(3.2 ppm) for 2 hours. A dose-dependence of lung pathology and mortality was reported. No mortality was observed during the subsequent 15 days following the 1 hour exposure, while 50% mortality and more severe lesions were seen during the first 5 days following the 2 hour exposure.

In a study of pulmonary effects of mercury inhalation, as well as the possible role of metallothionein (MT), Yoshida et al. (1999) exposed both MT-null and wild-type mice to 6.6 - 7.5 mg/m^3 (0.79 - 0.90 ppm) mercury vapor for 4 hours on 3 consecutive days. Examination of the lungs 24 hours after exposure revealed severe congestion, atelectasis (incomplete expansion of the lung), and mild hemorrhage of the alveoli in MT-null mice, along with 60% mortality. Among wild-type mice, these pulmonary effects were much less severe, pulmonary MT expression was markedly increased, and no lethality was observed. Mercury was found bound to MT in the lungs of wild-type, but not in MT-null mice. MT thus appears to ameliorate the effects of mercury inhalation.

The neurobehavioral manifestations in the offspring of mice with maternal exposure to mercury vapor during pregnancy suggest damage to motor control and learning centers. In the study upon which the acute REL derivation is based, Danielsson et al. (1993) exposed pregnant rats (12 per group) by inhalation to 1.8 mg/m^3 (0.22 ppm) of Hg^0 vapor for 1 hour/day (0.07 mg/kg/d) or 3 hours/day (0.2 mg/kg/d) during gestational days 11-14 and 17-20. The dose level was selected to avoid maternal toxicity. Tests of motor activity (locomotion, rearing, rearing time, total activity) in the offspring at 3 months of age revealed significant dose-dependent deficits compared to controls ($p < 0.01$). When tested at 14 months of age, the hypoactivity seen at 3 months was no longer apparent and, in the 0.2 mg/kg/d dose group, was replaced with significant hyperactivity (Table 5.3.1).

TABLE 5.3.2 EFFECTS OF PRENATAL METALLIC MERCURY ON MOTOR ACTIVITY

		3 months			14 months		
		Control	0.07	0.2	Control	0.07	0.2
Activity	Day	(SEM)	mg/kg/d	mg/kg/d	(SEM)	mg/kg/d	mg/kg/d
Locomotion	1	2785 (135)	2141 (104)*	2212 (135)*	1862 (119)	1289 (167)	1767 (127)
	2	2069 (127)	1432 (119)*	1385 (143)*	1194 (111)	1218 (104)	1512 (119)
	3	1719 (175)	1663 (191)	1090 (135)*	1162 (111)	915 (135)	1369 (119)
Rearing	1	404 (25)	321 (25)*	338 (25)*	204 (22)	143 (20)	210 (27)
	2	312 (29)	190 (20)*	161 (25)*	87 (22)	110 (28)	123 (22)
	3	247 (29)	238 (18)	157 (32)*	84 (18)	98 (25)	106 (18)
Rearing time	1	431 (19)	243 (20)*	232 (22)*	159 (21)	78 (24)	167 (26)
	2	269 (21)	138 (23)*	160 (24)*	66 (19)	99 (24)	114 (23)
	3	212 (21)	179 (23)	138 (21)*	87 (17)	76 (22)	138 (24)
Total activity	1	4854 (271)	3836 (318)*	3979 (302)*	3565 (302)	2435 (223)*	3151 (271)
	2	3804 (223)	2737 (239)*	2817 (350)*	2308 (255)	2324 (302)	3151 (334)*
	3	3183 (318)	3183 (350)	2132 (318)*	2228 (255)	2069 (271)	2546 (2711)

*p<0.01 Data estimated from Danielsson et al. (1993) Figure 1.

Significant learning deficits (swim maze performance) were observed in the 0.2 mg/kg/d-exposed, but not the lower-exposure rats tested at 15 months of age ($p < 0.05$) (Table 5.3.2). The brain concentrations of mercury in the 0.2 mg/kg/d dose group (0.012 mg/kg) were 2.5-fold higher than in the 0.07 mg/kg/d dose group (0.005 mg/kg), and 12-fold higher than in the control group (0.001 mg/kg).

TABLE 5.3.3 PRENATAL METALLIC MERCURY AND LEARNING DEFICITS

		7 months			15 months		
		Control	0.07	0.2	Control	0.07	0.2
Morris maze	Day		mg/kg/d	mg/kg/d		mg/kg/d	mg/kg/d
	1	53	48	46	42	40	29
	2	30	41	26	29	21	13*

*p<0.01 Data estimated from Danielsson et al. (1993) Figure 3.

These data indicate adverse effects of mercury exposure on the developing brain, but it is not clear at what nervous tissue levels effects first manifest.

To evaluate mercury deposition in neurons at low exposure levels, Pamphlett and Coote (1998) exposed female BALB/c mice to mercury vapor at 25 µg/m^3 (0.003 ppm) for 2-20 hr, or to 500 µg/m^3 (0.06 ppm) for 5-240 min. At 25 µg/m^3, mercury was first found in the perikarya of scattered large motor neurons in the lateral anterior horn of the spinal cord after 12 hr of exposure. Exposure at this level for 16 and 20 hr resulted in labeling of most of the large neurons of this area. By comparison, mercury was found in renal tubular epithelium after only 2 hr of exposure. Mice that survived longer than 6 weeks showed no mercury in the renal epithelia while mercury persisted in the brainstem motor neurons up to 30 weeks. At the higher dose of 500 µg/m^3, mercury labeling of spinal motor neurons was seen after only 30 min. The doses that resulted in mercury uptake into mouse motor neurons in these experiments are similar to those that workers in mercury-using occupations may receive in the course of a few hours. While the toxicological significance of the observed mercury labeling was not addressed in these mice, the accumulation of mercury in the motor neurons is consistent with the behavioral alterations reported above.

The effects of short term, high level exposure to mercury are not limited to pulmonary and nervous tissues. Severe cellular degeneration and necrosis were observed in the kidneys, brain, colon, and heart tissue of 2 rabbits exposed for 4 hours to 29.7 mg Hg/m³ (3.6 ppm) (Ashe et al., 1953). Exposure of rabbits to 31.3 mg Hg/m³ (3.8 ppm) for 1 hour resulted in moderate pathological changes (unspecified), but no necrosis, in the brain and kidney. In contrast, heart and lung tissues showed mild pathologic changes (Ashe et al., 1953). Increased duration (6 hours/day for 5 days) of exposure at this concentration was lethal.

6. Chronic Toxicity of Mercury

6.1 Chronic Toxicity to Adult Humans

This section briefly summarizes a large body of literature on mercury toxicity, emphasizing studies of inhalation exposure useful in the development of the 8-hr and chronic reference exposure levels. The reader is referred to OEHHA (1999) for more information on measuring toxicity by the oral route of exposure. The effects of chronic exposure to mercury vapor have been known for centuries and are most pronounced in the central nervous system. Toxic effects include tremors (mild or severe), unsteady gait, irritability, poor concentration, short-term memory deficits, tremulous speech, blurred vision, performance decrements, paresthesia, and decreased nerve conduction (Smith et al., 1970; Langolf et al., 1978; Fawer et al., 1983; Piikivi et al., 1984; Albers et al., 1988; Kishi et al., 1993). While some motor system disturbances can be reversed upon cessation of exposure, memory deficits may be permanent (Kishi et al., 1993). Studies have shown effects such as tremor and decreased cognitive skills in workers exposed to approximately 25 µg/m^3 (0.003 ppm) mercury vapor (Piikivi et al., 1984; Piikivi and Hanninen, 1989; Piikivi and Toulonen, 1989) (see discussion below).

The kidney is also a sensitive target organ of mercury toxicity. Effects such as proteinuria, proximal tubular and glomerular changes, albuminuria, glomerulosclerosis,

and increased urinary N-acetyl-β-glucosaminidase have been seen in workers exposed to approximately 25-60 μg/m^3 (0.003 - 0.007 ppm) mercury vapor (Roels et al., 1982; Bernard et al., 1987; Barregard et al., 1988; Piikivi and Ruokonen, 1989).

Chronic exposure to mercury vapors has also resulted in cardiovascular effects such as increased heart rate and blood pressure (Piikivi, 1989; Fagala and Wigg, 1992; Taueg et al., 1992), and in leukocytosis and neutrophilia (Fagala and Wigg, 1992).

A number of other studies with similar exposure levels also found adverse psychological and neurological effects in exposed versus unexposed individuals. Fawer et al. (1983) measured intention tremor with an accelerometer attached to the third metacarpal of the right hand in 26 male workers (mean age of 44 years) exposed to low concentrations of mercury vapor. The men worked either in a chloralkali plant (n = 12), a fluorescent tube manufacturing plant (n = 7), or in acetaldehyde production (n = 7). Twenty-five control subjects came from different parts of the same plants and were not occupationally exposed to mercury. The average exposure as measured by personal air sampling was 0.026 mg/m^3 (0.003 ppm) and the average duration of exposure was 15 years. The measurements of intention tremor were significantly higher in exposed workers than in controls ($p = 0.011$). Using the average exposure as a LOAEL and adjusting for occupational ventilation rates and workweek, the resultant LOAEL is 0.009 mg/m^3 (0.001 ppm).

Piikivi and Tolonen (1989) studied the effects of long-term exposure to mercury vapor on electroencephalograms (EEGs) of 41 chloralkali workers exposed for a mean of 15.6 years as compared to 41 matched controls. EEGs were analyzed both qualitatively and quantitatively. In the qualitative analysis, EEGs were interpreted visually with classification of normality and abnormality based on a previously established scale that separated focal, generalized and paroxysmal disturbances into four classes (normal, or mildly, moderately, or severely disturbed). Exposed workers, who had blood mercury levels of 11.6 μg/L, tended to have an increased number of EEG abnormalities and brain activity was found to be significantly lower than matched controls ($p < 0.001$). The abnormalities were most prominent in the parietal cortex, but absent in the frontal cortex. The authors used a conversion factor calculated by Roels et al. (1989) to extrapolate from blood mercury levels of 12 μg/L to an air concentration of 25 μg/m^3 (0.003 ppm).

Another study by Piikivi (1989) examined subjective and objective symptoms of autonomic dysfunction in the same 41 chloralkali workers described above. The exposed workers had mean blood levels of 11.6 μg/L corresponding to a TWA exposure of 25 μg Hg/m^3 in air (Roels et al., 1987). The workers were tested for pulse rate variation in normal and deep breathing, the Valsalva maneuver, vertical tilt, and blood pressure responses during standing and isometric work. The only significant difference in subjective symptoms was an increased reporting of palpitations in exposed workers. The objective tests demonstrated an increase in pulse rate variations at 30 μg Hg/m^3 (0.006 ppm; extrapolated from blood levels based on methods of Roels et al. (1987)), which is indicative of autonomic reflex dysfunction.

Piikivi and Hanninen (1989) studied subjective symptoms and psychological performance on a computer-administered test battery in 60 chloralkali workers exposed to approximately 25 μg/m^3 mercury vapor for a mean of 13.7 years. The subjective symptoms, evaluated by questionnaire, included the frequency or intensity of memory disturbances, difficulties concentrating, sleep disorders, and hand tremors. In addition a mood scale was used to evaluate tension, depression, anger, fatigue, and confusion. The psychomotor tests included finger tapping, eye-hand coordination, symbol digit substitution, pattern comparison, and a continuous performance test. Memory and learning effects were captured on tests of associate learning, associate memory, pattern memory, and serial digit learning. A statistically significant increase in subjective symptoms of sleep disturbance and memory disturbance was noted in the exposed workers ($p < 0.001$), as were increased anger, fatigue and confusion ($p < 0.01$). There were no differences in objective measures of memory, learning, or motor abilities, with the exception of poorer eye-hand coordination ($p < 0.001$).

A study by Ngim et al. (1992) assessed neurobehavioral performance in a cross-sectional study of 98 dentists exposed to a TWA concentration of 14 μg Hg/m^3 (range 0.7 to 42 μg/m^3) compared to 54 controls with no history of occupational exposure to mercury. Exposed dentists were matched to the control group for age, amount of fish consumption, and number of amalgam fillings. Air concentrations were measured with personal sampling badges over typical working hours (8-10 hours/day) and converted to a TWA. Blood samples were also taken (average 9.8 μg/L). The average concentration in air was estimated at 23 μg Hg/m^3 when the methods of Roels et al. (1987) were used. The average duration in this study of dentists was only 5.5 years, shorter than the above studies. The performance of the dentists was significantly worse than controls on a number of neurobehavioral tests measuring motor speed (finger tapping), visual scanning, visuomotor coordination and concentration, visual memory, and visuomotor coordination speed ($p < 0.05$). These neurobehavioral changes are consistent with central and peripheral neurotoxicity commonly observed in cases of chronic mercury toxicity.

Liang et al. (1993) investigated workers in a fluorescent lamp factory with a computer-administered neurobehavioral evaluation system and a mood-inventory profile. The cohort consisted of 88 individuals (19 females and 69 males) exposed for at least 2 years prior to the study. Exposure was monitored with area samplers and ranged from 8 to 85 μg Hg/m^3 across worksites. The average level of exposure was estimated at 33 μg Hg/m^3 and the average duration of exposure was estimated at 15.8 years. The exposed cohort performed significantly worse than the controls on tests of finger tapping, mental arithmetic, two digit searches, switching attention, and visual reaction time ($p < 0.05$-0.01). The effects on performance persisted after controlling for chronological age as a confounding factor.

6.2 Chronic Toxicity to Infants and Children

A number of case studies indicate that long-term exposure to Hg^0 in children is associated with severe arterial hypertension, acrodynia, seizures, tachycardia, anxiety,

irritability and general malaise (Sexton et al., 1978; Torres et al., 2000). These symptoms are consistent with the brain and kidneys as the principal target organs for Hg^0. By comparison, for methylmercury (MeHg), the brain is the most toxicologically relevant organ. An extensive literature supports the association between chronic MeHg exposure and neurological and developmental deficits in children (Choi, 1989; Harada, 1995; Grandjean et al., 1999). Unlike inorganic mercury, both Hg^0 and MeHg easily cross cell membranes, the blood brain barrier, and the placenta (Ask et al., 2002). Intracellular oxidation of Hg^0 and the slower demethylation of MeHg both lead to the mercuric ion that binds cellular macromolecules, trapping it within the cell and contributing to the toxicity associated with exposures to the respective forms. While the complete mechanisms of toxicity for the two forms are not well understood and are likely not identical, there are important similarities. Methylmercury and the mercuric ion formed from Hg^0 avidly bind to protein sulfhydryls and may inactivate enzymes. Disruption of protein synthesis has been reported after exposure to either Hg^0 or MeHg, although the former is the more powerful inhibitor (NAS, 2000). The neurotoxic effects observed in adult rats following *in utero* exposure to Hg^0, MeHg, or both, are reportedly similar with MeHg potentiating the effects of Hg^0 (Fredriksson et al., 1996). Given the high susceptibility of children to MeHg and the apparent similarities in mechanisms with Hg^0, children are expected to be more susceptible to Hg^0 toxicity as well.

There is a considerable body of evidence from human poisoning episodes that mercury exposure in utero and postnatally results in developmental neurotoxicity (McKeown-Eyssen et al., 1983; Grandjean et al., 1994; Harada, 1995; Grandjean et al., 1997). Thus, infants and children are susceptible subpopulations for adverse health effects from mercury exposure. These effects fall into several general categories: 1) effects on neurological status (Castoldi et al., 2001); 2) age at which developmental milestones are achieved (Marsh et al., 1979); 3) infant and preschool development (Kjellstrom et al., 1986; Kjellstrom et al., 1989); 4) childhood development (age 6 and above) (Grandjean et al., 1997); and 5) sensory or neurophysiological effects (Murata et al., 1999). These studies and others are extensively reviewed by the U.S. EPA (2000) and the NAS (2000)

Whereas MeHg and elemental mercury readily cross the blood-brain barrier and the placental barrier, the mercuric ion (Hg^{2+}) does not readily cross these barriers. However, in fetuses and neonates mercuric species concentrate more in the brain because the blood-brain barrier is incompletely formed. Methylmercury and elemental mercury are lipophilic and are distributed throughout the body. In adults mercuric species accumulate more in the kidney. However, in neonates mercuric species do not concentrate in the kidneys but are more widely distributed to other tissues (NAS, 2000). It is possible that the increased distribution of mercuric species to the brain in fetuses and neonates accounts for some of the sensitivity of the brain to mercury during these developmental periods. The sensitivity of the fetal brain might also be due to the high proportion of dividing and differentiating cells during neuronal development in the fetal and neonatal periods. These dividing cells may be more sensitive to damaging effects of mercury-protein complexes. Furthermore, neurodevelopment is a “one-way street”. Disruption along the route results in permanent deficits. Methylmercury can also alter

the relative levels of thyroid hormones to which the fetus is exposed and upon which normal neurodevelopment depends.

In addition to prenatal and postnatal dietary exposure, neonates may receive added postnatal dietary exposure to mercuric species and MeHg from breast milk (Drexler and Schaller, 1998; Sundberg et al., 1999). Animal data suggest that suckling rats retain a higher percentage of ingested organic mercury than do adults, with much higher concentrations in the brain (Kostial et al., 1978). School children can be accidentally exposed to elemental mercury which is a curiosity and an attractive nuisance (George et al., 1996; Lowry et al., 1999). Younger children may also be exposed when elemental mercury is spilled on floors and carpets where they are more active.

6.3 Chronic Toxicity to Experimental Animals

Studies of the effects of mercury in experimental animals generally employ mercury levels in excess of those to which humans are exposed in most settings, thus limiting their ability to model the consequences of long-term, low level exposures. To address this issue, and to test for a role of metallothionein (MT) in mitigating mercury's effects ,Yoshida et al. (2004) exposed wild type and MT-null mice to mercury vapor at 0.06 mg/m^3 (0.007 ppm), 8 hr/day for 23 weeks. Neurobehavioral effects in open field and passive avoidance tests were evaluated at 12 and 23 weeks, and brain levels of mercury were determined. Mercury levels in the brains of mice were 0.66 and 0.97 µg/g tissue for MT-null and wild type, respectively. For comparison, the authors cite human brain mercury levels ranging from 0.3 µg/g in dental personnel to 33 µg/g in retired mercury miners. Mercury-exposed mice showed enhanced motor activity that was statistically significant for both strains at 12 weeks ($p < 0.01$), and for the MT-null mice at 23 weeks ($p < 0.05$). In a learning task (passive avoidance of an electric shock), there were no significant differences between controls and either strain of mouse at 12 weeks of exposure. However, after 23 weeks of exposure, MT-null, but not wild type mice, showed significantly less avoidance than controls ($p < 0.05$) suggesting impaired long-term memory. These data suggest that long-term mercury exposure that results in brain levels of mercury comparable to those seen in occupationally-exposed humans, causes changes in neurobehavior, an effect that is exacerbated by low levels of MT. For comparison, Fawer et al (1983) reported increased intention tremor in human workers exposed to an average of 0.003 ppm for an average of 15 years (Section 6.1).

There is a substantial body of work delineating the neurotoxic effects of MeHg exposure on animals exposed in utero. A comparison between mercury vapor and MeHg, separately and in concert, was conducted in rats. Fredriksson et al. (1996) exposed pregnant rats to MeHg by gavage (2 mg/kg/d during days 6-9 of gestation), and metallic mercury (Hg^0) vapor by inhalation (1.8 mg/m^3 (0.22 ppm) for 1.5 h per day during gestation days 14-19), or both. Controls received the combined vehicles for each of the two treatments. The dose by inhalation was approximately 0.1 mg Hg^0/kg/day. No differences were observed among groups in clinical observations and developmental markers up to weaning. Tests of behavioral function, performed at 4-5 months of age, included spontaneous motor activity, spatial learning in a circular bath, and instrumental maze learning for food reward. Offspring of dams exposed to Hg^0 showed hyperactivity

over all three measures of motor activity: locomotion, rearing and total activity. This effect was enhanced in the animals of the MeHg + Hg^0 group. Compared to either the control or MeHg groups in the swim maze test, rats in the MeHg + Hg^0 and Hg^0 groups took longer to reach a submerged platform whose location they had learned the previous day. Similarly, both the MeHg + Hg^0 and Hg^0 groups showed more ambulations and rearings in the activity test prior to the learning trial in the enclosed radial arm maze. During the learning trial, these same animals showed longer latencies and made more errors in acquiring the food reward. Generally, the results indicated that prenatal exposure to Hg^0 caused alterations to both spontaneous and learned behaviours, suggesting some deficit in adaptive functions. In these experiments, exposure to MeHg was not observed to alter these functions but rather appeared to potentiate the effects of Hg^0.

The similarities in the effects of MeHg and Hg^0 imply similar targets in the brain, which appears to be the case. Pregnant squirrel monkeys were exposed to mercury vapor (0.5 or 1 mg/m^3 (0.06 or 0.12 ppm)) for 4 or 7 hours per day starting in the fifth to the seventh week of gestation and generally ending between 18 and 23 weeks of gestational age (Warfvinge, 2000). The concentration of mercury was found to be higher in maternal (0.80-2.58 µg/g tissue) than in offspring (0.20-0.70 µg/g) brains, but with similar cerebellar distributions. In this study, mercury was localized mainly to Purkinje cells and Bergmann glial cells, similar to the distribution seen after MeHg exposure. The nuclei affected in these and other studies are part of the motor system.

In rats exposed to mercury vapor at ~1 mg/m^3 (0.12 ppm) for 6 h/d, 3 d/wk for 5 wk (low dose), or 24 h/d, 6 d/wk for 5 wk (high dose), an exposure duration-dependent loss of Purkinje cells and proliferation of Bergmann glial cells were observed (Hua et al., 1995). Whereas mercury accumulated to a higher degree in kidney compared to brain, the mercury level in kidney only increased 17% (90 to 105 µg/g tissue) from low to high doses, while that of the brain increased 608% (0.71 to 5.03 µg/g). These neuropathological changes were observed at the same mercury doses as this group reported previously for kidney autoimmune disease (Hua et al., 1993). The brain is a more sensitive target for mercury toxicity in part due to its greater ability to concentrate the metal.

7. Developmental and Reproductive Toxicity

Occupational exposure to mercury vapor has been associated with reproductive problems in a number of epidemiological studies. In a study of 418 dental assistants, Rowland et al. (1994) reported that the fecundability of the women with high exposure to dental amalgams was 63% (95% CI 42-96%) of that reported for the dental assistants with no amalgam exposure. Similarly, in a Chinese study by Yang et al. (2002), there was a significantly higher prevalence of abdominal pain (OR 1.47, 95% CI 1.03: 2.11) and dysmenorrhea (OR 1.66, 95% CI 1.07; 2.59) among female factory workers exposed to ambient mercury vapor (0.001-0.200 mg/m^3) compared with factory workers without mercury exposure. In another study of female factory workers exposed to mercury vapors, the frequency of adverse birth outcomes, especially congenital anomalies, was higher among those exposed to mercury levels at or substantially lower than 0.6 mg/m^3 (Elghany et al., 1997).

The adverse effects of elemental mercury exposure have also been demonstrated in animal models. In rats, elemental mercury readily crosses the placental barrier and accumulates in the fetus following inhalation (Morgan et al., 2002). Pregnant rats exposed by inhalation to 1.8 mg/m^3 of metallic mercury for 1 hour or 3 hours/day during gestation (days 11 through 14 plus days 17 through 20) bore pups that displayed significant dose-dependent deficits in behavioral measurements 3-7 months after birth compared to unexposed controls (Danielsson et al., 1993). Behaviors measured included spontaneous motor activity, performance of a spatial learning task, and habituation to the automated test chamber. The pups also showed dose-dependent, increased mercury levels in their brains, livers, and kidneys 2-3 days after birth.

Morgan et al. (2002) exposed pregnant rats for 2 hr per day to 1, 2, 4, or 8 mg/m^3 mercury vapor during gestation days (GD) 6-15, and found a dose-dependent distribution of mercury to all maternal and fetal tissues. Adverse effects on resorptions, postnatal litter size and neonatal body weights were only observed at the highest mercury dose, which was also maternally toxic. It is of interest to note that following cessation of maternal exposure on GD 15, the mass of the fetal brain and its content of mercury both increased 10-fold. Thus the fetal brain continued to accumulate mercury eliminated from maternal tissues. This suggests that the period of fetal exposure is longer than that of maternal exposure, and may affect more neurodevelopmental stages than the timing of the maternal exposure would suggest.

Mercury and mercury compounds, including inorganic forms, are listed under California Proposition 65 (Cal/EPA, Safe Drinking Water and Toxic Enforcement Act of 1986) as developmental toxins. It should be noted that there is substantial evidence in humans of the developmental toxicity of methylmercury exposure. However, this REL summary is meant to be applied to elemental and inorganic mercury, and thus we are not describing methylmercury toxicity in depth in this document.

8. Derivation of Reference Exposure Levels

8.1 Mercury Acute Reference Exposure Level

Study	Danielsson et al., 1993
Study population	groups of 12 pregnant rats
Exposure method	inhalation of metallic mercury vapors
Exposure continuity	
Exposure duration	1 hour per day
Critical effects	CNS disturbances in offspring
LOAEL	1.8 mg/m³
NOAEL	not observed
Benchmark concentration	not derived
Time-adjusted exposure	
Human Equivalent Concentration	n/a
LOAEL uncertainty factor (UF_L)	10 (default; severe effect, no NOAEL)
Subchronic uncertainty factor (UFs)	
Interspecies uncertainty factor	
Toxicokinetic (UF_{A-k})	√10 (default, animal study)
Toxicodynamic (UF_{A-d})	10 (greater human vs rat susceptibility)
Intraspecies uncertainty factor	
Toxicokinetic (UF_{H-k})	√10 (default: critical study in young)
Toxicodynamic (UF_{H-d})	√10 (default: critical study in young)
Cumulative uncertainty factor	3000
Reference Exposure Level	**0.6 µg Hg/m³ (0.07 ppb Hg^0)**

Acute Reference Exposure Levels are levels at which intermittent one-hour exposures are not expected to result in adverse health effects (see Section 5 of the Technical Support Document (TSD)).

In the absence of acute inhalation studies in humans, the study by Danielsson et al. (1993) was selected as the critical study since it used a sensitive endpoint, neurotoxicity, in a highly susceptible, developmental stage. Maternal rats were exposed by inhalation to 1.8 mg/m³ of metallic mercury vapor for 1 hour/day or 3 hours/day during gestation. The offspring displayed significant dose-dependent deficits in behavior 3-7 months after birth compared to controls. The default uncertainty factor of 10 is applied for the use of a LOAEL for moderate to severe effects in the absence of a NOAEL.

A default interspecies uncertainty factor of √10 for toxicokinetic (UF_{A-k}) variability was used, while a larger interspecies UF_{A-d} of 10 for toxicodynamic differences was used to reflect the potentially greater developmental susceptibility of humans versus rats. This is based, in part, on Lewandowski et al. (2003) who used a comparative approach to analyze in vivo and in vitro data on the responses of neuronal cells of rats, mice, and humans to MeHg. Their analysis suggests that humans may be up to 10-fold more sensitive to MeHg than are rats. Application of Lewandowski's analysis assumes that

the human and rat responses to elemental mercury are comparable with those to MeHg. The study by Fredriksson et al. (1996) (above) supports this assumption for neurobehavioral effects. A greater susceptibility of humans to adverse neurobehavioral effects following early-life exposures compared with experimental animals has also been seen with other metals, especially lead. For example, Schwartz (1994) reported no evidence for a threshold for neurobehavioral effects in children with blood lead levels of 1 µg/dL compared with less than 15 µg/dL in primates (Gilbert and Rice, 1987) and less than 20 µg/dL in rats (Cory-Slechta et al., 1985).

Since the critical study involved early life exposures, the default intraspecies toxicodynamic uncertainty factor (UF_{H-d}) of $\sqrt{10}$ was employed to account for individual variability. The intraspecies toxicokinetic uncertainty factor of $\sqrt{10}$ reflects the absence of data in young humans, but also the lack of reason to expect major age differences, at least in the short-term kinetics. The resulting acute REL was 0.6 µg/m^3 (0.07 ppb).

This REL is developed for metallic mercury vapor but would be expected to be protective for inhalation of mercury salts. Although mercury salts have no significant vapor pressure under normal atmospheric conditions, they are of concern as hazards if aerosolized or produced during combustion. Animals exposed to mercury vapor inhalation had ten-fold higher brain mercury levels than animals exposed to a similar amount of injected inorganic mercury (mercuric nitrate) (Berlin et al., 1969); however the relationship between kinetics of mercury vapor and mercuric salts has not been extensively studied and may be complex, and dependent on the route, level and timing of exposure.

8.2 Mercury 8-Hour Reference Exposure Level

The 8-hour Reference Exposure Level is a concentration at or below which adverse noncancer health effects would not be anticipated for repeated 8-hour exposures (see Section 6 of the Technical Support Document).

The half life of elimination of mercury in humans following a single inhalation exposure of 14-24 min. was 21 days from the head, 64 days from the kidney, and 58 days from the body as a whole (Hursh et al., 1976). Urinary elimination among workers occupationally exposed for several years had an elimination half life of 55 days (Sallsten et al., 1994). Thus, since mercury is only slowly eliminated, the intervals between daily 8-hr exposures, and between weeks are not long enough for the elimination of significant amounts of the metal and it will accumulate in the body with repeated exposure. In view of this bioaccumulative property of mercury exposure in humans, it was considered necessary to use the same study and derivation (in terms of exposure for seven vs only five days per week) for the 8-hour REL as for the chronic REL described below. However, the exposure duration adjustment used in this case reflects a repeated exposure of 8 hours per day with an activity-related air intake of 10 m^3 per day (i.e. half that assumed for a 24-hour period for the chronic REL). As a result, the time-adjusted exposure is twice that for the chronic REL. This adjustment reflects the expectation that activity levels, and hence breathing rates, will be higher during the

exposure period than during the remaining 16 hours. The increased breathing rate enhances mercury inhalation during the 8 hour exposure period.

Study	Piikivi and Hanninen (1989); Fawer et al. (1983); Piikivi and Tolonen (1989); Piikivi (1989); Ngim et al. (1992)
Study population	Humans (236)
Exposure method	Inhalation of workplace air
Exposure continuity	8 hours per day, 5 days/week
Exposure duration	13.7 to 15.6 years
Critical effects	Neurotoxicity as measured by: intention tremor; memory and sleep disturbances; decreased performance on neurobehavioral tests (finger tapping, visual scan, visuomotor coordination, visual memory); decreased EEG activity
LOAEL	25 μg/m^3 (3 ppb)
NOAEL	not observed
Benchmark concentration	not derived
Time-adjusted exposure	18 μg/m^3 for LOAEL group (25 x 5/7)
LOAEL uncertainty factor (UF_L)	10 (default, severe effect, no NOAEL)
Subchronic uncertainty factor (UFs)	1
Interspecies uncertainty factor	
Toxicokinetic (UF_{A-k})	1 (default: human study)
Toxicodynamic (UF_{A-d})	1 (default: human study)
Intraspecies uncertainty factor	
Toxicokinetic (UF_{H-k})	√10 (default for inter-individual variability)
Toxicodynamic (UF_{H-d})	10 (greater susceptibility of children and their developing nervous systems)
Cumulative uncertainty factor	300
Reference Exposure Level	**0.06 μg Hg/m^3 (0.007 ppb Hg^0)**

The studies chosen for determination of the 8-hr REL examined neurotoxicity in humans as a sensitive endpoint following long-term exposures. They all point to a LOAEL of approximately 25 μg/m^3 (3 ppb) with a time-adjusted value of 18 μg/m^3 (25 x 5/7). In the absence of a NOAEL, we applied an uncertainty factor of 10, the default with neurotoxicity considered a moderate to potentially severe effect. The critical study was conducted in humans and was not a subchronic study so no interspecies or subchronic uncertainty factors were applied. To allow for interindividual variability and to specifically account for greater susceptibility among children, an overall intraspecies uncertainty factor of 30 was applied with a toxicokinetic factor (H-k) of √10 to reflect interindividual variability, and a toxicodynamic factor of 10 that reflects the higher susceptibility of the developing nervous system. The cumulative uncertainty is 300, and the resultant 8-hour REL is thus 0.06 μg Hg/ m^3 (0.007 ppb Hg °).

8.3 Mercury Chronic Reference Exposure Level

Study	Piikivi and Hanninen (1989); Fawer et al. (1983); Piikivi and Tolonen (1989); Piikivi (1989); Ngim et al. (1992)
Study population	Humans (236)
Exposure method	Inhalation of workplace air
Exposure continuity	8 hours per day (10 m^3/workday), 5 days/week
Exposure duration	13.7 to 15.6 year
Critical effects	Neurotoxicity as measured by: intention tremor; memory and sleep disturbances; decreased performance on neurobehavioral tests (finger tapping, visual scan, visuomotor coordination, visual memory); decreased EEG activity
LOAEL	25 $\mu g/m^3$ (3 ppb)
NOAEL	not observed
Benchmark concentration	not derived
Time-adjusted exposure	9 $\mu g/m^3$ for LOAEL group (25 x 10/20 x 5/7)
LOAEL uncertainty factor (UF_L)	10 (default, severe effect, no NOAEL)
Subchronic uncertainty factor (UFs)	1
Interspecies uncertainty factor	
Toxicokinetic (UF_{A-k})	1 (default: human study)
Toxicodynamic (UF_{A-d})	1 (default: human study)
Intraspecies uncertainty factor	
Toxicokinetic (UF_{H-k})	$\sqrt{10}$ (default for inter-individual variability)
Toxicodynamic (UF_{H-d})	10 (greater susceptibility of children and their developing nervous systems)
Cumulative uncertainty factor	300
Reference Exposure Level	**0.03 μg Hg/m^3 (0.004 ppb Hg^0)**

The chronic Reference Exposure Level is a concentration at which adverse noncancer health effects would not be expected from chronic exposures (see Section 7 in the Technical Support Document).

To calculate the chronic REL, studies were chosen that examined a sensitive endpoint (neurotoxicity) in humans following long-term exposures. They all point to a LOAEL of approximately 0.025 mg/m^3 (3 ppb). When adjusted for worker ventilation and workweek exposure, the LOAEL becomes 9 µg/m^3 (25 µg/m^3 x 10 m^3/20 m^3 x 5 d/7 d). In the absence of a NOAEL, we applied an uncertainty factor of 10, the default with neurotoxicity considered a moderate to potentially severe effect. The critical study was conducted in humans and was not a subchronic study so no interspecies or subchronic uncertainty factors were applied. To allow for interindividual variability and to specifically account for greater susceptibility among children, an overall intraspecies

uncertainty factor of 30 was applied with a toxicokinetic factor (H-k) of √10 to reflect interindividual variability, and a toxicodynamic factor of 10 that reflects the higher susceptibility of the developing nervous system. The cumulative uncertainty is 300, and the resultant chronic REL is thus 0.03 µg Hg/ m^3 (0.004 ppb Hg °).

The U.S.EPA (1995) based its RfC of 0.3 $\mu g/m^3$ (0.04 ppb) on the same study but used an intraspecies uncertainty factor of 3, a LOAEL uncertainty factor of 3 and included a Modifying Factor (MF) of 3 for database deficiencies (lack of developmental and reproductive toxicity data). This modifying factor was not used by OEHHA since allowance was made via the UF_{H-d} for the known sensitivity of children to the neurodevelopmental impacts of mercury.

It is noteworthy that none of the above studies discussed in sufficient detail a dose-response relationship between mercury vapor inhalation and the toxic effects measured. Because none of the studies mention a level below which toxic effects were not seen (a NOAEL), the extrapolation from a LOAEL to a NOAEL should be regarded with caution. Secondly, one study (Ngim et al., 1992) demonstrated neurotoxic effects from mercury inhalation at an exposure level slightly above the other studies, but for a shorter duration. It is possible that mercury could cause neurotoxic effects after a shorter exposure period than that reported in the study used in derivation of the chronic REL.

As mentioned above, OEHHA (1999) has developed a PHG for inorganic mercury in drinking water of 0.0012 mg Hg/L (1.2 ppb) as a level of exposure expected to be without significant health risk from daily water consumption. This value was based on data from a 1993 study by the National Toxicology Program that supported a NOAEL of 0.16 mg Hg/kg-day for renal toxicity in rats with chronic oral exposure. Application of the cumulative uncertainty factor of 1,000 (10 for use of a subchronic study, and 10 each for inter- and intraspecies variability) used in the PHG derivation, gives an oral REL of 0.16 µg Hg/kg-day. This value is several-fold higher than the chronic REL developed above for inhalation of elemental mercury, and reflects the greater ease with which elemental mercury (vs. inorganic mercury) penetrates membranes, especially when exposure is via inhalation versus the oral route.

8.4 Mercury as a Toxic Air Contaminant that Disproportionately Impacts Children

In view of the differential impacts on infants and children identified in Section 6.2.1, and the possibility of direct (inhalation) and indirect exposure (through a diet containing aquatic animals contaminated with methylmercury), OEHHA recommends that elemental mercury be identified as a toxic air contaminant (TAC) which disproportionately impacts children under Health and Safety Code, Section 39699.5.

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Nickel and Nickel Compounds, including Nickel Oxide. Reference Exposure Levels

1 Summary

The Office of Environmental Health Hazard Assessment (OEHHA) is required to develop guidelines for conducting health risk assessments under the Air Toxics Hot Spots Program (Health and Safety Code Section 44360 (b) (2)). OEHHA developed a Technical Support Document (TSD) in response to this statutory requirement that describes acute, 8 hour and chronic reference exposure levels (RELs) and was adopted in December 2008. The TSD presents methodology reflecting the latest scientific knowledge and techniques, and in particular explicitly includes consideration of possible differential effects on the health of infants, children and other sensitive subpopulations, in accordance with the mandate of the Children's Environmental Health Protection Act (Senate Bill 25, Escutia, chapter 731, statutes of 1999, Health and Safety Code Sections 39669.5 *et seq.*). These guidelines have been used to develop acute, 8-hour and chronic RELs for nickel and nickel compounds. The nickel RELs are applicable to the chemicals listed in Table 4 below, with the exception of nickel carbonyl because of its unique toxicity. In addition, nickel oxide has a separate chronic REL.

TABLE 4. NICKEL AND COMMON COMPOUNDS

Molecular Formula	Molecular Weight	Synonyms	CAS Registry Number
Ni	58.69	elemental nickel nickel metal	7440-02-0
NiO	74.69	nickel oxide green nickel monoxide nickel(II) oxide	1313-99-1
Ni_2O_3	165.36	nickel oxide black	
$Ni(OH)_2$	92.71	nickel hydroxide nickelous hydroxide	12054-48-7
$NiCl_2$	129.6	nickel chloride nickel dichloride	7718-54-9
$NiSO_4$	154.75	nickel sulfate nickelous sulfate	7786-81-4
$NiSO_4 \cdot 6H_2O$	262.85	nickel sulfate hexahydrate	10101-97-0
$NiCO_3$	118.7	nickel carbonate carbonic acid nickel(2+) salt nickelous carbonate	3333-67-3
Ni_3S_2	240.2	nickel subsulfide trinickel disulfide Heazlewoodite	12035-72-2

TABLE 4. NICKEL AND COMMON COMPOUNDS

Molecular Formula	Molecular Weight	Synonyms	CAS Registry Number
NiS	90.8	nickel sulfide nickel monosulfide Millerite	11113-75-0
$Ni(NO_3)_2 \cdot 6H_2O$	290.8	nickel nitrate hexahydrate	13478-00-7
$Ni(O_2CCH_3)_2$	178.8	nickel acetate	373-02-4
$Ni_3(CO_3)(OH)_4$	304.1	nickel carbonate hydroxide	12607-70-4
$Ni(CO)_4$	170.7	nickel carbonyl	13463-39-3

Nickel causes a variety of non-carcinogenic toxic effects including occupational contact dermatitis, occupational asthma, and reproductive toxicity in humans. Studies in experimental animals exhibit immune suppression, nephrotoxicity, pneumotoxicity, perinatal mortality and altered gene expression. The most sensitive effects appear to be in the lung and immune system. Descriptions of toxicokinetics, standard acute and chronic toxicity, immunotoxicity and reproductive toxicity appear below in Sections 4 to 8. Selection of key studies and derivation of RELs are presented in Section 9. Other observations on toxic effects and related studies which are important in defining the overall toxicity profile of nickel and its compounds, but do not contribute to the derivation of the RELs are described in Appendix A. The findings suggest that nickel be identified as a toxic air contaminant which may disproportionately impact children, pursuant to Health and Safety Code, Section 39669.5(c). The key values are summarized below.

1.1 Acute Toxicity (for a 1-hour exposure)

Inhalation reference exposure level **0.2 µg Ni/m³**
Critical effect(s) Immune system
Hazard Index target(s) Immune system

1.2 8-Hour REL (for repeated 8-hour exposures)

Inhalation reference exposure level **0.06 µg Ni/m^3**
Critical effect(s) Lung lesions, immunotoxicity
Hazard Index target(s) Respiratory system; immune system

1.3 Chronic REL Nickel and Nickel Compounds (except NiO)

Inhalation reference exposure level **0.014 µg Ni/m^3**
Critical effect(s) Lung, nasal epithelial and lymphatic pathology in male and female rats
Hazard index target(s) Respiratory system; hematopoietic system

1.4 Chronic REL Nickel Oxide

Inhalation reference exposure level	**0.02 µg Ni/m^3**
Critical effect(s)	Lung pathology in male and female mice
Hazard index target(s)	Respiratory system

1.5 Chronic Oral REL Nickel and Nickel Compounds

Oral Reference exposure level	**0.011 mg Ni/kg-day**
Critical effect(s)	Perinatal mortality in rats
Hazard index targets(s)	Developmental system

2 Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	Ni metal: silvery metal NiO: black crystals $NiCl_2$: yellow deliquescent crystals (U.S.EPA, 1985)
Density	8.9 g/cm^3 (Ni) 2.07 g/cm^3 ($NiSO_4 \cdot 6H_2O$) 6.67 g/cm^3 (NiO)
Boiling point	2730°C (Ni)
Melting point	1455°C (Ni); 1030°C ($NiCl_2$)
Vapor pressure	not applicable for dust
Flashpoint	not applicable
Explosive limits	Nickel dust or powder is flammable (CDTSC, 1985).
Solubility	Elemental nickel, nickel subsulfide, and nickel oxide are insoluble in water, but are soluble in dilute nitric, hydrochloric, and sulfuric acids. The chloride and sulfate forms of nickel are water-soluble.
Odor threshold	odorless
Metabolites	Ni^{2+}
Oxidation states	0, +1, +2, +3 (Von Burg, 1997)

2.1 Physicochemical Properties Affecting Toxicity

Aerosols, liquid or solid particulate matter (PM) suspended in air are present in the atmosphere as a result of dust storms, forest and grass fires, vegetation, sea spray, vehicular and industrial emissions, and atmospheric chemical reactions (Rostami, 2009). Anthropogenic activities account for about 10% of atmospheric aerosols.

The toxicity of inhaled aerosols depends upon the extent of deposition in the head or extra-thoracic region, upper and lower airways of the lung (bronchi and alveoli), chemical composition, and subsequent fate, including clearance. The deposition of airborne particles depends on physical properties, the size or diameter of the particle

(and distribution thereof), the concentration, and the density. The clearance of deposited particles depends on location of deposition, solubility, and the mass deposited or burden. In general deposited PM is more rapidly cleared from the upper airways (tracheobroncheal region, TB) than from the pulmonary region (alveoli) and soluble particles are more rapidly cleared than insoluble particles. Removal of particles from the alveoli may require engulfment by alveolar macrophages. Several computational models are available for the prediction of airway deposition and clearance (Jarabek et al., 2005; Brown et al., 2005; Rostami, 2009).

In the inhalation studies described and analyzed in this document nickel particles are usually described as having a mass median aerodynamic diameter (MMAD) in µm, a geometric standard deviation (for lognormal size distribution), and a particle density in g/cm^3. All three parameters and the aerosol concentration are required inputs in the Multiple Path Particle Dosimetry (MPPD2) model used to assess airway deposition in the calculation of chronic RELs. The model was also used in deposition and clearance mode to estimate nickel particle retention over various timed simulations for age-specific human models (µg Ni/day/m^2 alveolar surface area). However, retention estimates are less certain than deposition values since they depend on factors other than size, particularly solubility of the various nickel compounds in the lung surface layers.

Emissions of nickel particles from facilities subject to risk assessments under the Air Toxics Hot Spots program will vary in size and distributional characteristics. These characteristics are not necessarily reported in the emissions inventory, which forms the basis of the site-specific risk assessments. Thus, there is an implicit assumption that the size distributions are similar enough to those used in the toxicity studies that form the basis of the Reference Exposure Level.

In the studies used as a basis for the chronic RELs, animals were exposed to particle size distributions more or less centered on 2.5 µm mean diameter. CARB (2009) estimated that for 2010, $PM_{2.5}$ from stationary sources comprised about 15% of $PM_{2.5}$ emissions from all sources and about 38% of PM from stationary sources. Kleeman and Cass (1999) concluded that $PM_{2.5}$ from various stationary sources ranged from 11 to 50% of total PM emissions (tons/day), the remainder essentially was PM_{10}.

Linak et al. (2000) evaluated particle size distributions (PSDs) and elemental partitioning with three coal types and residual fuel oil combusted in three different systems simulating process and utility boilers. Uncontrolled PM emissions from the three coals ranged from 3800 to 4400 mg/m^3 compared to 90 to 180 mg/m^3 for fuel oil. The mass and composition of particles between 0.03 and >20µm in aerodynamic diameter showed that PM for the combustion of these fuels produced distinctive bimodal and trimodal PSDs. The trace element concentrations (µg/g) in emitted PM size fractions indicated that Ni was somewhat higher in the <2.5µm fraction than in the >2.5µm fraction: Western Kentucky coal, 110/86.2; Montana coal, 41.5/29.3; Utah coal, 109/39.4; and high sulfur No.6 oil, 8000/2270, respectively.

Krudysz et al. (2008) investigated spatial variation of PM in an urban area impacted by local and regional PM sources. Weekly size-segregated (<0.25, 0.25-2.5, and >2.5 µm)

PM samples were collected in the winter of 2005 in the Long Beach, California area. Coefficients of divergence analyses were conducted for size-fractionated PM mass, organic and elemental carbon, sulfur and 18 other metals and trace elements. For most metal species the highest concentrations were present in the coarse particles (>2.5µm), followed by the 0.25 to 2.5 µm fraction with significantly lower concentrations in the <0.25µm fraction. However, vanadium, nickel, cadmium, zinc and lead concentrations were highest in the <0.25µm and 0.25 to 2.5µm fractions. Nickel concentrations in the three fractions were approximately 2 ng/m^3, <0.25µm; 1 ng/m^3, 0.25-2.5µm; and 1.5 ng/m^3, >2.5µm (their Fig. 4).

On this basis we think that the particle size distributions used in the animal studies are a reasonable surrogate for $PM_{2.5}$ and PM_{10} emitted from stationary and possibly mobile sources.

The aqueous solubility of nickel compounds has a significant effect on their uptake and tissue distribution. In rodent studies with several water soluble and insoluble compounds, the water soluble compounds (e.g., $NiSO_4$, $NiCl_2$, $Ni(NO_3)_2$) were generally found in 10 to 100 fold higher concentrations in lung, liver, kidney, heart, brain and blood than the water insoluble compounds (e.g., NiS, Ni_3S_2, NiO). Insoluble compounds have solubility <0.01 mol/L, soluble compounds have solubility >0.1 mol/L and slightly soluble compounds range between 0.01 and 0.1 mol/L. Insoluble nickel compounds have solubility products that range from about 1 x 10^{-9} to 1 x 10^{-31} (Table 5).

TABLE 5. AQUEOUS SOLUBILITY AND SOLUBILITY PRODUCTS OF NICKEL COMPOUNDS

Name	Formula	Solubility g/L @ 20ºC	Ksp @ 25ºC
	Soluble Compounds		
Nickel chloride	$NiCl_2$	553	
Nickel nitrate hexahydrate	$Ni(NO_3)_2•6H_2O$	600	
Nickel sulfate hexahydrate	$NiSO_4•6H_2O$	400	
Nickel acetate tetrahydrate	$Ni(CH_3CO_2)_2•4H_2O$	270 @ 0ºC	
	Insoluble Compounds		
Nickel carbonate	$NiCO_3$	90 mg/L	6.6×10^{-9}
Nickel hydroxide	$Ni(OH)_2$		2.0×10^{-15}
Nickel sulfide	NiS		3.0×10^{-19}
Nickel sulfide α	NiS		4.0×10^{-20}
Nickel sulfide β	NiS		1.3×10^{-25}
Nickel arsenate	$Ni(AsO_4)_2$		3.1×10^{-26}
Nickel cyanide	$Ni(CN)_2$		1.7×10^{-9}
Nickel ferrocyanide	$Ni_2[Fe(CN)_6]$		1.3×10^{-15}
Nickel oxalate	NiC_2O_4		4.0×10^{-10}
Nickel iodate	$Ni(IO_3)_2$		4.7×10^{-5}
Nickel phosphate	$Ni_3(PO_4)_2$		4.7×10^{-32}

Sources:
http://chemed.chem.wisc.edu/chempaths/Table-of-Some-Solubility-Products-at-25ºC;
http://www.csudh/oliver/chemdata/data-ksp.htm;
http://www.ktf-split.hr/periodni/en/abc/kpt.html;
Occupational Health Guide for Nickel Metal and Soluble Nickel Compounds, National Institute for Occupational Safety and Health, September, 1978.

3 Major Uses or Sources of Exposure

The most common airborne exposures to nickel compounds are to insoluble nickel compounds such as elemental nickel, nickel sulfide, and the nickel oxides from dusts and fumes. Contributions to nickel in the ambient air are made by combustion of fossil fuels, nickel plating, and other metallurgical processes. The most common oxidation state of nickel is the divalent (Ni(II) or Ni^{2+}) form (U.S.EPA, 1985). Elemental nickel is a malleable, silvery-white metal that is highly resistant to strong alkali. Because of its corrosion resistance, about 40% of nickel is used in the production of stainless steel, permanent magnets, and other alloys that require resistance to extremes of temperature or stress (U.S.EPA, 1985). About 20% of nickel is produced as nickel sulfate and hydroxide used in electroplating baths, batteries, textile dyes, and catalysts (U.S.EPA, 1985, Von Burg, 1997). Nickel dust or powder is flammable (CDTSC, 1985). Nickel carbonyl also is volatile. However, because of its unique toxicity relative to the inorganic nickel compounds, this REL is not applicable to nickel carbonyl.

3.1 Air

The primary stationary source categories that emit nickel into ambient air in California are fuel combustion, nickel alloy manufacture, cement production, asbestos mining and milling, municipal waste sludge incineration, iron and steel foundries, secondary metal recovery, cooling towers, coal gasification petroleum processing, and electroplating. Also nickel has been detected in vehicular exhaust, tobacco smoke, and indoor smoke from home-heating and cooking fuels (CARB, 1991). The United States Environmental Protection Agency (U.S. EPA, 1986) estimated that particles found in ambient air as a result of oil combustion might contain nickel in the form of nickel sulfate, with smaller amounts of nickel oxide and complex metal oxides containing nickel. The majority of the nickel in the atmosphere is thought to be associated with human activities. Up to one-third of atmospheric nickel could come from windblown dusts, forest fires and volcanic emissions (CARB, 1991). The annual average ambient air concentration of nickel as measured by the air monitoring network operated by the California Air Resources Board and local air districts in 2002 was 4.5 ± 4.1 SD ng/m^3 (CARB, 2008). This value is quite similar to the values reported for earlier years 1992 to 2001 (CARB, 2008). Recent data from the south coast air basin (SCAQMD, 2008) show average sampled concentrations of nickel in total suspended particulate of around 6 ng/m^3. The highest individual area was West Long Beach at about 11 ng/m^3 possibly resulting from increased shipping activity at the ports since nickel is naturally present in bunker fuel used in ships. Some additional recent studies of nickel in ambient air are listed in Table 6. In general concentrations range from 2 to 9 ng Ni/m^3. Besides ambient and occupational exposures, nickel has been measured in mainstream cigarette smoke in concentrations higher than other metals such as copper, cadmium and iron: 0.2-0.51, 0.19, 0.07-0.35, and 0.042 µg/m^3, respectively (IARC, 1986).

TABLE 6. ATMOSPHERIC NICKEL CONCENTRATIONS AND DRY DEPOSITION RATES IN SOME RECENT STUDIES

Study	Region	No. sites sampled	Analyte(s)	Sample period	Ni, ng/m^3	Deposition Rate, µg Ni/d/m^2
Agrawal et al., 2009	Los Angeles, CA Air Basin	10	Metals, $PM_{2.5}$	2 years	3-7.5	N.A.
Armami et al., 2009	Los Angeles, CA, Long Beach	6	Metals, $PM_{2.5-10}$ $PM_{0.25-2.5}$ $PM_{0.25}$QUF	7 weeks	2-8 5-9 4-9	N.A.
Lim et al., 2006	Los Angeles, CA	7	Metals, PM_{6-11} PM_{11-20}	24 hr x 4 seasons	9.2	9.4
Polidori et al., 2009	So. Calif indoor and outdoor retirement communities	4	Metals, $PM_{<0.25}$ $PM_{0.25-2.5}$ $PM_{2.5-10}$	2 x 6 weeks/site	4 indoor 5 outdoor S.Gabriel	N.A.
Sabin et al., 2006	Los Angeles, CA. I-405 highway proximity	4 10-400m	Metals, $PM_{<6}$ PM_{6-11} PM_{11-20} PM_{20-29} $PM_{>29}$	3 weeks, 8AM- 5 PM 300,000 vehicles/day	10	1-3
Sabin et al., 2008	So. Calif coast, Santa Barbara to San Diego	8	Metals	3months 10/site		0.21-5.4
Hays et al., 2011	Raleigh, NC I-440 highway	1 20m	Metals, $PM_{2.5-10}$ $PM_{0.1-2.5}$ $PM_{0.1}$	2 months, 125,000 vehicles/d	0.7 1.1 0.2	N.A.
Bell et al., 2010	Connecticut, and Mass. Low birth weight in 76,788 infants of exposed mothers	4	Metals, $PM_{2.5}$	Weekly averages for 39 week gestation period	3.1±1.5	N.A.

3.2 Soil

Nickel occurs naturally in the Earth's crust at an average concentration of 0.0086% (86 ppm) (Duke, 1980). The nickel content of soil can vary widely depending on local geology. Both the southeastern United States and southern Quebec can have nickel concentrations greater than 1000 ppm due to local ultramafic rock, which is rich in

nickel. Typical nickel soil concentrations range from 4 to 80 ppm (ATSDR, 2005). A soil survey by the U.S. Geological Survey throughout the U.S. reported concentrations from <5 to 700 ppm, with a geometric mean of 13.0 ± 2.31. Nickel ranked 15th among 50 elements included in the study (Shacklette and Boerngen, 1984). Auto emissions can also raise the level of nickel in soil. Lagerwerff and Sprecht (1970) found nickel concentrations from 0.9 to 7.4 ppm in roadside soils. The concentrations were lower at greater distances from the road and at greater soil depths. Munch (1993) found 32 ppm Ni in soil lying directly at the roadside edge of a busy forest road (3200 vehicles/day) in Germany. Haal et al. (2004) reported nickel roadside soil concentrations of 12 to 33 ppm 5 to 15 m from the roads in Tallinn, Estonia. They noted that while lead had decreased over the past decade, Zn and Ni had doubled.

3.3 Water

Nickel enters groundwater and surface water via dissolution of rocks and soils, from atmospheric deposition, from biological decay, and from waste disposal. Nickel compounds are relatively soluble in water and usually exist as nickel ions in aqueous environments. Uncontaminated surface freshwater and seawater usually contain low concentrations of nickel (<0.3 μg/L, Barceloux, 1999). The nickel concentration of fresh surface water has been reported to average between 15 and 20 μg/L (Grandjean, 1984; ATSDR, 2005). The nickel concentration in groundwater is normally less than 20 μg/L (U.S.EPA, 1986), and levels appear similar in raw, treated, and distributed municipal water.

Elevated nickel in drinking water may result from corrosion of nickel-containing alloys used in valves and other components in the water distribution system as well as from nickel-plated faucets. Tap water that is used for drinking purposes generally contains nickel at concentrations ranging from 0.55 to 25 µg Ni/L in the United States (ATSDR, 2005; FDA 2000; O'Rourke et al. 1999; Thomas et al. 1999). Nickel concentrations in tap water measured in the Total Diet Study 1991–1999 ranged from 0 to 0.025 mg Ni/kg (0–25 µg Ni/L) with a mean value of 0.002 mg/kg (2 µg Ni/L) (FDA 2000). Analysis of data obtained during 1995 - 1997 from the National Human Exposure Assessment Study (NHEXAS) yielded median concentrations of nickel in tap water (used as drinking water) of 4.3 µg Ni/L (10.6 µg Ni/L, 90th percentile) in the Arizona study and 4.0 µg Ni/L (11 µg Ni/L, 90th percentile) in the U.S. EPA Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) study (O'Rourke et al., 1999; Thomas et al., 1999). In a 1969–1970 survey of 969 water supplies in the United States representing all water supplies in eight metropolitan areas and one state (2,503 samples), 21.7% of samples had concentrations <1 µg Ni/L, 43.2% of the samples contained between 1 and 5 µg Ni/L, 25.6% of the samples contained between 6 and 10 µg Ni/L, 8.5% of the samples contained between 11 and 20 µg Ni/L, and 1% had levels >20 µg Ni/L (NAS 1975).

Nickel has been detected in California drinking water sources. According to the monitoring data collected by the California Department of Health Services (DHS) between 1984 and 1997, the highest, average and median concentrations of nickel in

water were 540 μg/L, 26 μg/L, and 17.9 μg/L, respectively (DHS, 1998). The detection limit for the purposes of reporting for nickel is 10 μg/L (10 ppb).

3.4 Food

Terrestrial plants take up nickel from soil mainly via the roots. The amount of uptake depends on the concentration in soil, soil pH, organic matter content and the type of plant. The nickel concentration in most natural vegetation ranged from 0.05 to 5.0 mg Ni/kg dry weight (dw) (NRC, 1975). Some food sources such as chocolate, nuts, beans, peas, and grains are relatively rich in nickel.

There have been several studies regarding nickel content in an average diet (ATSDR, 2005). Current information on the dietary intake of nickel in the United States is based on data gathered from the NHEXAS study. Nickel concentrations were measured in duplicate diet samples, which, in combination with study participant's estimates of food and water intake, were used to determine both the overall concentration of nickel in combined solids and liquids in the total diet and the average nickel intake of study participants. In the U.S. EPA Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) study, the mean and median concentrations of nickel in combined dietary solids and liquids were 47 and 43 μg Ni/kg, respectively (Thomas et al., 1999).

Calamarie et al. (1982) showed that nickel is not likely to accumulate in fish. They exposed rainbow trout (*Salmo gairdneri*) to nickel contaminated water at 1.0 mg Ni/L for 180 days and found 2.9 mg Ni/kg wet weight in liver, 4.0 mg/kg in kidneys, and 0.8 mg/kg in muscle. Initial study values for these tissues were 1.5, 1.5, and 0.5 mg Ni/kg, respectively.

Myron et al. (1978) studied nickel levels in meals sampled from the University of North Dakota and from a hospital. The average nickel concentration of the student meals ranged from 0.19 to 0.29 μg Ni/g dry weight and for the hospital meals from 0.21 to 0.41 μg Ni/g dry weight. Based on the nine diets examined, the authors estimated an average daily dietary intake of 168 ± 11 μg nickel. This value is similar to those estimated in other studies (ATSDR, 2005).

4 Toxicokinetics

4.1 Absorption

Ishimatsu et al. (1995) demonstrated that the absorption fraction of orally administered nickel compounds in rats was closely related to their water solubility. They administered eight nickel compounds and nickel metal. The solubilities in saline solution were in the following order: [$Ni(NO_3)_2$ > $NiCl_2$ > $NiSO_4$] >> [NiS > Ni_3S_2] > [NiO (black) > Ni (metal) > NiO (green)]. The insoluble nickel metal and nickel oxides ranged from 0.01 to 0.09% absorbed. The absorption of the slightly soluble nickel subsulfide and nickel sulfide was 0.5% to 2.1% and the soluble nickel compounds (sulfate, nitrate and chloride) ranged from 10 to 34 percent. In rats administered $NiCl_2$, $NiSO_4$, and NiS 84-87% of recovered nickel was detected in the kidneys. Lesser kidney ratios were found for Ni_3S_2, $Ni(NO_3)_2$, NiO(B) and Ni(M): 76%, 73%, 62%, and 51%, respectively. However, NiO(G) showed greater recovery from liver than kidney.

Ho and Furst (1973) reported that gavage administration of rats with $^{63}NiCl_2$ in 0.1N HCl led to 3 to 6 percent absorption of the labeled nickel, independent of dose level (4, 16, and 64 mg Ni/kg body weight (bw)). One day after administration 94 to 97 percent of the dose was excreted in the feces and 3 to 6 percent in the urine. Nielsen et al. (1993) administered $^{57}NiCl_2$ at 3 to 300 μg Ni/kg bw by gavage to male mice, and estimated that intestinal absorption ranged from 1.7 to 7.5 percent of administered dose.

Nickel is absorbed in the gastrointestinal (G.I.) tract of humans either as free ions or as complexes. The degree of uptake or bioavailability depends on the vehicle (water or food) and has ranged from 1% to 40% in several studies (Table 7).

Cronin et al. (1980) reported that ingestion of a soluble nickel compound during fasting by a group of female subjects resulted in urinary elimination of four to 20 percent of the dose. Sunderman et al. (1989) found that about 40 times more nickel was absorbed from the G.I. tract when nickel sulfate was given to human volunteers in drinking water (27 ± 17 %, mean ± SD) than when it was given in food (0.7 ± 0.4 %). Sunderman et al. (1989) also reported that absorption fraction was independent of dose at 12, 18, or 50 μg Ni/kg bw.

TABLE 7 ABSORPTION OF INGESTED NICKEL IN HUMANS FROM BIOAVAILABILITY STUDIES (DIAMOND ET AL., 1998; ATSDR, 2005)

Study	Number of subjects	Vehicle	Duration	Fasting status	Absorption (% of Dose)
Nielsen et al., 1999	8	Water plus scrambled eggs	Acute	Fasted	25.8 to 2.5
Patriarca et al., 1997	4	Water	Acute	Fasted	29-40
Sunderman et al., 1989	8	Water	Acute	Fasted	29.3
Sunderman et al., 1989	8	Food	Acute	Fasted	1.8
Cronin et al. , 1980	5	Capsule plus 100 mL water	Acute	Fasted	12-32
Christensen & Lagassoni, 1981	8	Capsule	Acute	With meal	5.7
Gawkrodger et al., 1986	3	Capsule	Acute	With meal	2.7, 2.8
Menne et al., 1978	6	Capsule	Acute	Not fasted	2.2 (women)
Menne et al., 1978	7	Capsule	Acute	Not fasted	1.7 (men)
Horak & Sunderman, 1973	10-50	Food	Chronic	Not fasted	1.0
McNeeley et al., 1972	19	Food & water	Chronic	Not fasted	1.6
McNeeley et al., 1972	20	Food	Chronic	Not fasted	1.2

Solomons et al. (1982) and Nielson et al. (1999) reported similar results. They found that plasma nickel concentrations in five fasted human subjects were significantly elevated when they were given nickel sulfate (5 mg Ni) in drinking water with a peak level of about 80 μg Ni/L at three hours after oral administration. When five mg Ni (as nickel sulfate) were administered in whole cow-milk, coffee, tea, orange juice, or Coca Cola®, the rise in plasma Ni was significantly suppressed with all but the Coca Cola®. By four days after administration, 26% of a dose given in water was excreted in urine and 76% in feces. When the nickel dose was given in food, 2% was excreted in the urine and the balance in feces. The elimination half-life for absorbed nickel averaged 28 ± 9 hours (Sunderman et al., 1989).

Solomons et al. (1982) showed that plasma nickel levels of subjects who consumed a typical Guatemalan meal with 5 mg nickel or a North American breakfast with 5 mg nickel were only about 5 to 20 percent of that which resulted from the consumption of 5 mg nickel in water. Nielsen et al. (1999) administered nickel in drinking water

(12 μg Ni/kg bw) to eight fasted volunteers at different time intervals, with standardized portions of scrambled eggs. They found that the highest fraction of nickel dose (25.8%) excreted in urine was observed when the scrambled eggs were taken four hours prior to nickel in drinking water. A much lower fraction of nickel dose (2.5%) was excreted when the nickel was mixed into the eggs or when the drinking water was taken together with the eggs (3.4%).

Patriarca et al. (1997) studied nickel metabolism in humans using the stable isotope ^{62}Ni (98.83%, as metal). Four healthy adult subjects (two women and two men) were fasted overnight and administered 10 μg ^{62}Ni/kg bw in water. Blood samples were drawn in fixed intervals and the total daily output of urine and feces was collected for the first five days after dose ingestion. ^{62}Ni was measured in plasma, urine and feces by isotope dilution using ^{61}Ni and plasma-mass spectrometry. Fecal excretion of ^{62}Ni averaged 66.9 ± 4.9 % of administered dose with an absorbed fraction of 33.1 ± 4.9 %. Urinary excretion over five days ranged from 51% to 82% (mean ± SD= 65.2 ± 13.4 %) of absorbed dose. Plasma ^{62}Ni peaked between 1.5 and 2.5 hours after ingestion with concentrations ranging between 269 and 344 nM; ^{62}Ni was rapidly cleared from the plasma but was still detectable at 96 hr post ingestion (< 32 nM). The authors reported no evidence of biliary excretion or enterohepatic circulation of ^{62}Ni as indicated by the appearance of secondary peaks in plasma or urinary nickel concentrations. Also the elimination of ^{62}Ni in feces followed the same pattern as the fecal marker (radio-opaque pellets) indicating that biliary excretion is very low or absent in humans, albeit with a limited number of subjects.

Nickel has been reported as an essential element in several animal species. Signs of Ni deficiency include depressed growth and reduced hematocrit (Nielsen, 1996). In the case of human nutrition the essentiality of Ni has yet to be established (IOM, 2001).

Animal models have been used to estimate the inhalation absorption of water-soluble and water-insoluble nickel compounds. English et al. (1981) administered nickel chloride and nickel oxide intratracheally to rats and reported greater than 50% of the soluble nickel chloride was cleared from the lungs within three days. Most of the nickel was excreted in the urine. In contrast, the water-insoluble nickel oxide persisted in the lung for more than 90 days, and the nickel was excreted equally in urine and feces.

Valentine and Fisher (1984) administered slightly soluble nickel subsulfide intratracheally to mice and observed the pulmonary clearance to have two distinct components with initial and final half-lives of 1.2 and 12.4 days, respectively. The excretion of the chemical (measured as ^{63}Ni) was 60% in the urine and 40% in the feces. Similar findings were reported by Finch et al. (1987) who observed that the pulmonary clearance of intratracheally administered nickel subsulfide in mice was biphasic with clearance half-lives of two hours and 119 hours for initial and final phases, respectively.

Tanaka et al. (1985) exposed male Wistar rats to NiO aerosols of mass median aerodynamic diameter (MMAD) and geometric standard deviation (gsd) of 1.2 μm, 2.2 gsd and 4.0 μm, 2.0 gsd. The average exposure concentration was 0.6 mg/m^3 or

70 mg/m^3 and total exposure time was 140 hours. Some rats were sacrificed after exposure while others were kept for 12 and 20 months prior to sacrifice. The biological half-lives of NiO deposited in the lungs based on the assumption of first order clearance kinetics were 11.5 and 21 months for 1.2 and 4.0 µm MMAD aerosols, respectively. The relation used was $T_{50} = -0.301/\log(1- f)$, where f , the clearance ratio, was selected as 0.002 or 0.001 depending on fit to the experimental data.

Following a single 70-minute inhalation exposure of rats to green nickel oxide (^{63}NiO; 9.9 mg Ni/m^3; AMAD 1.3 µm, 2.0 gsd), the fraction of the inhaled material deposited in the total respiratory tract was 0.13, with 0.08 deposited in the upper respiratory tract and 0.05 deposited in the lower respiratory tract (Benson et al. 1994). During the 180 days post-exposure, nickel was not detected in extra-respiratory tract tissues.

Tanaka et al. (1988) studied the biological half-life of amorphous NiS aerosols in exposed rats. The rats were exposed to a NiS aerosol with MMAD of 4.0 µm (gsd = 2.0) and either a single four hr exposure of 107 mg/m^3 or repeated 8.8 mg/m^3 for 7 hr/day, 5 days/week for one month. After exposure, the nickel contents in lung, liver, kidney, spleen, blood and urine were measured. In sharp contrast to the findings with NiO (above), NiS was rapidly cleared from lung tissue following a four-hour exposure with a half-life of 20 hours (f = 0.57). Repeated exposures of NiS at lower concentration showed no accumulation of NiS in the lung and similar clearance kinetics following the final exposure (their Fig. 2).

Following a single 120 minute inhalation exposure of rats to nickel subsulfide ($^{63}Ni_3S_2$; 5.7 mg Ni/m^3 AMAD 1.3 µm, gsd 1.5), the fraction of inhaled material deposited in the upper respiratory tract was similar to that observed for nickel oxide (0.14 in the total respiratory tract, 0.09 in the upper respiratory tract, and 0.05 in the lower respiratory tract). In contrast to nickel from nickel oxide, nickel from nickel subsulfide was detected in the blood, kidneys, and carcass between 4 and 24 hours after the exposure (Benson et al., 1994).

Data in rats and mice indicate that a higher percentage of less-soluble nickel compounds was retained in the lungs for a longer time than soluble nickel compounds (Benson et al. 1987, 1988; Dunnick et al. 1989; Tanaka et al. 1985) and that the lung burden of nickel decreased with increasing particle size ($\leq$ 4 µm) (Kodama et al. 1985a, 1985b). Nickel retention was six times (mice) to 10 times (rats) greater in animals exposed to less-soluble nickel subsulfide compared to soluble nickel sulfate (Benson et al. 1987, 1988).

The lung burdens of nickel generally increased with increasing exposure duration and increasing levels of the various nickel compounds (Dunnick et al. 1988, 1989). From weeks 9 to 13 of exposure, lung levels of nickel sulfate and nickel subsulfide remained constant while levels of nickel oxide continued to increase (Dunnick et al. 1989). Slow clearance of nickel oxide from the lungs was also observed in hamsters (Wehner and Craig 1972). Approximately 20% of the inhaled concentration of nickel oxide was retained in the lungs at the end of exposure for two days, three weeks, or three months. The retention was not dependent on the duration of exposure or exposure

concentration. By 45 days after the last exposure to nickel oxide (two-day exposure), 45% of the initial lung burden was still present in the lungs (Wehner and Craig 1972).

Workers occupationally exposed to nickel have higher lung burdens of nickel than the general population. Dry weight nickel content of the lungs at autopsy was 330 ± 380 µg/g in roasting and smelting workers exposed to less-soluble compounds, 34 ± 48 µg/g in electrolysis workers exposed to soluble nickel compounds, and 0.76 ± 0.39 µg/g in unexposed controls (Andersen and Svenes 1989). In an update of this study, Svenes and Andersen (1998) examined 10 tissue samples taken from different regions of the lungs of 15 deceased nickel refinery workers; the mean nickel concentration was 50 µg/g dry weight. Nickel levels in the lungs of cancer victims did not differ from those of other nickel workers (Kollmeier et al. 1987; Raithel et al. 1989).

Nickel levels in the nasal mucosa are higher in workers exposed to less-soluble nickel compounds relative to soluble nickel compounds (Torjussen and Andersen 1979). These results indicate that, following inhalation exposure, less-soluble nickel compounds remain deposited in the nasal mucosa. Higher serum nickel levels have been found in occupationally exposed individuals compared to non-exposed controls (Angerer and Lehnert 1990; Elias et al. 1989; Torjussen and Andersen 1979). Serum nickel levels were found to be higher in workers exposed to soluble nickel compounds compared to workers exposed to less-soluble nickel compounds (Torjussen and Andersen 1979). Concentrations of nickel in the plasma, urine, and hair were similar in nickel-sensitive individuals compared to non-sensitive individuals (Spruit and Bongaarts 1977).

Serita et al. (1999) evaluated pulmonary clearance and lesions in rats after a single inhalation of ultrafine metallic nickel (Uf-Ni, 20 nm average particle diameter). Wistar rats (sex unspecified) were exposed to 0.15 (Low), 1.14 (Medium), or 2.54 (High) mg Uf-Ni/m^3 for five hours. Groups of five rats per dose group were sacrificed at 0 hr and 1, 3, 7, 14, and 21 days post exposure. The amount of nickel in the lung accumulated in a dose-dependent manner (1.4, 10.1, 33.5 µg Ni/lung, respectively). The half times for nickel in the lung averaged about 32 days and appeared independent of initial dose.

4.2 Distribution

Several studies of nickel administered to rodents via the oral route show that nickel was mainly concentrated in the kidneys, liver, and lungs, and the absorbed nickel was excreted primarily in the urine (Borg and Tjalve, 1988; Jasim and Tjalve, 1984, 1986a, 1986b; Dieter et al., 1988). Nielsen et al. (1993) showed that retention and distribution of nickel in mice was dependent on the route of administration. As shown in Table 8, Nielsen et al. (1993) showed that 20 hours after nickel administration, deposition in body tissues resulting from intraperitoneal (i.p.) injection was much greater than that observed after gavage administration.

TABLE 8. MEDIAN NICKEL BODY BURDEN AND CONTENTS OF MAJOR ORGANS IN MICE AS PERCENTAGE OF ADMINISTERED DOSE (FROM NIELSEN ET AL., 1993)*.

Tissue	Gastric Intubation	Intraperitoneal Injection
Liver	0.0439 (0.046)[a]	0.255 (0.044)[b]
Kidneys	0.029 (0.030)	1.772 (0.306)
Lungs	<0.010 (0.010)	0.114 (0.020)
Carcass	0.106 (0.111)	3.164 (0.546)
Stomach	0.014 (0.015)	<0.010 (0.002)
Intestine	0.762 (0.799)	0.490 (0.084)
Total body burden	0.954 (1.0)	5.794 (1.0)

*Note: a) Measurements made 20 hr after oral dose of 10 µmol Ni/kg bw. b) Measurements made 20 hr after intraperitoneal injection of 1.0 µmol Ni/kg bw. Values in parentheses are ratios of relative tissue burden over total body burden.

Ishimatsu et al. (1995) evaluated the distribution of various nickel compounds in rat organs 24 hours after oral administration. Male Wistar rats (10 weeks old, 8/compound) were administered the nickel compounds by gavage as 10 mg of Ni dissolved in a 5% starch saline solution. The animals were sacrificed at 24 hr after dosing and organs and blood taken for Ni determination. Selected results are presented in Table 9. The kidney stands out as the major site of nickel deposition. This table also demonstrates the high bioavailability of soluble nickel compounds compared to poorly soluble compounds.

Obone et al. (1999) measured the accumulation of nickel in tissues of rats exposed to $NiSO_4$ in drinking water for 13 weeks. Accumulation in all organs examined was observed to increase with increasing dose level. The order of accumulation compared to the control was kidneys > testes > brain > spleen > lung = heart= liver (Table 10).

Absorbed nickel is unlikely to exist as free ionic Ni^{2+}, but rather as nickel complexes. Sunderman and Oskarsson (1991) noted that in humans absorbed nickel is transported by binding to a metalloprotein (nickeloplasmin), albumin, and ultra-filterable ligands, such as small polypeptides and L-histidine. Van Soestbergen and Sunderman (1972) administered nickel chloride (as ^{63}Ni) to rabbits by intravenous injection at 0.24 mg Ni/kg bw. They found that between two and 24 hr after injection, approximately 90% of serum ^{63}Ni was bound to proteins (e.g., albumin) with molecular weights greater than 10,000 and the remaining label was bound to small organic molecules such as short peptides and amino acids.

TABLE 9. MEAN NICKEL CONCENTRATIONS IN RAT ORGANS 24 HOURS AFTER ORAL ADMINISTRATION (ADAPTED FROM ISHIMATSU ET AL., 1995)*

Ni Compound	Lung µg/g	Liver µg/g	Kidney µg/g	Heart µg/g	Brain µg/g	Blood µg/mL
NiO (Green)	0.04	0.02	0.03	0.03	0.03	0.03
Ni metal	0.18	0.04	0.31	0.04	0.02	0.02
NiO (Black)	0.08	0.04	0.32	0.04	0.02	0.05
Ni_3S_2	0.17	0.07	1.2	0.04	0.02	0.05
NiS	0.34	0.11	6.4	0.60	0.04	0.21
$NiSO_4$	2.5	0.57	25.5	0.47	0.04	0.28
$NiCl_2$	3.7	0.53	28.7	1.2	0.18	0.31
$Ni(NO_3)_2$	6.3	1.1	32.6	2.4	0.15	2.25
Control	0.04	0.03	0.03	0.03	0.02	0.03

* Note 8 animals/compound; 10 mg Ni oral dose by gavage

TABLE 10. MEAN NICKEL CONCENTRATIONS IN RAT ORGANS AFTER 13 WEEKS EXPOSURE TO $NISO_4$ IN DRINKING WATER (µG NI/G TISSUE, OBONE ET AL., 1999)*

Treatment NiSO4	Liver	Kidney	Spleen	Heart	Lungs	Brain	Testis
0%	1.58	1.39	1.51	1.60	1.22	1.59	1.50
0.02%	1.60	1.88	1.85	1.74	1.60	1.68	1.85
0.05%	1.63	3.45	1.86	1.83	1.95	1.77	2.05
0.1%	2.08	5.48	2.26	2.12	2.11	2.78	2.84

*Note: Values are means of three different experiments. Measurements made 24 hr after termination of exposure.

Chelation of Ni^{2+} by organic compounds has a significant effect on the cellular uptake, absorption, and distribution of Ni^{2+} (Sakar, 1984; Nierborer et al., 1984; Borg and Tjalve, 1988; Hopfer et al., 1987). Nierborer et al. (1984) studied cellular uptake of Ni^{2+} in human B-lymphoblasts, human erythrocytes and rabbit alveolar macrophages. They observed that addition of L-histidine or human serum albumin at physiological concentrations to the cell cultures reduced Ni^{2+} uptake by up to 70%. The concentration of Ni^{2+} used in the study was 7×10^{-8} M (4.1 µg/L); it was comparable to serum nickel levels observed in workers occupationally exposed to nickel.

Rezuke et al. (1987) measured nickel concentrations in human postmortem samples in seven to 10 adults. In decreasing order the mean and range in µg Ni/kg dry weight in the tissue specimens were: lung 173 (71-371); thyroid 141 (41-240); adrenal 132 (53-

241); kidney 62 (19-171); heart 54 (10-110); liver 50 (11-102); brain 44 (20-65); spleen 37 (9-95); and pancreas 34 (7-71). In five specimens of bile, nickel concentrations averaged 2.3 ± 0.8 µg/L (range 1.5-3.3 µg/L). These values differ markedly from the distribution of Ni in the rat noted in Table 10 above. The relatively high Ni burden in the human lung and low burden in the human kidney may indicate significantly more inhalation exposure in humans and/or significant differences in the chemical state of nickel absorbed in laboratory rodent versus human environmental exposures.

Nickel has been shown to cross the human placenta; it has been found in both fetal tissue (Schroeder et al., 1962) and the umbilical cord blood serum (McNeely et al., 1971). Similar findings have been reported in animal studies. Szakmary et al. (1995) administered a single gavage dose of 5.4, 11.3, or 22.6 mg Ni/kg bw as nickel chloride to pregnant rats. Twenty-four hours after exposure, nickel levels in fetal blood were raised from 10.6 (control) to 14.5, 65.5, and 70.5 µg/L for the low, medium, and high dose groups, respectively. Jacobsen et al. (1978) observed that when pregnant mice were given a single i.p. injection of ^{63}Ni chloride (0.14 mg/kg bw) on day 18 of gestation, passage of ^{63}Ni from mother to fetus was rapid and concentrations in fetal tissues were generally higher than those in the dam.

The distribution of nickel chloride in pregnant and lactating rats following its injection has been studied by a number of authors (Dostal et al., 1989; Mas et al., 1986; Sunderman et al., 1978). Half-lives of nickel in whole blood following i.p. treatment of pregnant and non-pregnant rats were similar (3.6–3.8 hours), while the half-life for nickel in fetal blood was 6.3 hours following treatment on gestation days 12 or 19 (Mas et al., 1986). Intramuscular injection of nickel chloride (12 mg Ni/ kg/day) into pregnant and non-pregnant rats resulted in a greater accumulation of nickel in the pituitary of pregnant rats (Sunderman et al. 1978).

Tallkvist et al. (1998) evaluated the olfactory transport and subcellular distribution of $^{63}Ni^{2+}$ solution instilled intra-nasally in rats (4 µg/nostril). Cellular fractionation was conducted at one day, one week and three weeks after exposure. Of the $^{63}Ni^{2+}$ present in the olfactory epithelium, 60% to 70% was present in the supernatant, whereas in the olfactory bulb and the basal hemisphere about 70% - 80% of the nickel was bound to particulate cellular constituents. Gel filtration of the cytosol indicated that the $^{63}Ni^{2+}$ eluted with a molecular weight of about 250, identical to that obtained with histidine. Also, in olfactory tissues $^{63}Ni^{2+}$ was partly present in the cytosol associated with a 25,000 molecular weight component. The authors conclude that: 1) nickel is transported in the primary olfactory neurons via slow axonal transport; (2) the metal is bound to both soluble and particulate cytosolic constituents; and (3) the metal also shows this subcellular distribution in other parts of the olfactory system. The authors also note that neuronal transport of nickel was about 20 times slower than cadmium ($^{109}Cd^{2+}$) or manganese ($^{54}Mn^{2+}$) studied earlier.

Schwerdtle and Hartwig (2006) evaluated the subcellular distribution of $NiCl_2$ and black NiO in human lung A549 cells exposed for 20 and 24 hr, respectively. Cells treated with $NiCl_2$ at 0, 50, 100, 250, or 500 µM exhibited dose-dependent uptake of Ni into the cytoplasm and nuclei. Intracellular Ni concentrations in cytoplasm were about 10, 20,

50, 275, and 550 µM, respectively. Concentrations in the nuclei were much lower at about 5, 10, 15, 40, and 110 µM, respectively. Cells treated with black NiO at 0, 0.2, 0.5, 1.0, and 2.0 µg NiO/cm^2 showed a similar pattern of intracellular distribution with greater relative concentrations in the nuclei. For cytoplasmic distribution the Ni concentrations were about 5, 110, 150, 240, and 450 µM, respectively. For nuclear distribution the Ni concentrations were about 2, 60, 70, 125, and 230 µM, respectively. The authors concluded that particulate Ni(II) exhibits greater toxicity due to its longer retention times rather than a different MOA which still involves Ni(II) ions as the direct or indirect genotoxicant.

4.3 Excretion

Nickel burden in humans does not increase with age. A majority of nickel absorbed from environmental media and diet is rapidly excreted via the urine. Solomons et al. (1982) found that nickel in water was quickly absorbed and excreted by humans; they estimated a biological half-life of about eight hours. Hogetveit et al. (1978) reported that elevated levels of nickel were detected in urine samples collected from workers exposed to soluble or insoluble nickel through inhalation.

The kinetics of nickel elimination in humans and animals appear to be similar. Onkelinx et al. (1973) injected nickel chloride i.v. to rats and rabbits and followed the nickel in plasma over time. Elimination profiles were similar in both species with early and later phases of elimination from plasma exhibiting first-order kinetics with half-lives of 6 and 50 hr for rats and 8 and 83 hr for rabbits, respectively.

Sweat and milk are also possible excretion routes for absorbed nickel in humans. Hohnadel et al. (1973) observed that, in sauna bathers, the mean concentrations of nickel in the sweat from healthy men and women were significantly higher than the mean concentrations in urine. Several studies have demonstrated that excretion of nickel in human milk is quite low and should be considered a minor route of excretion in lactating women (Feeley et al., 1983; Mingorance and Lachica, 1985). Casey and Neville (1987) reported a mean nickel concentration of 1.2 ± 0.4 µg/L in 46 human milk samples from 13 women during the first month of lactation with an average estimated daily infant intake of 0.8 µg Ni. Krachler et al. (2000) measured trace elements in 27 human milk samples and found a median nickel concentration of 0.79 µg/L (range < 0.13-6.35 µg/L).

Graham et al. (1978) measured the clearance of $NiCl_2$ aerosol in mice exposed to 644 µg Ni/m^3 for two hours. Immediately following exposure and at 24 hr intervals thereafter the mice were sacrificed, their lungs and spleens were removed and weighed, and nickel concentrations were determined by atomic absorption spectroscopy. Clearance of nickel from the lung followed first-order kinetics with a fitted curve of Y = 7.569exp (-0.291t), where Y is µg Ni/g dry weight lung and t is days post exposure. The spleen did not exhibit a significant uptake of nickel following exposure.

Koizumi et al. (2004) measured the urinary excretion of nickel nitrate hexahydrate in rats by inductively coupled plasma argon emission spectroscopy (ICPAES). Male

Wistar rats received single oral doses of 0, 0.005, 0.01, 0.025, 0.05, 0.075, 0.1, 0.125, 0.25, 0.5, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, 10.0, 20.0, and 50.0 mg $Ni(NO_3)_2 \cdot 6H_2O$/kg bw. Five animals were used for analysis at each dose level. The 24-hr urinary excretion of nickel was observed to fit the relation $Y = 62.68X^{0.8527}$, R = 0.9488, where Y is the excreted Ni in µg and X is the oral dose in mg/kg bw. The proportion of total nickel elimination decreased from 25% at 0.01 mg/kg to about 5% at 0.1 mg/kg and higher doses. Urological analysis of markers of renal toxicity, N-acetyl-β-D-glucosamine (NAG), β_2-microglobulin, urine albumin, and urine protein, showed no indication of toxicity at any dose level used.

Dostal et al. (1989) showed that milk is an excretion pathway of nickel chloride in rodents. Daily subcutaneous injections of lactating rats with 3 or 6 mg Ni/kg bw for four days raised nickel levels in milk from < 2 µg/L to 513 ± 54 and 1030 ± 66 µg/L, respectively. They also showed that nickel treatment significantly changed the composition of milk by increasing the milk solids (42%) and lipids (110%) and decreasing milk protein (29%) and lactose (61%).

Oyabu et al. (2007) studied the biopersistence of inhaled NiO particles in the rat lung. Thirty male Wistar rats were exposed to NiO particles (geometric mean diameter = 139±12 nm, average exposure concentration = $1.0 \pm 0.5 \times 10^5$ particles/m^3) for six hr/day for four weeks. At four days and one and three months after inhalation, a group of 10 rats was sacrificed and the NiO particles deposited in the lung determined by chemical analysis. The retained Ni particle content of the lung decreased exponentially with a calculated half time of 62 days.

Oliveira et al. (2000) studied urinary nickel excretion in 10 workers from a galvanizing plant using $NiSO_4$, a soluble nickel compound, and 10 control subjects. Personal air monitors were used with 0.8 µm filters (OSHA method). No other particle size information was provided. Nickel airborne levels varied between 2.8 and 116.7 µg/m^3. Pre- and post-shift urinary Ni levels were taken on five consecutive workdays. Post-shift values ranged from 4.5 to 43.2 µg Ni/g creatinine. A significant correlation was observed between urinary and airborne nickel ($r = 0.96$, $P \leq 0.001$) with the relation urinary Ni (µg/g creatinine) = 6.00 + 0.43(airborne Ni, µg/m^3). No differences were observed with respect to different workdays.

Yokota et al. (2007) studied the urinary elimination of nickel and cobalt in relation to airborne exposures in a battery plant. The workers were exposed to nickel hydroxide, metallic cobalt, and cobalt oxyhydroxide. Nickel in the air was several fold higher than cobalt and positively correlated ($r^2 = 0.958$). Cobalt in air and post-shift urine gave a regression equation of $Co\ (\mu g/L)_{urine} = 15.8 + 243.8\ Co\ (mg/m^3)_{air}$ with a poor correlation coefficient (r = 0.491). No correlation was found between Ni in air and post-shift urine [$Ni\ (\mu g/L)_{urine} = -17.3 + 7.33\ Ni\ (mg/m^3)_{air}$, r = 0.272, P = 0.15]. The authors note that the workers were using respiratory protection which presumably reduced inhalation exposure to $Ni(OH)_2$. They also note discrepancy with treatment of Ni inhalation by the DFG (Deutsche Forschungsgemeinschaft, 2005) which gives the relations for airborne nickel exposure and urinary nickel for water-soluble and water-insoluble compounds. For soluble nickel compounds including the hydroxide, acetate, chloride, sulfate and

similar salts they give Ni $(\mu g/L)_{urine}$ = 10 + 600 Ni$(mg/m^3)_{air}$. For insoluble nickel compounds including the metal, oxide, carbonate, sulfide, and sulfidic ores they give Ni $(\mu g/L)_{urine}$ = 7.5 + 75 Ni$(mg/m^3)_{air}$. The authors argue that $Ni(OH)_2$ should be treated as an insoluble compound with respect to urinary excretion rather than a soluble one.

Afridi et al. (2006) measured metal content in biological samples from 56 production workers (PW) and 35 quality control workers (QCW) of a steel mill and 75 unexposed normal controls (all male, age range 25-55 yr). For nickel in scalp hair the PW showed the highest Ni concentration of 13.76 ± 4.48 µg Ni/g with QCW lower at 9.02 ± 2.64 µg Ni/g. These values were significantly higher than the non-occupationally exposed controls at 5.25 ± 1.46 µg Ni/g hair ($P < 0.02$). Surprisingly the mean lead values were quite similar at 16.21, 10.33, and 6.84 µg Pb/g hair, respectively. Urine concentrations were also measured and showed lesser, but also significant, differences i.e. 9.47, 7.62, and 6.31 µg Ni/L urine, respectively.

Ohashi et al. (2006) evaluated selected urinary metals in 1000 women in the general Japanese population. The geometric mean concentration for nickel was 2.1 µg Ni/L or 1.8 µg Ni/g creatinine. Unlike copper and manganese both nickel and cobalt showed no substantial age dependency for urinary excretion.

4.4 Physiological Models

Onkelinx et al. (1973) conducted a kinetic analysis of $^{63}Ni^{2+}$ clearance in rats and rabbits following a single intravenous injection of $^{63}NiCl_2$ (specific activity 5.9 µCi/µg Ni). In both species $^{63}Ni^{2+}$ was rapidly cleared from plasma or serum during the first two days, and more slowly after two days. The blood elimination data were best described by the bi-exponential relations:

Rats: $S = 226 \exp[-0.11t] + 0.57 \exp[-0.014t]$ for 17 µg Ni/rat (82 µg Ni/kg bw);

Rabbits: $S = 1165 \exp[-0.092t] + 4.95 \exp[-0.0084t]$ for 816 µg Ni/rabbit (240 µg Ni/kg bw);

where S is the plasma concentration of Ni^{2+} (µg/L) and t is the time after injection (hr). A two-compartment model derived from the data successfully predicted serum or plasma concentrations of Ni^{2+} in animals receiving continuous infusions or repeated daily injections of $^{63}NiCl_2$.

Sunderman et al. (1989) developed a model to predict nickel absorption, serum levels, and excretion following oral exposure to nickel in water and food. The model was developed based on two experiments in humans in which serum nickel levels and urinary and fecal excretion of nickel were monitored for two days before and four days after eight subjects were given an oral dose of nickel as nickel sulfate (12, 18, or 50 µg Ni/kg bw) in water or in food. The data were then analyzed using a four-compartment toxicokinetic model consisting of Gut, Serum, Urine and Tissues. Two inputs of nickel, the single oral dose, in which uptake was considered to be a first-order process, and the baseline dietary ingestion of nickel, in which uptake was considered to be a pseudo-zero order process were used. Model parameters were determined for the model from the two experiments. No further model validation (i.e. with independent data) was

described. A sample model code implemented in Berkeley Madonna software is given in Appendix B.1 for a single 50 µg Ni/kg bw dose in water.

Uthus (1999) proposed a 16-compartment biokinetic model to describe the uptake and metabolism of orally administered $^{63}NiCl_2$. The compartments were either in groups representing the GI tract, Blood, Liver or Body, or individual for Urine and Feces. Transfer of Ni mass between compartments was governed by first order rate constants. Oral dosing of female Sprague-Dawley rats with 0.84 µg ^{63}Ni (10.7 µCi) resulted in seven day cumulative urinary and fecal excretions of 2.46% and 97.5% of dose, respectively. For liver, peak ^{63}Ni radiolabel occurred within 30 min of dosing and reached 0.09% of dose. Peak radiolabel in kidney was 0.04% of dose and in bone 0.001% of dose. The model predicts 2.54% and 96.4% of dose excretions for urine and feces, respectively. Retention of Ni in grouped organs was predicted to amount to 0.34% seven days after dosing. Model code for a single oral dose is provided in Appendix B.

Franks et al. (2008) describe a mathematical model of the in vitro keratinocytes response to chromium or nickel exposure. The model tracks the interaction between metal ions (in both intra- and extra-cellular states) and their effect on the viability of keratinocytes and the release of the pro-inflammatory cytokine interleukin-1α (IL-1ά). The model is intended to describe a monolayer of freshly isolated keratinocytes (10 µm), which has been grown to confluence and dosed with media containing, e.g., 0.01 to 10,000 µM $NiCl_2$ for 24 hours. The metal ion is assumed to be in equilibrium between extracellular concentration (A_c) and intracellular concentration (A_i), with the latter inducing the cytokine response. The volume fraction of keratinocytes is (n) and the amount of metal associated with the cell is given by (nA_i). The volume fraction of keratinocytes in the system is described by $dn/dt = - K_d n$, where $K_d = \delta_{ni}A_i + \delta_n$. This accounts for death due to the toxic effects of the intracellular ion ($\delta_{ni}A_i$) and the net birth and natural death of cells (δ_n). Control experiments indicated that 80% of cells were still alive after 24 hr, indicating that $\delta_n > 0$. The model assumes: (1) an exchange between extra- and intracellular metal ions; (2) cell death releases metal ions to the extracellular region; and (3) partitioning between extra- and intracellular states according to a partition coefficient (μ_n). The main equations for extra- and intracellular metal ions, respectively, are as follows:

$$d/dt((1 - n)A_c) = -k_n n(\mu_n A_c - A_i) + K_d n A_i;$$

$$d/dt(nA_i) = k_n n(\mu_n A_c - A_i) - K_d n A_i.$$

Keratinocytes with metal bound to them release a variety of chemokines and cytokines, in particular IL-1ά, release of the latter is described in the model by:

$$d/dt((1 - n)c) = \beta_{cn} n + \beta_{ci} n A_i - \delta_c(1 - n)c;$$

where β_{cn} is the rate of cytokine release by unaffected cells, β_{ci} is the rate of cytokine release by affected cells, δc is the rate of natural decay of cytokines in the media, and c is the concentration of IL-1ά. In comparing model predictions to experimental data for nickel the authors report no apparent relationship between nickel dose and IL-1ά

release except a decrease at high nickel concentrations (> 100 µM). Good agreement between model predictions and existing experimental data was observed. An example implementation of the Franks et al. model in Berkeley Madonna code is given in the Appendix B.2. Approximate parameter values obtained by curve fitting to experimental data were: δ_{ni} =6.3 x 10^{-5}/µM-d; β_{ci} = 0/day; K_n = 320/day; μ_n = 2.2 unitless; δ_n = 0.21/day; δ_c = 3.2/day; β_{cn} = 1.5 x 10^{-3}/µM-d. The initial concentration of cells (n_0) was estimated to be 0.0165 and the molecular mass of IL-1α was 17.7 kDa.

The only PBPK models for nickel compounds identified in the published literature were those of Menzel et al. (1987) and Menzel (1988). These rat models are interesting but few details were provided by the authors and they would be difficult to reproduce. An example of what an alternative nickel PBPK model might look like is given in Appendix B.4. This example is based in part on the manganese rat PBPK model of Teeguarden et al. (2007). The model was adjusted for nickel using data from Ishimatsu et al. (1995), Benson et al. (1994) and Tanaka et al. (1985). The model represents six perfused tissues: upper and lower respiratory tracts, bone, liver, kidneys, and muscle. Each of these tissues has a shallow tissue pool in rapid equilibrium with blood and a deep tissue store connected to the shallow tissue by transfer rate constants. Exchange of nickel between the shallow tissue pools and venous blood is controlled by tissue/blood partition coefficients (Ishimatsu et al., 1995). Absorption of airborne nickel oxide includes transport of deposited nickel into shallow tissue pools and mechanical removal from respiratory surfaces to the gastro-intestinal tract. The model includes fecal, urinary and biliary excretion of absorbed or ingested nickel. Comparisons of model predictions with observed data of Tanaka et al. (1985) for prolonged exposures to NiO aerosol were good for lung tissue Ni concentrations at high and low exposure concentrations and for liver and kidney concentrations at high exposure concentration (Appendix B.4).

Hack et al. (2007) describe a physiological model of the intracellular dosimetry of inhaled nickel. The model consists of seven intracellular compartments of the tracheobronchial epithelial cell: Cytoplasm, Cytoplasmic Proteins, Vacuolar Particles, Perinuclear Cytoplasm, Perinuclear Cytoplasmic Proteins, Nucleus, and Nuclear Proteins. Extracellular compartments consist of Surface Particles, GI Tract, Ionic Ni in Mucus, and Venous Blood. The model accepts the deposited dose into the mucous layer following inhalation of nickel particles or aerosols.

Particulate nickel compounds are either cleared from the mucous layer by mucociliary action, dissolved into Ni^{2+} ions, or taken up by the cells. Phagocytosis of nickel particles, such as Ni_3S_2 or crystalline NiS, results in the formation of a vacuole in which nickel particles are encased and ultimately dissolved. Extracellular dissolution of soluble nickel compounds results in the release of ionic nickel, which enters the cell via divalent ion transport systems (e.g., magnesium). Both influx and efflux of nickel ions are described by saturable Michaelis-Menten kinetics. Once in the cytoplasm nickel ions may bind with cytosolic proteins or diffuse through the cytoplasm to the perinuclear cytoplasm. Once there, nickel ions may bind reversibly to perinuclear proteins, enter the nucleus and bind to nuclear proteins. Model processes are mostly modeled with first order rate constants for forward and reverse directions. An exception is the Michaelis-Menten kinetics for influx and efflux of Ni from mucous to cytoplasm to

venous blood. In this respect the Hack et al. model resembles a biokinetic model. Model parameters were based mostly on published values. An example of this model implemented in Berkeley Madonna code is given in Appendix B.3.

The model for uptake of $NiCl_2$ by cultured pneumocytes predicted steady state concentrations better than the rate of uptake where the model underpredicted intracellular levels in the first half hour after exposure (data of Saito and Menzel, 1986). Model comparisons with the data of Costa et al. (1981) gave good observed/predicted ratios (O/P) of 1.57 to 0.94 for Ni_3S_2 in the nucleus (nmol/mg protein), 0.65 for $NiCl_2$ in the whole cell, 0.3 for $NiCl_2$ in the cytoplasm, and 0.5 for $NiCl_2$ in the nucleus (all nmol/mg protein). With the data of Abbracchio et al. (1982) agreement was more variable for O/P: $NiCl_2$ in the nucleus, 2.5 to 5.7; $NiCl_2$ in cytoplasm, 0.18; crystalline NiS in the nucleus 0.96 to 3.5; crystalline NiS in the particulate fraction 1.02; crystalline NiS in the cytoplasmic fraction 1.10.

Hsieh et al. (1999a) proposed a dosimetric model of nickel deposition and clearance from the rat lung. The model was developed using lung burden data from the National Toxicology Program (NTP) studies of nickel sulfate (NTP, 1996c), nickel subsulfide (NTP, 1996b), and nickel oxide (NTP, 1996a) and earlier models (Yu and Xu, 1986). The model consists of a single alveolar compartment. Deposited particles are removed from the lung by two principal mechanisms: (1) mechanical clearance via mucociliary transport; and (2) clearance by dissolution. For moderately soluble Ni_3S_2 particles both mechanisms are operable. The lung burden buildup in the alveolar region of the rat lung is described by the following equations:

$$dM_i/dt = r_i - \lambda_i M_i \quad (1);$$

$$r_i = C_i \times \eta \, MV \quad (2);$$

$$\lambda_i = a_i \times \exp[-b_i\{m_s/m_{s0})^{ci}] \quad (3);$$

where M is the mass burden, i indicates the particular nickel compound, r is the deposition rate, λ_i is the total alveolar clearance rate coefficient, η is the alveolar deposition fraction, C_i is the air concentration, MV is the minute ventilation, a_i, b_i, c_i are compound specific clearance rate coefficient constants, m_s = M/S in which M is the lung mass burden and S is the total alveolar surface area ($m_s = 5.38 \times 10^3$ cm^2 for rats), and m_{s0} = 1 mg/cm^2 is the dimensional constant introduced to normalize m_s. For $NiSO_4$, the a, b, c parameter values were 10.285, 17.16, and 0.105, respectively. For Ni_3S_2, the a, b, c parameter values were 0.00768, -20.135, and 0.266, respectively. For NiO, the a, b, c parameter values were 0.0075, 300, and 0.95, respectively.

Hsieh et al. (1999b) modified the rat model to develop a model of deposition and clearance of nickel in humans. Deposition rates were calculated for six scenarios: nose-breathing at rest, nose-breathing at light work, nose breathing at moderate work, mouth breathing at rest, mouth breathing at light work, and mouth breathing at moderate work. The clearance rate coefficient constants for humans were modified from the rat values. For nickel oxide, clearance rate coefficient constant *a* was estimated to be 1/7.6 times the rat value; constants *b* and *c* were assumed to be the same as rats. For nickel subsulfide, clearance is due to mechanical transport and dissolution; the clearance rate

coefficient constant *a* was estimated to be the sum of the clearance rate coefficient constant *a* for insoluble nickel (nickel oxide) and the difference between the clearance coefficient constant for nickel oxide and for nickel subsulfide for rats. For nickel sulfate, clearance rate coefficient constants in humans were assumed to be the same as in rats.

Hsieh et al. (1999c) developed a model for deposition, clearance and retention kinetics in the respiratory tract for inhaled nickel compounds in the mouse. The nickel compounds studied were NiO (green), Ni_3S_2, and $NiSO_4 \cdot 6H_2O$. The approach and equations for alveolar deposition and clearance are similar to those given above for the rat (Hsieh et al., 1999a). In this case the compound specific clearance coefficients a, b, c were: NiO, 0.0085, 180, 0.95; Ni_3S_2, 0.011, -9.293, 0.266; and $NiSO_4$, 10.285, 15.78, 0.105, respectively. The model predictions were compared with experimental data for the normalized lung burden metric (Ni-lung burden/g lung/unit concentration) and the calculated results did not always show good agreement. Because of lower deposition rates and faster clearance rates, mice have lower lung burdens than rats when exposed to the same concentrations of NiO or $NiSO_4$ particles. For Ni_3S_2, the lung burden/gram of lung in mice can be lower or higher than in rats depending upon exposure concentration and duration.

The Yu et al. (2001) modification of the model was used to predict lung burdens in nickel refinery workers and comparison with measured lung Ni burdens in deceased refinery workers showed good agreement between predicted and measured values. The model treats the alveolar region of the human lung as a single compartment. The kinetic expressions governing the change in mass with time in this compartment for NiO, Ni_3S_2 and $NiSO_4$ are as follows:

$$dM_{NiO}/dt = r_{NiO} - \lambda_{NiO} M_{NiO};$$

$$dM_{Ni3S2}/dt = r_{Ni3S2} - \lambda_{Ni3S2} M_{Ni3S2};$$

$$dM_{NiSO4}/dt = r_{NiSO4} - \lambda_{NiSO4} M_{NiSO4};$$

where M is the mass burden, r is the deposition rate and λ is the total alveolar clearance rate coefficient (/day) over all clearance pathways. For a given concentration, r in the above expressions is equal to concentration x alveolar deposition fraction (η) x minute ventilation (MV). The clearance rate coefficients are based on extrapolation from rat data, e.g.

$$\lambda_{NiO} = 0.00099 \exp[-300(V/V_{AM})^{0.95}] \text{ (/day)};$$

where V is the total volume of Ni compounds retained in the lung (mm^3) and $V_{AM} = 1.75 \times 10^4$ mm^3 is the total alveolar macrophage volume in humans. When the dosimetry model is applied to worker exposure, three additional factors are incorporated in the model: inhalability, mixed breathing mode, and clearance rate coefficient of a Ni compound mixture. The inhalability expression is based on the recommendation of the International Commission on Radiological Protection (ICRP ,1994):

$$\eta_{inhalability} = 1\text{-}0.5 \times (1\text{-}(7.6 \times 10^{-4} d_a^{2.8} + 1)\text{-}1 + 1.0 \times 10^{-5} U^{2.75} \exp(0.055 d_a);$$

where d_a is the aerodynamic diameter of the particle in μm and U is the wind speed in m/s, usually taken to be zero for workplace calculations. Deposition rates are calculated for three different ventilations: at rest, light work, and moderate work.

This modified dosimetry model was applied to the data on lung Ni burden for 39 workers reported by Andersen and Svenes (1989). Since particle sizes were not measured in the study, values from the same facility measured by Vincent (1996) were used. Particle sizes ranged from 42 to 62 μm MMAD for roasting and smelting and 1.4 to 51 μm MMAD for electrowinning work areas. These values are much greater than the 2 to 3 μm MMAD used in the chronic rat inhalation study. The correspondence of observed vs. predicted lung burdens for the two work areas are presented by the authors (their Figs. 1 and 2) but no statistical correlations were provided. Nevertheless several points fall on or close to the 1:1 correlation line generally supporting their claim of good agreement.

5 Acute Toxicity

5.1 Acute Toxicity Summary

Studies of acute toxicity of nickel and compounds are summarized in Table 11 and Table 12. The acute toxicity of inhaled nickel compounds is affected by their solubility and particle size distribution. Similar toxic effects were seen in both exposed humans and experimental animals, primarily lung lesions, decreased lung function and immunotoxicity. The immunotoxicity endpoint appears to form the best basis for deriving an acute reference exposure level.

5.2 Acute Toxicity to Humans

A group of seven metal plating workers with occupational asthma were evaluated for atopy and pulmonary function challenge in response to inhalational challenge with nickel sulfate hexahydrate and other metals (Cirla et al., 1985). Three of the asthmatics tested positive for the presence of nickel-specific IgE antibodies. Positive reactions to skin testing with nickel were found in 3 of the asthmatic workers who also had dermatitis. Six out of the seven asthmatics exhibited significantly decreased FEV_1 (> 15%) when exposed to 0.3 mg/m^3 nickel sulfate aerosol for 30 minutes. Control challenges with other metal salts did not reveal similar deficits in FEV_1. No particle size information was provided by the authors.

The study by Cirla et al. (1985) has been used in previous analyses of nickel health effects by OEHHA and U.S. EPA, but was considered inadequate for the present purpose. Other studies of acute toxicity to humans are reported in Table 11 below.

Soluble nickel compounds appear to be the greatest concern for acute health effects. The soluble forms of nickel are absorbed as Ni^{2+} (Coogan *et al*., 1989). Divalent nickel competes with copper for binding to serum albumin and is systemically transported in this way (Sunderman, 1986). The kidneys, lungs, and placenta are the principal organs for systemic accumulation of nickel (Sunderman, 1986). In contrast to the long half-life of the insoluble forms of nickel in the nasal mucosa, the elimination half-life of Ni^{2+} in the plasma is 1-2 days in mice (Nieboer *et al*., 1988).

A two-year-old child died after accidentally ingesting an oral dose of approximately 570 mg/kg bw of nickel sulfate (Daldrup et al., 1983). Cardiac arrest occurred four hours after the ingestion, and the child died eight hours after the accident. Webster (1980, cited in Norseth, 1984) reported nickel intoxication in a group of 23 dialysis patients. The source of nickel was plated stainless steel in a water heater tank. The concentration of nickel was approximately 250 µg/L in the dialysate. This level was much higher than those found in five other dialysis units (average 3.6 µg/L, range 2.5 to 4.5 µg/L). Symptoms observed included nausea, weakness, vomiting, headache and palpitations.

Remission was relatively rapid, occurring in three to 13 hours after cessation of dialysis. Sunderman et al. (1988) report on an episode of 32 workers in an electroplating plant accidentally drinking water containing $NiSO_4$ and $NiCl_2$ with a concentration of 1.63 g Ni/L. Twenty workers experienced nausea, vomiting, abdominal discomfort, diarrhea, giddiness, lassitude, headache, cough and shortness of breath, which lasted for a few hours to several days. Nickel intakes were estimated at between 0.5 and 2.5 g. Serum concentrations ranged from 13 to 1340 µg Ni/L and urine concentrations from 0.15 to 12 mg Ni/g creatinine. Elimination half times ranged from 27 hr with induced diuresis to 60 hr in non-induced subjects.

Nickel fumes from high nickel alloy welding (mean concentration = 440 µg Ni/m³, range = 70-1,100 µg Ni/m³) caused complaints of upper respiratory irritation and headache in welders exposed for 4 weeks (Akesson and Skerfving, 1985).

Exposure to nickel in occupational settings causes dermatitis and asthma in some individuals with repeated exposures (Davies, 1986). The nickel ion, bound to proteins in the dermis, acts as an antigen eliciting a type IV (delayed type) hypersensitivity response. This response, mediated by T-lymphocytes, causes dermal hypersensitivity. This hypersensitivity can be diagnosed by patch testing (Menne and Maibach, 1989).

Phillips et al. (2010) re-examined a case report of a 38-year-old healthy male who inhaled nanoparticles of nickel while spraying nickel onto bushes for turbine bearings using a metal arc process. The spraying process lasted about 90 minutes and the subject was observed to remove a protective half face mask during the spraying process. The subject complained of feeling unwell and went home and the next day he complained of cough, shortness of breath, and a tight chest. Four days after exposure he was admitted to the hospital and was tachypneic, pyrexial and cyanosed. He was treated with supplemental oxygen and antibiotics but died of respiratory failure 13 days after exposure (official cause of death was adult respiratory distress syndrome, ARDS). Nickel nanoparticles (< 25 nm) were identified in lung macrophages using transmission electron microscopy. High levels of nickel were measured in the subject's urine (780 µg/L) and his kidneys showed evidence of tubular necrosis. In addition, there was hematuria and proteinuria also indicative of kidney toxicity. The updated examination supports the idea that inhaled nickel can be absorbed systemically and affect other organs.

TABLE 11. SUMMARY OF ACUTE NICKEL TOXICITY IN HUMANS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Dalrup *et al*., 1983	$NiSO_4$	Accidental ingestion of a single dose, ca. 570 mg/kg	Mortality at 8 hr via cardiac arrest	2-yr old child.
Webster, 1980	Ni^{2+} form not specified	Dialysis patients, 250 µg Ni/L in dialysis fluid, N = 23	Nausea, weakness, vomiting, headache, palpitations	Remission in 3-13 hr after cessation of dialysis.
Sunderman *et al*., 1988	$NiSO_4$ $NiCl_2$	Accidental ingestion of contaminated drinking water with 1.63 g Ni/L N = 20 electroplating workers	Nausea, vomiting, abdominal discomfort, diarrhea, giddiness, lassitude, headache, cough, shortness of breath	Ni intake estimates 0.25 to 2.5 g. Serum concentrations 13-1340 µg Ni/L, urine concentrations 0.15-12 mg Ni/g creatinine
Cirla *et al*., 1985	$NiSO_4$ aerosol	Metal plating workers with occupational asthma. N = 7, 0.3 mg Ni/m^3 x 30 min	6/7 had FEV_1 reductions > 15%	No particle size information, 3/7 positive for Ni-specific IgE antibodies.
Phillips *et al*., 2010	Ni nanoparticles, <25 nm diameter	Occupational exposure during spraying 90 min	ARDS, respiratory failure and death 13 days after exposure	Ni nanoparticles found in lung macrophages, high levels of Ni in urine (780 µg/L) and kidneys. Evidence of kidney tubular necrosis.

Note: ARDS = adult respiratory distress syndrome; FEV1 = forced expiratory volume 1 second.

5.3 Acute Toxicity to Experimental Animals

Ishihara et al. (2002) studied inflammatory responses and mucus secretion in rats with acute bronchiolitis induced by nickel chloride inhalation. Male Wistar-jcl strain SPF rats at age 10 weeks were exposed (5 animals/group) via whole body to aerosols of nickel chloride with an ultrasonic nebulizer 5 hours/day for 5 days. The average concentrations of the aerosols were 0.85 mg Ni/m^3 in day one and 0.24 mg Ni/m^3 during days two to five. Following exposure the animals were given clean air on days six to eight prior to sacrifice. The nickel aerosols had a MMAD of 1.8 µm with a gsd of 1.6. The measured inflammatory biomarkers were total protein concentration, total elastolytic activity, α1-antitrypsin, and β-glucuronidase activity. Sialic acid and fucose were measured as mucus components. Also measured were soluble L-selectin, cytokine-induced neutrophil chemoattractant (CINC) and growth-regulated gene products (GRO). Total protein concentrations, total elastolytic activity, trypsin inhibitory capacity, β-glucuronidase, fucose, and sialic acid in bronchoalveolar lavage fluid (BALF) were significantly greater than control ($P < 0.05$ vs. control, $N = 5$) at day 3 to day 8 time points following nickel exposure. CINC/GRO and soluble L-selectin were significantly increased at days 3-6 and days 5-6, respectively. The extent of lung tissue injury was scored by histopathological observations. There was no exfoliation of the airway epithelium found on exposure day five when bronchiolitis developed. The data indicate that nickel chloride inhalation caused an acute inflammatory response with hypersecretion of mucus, which cleared in one month.

The data of Ishihara et al. were analyzed using benchmark dose methodology. Doses were calculated as mg Ni^{2+} inhaled with the average body weight of 0.289 kg and the relation Inhalation in rats (m^3/day) = 0.105 x (bodyweight, kg/0.113)$^{2/3}$. Adequate model fits ($P \geq 0.1$) were obtained for continuous benchmark doses at the one standard deviation point with linear, power or polynomial models. The 95% lower bounds on the benchmark doses for a one standard deviation change in the respective endpoints ($BMDL_{1SD}$) were 5.5 µg (linear, $P = 0.132$), for total cells/µL BALF; 18.6 µg (power, $P= 0.156$), for total protein mg/mL BALF; 50 µg (polynomial, $P = 0.19$), for total elastolytic activity as nmol succinyl trialanine *p*-nitroanilide hydrolyzed/hr/mL BALF; and 13.5 µg (power, $P = 0.34$) for sialic acid µg/mL BALF. For the five hours/day times five days inhaled exposure volume of 0.2 m^3, the $BMDL_{1SD}$ equivalent concentrations for the four endpoints would be 27.5, 93, 250, and 67.5 µg/m^3, respectively. These values appear significantly lower than the BMDL of 165 µg/m^3 for inhibition of antibody production in mice (data of Graham et al., 1978) but are consistent with the more extensive exposure protocol (5hr/day x 5 days).

It has been shown that water-soluble nickel compounds are more acutely toxic than the less soluble compounds by ingestion. The single dose oral LD_{50}'s in rats for less-soluble NiO and Ni_3S_2 were > 3000 mg Ni/kg bw, while the oral LD_{50}'s for the more soluble $NiSO_4$ and nickel acetate ranged from 39 to 141 mg

Ni/kg bw in rats and mice (Mastromatteo, 1986; Haro et al., 1968). Soluble nickel compounds appear to be more toxic by intraperitoneal (i.p.) injection than by intramuscular (i.m.) or subcutaneous (s.c.) injections. Acute LD_{50} values for $NiCl_2$ in rats were 5 mg Ni/kg bw by i.p. injection, 23 mg Ni/kg bw by i.m. injection, and 25 mg Ni/kg bw by s.c. injection (Knight et al., 1991).

Jia et al. (2010) conducted a mechanistic study of nickel-induced olfactory impairment. Male mice were intranasally instilled with $NiSO_4$ or saline followed by ATP, purinergic receptor antagonists, or saline. The olfactory epithelium was examined histologically and with immunochemistry 1 to 7 days postinstillation. Doses of 0, 0.1, 0.5, or 2.5 mg/kg body weight showed both time and dose dependence in nasal toxicity indicated by decreases in thicknesses of the ectoturbinate 2 and endoturbinate 2 regions. Decreases in thickness ranged up to 30 and 15 µm at the top doses, respectively. No effects were seen in the nasal septum. Reductions in thickness were due to sustentacular cell loss measured by terminal dUTP nick-end labeling (TUNEL) staining at 1-day postinstillation and caspase-3-dependent apoptosis of olfactory sensory neurons at 3-days postinstillation. An increase in cell proliferation was observed by BrdU incorporation at 5 and 7 days postinstillation. Treatment with purinergic receptor antagonists reduced cell proliferation whereas exogenous ATP significantly increased cell proliferation. The authors conclude that ATP has neuroproliferative and neuroprotective roles in normal and injured olfactory epithelium.

Subcutaneous injections of 10 mg/kg nickel chloride have been shown to increase prolactin secretion in rats one day following administration (Clemons and Garcia, 1981). However, an earlier study showed that prolactin secretion in rats is specifically inhibited for 30 minutes following intravenous exposure to 100 µg Ni^{2+} as $NiCl_2$ (LaBella *et al*., 1973).

Donskoy et al. (1986) found that s.c. injection of 125 to 750 µmol Ni/kg to male Fischer 344 rats resulted in acute hepatic toxicity within 24 hr as evidenced by enhanced lipid peroxidation, microvesicular steatosis, and increased serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The latter serum enzymes were significantly increased about two-fold by the low dose of 125 µmol Ni/kg compared to control animals ($P < 0.05$, $N = 14$).

Subacute (12-day) inhalation exposures (5 days/week, 6 hours/day) of 10 mice to nickel, as 10 mg Ni_3S_2/m^3 (AMAD = 1.3µm, gsd = 1.5), caused 100% mortality (Benson *et al*., 1987). Two of 10 rats also died from this exposure. Although no effect was seen on natural killer cell activity in these animals, lesions in the nasal and lung epithelium and in bronchial lymph node were observed. Pathology revealed emphysematous changes in the lungs of rats exposed to 5 or 10 mg Ni_3S_2/m^3, and fibrosis in mice exposed to 5 mg Ni_3S_2/m^3. Atrophy of lymphoid tissues, including spleen, thymus, and bronchial lymph nodes, was observed in mice and rats exposed to 5 or 10 mg Ni_3S_2/m^3.

Nickel distributes preferentially to the lungs and kidneys following intratracheal administration of $NiCl_2$ to rats (Carvalho and Ziemer, 1982). The electrophilic Ni^{2+} ion is reported to be the causative agent of nephrotoxicity in rats; it binds to intracellular nucleophiles in kidney tissue such as guanine, adenine, and glutathione two hours following intraperitoneal exposure to 10 mg Ni/kg as $NiCO_3$ (Ciccarelli and Wetterhahn, 1984).

Toya et al. (1997) evaluated the effects of single and repeated intratracheal instillations of nickel fumes (about 10 nm in diameter), Ni_2O_3 (2.0 µm geometric mean diameter and 1.69 gsd) and NiO (2.2µm geometric mean and 1.68 gsd) powders, all dispersed in saline and sonicated immediately prior to instillation, in the Sprague-Dawley rat. The LD_{50} of nickel fumes was estimated to be 38.2 mg/kg bw. Body weight gain was retarded by single doses of 13.0 mg Ni_2O_3/kg, 14.3 mg Ni fumes/kg, or 13.0 mg NiO/kg compared to controls. The lung lesions induced by a single nickel exposure were characterized by goblet cell hyperplasia, perivascular inflammatory cells and edema in the alveolar space. Nickel fumes and Ni_2O_3 produced goblet cell hyperplasia, focal granuloma, and inflammatory cells in the alveolar space but NiO did not produce lesions. Repeated instillations of nickel fumes (5.9 mg/kg-d for four days to one week) produced a secretion of proteinaceous materials in the alveolar space. The authors note that although the Ni fumes were composed of about 3% Ni_2O_3 and the remainder NiO, its toxicity was greater on a weight basis than Ni_2O_3 administered alone. They speculate that the difference in toxicity was due to the presence of ultrafine particles in the Ni fumes.

Serita et al. (1999) studied lesions formed in rat lungs after a single five hour inhalation exposure to agglomerated ultrafine metallic nickel (Uf-Ni) with an initial 20 nm average particle diameter and an exposure aerosol of MMAD = 1.3 µm, and geometric standard deviation (gsd) = 1.54. Sixty to 80 Wistar rats per dose group (sex unspecified) were exposed to 0.15 (Low), 1.14 (Medium), or 2.54 (High) mg Uf-Ni/$m^3$for five hours. Five animals /dose group were sacrificed at 0 hr and 1, 3, 7, 14, and 21 days post exposure. The Low group also had sacrifices at 28, 56, and 84 days post exposure. The toxicological findings included: (1) a significant increase in lung weight in the Medium and High groups; (2) accumulation of foamy alveolar macrophages (AM) and debris of burst AM which may restrict pulmonary ventilation; (3) degenerated AM indicating alveolar lipoproteinosis which was aggravated for up to four weeks in the High group; and (4) acute calcification of the degenerated AM possibly related to a disruption of Ca^{2+} ion transport by solubilized Ni^{2+} ion. This study indicates a LOAEL of 1.14 mg Ni/m^3 and a NOAEL of 0.15 mg Ni/m^3 for a single five-hour exposure to metallic nickel. However, as the authors point out, if half of the amount of Ni deposited in the lung in the Low group were carried over to the next day, the amount of deposition after 30 days at 5hr/d would exceed the single exposure deposition for the High group. Therefore, it is difficult to accept 0.15 mg/m^3 as a true NOAEL applicable to repeated exposure scenarios.

Prows and Leikauf (2001) studied the genetic determinants underlying the susceptibility to acute nickel-induced lung injury in sensitive and resistant mouse strains. The mice were exposed 6 times over one year in an inhalation chamber to air containing 152 ± 12 μg Ni/m^3 (0.2 μm MMAD) generated from 50 mM (10^{-3} M) $NiSO_4 \cdot 6H_2O$ (duration of individual exposures not given). Quantitative trait loci (QTL) analysis of 307 backcross mice generated from the sensitive A/J and resistant C57BL/6J mouse strains identified a significant linkage on chromosome 6 (designated *Aliq4*) and suggestive linkages on chromosomes 1 and 12. Analysis of phenotypic extreme responders to nickel-induced lung injury, including 55 most sensitive (survival times ≤ 66 hr) and 54 most resistant (survival times ≥ 112 hr) backcross mice, identified possible linkages on chromosomes 1, 6, 8, 9, and 12, which explained 62% of the genetic variance in the extreme phenotypic cohort. Comparing mean survival times of backcross mice with similar haplotypes gave an allelic combination of four QTLs that could account for the survival differences. The QTL intervals on chromosomes 6 and 12 were previously identified with ozone sensitivity. Candidate genes for chromosome 6 locus include *Tbxas1* (thromboxane A synthase 1), *Aqp1* (aquaporin-1), *Crhr2* (corticotropin releasing hormone receptor-2), *Sftpb* (surfactant-associated protein-B), *Pecam* (platelet/endothelial cell adhesion molecule), and *Tgfa* (TGF-α). The results suggest that relatively few genes might be important for irritant-induced acute lung injury. In a subsequent study (Prows et al., 2003) examined gene expression in sensitive and resistant strains (see Appendix A, Section A3.2)

Nishi et al. (2009) evaluated the effects of NiO nanoparticles on inflammation and chemokine expression in rats exposed intratracheally. The mass median diameter of NiO agglomerates suspended in distilled water was 26 nm (8.41 nm weighted average surface primary diameter and 104.6 m^2/g specific surface area). The particle size distribution of the sample nanoparticles was determined by a dynamic light scattering technique (diameter range ca. 10 to 60 nm). Male Wistar rats were exposed to 0.1 mg (0.33 mg/kg) or 0.2 mg (0.66 mg/kg) followed by sacrifice at 3 days, 1 week, and 1, 3, and 6 months following a single instillation. Control animals received intratracheal instillation of distilled water. Cytokine-induced neutrophil attractant-1 (CINC-1), CINC-2αβ, and CINC-3 in lung tissue and BALF were determined by measurement of protein by ELISA. Both CINC-1 and CINC-2αβ were elevated from day 3 to 3 months in lung tissue and from 3 to 6 months in BALF. CINC-3 was elevated on day 3 both in lung tissue and BALF, then decreased. Total cell and neutrophil counts in BALF were increased from day 3 to 3 months. In lung tissue, infiltration of neutrophils and alveolar macrophages was seen from day 3 to 6 months in alveoli. Dose-responses were observed for total cells at 1, 3 , and 6 months; CINC-1 in lung at 3 days, 1 week and 3 months and in BALF at 3 days, and 6 months; CINC-2 at 3 days, 1 week, and 3 months in lung and 3 days, 1 month and 6 months in BALF; and CINC-3 at 3 days and 1 week in lung and 3 days, 1 week and 1 month in BALF. The data indicate the involvement of CINC in NiO nanoparticle induced lung injury.

Singla et al. (2006) found that acute oral administration of $NiSO_4$ (50 mg/kg-d x 7 days) to rats affected the structural and functional integrity of the intestine. The activities of the brush border enzymes maltase ($P < 0.05$), lactase ($P < 0.05$), alkaline phosphatase ($P < 0.05$) and leucine amino peptidase ($P < 0.05$) were increased in purified brush borders from Ni-treated rats compared to controls. Alternatively, sucrase, trehalase ($P < 0.01$) and glutamyl transpeptidase ($P < 0.05$) were reduced in nickel fed animals compared to controls. Kinetic analysis of alkaline phosphatase and sucrase indicated that quantity of enzymes (Vmax) was altered by nickel exposure rather than their activity (Km). Regional analysis indicated that the changes in enzyme activity were mainly located in the villus tip and mid villus regions, rather than the crypt base. The authors conclude that acute feeding of nickel affects the development of various brush border enzymes along the crypt-villus axis of the rat intestine.

TABLE 12. SUMMARY OF ACUTE NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Mastromatteo, 1986	NiO, Ni_3S_2	Single dose oral toxicity in mice and rats.	LD_{50}s > 3000 mg/kg.	
Haro *et al.*, 1986	$NiSO_4$, Ni acetate	Single dose oral toxicity in mice and rats.	LD_{50}s 39 to 141 mg/kg.	
Knight *et al.*, 1991	$NiCl_2$	Intraperitoneal (i.p.), intramuscular (i.m.) and subcutaneous (s.c.) injection in rats.	Acute LD_{50}s: i.p. = 5 mg/kg i.m. = 23 mg/kg; s.c. = 25 mg/kg	
Donskoy *et al.*, 1986	$NiCl_2$	s.c. injection of 125-750 µmol Ni/kg in male F344 rats.	Acute hepatic toxicity within 24 hr.	Enhanced lipid peroxidation at 750 µmol Ni/kg, 4-fold increase in thiobarbituric acid chromogens in hepatic cytosol.
Benson *et al.*, 1987	Ni_3S_2 AMAD = 1.3 µm, gsd = 1.5	Inhalation exposure 6hr/d. 5d/wk, 12 days, 5 or 10 mg/m^3 to mice and rats	Mortality 100 % in mice, 20% in rats	Lesions in nasal and lung epithelium and lymph nodes. Atrophy of lymphoid tissues incl. spleen, thymus, bronchial lymph in mice and rats at both doses.
Graham *et al.* 1975, 1978	$NiCl_2$, 99% < 3 µm	Inhalation of 0, 100, 250, 375, 490 µg Ni/m^3 in mice for 2 hr. Challenge with sheep RBC.	Immunotoxicity, decrease in splenic antibody formation with linear dose response.	BMDL based on loss of 100 hemolytic plaques per 10^6 spleen cells.
Condevaux *et al.*, 2001	$NiCl_2$	Natural killer (NK) cell activity with 0, 1, 10, 100 µg Ni/mL monkey and rat cells *in vitro*	NK activity: in monkey 34-42% ↓: in rat 22-24% ↓.	
Haley *et al.*, 1987, 1990	Ni_3S_2 NiO	Intratracheal instillation of 0.06 µmol Ni/g lung in monkey and mice	Impaired pulmonary macrophage phagocytic function.	Secondary increase in NK cell-mediated killing of target AM cells.

TABLE 12. SUMMARY OF ACUTE NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Adkins *et al*., 1979	$NiCl_2$, 86-96% < 1.4µm, 99% < 3µm	Host resistance in 80-120 mice/dose group: 0, 289, 369, 499 µg Ni/m^3 x 2 hr.	Response to experimental infection with *Streptococcus pyogenes* 24 hr after Ni dose gave increase in mortality	BMDL of 365 µg Ni/m^3 for a doubling of mortality increase (3.74 to 7.4%). Supporting study for aREL.
Toya *et al*., 1997	Ni_2O_3, NiO powders and Ni fumes in particulate suspensions	Intratracheal instillation in rats: 23 -30 /group. Ni_2O_3 1.4, 13 mg/kg; NiO 13 mg/kg; Ni fumes 3.8, 14.3 mg/kg and repeated 4 x 5.9 mg/kg in 8 weeks.	Mortality of Ni fumes LD_{50} = 38.2 mg/kg. Reduced BW gain at 13 mg/kg Ni_2O_3, 14 mg/kg Ni fumes, and 13 mg/kg NiO.	Lung lesion induced by single exposures of Ni fumes and Ni_3O_2 but not NiO.
Serita *et al*., 1999	Ultrafine Ni 20 nm MMAD = 1.3 µm, gsd = 1.54	Single inhalation study in rats, 60-80 rats/dose. 0.15, 1.14, 2.54 mg/m^3 for 5 hr. Rats sacrificed at intervals up to 84 days	Lung lesions observed at 1.14 mg Ni/m3	Lung weight ↑ Foaming alveolar macrophages (AM) ↑ Degenerated AM with alveolar lipoproteinosis ↑ Acute calcification of degenerated AM ↑
Ishihara *et al*., 2002	$NiCl_2$ aerosol MMAD = 1.8µm, gsd = 1.6	Inhalation in male rats 5hr/d x 5 d 0.85 (d1) to 0.24 (d2-5) mg Ni/m^3.	Inflammatory biomarkers in BALF: total protein concentration ↑; Total elastolytic activity ↑; trypsin inhibitory capacity ↑; β-glucuronidase ↑.	Fucose ↑; sialic acid ↑; L-selectin ↑ BMDLs estimated for total cells, total protein, total elastolytic activity and sialic acid.
Nishi *et al*., 2009	NiO nanoparticles MMAD = 26 nm, 10-60 nm distribution by light scattering.	Intratracheal instillation, inflammation and chemokine expression in rats. 0.1 or 0.2 mg single instillation sacrifice 3d to 6 mo.	Cytokine –induced neutrophil attractant 1(CINC-1) ↑ and CINC-2αβ ↑ in BALF at both doses $P < 0.01$ vs. control.	CINC-3 ↑ at 3 days then decreased.

TABLE 12. SUMMARY OF ACUTE NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Singla *et al.*, 2006	$NiSO_4$	Oral exposure in rats 50 mg/kg-d x 7 days.	Functional integrity of intestine, activity of brush border enzymes: maltase ↑, lactase ↑, alkaline phosphatase ↑, leucine amino peptidase ↑ all P < 0.05.	Sucrose ↓ p <0 .01, trehalase ↓p < 0.01, glutamyl trans-peptidase↓ p < 0.05.
Jia *et al.*,2010	$NiSO_4$	Intranasal instillation in mice, 0, 0.1, 0.5, 2.5 mg/kg bw. Histological and immuno-chemical analysis at 1-7 d post treatment.	Nasal toxicity time and dose dependent decreases in thickness of ectoturbinate 2 and endoturbinate II regions.	$BMDL_{05}$ estimates of 10.6 to 24.3 µg Ni/kg bw for endoturbinate II data set.

Note: AM = alveolar macrophages; AMAD = activity median aerodynamic diameter; MMAD = mass median aerodynamic diameter ARDS = adult respiratory distress syndrome; BMDL 95% lower bound on a specific response level (e.g. BMDL05 = lower bound on a 5% response); BALF = bronchial alveolar lavage fluid; CI = 95% confidence interval; NK = natural killer;; ↑ = increase; ↓ = decrease.

5.4 Predisposing Conditions for Nickel Toxicity

Medical: Asthmatics or atopic individuals may be especially at risk for developing nickel-induced asthma (Cirla *et al*., 1984). Cigarette smokers may receive greater nickel exposure, since cigarette smoke contains nickel (Menden et al., 1972; Smith et al., 1997; Reprotext, 1999; Torjussen et al., 2003). These authors report about 0.5 to 2.5% of cigarette tobacco nickel appeared in the particulate phase of mainstream smoke. Additionally, a review of the literature on nickel toxicity showed that Ni^{2+} causes vasoconstriction in animals and humans, which may potentiate the effects of a primary ischemic lesion in the cardiovascular system (U.S.EPA, 1985).

Chemical: In rats, rabbits, and dogs, one mg/kg nickel chloride antagonizes the cardiac arrhythmia induced by digoxin by competing with calcium at cardiac membrane sites (Prasad *et al*., 1980). The implications of this effect for persons with congestive heart failure have not been investigated.

6 Reproductive and Developmental Toxicity

6.1 Reproductive and Developmental Toxicity Summary

Studies of reproductive and developmental toxicity of nickel and compounds are summarized below. Human studies (Table 13) of workers exposed to nickel compounds by the inhalation route suggest increased incidence of spontaneous abortions in females and spermatotoxicity in males. In experimental animals (Table 14), no inhalation studies were identified. But oral exposures resulted in spermatotoxicity in mice and rats involving both induction of mutation and endocrine disruption, and reduced reproduction in rats (both sexes exposed separately and together). Nickel-exposed mice and rats also exhibited significantly increased perinatal mortality.

Although reproductive and developmental effects are a substantial source of concern, none was selected as the basis of any of the inhalation RELs. The animal studies used less relevant routes of exposure. The human studies involved fairly high exposures, where these were quantified. The inhalation-based acute, 8-hour and chronic RELs derived in this document are at least 50-fold lower than the chronic oral REL which is based on perinatal mortality in rats (see section 9.8).

6.2 Human Studies

Chashschin et al. (1994) reported that an increase in spontaneous abortions was observed among 290 women (15.9%) who worked in a nickel hydrometallurgy refining plant in Russia, compared with 336 female construction workers without any occupational nickel exposure as controls (8.5%). The workers were exposed to primarily nickel sulfate at 0.11 to 0.31 mg Ni/m^3, but no particle size information was provided. In the same study, the authors also noted a statistically significant increase in structural malformations among offspring born to 356 workers (16.9%) compared to 342 controls (5.8%). They reported relative risks were 2.9 for all kinds of defects, 6.1 for cardiovascular system defects, and 1.9 for musculoskeletal defects. They noted heavy manual activity and heat stress as potential confounders. No confidence intervals or other statistical analyses were provided by the authors.

Benoff et al. (2000) studied the effects of metal ions on human sperm mannose receptor expression, a biomarker of spermatotoxicity. Exposure of human sperm to Ni(II) had a biphasic effect with a low concentration of 4.21 nM Ni(II) stimulating the mannose receptor expression ($P < 0.01$) and higher concentrations of 421 nM and 42 µM Ni(II) decreasing expression ($P < 0.014$).

Danadevi et al. (2003) studied semen quality of Indian welders occupationally exposed to nickel and chromium. Fifty-seven workers from a welding plant in South India and 57 controls were monitored. Blood nickel and chromium

concentrations (oxidation states unspecified) were determined by inductively coupled plasma mass spectrometry (ICP-MS). World Health Organization criteria were employed in analyzing semen samples. The nickel and chromium blood concentrations for 28 exposed workers were 123±35 and 131±53 µg/L, respectively. The control levels (N = 27) were much lower at 16.7±5.8 and 17.4±8.9 µg/L, respectively. Sperm concentrations were 14.5±24.0 x 10^6/mL for exposed workers vs. 62.8±43.7 x 10^6/mL in the controls. Rapid linear sperm motility was decreased in the exposed subjects compared to controls and there was a significant positive correlation between the percentage of sperm tail defects and blood nickel in exposed workers (R = 0.485, P = 0.036). These investigators also report a negative correlation of sperm concentration with blood chromium in exposed workers (R = -0.424, P = 0.025).

Vaktskjold et al. (2006) investigated the incidence of genital malformations in newborns of women nickel-refinery workers. In this register-based cohort study, data about pregnancy outcome and occupation were obtained from the Kola Birth Registry, covering the township of Monˇegorsk in Northwestern Russia. The reference population comprised delivering non-Ni-exposed women from Monˇegorsk. Nickel exposure was characterized by using as a guideline the water-soluble Ni subfraction of the inhalable aerosol fraction obtained by personal monitoring for nickel- and copper-refinery workers and/or measured urinary-Ni concentrations. The following exposure categories were assigned according to the occupation the delivering woman had at the time of becoming pregnant: background, observed urinary Ni concentration < 10 µg/L; low, <70 µg/L; high, ≥ 70 µg/L, which roughly corresponds to airborne exposure concentrations ≥160 µg/m^3 of the water-soluble inhalable subfraction. This registry and exposure classifications were also used in the other studies by Vaktskjold et al. described below. The association of the outcome with assigned exposure ratings was analyzed with a logistic regression model, adjusted for parity, maternal malformation, exposure to solvents and infection in early pregnancy. There was no association between nickel exposure and genital malformations in this study. The odds ratio (OR) for nickel-exposed women delivering a newborn with a genital malformation was 0.81(95% C.I. 0.52-1.26) and that for undescended testicle was 0.76(95% C.I. 0.40-1.47). The study is limited by few cases in the higher exposure groups.

Vaktskjold et al. (2007) evaluated the possible association between nickel exposure in early pregnancy and the delivery of small-for gestational-age (SGA) newborns. Live births and stillbirths after at least 28 weeks' gestation from the Kola Birth Registry were considered. The study population consisted of 22,836 births and SGA was defined as birth weight below the tenth percentile for the gestational age in the source population. There were 2,096 (9.2%) newborns defined as SGA. The mothers of 10.6 percent of the SGA and 13 percent of the reference infants were employed at jobs with Ni exposure above the background level. The unadjusted odds ratio (OR) for an SGA birth per unit increase in exposure category was 0.79 (95% C.I. = 0.68-0.91) and the adjusted OR (Model 1) was 0.84 (95% C.I. = 0.75-0.93). The authors concluded that the maternal

exposures to water-soluble nickel in the first part of pregnancy did not increase the risk of an SGA newborn without trisomy in the study population. (The marginal decrease in OR for SGA with exposure category, which was reduced by adjustment, was not considered biologically significant.)

Vaktskjold et al. (2008a) studied the incidence of musculoskeletal defects in the offspring of women occupationally exposed to nickel in early pregnancy, based on the Kola registry and exposure categories described above. In total, the study population consisted of 22,965 births. Three hundred and four infants (13.3/1000 births; 95% C.I. 11.9-14.7) were diagnosed with isolated musculoskeletal defects(s) at birth. The adjusted odds ratio for the association between maternal exposure to nickel and the observed defects was 0.96 (95% C.I. 0.76-1.21). The authors concluded that despite the high incidence of defects there was no apparent association with maternal nickel exposure.

Similarly, Vaktskjold et al. (2008b) studied the incidence of spontaneous abortion among nickel-exposed female refinery workers. A case-control study involved women employed in nickel-exposed work areas in early pregnancy. Each pregnancy record was assigned a categorical nickel exposure rating according to occupation at pregnancy onset. The guidelines were the water-soluble Ni subfraction of the inhalable aerosol fraction obtained by personal monitoring for nickel- and copper-refinery workers and/or measured urinary-Ni concentrations. The cut-off between low and high exposure levels was 70 µg Ni/L urine corresponding to about 160 µg Ni/m^3 of the water soluble sub-fraction. The unadjusted OR for the association between maternal Ni exposure and spontaneous abortion was 1.38 (95% C.I. 1.04-1.84), and the adjusted OR was 1.14 (95% C.I. 0.95-1.37). Adjustments included previous induced abortion, previous delivery, solvent or paint exposure, heavy lifting, and maternal age >34 years. Addition of maternal smoking did not significantly change the OR, 1.15(0.96-1.39). The authors concluded that no statistical association was established; however they note that the findings do not exclude the possibility of a weak excess risk.

TABLE 13. SUMMARY OF HUMAN REPRODUCTIVE OR DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Chashschin *et al*., 1994	$NiSO_4$	Airborne exposure of female refinery workers, 0.11 to 0.31 mg Ni/m^3, N = 290 *vs*. 336 controls	Spontaneous abortion (SA): 15.9% in exposed vs.8.5% in controls. No confidence interval (CI).	Significant increase in structural malformations (16.9%) vs. 5.8% in controls. RR = 2.9 for all defects, 1.9 for musculoskeletal defects. No CI's.
Benoff *et al*., 2000	Ni^{2+}	In vitro treatment of human spermatozoa: 4.21 nM, 421 nM, 42 µM Ni^{2+}.	Mannose receptor expression a biomarker for spermatotoxicity. 4.21 nM ↑, 421 nM ↓, 42 µM ↓	P < 0.014 for observed decreases in mannose receptor expression.
Danadevi *et al*., 2003	Ni, Cr	Semen quality in Indian welders. N = 57 exposed *vs* 57 controls	Sperm concentrations 14.5 ± 24.0 x 10^6/mL in exposed vs. 62.8 ± 43.7 x 10^6/mL in controls.	Linear sperm motility ↓, sperm tail defects ↑. Effects correlate with blood Ni.
Vaktsjold *et al*., 2006	Ni, water soluble inhalable	Female Ni refinery workers. Urinary Ni < 10µg/L control, < 70 µg/L low exposure group, ≥ 70 µg/L high exposure group	Genital malformations: OR = 0.81 (95% CI = 0.52-1.26); undescended testicle OR = 0.76 (95% CI = 0.75-0.93)	Few cases in high exposure group. Only 103 newborns diagnosed with one or more malformation (44.5/10,000)
Vaktsjold *et al*., 2007	Ni, water soluble inhalable	Female Ni refinery workers. Urinary Ni < 10µg/L control, < 70 µg/L low exposure group, ≥ 70 µg/L high exposure group.	Small for gestational age (SGA) newborns: unadjusted OR = 0.79(95%CI = 0.68-0.91); adjusted OR = 0.84(95%CI = 0.75-0.93)	SGA = birth weight below 10^{th} percentile. 2096 (9.2%) defined as SGA

TABLE 13. SUMMARY OF HUMAN REPRODUCTIVE OR DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Vaktsjold *et al*., 2008a	Ni, water soluble inhalable	Female Ni refinery workers. Urinary Ni < 10µg/L control, < 70 µg/L low exposure group, ≥ 70 µg/L high exposure group.	Musculoskeletal (MS) defects: adjusted OR = 0.96 (95% CI = 0.76-1.21)	No Ni-induced MS defects despite high incidence: 304 (13.3/1000).
Vaktsjold *et al*., 2008b	Ni, water soluble inhalable	Female Ni refinery workers. 474 cases, 4571 controls. Urinary Ni < 10µg/L control, < 70 µg/L low exposure group, ≥ 70 µg/L high exposure group	Spontaneous abortion (SA): unadjusted OR 1.38 (95% CI = 1.04-1.84); adjusted OR = 1.14 (95% CI = 0.95-1.37).	Possible weak effect or increased excess risk in early pregnancy.

Note: CI = 95% confidence interval; MS = musculoskeletal; OR = odds ratio; SA = spontaneous abortion; SGA = small for gestational age; ↑ = increase; ↓ = decrease.

6.3 Animal Studies

Animal studies of the developmental and reproductive toxicity of nickel compounds are summarized in Table 14.

The studies of NiPERA (2000a,b) showing perinatal mortality in nickel treated rats were selected as the basis of the chronic oral REL. The details of the derivation are given in section 9.8.

NiPERA (2000a) sponsored a one-generation reproduction study in Sprague-Dawley rats with nickel sulfate hexahydrate. Eight animals per sex/dose group were administered 0, 10, 20, 30, 50 or 75 mg/kg-d by daily aqueous gavage to the F0 parental animals and selected F_1 offspring. Dosing of the F0 animals began two weeks prior to mating and dosing of F_1 offspring began on PND 22. All doses were given at constant volume of 10 mL/kg. Both F_0 and F_1 animals were examined for indications of toxicity. Experimental endpoints for F_0 animals included clinical observations, body weights, food and water consumption, mating, parturition, lactation and offspring growth and viability. Experimental endpoints for selected F_1 animals included survival, clinical observations and body weight during the F_1 dosing phase. All F_0 and F_1 animals were subjected to gross necropsy examination at time of death or terminal sacrifice. For the F_0 animals post-implantation loss (implantation scar count minus the number of live pups on Day 0) was significantly increased at the 30, 50, and 75 mg/kg-d dose levels and increased at the 10 and 20 mg/kg-d levels (mean loss values: 0.4 control; 2.6; 1.5; 2.3 ($P<0.05$); 2.7 ($P<0.01$); 4.8 ($P<0.01$)). For F_1, pup viability was significantly decreased at all dose levels except 50 mg/kg-d compared to the control (dead/live: 1/128 control; 12/100; 10/106; 10/92; 4/89; 23/80 all $P < 0.01$ except 50 mg/kg-d). For this study a LOAEL of 10 mg/kg-d equivalent to 2.1 mg Ni/kg-d was identified.

NiPERA (2000b) sponsored a two-generation reproduction study in Sprague-Dawley rats with nickel sulfate hexahydrate. Twenty-eight animals per sex per group were administered 0, 0.22, 0.56, 1.12, or 2.23 mg Ni/kg-d by aqueous gavage. The animals were exposed from ten weeks prior to mating for F_0, through gestation, and until PND 21 (13 weeks to delivery of F_1 offspring). Exposure for F_1 was from *in utero*, during lactation, through development from PND 22 to about PND 92 (a minimum of 70 days of treatment). In contrast to the one-generation study the F0 animals showed no statistically significant effects of nickel administration on implantation and post-implantation losses. Statistically significant differences in F_0 organ weights consisted of decreased absolute and relative liver weights in the high dose males, decreased absolute brain weight in the mid dose females, and increased relative liver weight in 0.56, 1.12 and 2.23 mg/kg-d group females. The investigators did not consider these organ weight effects to be toxicologically meaningful. The percent of dead pups/total in the respective dose groups were: 2.2 (control); 3.7; 2.2; 2.1; 4.2 ($P = 0.105$ vs.

control by one-sided Fisher exact test). For this study a NOAEL of 2.23 mg Ni/kg-d was identified by the authors.

Schroeder and Mitchener (1971) conducted a three-generation reproduction study in Long-Evans rats administered drinking water containing five mg Ni/L (0.43 mg Ni/kg-d, U.S.EPA, 1988). Five pairs of rats were randomly selected at the time of weaning, placed in separate cages and given nickel in drinking water *ad libitum*. The rats were allowed to breed for up to nine months of age or longer. At weaning, pairs were randomly selected from the first, second and third litter (F_1) and allowed to breed and to produce the F_2 generation. Pairs were likewise selected at random from the F_2 litters to breed the F_3 generation. They observed that all nickel-exposed animals in the three generations gave birth to litters that exhibited significantly increased perinatal mortality ($P < 0.0001$), and there was a significantly increased number of "runts" in the first ($P < 0.025$) and third ($P < 0.0001$) generations. The study suffers from small sample size, and the fact that matings were not randomized and that the males were not rotated.

Ambrose et al. (1976) studied the effects of dietary administration of nickel sulfate hexahydrate in a three-generation study in rats. Male and female rats in the parent generation were exposed to 0, 250, 500, or 1000 ppm nickel, starting at 28 days of age. Mating was initiated after 11 weeks of nickel exposure. Rats in the first, second and third generations were also given the same diet as the parent generation. At each mating, 20 females from each dose level were transferred to individual breeding cages and mated with a male from the same dietary nickel level. The authors did not observe any adverse effect on fertility, pregnancy maintenance, or postnatal survival of offspring in the three generations. They did report a dose-dependent decrease in the number of siblings weaned per litter averaging 8.1, 7.2, 6.8, and 6.4, respectively. Weanling body weight was clearly affected at the top dose level averaging 73% of the controls. The study suffers from small sample size and the use of pups rather than litters as the unit of comparison.

In a two-generation study (RTI, 1988), nickel chloride was administered in drinking water to male and female CD rats (30/sex/dose) at dose levels of 0, 50, 250, or 500 ppm (mg Ni^{2+}/L) for 90 days before breeding. A significant decrease in the P_0 maternal body weight was observed at the highest dose level. A significant decrease in live pups/litter and average pup body weight versus controls was also seen at the 500 ppm level in the F_{1a} generation. Similar effects were seen in the F_{1b} litters of P_0 dams exposed to the 500 ppm dose level. Increased pup mortality and decreased live litter size were also observed in the 50 and 250 ppm dose groups in the F_{1b} litters. These latter findings are questionable due to increased temperature and humidity experienced by the F_{1b} litters, which could have influenced the observed effects (Edwards, 1986). F_{1b} males and females were randomly mated on postnatal day (PND) 70 and their offspring were evaluated through PND 21. The 500 ppm dose level caused a significant body weight depression of both mothers and pups, and increased neonatal mortality. The 250 ppm dose level produced transient depression of

maternal weight gain and water intake during gestation of the F_{2b} litters. A significant increase in short ribs was observed in the 50 ppm dose group, but since this was not seen in the higher doses, it is not considered to be biologically significant.

Kakela et al. (1999) evaluated the effect of $NiCl_2$ administered in drinking water on reproduction in Wistar rats. Four groups of six female rats were exposed to 10-100 ppm Ni^{2+} for up to 100 days prior to conception and through gestation and lactation. Two groups of male rats were exposed to 30 ppm Ni^{2+} for 28 and 42 days prior to conception and one group of males and females were exposed to 30 ppm Ni^{2+} for 28 days prior to conception. Exposure was continued for the females through lactation. The males were sacrificed at conception. When males were exposed to Ni^{2+} both the number of pregnancies and the number of pups born were reduced. The control value for gestation index (number of live pups per dam) was 10.2 ± 1.5 SE versus 2.7 ± 1.4 ($P < 0.01$) for 28 day exposures and 7.8 ± 2.0 for 42 day exposures. The litter sizes were 9.2 ± 1.5, 1.3 ± 0.9 ($P < 0.01$), and 6.2 ± 2.0, respectively. Females exposed to 100 ppm Ni^{2+} 14 days prior to conception also gave reduced litters: 4.0 ± 1.0 ($P < 0.05$). Histological examination of testes in nickel-exposed rats revealed shrinkage of the seminiferous tubules and decreased number of basal spermatogonia. When both parents were exposed to nickel, pup mortality during lactation was high.

Administration of 25 µmol Ni/kg-d for 5 days only marginally affected mating efficiency of males (75% vs. 80-90% in controls). No significant difference was seen in the total number of implantations among pregnancies resulting from nickel-treated males. Total implantations/litter from nickel-treated males ranged from 10.9 to 11.4. However there was a marked decrease in the number of live implantations among the nickel animals during weeks 1 to 3. The mean incidence of dead implantations during these three weeks was 1.9, 3.2, and 2.2, respectively (all $P < 0.05$ vs. control). These values compare with those for a single 100 mg/kg dose of cyclophosphamide, a dominant lethal mutagen, of 5.3, 6.33, and 3.6, respectively (all $P < 0.001$ vs. control). The percentage of dead implantations/litter expressed as a percentage of total implants for weeks 1, 2, and 3 were: control, 8.69, 8.03, 10.9; nickel, 16.5 ($P < 0.05$), 28.00 ($P < 0.001$), 19.64 ($P < 0.001$); cyclophosphamide, 60.27, 55.86, 35.00 (all $P < 0.002$). The results clearly suggest a specific Ni-induction of dominant lethal-type mutations.

TABLE 14. SUMMARY OF ANIMAL REPRODUCTIVE AND DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Schroeder and Mitchener, 1971	Ni in drinking water	3-generation reproduction study in rats, 0.43 mg Ni/kg-d	Increased perinatal mortality in all generations.	Small sample size, mating not randomized, males not rotated.
Ambrose *et al*., 1976	$NiSO_4 \cdot 6H_2O$	3-generation study in rats: 0, 250, 500, 1000 ppm Ni	Reproductive effects: dose-dependent decreases in number of siblings/litter, 8.1, 7.2, 6.8, 6.2, respectively.	Small sample size, use of pups rather than litters as unit of comparison.
RTI, 1988	$NiCl_2$	2-generation study in rats, 30/sex/dose. 0, 50, 250, 500 ppm Ni in drinking water for 90 d before breeding.	Reproductive effects: P_0 maternal BW ↓, live pups/litter ↓, avg. pup weight in F_{1a} and F_{1b} ↓.	500 ppm considered significant BW ↓ in mothers and pups, and increased neonatal toxicity.
Kakela *et al*., 1999	$NiCl_2$	Reproduction in female rats 10, 30, 100 ppm Ni, and 30 ppm Ni in male rats.	Reproductive effects: females exposed t o100 ppm Ni 14 d prior to conception gave reduced litters. Males exposed gave reduced number of pregnancies and number of pups born.	Histology of males showed shrinkage of the seminiferous tubules and decreased number of basal spermatogonia. Perinatal mortality seen when both parents were exposed.
NiPERA, 2000a	$NiSO_4 \cdot 6H_2O$	1-generation reproduction study in rats, 8/sex/dose group, 0, 10, 20, 30, 50, or 75 mg/kg-d, aqueous gavage.	Reproductive effects: F_1 pup viability significantly decreased at all dose levels except 50 mg/kg-d.	LOAEL = 10 mg/kg-d ≈2.1 mg Ni/kg-d.

TABLE 14. SUMMARY OF ANIMAL REPRODUCTIVE AND DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
NiPERA, 2000b	$NiSO_4 \cdot 6H_2O$	2-generation reproduction study in rats 28/sex/dose group; 0, 0.22, 0.56, 1.12, 2.23 mg Ni/kg-d.	Reproductive effects: % dead pups/total: 2.2, 3.7, 2.2, 2.1, 4.2 (P = 0.105), respectively. Suggestion of a specific Ni-induced dominant lethal mutation.	Decreased absolute brain weight in mid dose females, increase in relative liver weight at 0.56, 1.12, or 2.23 mg/kg-d.
Smith *et al.,* 1993	$NiCl_2$	2-generation reproduction study in rats 34 females/dose group; 0, 10, 50, 250 ppm Ni in drinking water for 11 weeks prior to mating.	Reproductive effects: maternal weight gain reduced. Increased perinatal mortality in G1 250 ppm (P<0.01) and in G2 10 ppm (P< 0.03); 50 ppm (P< 0.076), 250 ppm (P < 0.01).	LOAEL = 10 ppm ≈ 1.3 mg Ni/kg-d.
Slotkin & Seidler, 2008	$NiCl_2$	Neurodevelopmental cell model. PC12 pheochromocytoma cells treated with 30 µM $NiCl_2$, 5-8 cell cultures examined at 24, 72 hr post treatment.	Gene expression: Tryptophan hydroxylase (*tph*) ↓, vesicular monoamine transporter (*slc6a4*) ↑. Ni reduced net expression of 5HT receptor genes.	Significant decrements in *htr1d*, *htr2a*, and *htr3b*. Evidence of toxic action on specific neurotransmitter pathways.
Pandey *et al*., 1999	$NiSO_4$	Oral exposure of adult male mice 0, 5, 10 mg/kg bw, 5d/week x 35 days.	Dose-dependent decreases in absolute and relative weights of testes, epididymides, seminal vesicle, and prostate gland at 5 mg/kg-d (except epididymides) and 10 mg/kg-d.	Sperm motility ↓; Sperm concentration ↓. Altered marker testicular enzymes: γ-glutamyl trans-peptidase ↑; sorbitol dehydrogenase ↓; LDH ↑. All effects at 10 mg/kg-d, P < 0.05.

TABLE 14. SUMMARY OF ANIMAL REPRODUCTIVE AND DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Pandey and Srivastava, 2000	$NiSO_4$ $NiCl_2$	Oral exposure of young male mice, 6/dose group, 0, 5, 10, or 20 mg/kg-d x 5d/week x 35 days.	Same effects as above for reproductive tissue weights and sperm concentration and motility. Abnormal sperm head, neck and tail morphology with higher doses of either compound.	Curved neck, curved, bent, round, loop, or folded tails with higher doses of $NiSO_4$ or $NiCl_2$. $BMDL_{1SD}$ (motility decrease) = 2.91 mg/kg-d $NiSO_4$; $BMDL_{1SD}$ (sperm abnormality) = 0.46 mg/kg-d $NiSO_4$; 0.34 mg/kg-d $NiCl_2$.
Xie *et al*., 1995	$NiCl_2 \cdot 6H_2O$	Male ICR mice i.p. doses of 0, 0.5, 1.0, 3.0, or 5.0 mg Ni/kg bw. Mice sacrificed 24 hr post treatment and 5.0 mg/kg 7 days post treatment.	Dose dependent increases in testicular LPO, Ni, Ca, Fe ($P<0.05$, $N=5$). Lesser increases in Cu, Zn.	Testicular weight decrease 0.65% bw to 0.4% bw ($P<0.05$, $N=5$).
Das & Dasgupta, 1997	$NiSO_4 \cdot 6H_2O$	Adult male rats fed normal or protein restricted diets dosed with 20mg/kg i.p. on alternate days for 20 days.	Testicular steroido-genesis: $NiSO_4$ significantly reduced 3β-hydroxysteroid dehydrogenase (HSD) and 17β-HSD in both dietary regimes.	Significant recovery seen 15 days after cessation of nickel treatment.
Forgacs *et al*., 1998	$NiSO_4 \cdot 7H_2O$	Primary Leydig cell cultures with exposures *in vivo* or *in vitro*. Mice dosed s.c with $NiSO_4$ 0, 10, 20, 40 mg/kg bw every 3 days x 4.	Dose-dependent depression of human chorionic gonadotropin (hCG)-stimulated testosterone over 48 hr in cultured testicular interstitial cells.	*In vitro* exposure of 48 hr cultures of hCG-stimulated testicular interstitial cells to 0, 62.5, 125, 250, 500, and 1000 μM $NiSO_4$. Testosterone production 100, 105, 78*, 56*, 32*, 18*%, respectively (* $P < 0.05$, $N = 7$).

TABLE 14. SUMMARY OF ANIMAL REPRODUCTIVE AND DEVELOPMENTAL TOXICITY OF NICKEL

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Doreswamy *et al*., 2004	$NiCl_2$	Testicular oxidative stress in male mice 0, 12.5, 25, or 50 µmol $NiCl_2$/kg-d i.p. for 3-5 days. Mice sacrificed 24 hr after last dose.	LPO increased in: testicular homogenate (10-25%); mitochondria (20-45%); microsomes (25-60%); epididymal sperm (8-25%).	Antioxidant enzymes ↑: GSH peroxidase (8-26%); GST (15-26%); catalase (10-25%). Double stranded DNA↓ in testis and epididymal spermatozoa.

Note: BMDL 95% lower bound on a specific response level (e.g. BMDL05 = lower bound on a 5% response); G1,G2 = first and second generations; GSH = glutathione; GST = glutathione sulfotransferase; hCG = human chorionic gonadotropin; HSD = hydroxysteroid dehydrogenase; LDH = lactate dehydrogenase; LPO = lipid peroxidase; ↑ = increase; ↓ = decrease.

There are several reports of teratogenicity and other reproductive effects in laboratory animals exposed to nickel (Ambrose et al., 1976; Schroeder and Mitchener, 1971; RTI, 1987; Smith et al., 1993). Mice exposed during pregnancy to $NiCl_2$ by intraperitoneal injection bore offspring with numerous fetal malformations and skeletal anomalies. In addition there were increased fetal resorption rates and decreased fetal weights (Lu *et al*., 1979). Woollam (1972) showed that nickel acetate, when injected intraperitoneally into pregnant hamsters, caused significant fetal mortality at 25 mg/kg.

Intravenous exposure of pregnant rats to 11 mg Ni/kg caused increased fetal mortality and a 16% incidence of fetal malformations including anopthalmia, cystic lungs, and hydronephrosis (Sunderman et al., 1983). Temporary hyperglycemia was seen in pregnant rats exposed intraperitoneally to $NiCl_2$ at four mg/kg (Mas *et al*., 1985). The authors proposed that this hyperglycemia was a mechanism for teratogenicity.

Sunderman et al. (1978) administered nickel chloride (16 mg Ni/kg) to Fischer rats by intramuscular (i.m.) injection on day eight of gestation. The body weights of fetuses on day 20 of gestation and of weanlings four to eight weeks after birth were reduced. No congenital anomalies were found in fetuses from nickel-treated dams, or in rats that received 10 i.m. injections of 2 mg Ni/kg as nickel chloride twice daily from day 6 to day 10 of gestation.

Diwan et al. (1992) showed that intraperitoneal (i.p.) injection of nickel acetate to pregnant F344/NCr rats caused early mortality in the offspring. They administered four i.p. injections of nickel acetate (2.6 mg Ni/kg) on days 12, 14, 16, and 18 of gestation and reported that all offspring died within 72 hr after birth.

Smith et al. (1993) administered nickel chloride in drinking water at 0, 10, 50, or 250 ppm (0, 1.3, 6.8, or 31.6 mg/kg-d) to 34 female Long-Evans rats per group for 11 weeks before mating and subsequently during two sequential gestations (G1, G2) and lactation (L1, L2) periods. Pups were observed until weaning and breeder males were unexposed. Dams were rested for two weeks after weaning of the first litters before initiating the second breeding. During this time exposure to nickel was continuous. The animals were 6-7 months old when they produced their second litters. Throughout the study, there were no overt clinical signs of toxicity in any of the dose groups. Reproductive performance was unaltered by nickel exposure although maternal weight gain was reduced during G1 in the mid and high dose groups. The most significant finding was the increased frequency of perinatal death (Table 15). The authors reported that the proportion of dead pups per litter was significantly increased at the highest dose level in G1 ($P \leq 0.01$) and at the low ($P \leq 0.03$) and high ($P \leq 0.01$) dose levels in G2. The mid dose level in G2 was also increased ($P = 0.076$). Overall there was a dose related increase in perinatal mortality in both segments of the study. The authors concluded that 10 ppm $NiCl_2$ (1.3 mg Ni/kg-d) represented the LOAEL in the study.

TABLE 15. REPRODUCTIVE OUTCOMES OF BREEDING FEMALE RATS EXPOSED TO NICKEL CHLORIDE IN DRINKING WATER (SMITH *ET AL.*, 1993).

Concentration of nickel in water ppm Ni (No. females)	Sperm positive females	No. viable litters	Average no. of pups per litter (live and dead)	No. of litters with dead pups at birth	Total dead pups on post natal day 1(% dead pups per litter)
G1, L1					
0 (34)	29	25	12.9	5	5 (1.7)
10 (34)	30	25	12.2	5	9 (3.1)
50 (34)	30	24	11.7	0	0 (0)
250 (34)	32	27	13.2	11	35*** (13.2)**
G2, L2					
0 (29)	28	23	10.6	2	2 (1.0)
10 (29)	28	22	12.5	7	11** (4.3)**
50 (30)	29	24	13.3	6	16* (4.6)
250 (31)	31	25	11.3	10	22*** (8.8)***

Note: Significant levels, pairwise comparison to control: * $0.05 < P \leq 0.10$;
** $0.01 < P \leq 0.03$; *** $0.001 < P \leq 0.01$.

Slotkin and Seidler (2008) evaluated the effects on Ni^{2+} in a neurodevelopmental cell model. Neurodifferentiating rat PC12 pheochromocytoma cells were treated with 30 µM $NiCl_2$. The cell cultures were examined 24 and 72 hr after the start of exposure with five to eight independent cultures at each time point. Unlike organophosphorus (OP) agents studied with this system, nickel reduced expression of tryptophan hydroxylase (*tph*) and enhanced vesicular monoamine transporter (*slc6a4*). Nickel exposure reduced the net expression of serotonin (5HT) receptor genes more effectively than did diazinon or dieldrin. Significant decrements were seen for receptor genes *htr1d*, *htr2a* and *htr3b*. The authors conclude that the results provide "evidence connecting the direct, initial mechanisms of toxicant action on specific neurotransmitter pathways with their long-term effects on synaptic function and behavior."

Male rat reproductive toxicity (damage to epididymal tubules and abnormal spermatozoa) was observed following a single subcutaneous dose of 5 mg Ni/kg as Ni_3S_2 (Hoey, 1966). Benson et al. (1987) showed that mice and rats exposed to 5 or 10 mg Ni_3S_2/m^3 displayed degeneration of testicular germinal epithelium after 12 days exposure (6 hours/day, 5 days/week).

Pandey et al. (1999) administered $NiSO_4$ orally to adult male mice at 0, 5 or 10 mg/kg bw for 5 days/week for 35 days. Significant dose-dependent decreases were observed in absolute and organ-to-body weight ratios of testes, epididymides, seminal vesicles, and prostate gland. Also observed were decreases in sperm motility and count. Significant alterations of marker testicular enzymes were seen: γ-glutamyl transpeptidase, 28.76, 35.23, and 38.44*; sorbitol dehydrogenase, 7.88, 6.00, and 4.04*; and lactate dehydrogenase, 194, 237, 244*, respectively (* $P<0.05$, N=10, all activities nmol/min/mg protein).

Pandey and Srivastava (2000) reported spermatotoxic effects of nickel in mice. Young male mice (25 ± 5 g), six/dose group were administered 0, 5, 10, or 20 mg/kg bw of $NiSO_4$ or $NiCl_2$ orally by gavage in 0.2 mL distilled water five days/week for 35 days. The animals were sacrificed on day 36 and the testes, epididymides, seminal vesicles and prostate glands were removed and weighed. No overt toxicity was observed. The absolute and relative weights of testes, epididymides, seminal vesicles and prostate gland were significantly decreased at the top dose of 20 mg/kg bw. Dose-dependent reductions in sperm motility were observed at 10 and 20 mg/kg bw with nickel sulfate and nickel chloride ($P <0.05$). Dose-dependent decreases in sperm count were also seen with both nickel compounds but were statistically significant only at the top dose with $NiSO_4$. There was a significant increase in abnormal sperm including abnormalities of the head, neck and tail region. Curved neck and curved, bent, round, loop and folded tail were seen at both higher doses with $NiSO_4$ and $NiCl_2$. A continuous benchmark dose analysis of the sperm motility and sperm count data gave only one adequate fit, namely decrease in motility with $NiSO_4$ treatment ($BMDL_{1SD}$ = 2.91 mg/kg bw, linear model, P = 0.22). A similar analysis of sperm abnormality data gave adequate fits for both compounds: $NiSO_4$, $BMDL_{1SD}$ = 0.46 mg/kg, polynomial model, P = 0.97; and $NiCl_2$, $BMDL_{1SD}$ = 0.34 mg/kg, polynomial model, P = 0.12.

Xie et al. (1995) evaluated the effects of chelating agents on testicular toxicity in mice caused by acute nickel exposure. Male ICR mice were injected intraperitoneally with $NiCl_2•6H_2O$ at doses of 0, 0.5, 1.0, 3.0, or 5.0 mg Ni/kg bw and sacrificed 24 hr after injection. Nickel administration resulted in dose-dependent increases in testicular lipid peroxidation (LPO), and Ni, calcium (Ca) and iron (Fe) concentrations (all $P < 0.05$, N=5). Lesser increases in testicular copper (Cu) and zinc (Zn) were also seen. Treatment with 5.0 mg Ni/kg and seven days observation showed increasing LPO with a peak at two days after Ni administration followed by a gradual decrease. Testicular weight decreased from about 0.65% of body weight to 0.4% over the same period ($P < 0.05$, N = 5). Among five chelating agents tested *meso*-2, 3-dimercaptosuccinic acid (DMSA) and *N*-benzyl-D-glucaminedithiocarbamate (BGD) were the most effective in removing nickel from the testes, protecting against LPO and Ni-induced sterility.

Das and Dasgupta (1997) treated male Wistar rats with 20 mg $NiSO_4$/kg bw by intraperitoneal injection on alternate days for 20 days. Significant decreases were observed in testicular weight, lactate dehydrogenase, and protein

concentration and increases in testicular glycogen and cholesterol (all $P < 0.05$, $N = 6$). The differences from control animals were generally enhanced in parallel groups fed a protein-restricted diet with or without nickel sulfate administration.

Forgacs et al. (1998) evaluated the effects of Ni(II) on testosterone production of mouse Leydig cells in vitro following repeated in vivo or in vitro exposures. CFLP mice were injected s.c. (four treatments every three days) with 0, 10, 20, or 40 mg $NiSO_4 \cdot 7H_2O$/kg bw. Human chorionic gonadotropin (hCG)-stimulated testosterone response was reduced by Ni-treatment in 48 hr cultures of testicular interstitial cells from treated animals in a dose-dependent manner (100 (control), 88%, 80%*, and 59%*, respectively (* $P < 0.05$, $N = 4$)). Direct nickel effects were assessed in 48 hr cultures of hCG-stimulated testicular interstitial cells exposed to 0, 62.5, 125, 250, 500, or 1000 µM $NiSO_4$. Testosterone production relative to hCG control was 100% (control), 105%, 78%*, 56%*, 32%*, and 18%* respectively (* $P < 0.05$, $N = 7$). Cytotoxicity was assessed by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay following exposure and cell viability remained above 80% at all doses. The data indicate that the effect of nickel on the Leydig cell testosterone production is time and concentration dependent, and is not due to cytotoxicity.

Das and Dasgupta (2000) treated male Wistar rats with 20 mg $NiSO_4$/kg bw by intraperitoneal injection on alternate days for 20 days. Significant decreases in cauda epididymal sperm count and sperm motility were observed following treatment ($P < 0.05$). In addition decreases were seen in testicular DNA, RNA, and total protein concentrations ($P < 0.05$). The authors conclude that $NiSO_4$ is a likely gonadotoxicant that adversely affects the expression of genetic information via reduced nucleic acids and protein. In a subsequent study using a similar protocol in male rats Das and Dasgupta (2002) found that nickel treatment significantly reduced the activities of two testicular steroidogenic enzymes, 3β- and 17β-hydroxy steroid dehydrogenases (HSD), and plasma testosterone concentration. 3β-HSD was reduced from 8.97 ± 0.18 in control normal protein diet rats to 6.57 ± 0.23 units/mg ($P < 0.05$) in normal diet plus $NiSO_4$. For 17β-HSD the reduction was from 6.50 ± 0.29 to 5.10 ± 0.21 units/mg protein ($P < 0.05$), respectively. Plasma testosterone was reduced from 3.27 ± 0.06 to 2.43 ± 0.10 ng/mL ($P < 0.05$), respectively. Increases in testicular cholesterol and ascorbic acid were observed in the same groups of rats. Some reversibility of the effects was seen when treated animals were fed a normal diet during a withdrawal period.

Doreswamy et al. (2004) treated adult male CFT-Swiss mice with 0, 12.5, 25, or 50 µmol $NiCl_2$/kg bw/d by single i.p. injection for three or five treatments. The mice were sacrificed 24 hr after the final dose and evaluated for biochemical endpoints, DNA damage and fragmentation and at 1, 2, 3, and 5 weeks from the beginning of treatment for sperm head abnormalities. No clinical signs of toxicity were observed at any administered dose. Dose-dependent increases in lipid peroxidation were seen with whole testicular homogenates (10-25%), mitochondrial fractions (20-45%), microsomal fractions 25-60%), and epididymal

sperm (8-25%). Antioxidant enzymes were similarly increased: glutathione peroxidase (8-26%); glutathione *S*-transferase (15-26%); and catalase (10-25%). Nickel treatment also resulted in a dose-dependent decrease in double stranded DNA (ds-DNA) in the testis and in epididymal spermatozoa. For testis the proportion of ds-DNA was 83% (control), 80%, 65% ($P < 0.05$), and 62% ($P < 0.05$), respectively. For epididymal sperm the values were 90%, 85%, 82% ($P < 0.01$), and 80% ($P < 0.01$), respectively. Agarose gel electrophoresis of genomic DNA, visualized by ethidium bromide fluorescence, showed DNA damage at 6.25, 12.5, 25.0 and 50 µmol Ni/kg-d for three days. Caudal sperm counts did not differ from the control. However, nickel treatment induced a significant dose-dependent increase in the percentage of abnormal sperm, mainly amorphous heads, balloon heads, and hammerheads.

7 Chronic Toxicity

7.1 Chronic Toxicity Summary

Studies of human chronic toxicity of nickel and compounds, and also studies with human cells *in vitro,* are summarized in Table 16 and Table 17. Animal studies are summarized in Table 18. The most important toxic effect seen in both nickel-exposed humans and experimental animals by inhalation is pneumotoxicity. In humans exposed occupationally this is expressed as nickel-induced asthma, pulmonary fibrosis, decreased lung function (FEV_1), and increased lung abnormalities revealed by radiography. In experimental animals adverse lung effects included inflammatory lesions, macrophage hyperplasia, alveolar proteinosis, and fibrosis (rats only), in addition to bronchial lymph node hyperplasia and nasal epithelial atrophy. Numerous other adverse effects at the cellular level were also seen contributing to cytotoxicity, genetic toxicity, immunotoxicity, and other metal-induced toxicity (Beyersmann and Hartwig, 2008; Rana, 2008). However, the most sensitive adverse effects (occurring at lower doses/exposures) were seen in the lung.

7.2 Human Studies

A number of studies indicate that occupational inhalation exposure to nickel aerosols can result in development of asthma specific to nickel. Davies (1986) found 3 cases of asthma among 53 nickel-plating workers without a history of asthma prior to employment. Novey et al. (1983) described biphasic metal-specific bronchial responses in an individual metal-plating worker exposed to nickel and chromium salts. In another case, immunological studies conducted in a 24-year old man showed nickel-specific antibodies in the serum after several weeks of working in a nickel-plating shop using nickel sulfate (McConnell et al., 1973). Dermatitis was observed on exposed areas of his skin, and pulmonary function, measured by FEV_1 with and without isoproterenol challenge, was significantly impaired compared with a control subject and normal values. This worker reported dyspnea, non-productive cough, chest-tightness, and wheezing as symptoms during the work period.

Fernandez-Nieto et al. (2006) reported results obtained from four patients with work-related asthma due to exposure to metallic salts. Two subjects came from factories where potassium dichromate and nickel sulfate were used for electroplating, another worked in a cement factory (potassium dichromate), and one was a welder exposed to metal fumes, including nickel and chromium. All the patients had bronchial hyperresponsiveness (BH) to methacholine, which increased 24 hr after challenge with metal salts. Airway hyperresponsiveness to methacholine was assessed as the provocative concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}). The methacholine inhalation test was performed the day before the antigen challenge and again 24 hr after challenge. A two-fold or greater reduction of the PC_{20} compared to baseline value was

considered a significant change. Nickel sulfate challenge of subject 1 (electro-plating) elicited a BH response at a methacholine concentration of 10 mg/mL and in subject 2 (cement) of 0.1 mg/mL. Twenty-four hours after nickel challenge, the PC_{20} for subject 1 was 0.15 mg/mL.

Although asthma has been described in the above studies, occupational inhalation of nickel dusts has not been found to be associated with pulmonary fibrosis although an increase in irregular lung opacities was observed by Muir et al. (1993) with exposures ≥ five years in 149 nickel sinter plant workers. Pang et al. (1996) observed slight but not statistically significant increased relative risk of mortality due to non-malignant diseases of the respiratory system in nickel platers exposed to $NiCl_2$ and $NiSO_4$. The relative risk with adjustment for age, period of follow up, and year starting nickel work was 1.59 (95% CI, 0.58 to 4.36). The study suffers from low numbers (248 subjects total) and relatively brief soluble nickel exposures (mean = 2.1 yr, median 0.86 yr). An occupational epidemiology report by Broder et al. (1989) found no significant effects on pulmonary function in relation to nickel exposure in a nickel smelter.

Moulin et al. (2000) conducted a mortality study of 4898 stainless steel workers exposed to metallic alloys including nickel. Among the non-malignant endpoints included, no significant increases in standardized mortality ratios (SMRs) for chronic bronchitis, pneumoconiosis or other respiratory system effects were seen. Huvinen et al. (2002) studied 284 workers in a ferrochromium and stainless steel plant. Long-term workers (average 23 years) exposed to low levels of dusts and fumes containing molybdenum (0.3 $\mu g/m^3$), nickel (1.8 $\mu g/m^3$) and chromium (4.7 $\mu g/m^3$) did not show evidence of respiratory disease detectable by lung function tests or chest radiography. Similarly, Egedahl et al. (2001) studied mortality experience among employees at a hydrometallurgical nickel refinery and fertilizer complex in Alberta, Canada. A total of 1649 males who worked continuously for at least 12 months during the years 1954 to 1978 were followed for an additional 17 years. Exposure with this refining process involves nickel metal rather than soluble nickel or sulfides. The observed deaths due to respiratory disease were less than expected (SMR = 36, C.I. 13 to 79).

Berge and Skyberg (2003) reported evidence of increased radiographic lung abnormalities with increased exposure to soluble or sulfidic nickel, albeit with a relatively small number of cases (47/1046) and relatively mild effects. Exposure factors for 1046 refinery workers were, mean ± SD: total Ni, 5.59 ± 11.73; soluble Ni, 1.43 ± 2.23; sulfidic Ni, 0.55 ± 1.19; oxidic Ni, 3.09 ± 8.54; and metallic Ni, 0.52 ± 1.35 $(mg/m^3)yr$. For quantal dose response analysis the following mean exposures were used for sulfidic nickel: 0.03 (254 subjects), 0.27 (237), 1.03 (282), and 4.32 $(mg/m^3)yr$ (263). For soluble nickel the mean exposures were: 0.01 (264), 0.08 (237), 0.33 (282), and 1.73$(mg/m^3)yr$ (263). Pulmonary fibrosis was defined as a median reading of International Labor Organization (ILO) score ≥ 1/0. For soluble nickel exposure the crude odds ratio for pulmonary fibrosis was 4.34 (95% CI, 1.75 to 10.77). The risk adjusted for age, smoking, asbestos, and sulfidic nickel was 2.24 (95% CI, 0.82 to 6.16) with a dose-response. The

corresponding values for sulfidic nickel were crude 5.06 (95% CI, 1.70 to 15.09) and adjusted, as above except for substituting soluble nickel for sulfidic nickel, 2.04 (95% CI, 0.54 to 7.70). The prevalence values for pulmonary fibrosis and both soluble and sulfidic cumulative nickel exposure (their Tables 5 and 6) were acceptably fit by the multistage model. For soluble nickel a $BMDL_{01}$ (1 % excess risk) of 0.35 (mg Ni/m^3)-yr was obtained ($\chi^2 = 2.21$, P = 0.33). For sulfidic nickel the $BMDL_{01}$ was 0.19 (mg Ni/m^3-yr, $\chi^2 = 3.91$, P = 0.14). Dose responses on the adjusted data sets were not fit as well by the model as were the crude data. For example the soluble nickel gave a $BMDL_{01}$ of 0.69 ($\chi^2 = 3.11$, P = 0.08) when adjusted for smoking, age, asbestos and sulfidic Ni (g-adjustment) and a $BMDL_{01}$ of 0.56 (mg/m^3)-yr ($\chi^2 = 1.72$, P = 0.42) when adjusted for age, smoking and asbestos only (f-adjustment). For sulfidic nickel no BMD or BMDL could be calculated from the g-adjusted data sets and with f-adjustment the $BMDL_{01}$ was 0.34 (mg Ni/m^3)-yr ($\chi^2 = 4.16$, P = 0.125). As the authors note, the data are not strong but there is a measureable dose response for cumulative nickel exposure and pulmonary fibrosis. The mean and median exposure periods were 21.8 and 21.9 years, respectively.

Sivulka et al. (2007) reviewed the literature on nickel exposure and non-malignant respiratory disease and suggested that the failure to observe frank lung toxicity in exposed nickel workers may be related to the particle size to which the workers were exposed. The authors point out that in rat studies showing lung lesions, exposures have been to respirable-sized particles (< 4 μm diameter) whereas occupational exposures constitute largely non-respirable larger diameter particles.

TABLE 16. SUMMARY OF CHRONIC NICKEL TOXICITY IN HUMANS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Fernandez-Nieto *et al*., 2006	$NiSO_4$ $K_2Cr_2O_7$	Work-related asthma in electroplating and cement workers (N=4). Bronchial hyper-responsiveness (BH) to methacholine.	Specific inhalation challenge to reduce concentration of methacholine to cause a 20% reduction of FEV_1 (PC20) = increased BH. Both Ni and Cr gave positive responses.	Positive IgE determination for Cr and Ni was found in one subject. Skin tests negative for Cr and Ni.
Pang *et al*., 1996	$NiCl_2$ $NiSO_4$	Nickel platers, N = 248, exposure mean = 2.1 yr, median = 0.86 yr.	Mortality due to non-malignant diseases of the respiratory tract. Adjusted RR = 1.59 (95% CI = 0.58-4.36).	Low numbers and brief exposures.
Moulin *et al*., 2000	Metallic alloys incl. Ni	Steel workers N = 4898	Non-malignant endpoints, chronic bronchitis, pneumo-coniosis, and other respiratory system effects: no significant increases in SMRs.	
Berge & Skyberg, 2003	Soluble Ni Sulfidic Ni	Nickel refinery workers 47/1046, mean soluble Ni for exposure categories, 0.03, 0.27, 1.03, and 4.32 $(mg/m^3)yr$; mean sulfidic Ni 0.01, 0.08, 0.33, 1.73 $(mg/m^3)yr$.	Radiographic lung abnormalities indicative of pulmonary fibrosis (PF). Soluble Ni adjusted OR = 2.24 (95% CI = 0.82-6.16); sulfidic Ni adjusted OR = 2.04 (95% CI = 0.54-7.70).	Unadjusted data: soluble Ni $BMDL_{01}$ = 0.35 $(mg/m^3)yr$; sulfidic Ni $BMDL_{01}$ = 0.19 $(mg/m^3)yr$. Adjusted data: 0.56 and 0.34 $(mg/m^3)yr$, respectively. Data are weak but there is a measureable dose-response.

TABLE 16. SUMMARY OF CHRONIC NICKEL TOXICITY IN HUMANS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Jensen *et al.,* 2004	$NiSO_4 \cdot 6H_20$	Lymphocyte subpopulations and cytokine profiles in Ni-sensitive (N = 33) and normal (N=19) subjects. Ni-sensitive (7-10/group): 0, 0.3, 1.0, 4.0 mg Ni; controls (9-10/group) 0, 4.0 mg Ni.	PBMC isolated from blood 24 hr after Ni treatment for analysis. Ni-sensitive had significantly higher fractions of lymphocytes in their blood: $CD3^+$-type (P = 0.0035); $CD4^+$-type (P = 0.000095); $CD8^+$-type (P = 0.000007).	
Yoshioka *et al.*, 2007	Ni, Cd	Ni-Cd battery workers, N = 66	Ni in urine, Cd in blood, 8-OH-G in urine. Creatinine adjusted 8-OH-G correlated with age, Ni-U, Cd-B.	Combined effects of Ni and Cd not additive. Data suggest that Ni is the main stressor increasing 8-OH-G in urine.

Note: BMDL 95% lower bound on a specific response level (e.g. $BMDL_{01}$ = lower bound on a 1% response); 8-OH-G = 8-hydroxyguanine.

Yoshioka et al. (2007) studied the urinary excretion of 8-hydroxyguanine (8-OH-G), an oxidative stress marker, in nickel-cadmium battery workers. Sixty-six subjects (64 male and two female) provided urine and blood samples. The levels of cadmium in blood (Cd-B) and nickel in urine (Ni-U) were determined by graphite furnace atomic absorption spectroscopy. 8-OH-G in urine was analyzed by high performance liquid chromatography-electrochemical detector system. Creatinine-adjusted 8-OH-G was significantly correlated with age, Ni-U, and Cd-B in univariate analysis, while multivariate analysis revealed that Ni-U and Cd-B were significantly independent variables positively correlated with 8-OH-G. The data were analyzed for mixture toxicity. The subjects were divided into groups based on median concentration of Ni-U and Cd-B (2.86 µg/g creatinine and 0.23 µg/dL, respectively). Subjects with high Ni-U/high Cd-B (Group 4) had the highest levels of 8-OH-G (21.7, 2.0, GM, GSD), followed by those with high Ni-U/low Cd-B (11.5, 1.6, Group 3), those with low Ni-U/high Cd-B (Group 2, 8.9, 1.9) and those with low Ni-U/low Cd-B (Group 1, 8.5, 1.5). The p values of Student's t-tests between Group 1 and Group 2, 3, and 4 were 0.847, 0.050, and < 0.001, respectively. The combined effect of Cd and Ni on the urinary excretion of 8-OH-G departed from additivity. The results indicate that nickel exposure was the primary stressor resulting in increased production and excretion of 8-OH-G.

Carroll and Wood (2000) exposed monolayer cultures of human keratinocytes and fibroblasts to nickel sulfate at concentrations above 0.001 M. Cytotoxicity to both cell types was 50% based on decreased viability. ^{35}S-methionine labeling followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and immunoblotting with specific monoclonal antibodies indicated an increased synthesis of heat shock protein 90 (Hsp90) in keratinocytes at concentrations above 10^{-5} M and induction of heat shock protein 72 (Hsp72) above 10^{-4} M. For fibroblasts increased induction of Hsp90 was seen at all concentrations tested and a dose-related increase was observed for Hsp72. The results indicate a stress response to the toxic effects of nickel ions at fairly low concentrations.

Cell lines derived from monkey kidney (COS-7), human lung tumors (A549), or human liver tumors (HepG2) were cultured for four days with 0, 100, 200, or 400 µM Ni Cl_2. Nickel treatment decreased growth rates in all cell lines after four days in a dose dependent manner. In HepG2 cells GRP96 expression was significantly enhanced at 400 µM Ni(II) ($P < 0.05$) whereas Hsp72 and Hsp73 were significantly suppressed ($P < 0.01$). COS-7 cells showed a similar pattern. GRP96 was over-expressed in A549 cells at 400 µM Ni(II) and Hsp73 was moderately increased.

Au et al. (2006) studied the cytotoxicity of nickel(II) in human T-lymphocyte Jurkat cells in vitro. Jurkat cells were incubated with 0, 1, 10, or 100 µg/mL Ni^{2+} (compound unspecified: 100 µg/mL Ni^{2+} = 1.7mM) for 24 hours. The treatment reduced cell viability and proliferation in a dose-dependent manner. Cell viability

was reduced by 35% at 100 µg Ni/mL. A significant decrease in cell proliferation was also seen at 100 µg Ni/mL. Nickel(II) at 10 µg Ni/mL induced expression of caspase-3, but not at 100 µg Ni/mL. Cells incubated at 100 µg Ni/mL showed fragmented nuclei. Enumeration of Hoechst 33258-stained cells showed that Ni^{2+} at 100 µg/mL induced 16% of the cells to undergo apoptosis. In contrast the lower Ni concentrations were indistinguishable from the control. The authors note that the onset of apoptosis by metal ions may be due to a disruption in cell signaling, DNA damage, or changes in cell constituents such as Ca^{2+}.

M'Bemba-Meka et al. (2006) exposed isolated human lymphocytes to solubilized Ni_3S_2 in vitro to assess cytotoxicity. Lymphocyte suspensions were exposed to 0, 0.25, 0.50, 0.75, 1.0, 1.5, or 2.0 mM Ni_3S_2 for 3-4 hr and to 2.0 mM Ni_3S_2 for 30, 60, 90, 120, 180 or 240 min. Cell viability was assessed by trypan blue exclusion. Nickel(II) treatment resulted in both concentration- and time-dependent lymphocyte death. Significant increases in cell death were seen at 0.75 mM Ni_3S_2 for 4 hr and 1.0 mM Ni_3S_2 for 2 hr ($P < 0.05$). Increased production of H_2O_2 and superoxide anion (O_2^-), lipid peroxidation and depletion of cellular sulfhydryl contents were induced by 1 mM Ni_3S_2. Nickel-induced lymphocyte death was significantly prevented by pretreatment with scavengers of reactive oxygen species (catalase, superoxide dismutase, dimethylthiourea/mannitol, deferoxamine or glutathione/*N*-acetylcysteine). Co-treatment with cyclosporin A inhibited Ni_3S_2-induced disturbances of mitochondrial membrane potential ($\Delta\Psi m$), and significantly prevented Ni_3S_2-induced cell death ($P < 0.05$ vs. Ni_3S_2 alone treatment). Lymphocyte death was also significantly reduced by treatment with Ca^{2+} channel blockers (diltiazem, nifedipine, and verapamil) and intracellular Ca^{2+} antagonists (dantrolene, cyclosporin A, and ruthenium red). Treatment of lymphocytes with 1 mM Ni_3S_2 alone increased intracellular Ca^{2+} about three fold over three hours. The authors interpret the findings as indicative of an activation of cell death signaling pathways involving generation of reactive oxygen species (ROS) and oxidative stress, loss of mitochondrial membrane potential, and disruption of cellular calcium homeostasis.

Guan et al. (2007) also studied the toxicity of nickel(II) in human T-lymphocyte Jurkat cell line. The cells were exposed to 0, 20, 40, 60, or 80 µg Ni/mL $NiCl_2$ for 0, 6, 12, or 24 hr and viability measured by trypan blue staining assay. Viability was less than 10% when cells were incubated for 24 hr at 80 µg Ni/mL. Treated cells exhibited morphological changes and chromosomal condensation indicative of apoptosis. The apoptotic fraction increased in a dose- and time-dependent manner. After incubation with nickel(II) for 6 hr the concentration of NO increased linearly from ca. 0.9 (control) to 3.7 µM (80 µg Ni/mL) (monitored by release of NO_2^-/NO_3^- into the cell culture medium). Nickel(II) treatment was also observed to dissipate mitochondrial membrane potential and down regulate bcl-2 mRNA after 12 hr exposure at 60 µg Ni/mL possibly modulating Ni-induced cell apoptosis. The authors speculate that a key process in the immune cellular response to nickel(II) is nickel induced apoptosis mediated by a mitochondrial pathway associated with NO.

Ke et al. (2007) studied fluorescent tracking of nickel ions in human cultured cells. Water-insoluble nickel compounds such as NiS and Ni_3S_2 were shown in vitro to enter cells by phagocytosis. Using a dye that fluoresces when intracellular Ni^{2+} ion binds to it, the authors showed that both soluble and insoluble nickel compounds elevated Ni ions in the cytoplasm and nuclear compartments. However, soluble nickel compounds were more readily removed than the insoluble nickel compounds. Within 10 hours after $NiCl_2$ removal from the culture medium, Ni ions disappeared from the nucleus and were not detected in the cells by 16 hours. Insoluble Ni_3S_2 yielded Ni ions that persisted in the nucleus after 16 hours and were detected in the cytoplasm even after 24 hours following Ni removal.

Trombetta et al. (2005) evaluated the toxic effects of nickel in a three dimensional model of human epithelium (RHE) reconstituted from TR146 cells derived from a human squamous cell carcinoma of the buccal mucosa. The RHE cultures were exposed for 72 hr to eight concentrations of $NiCl_2$ ranging from 0.05 to 7.6 mM. Cell viability, assessed by the MTT assay, was significantly reduced at Ni(II) concentrations greater than 1.3 mM. Similarly the release of prostaglandin E2 and interleukin-6 into the culture medium was also significantly increased above 1.3 mM Ni(II). However no change was seen in interleukin-8 release at any nickel concentration. In addition to cytokines the effect of nickel on glutathione (GSH) was also measured. Nickel induced a non statistically significant reduction in GSH from 2.392 nmol/cm^2 in control cultures to 2.151 nmol/cm^2 at 7.6 mM Ni(II). By contrast an increase in tissue oxidized glutathione (GSSG) was seen at all nickel concentrations and was statistically significant above 0.7 mM ($P < 0.05$). Total tissue glutathione (GSH + GSSG) appeared to increase compared to controls after nickel exposure. The ratio of GSH/GSSG was significantly reduced at all nickel concentrations tested ($P < 0.05$). The results indicate that nickel exposures that are not toxic enough to affect cell viability or inflammatory cytokine release can affect cellular redox equilibrium. The authors also observed an increase in vacuolized cells and apoptotic cells in tissue cultures at all Ni concentrations ≤ 0.7 mM without evidence of cellular necrosis. Thus low “non-toxic” nickel exposure may modify cellular effectors of apoptosis.

Davidson et al. (2005) reported that $^{63}NiCl_2$ interfered with cellular iron homeostasis in human lung A549 cell cultures. Soluble nickel was observed to block the uptake of iron into transferrin-bound iron and non-transferrin-bound iron (NTBI) leading to cellular ferritin accumulation. Since excessive iron is toxic to cells, such nickel-induced blockage might be expected to lead to cytotoxicity. Nickel also decreased the binding of Von Hippel-Landau (VHL) protein to hypoxia inducible factor 1α (HIF-1α) possibly by competing for iron sites on prolyl hydroxylases. Prolyl hydroxylases 1-3 hydroxylate the ODD (oxygen-dependent degradation) domain in HIF-1α. VHL can bind to hydroxylated proline residues in the ODD domain of HIF-1α and target it for degradation. When the prolyl hydroxylases are not functional, no hydroxylation of proline residues occurs and VHL will not bind.

Cheng et al. (2003) quantified gene expression in microarrays with cDNA chips (ca. 8000 cDNAs) after exposure of human peripheral lung epithelial cells to nickel(II). Cultured human lung epithelial HPL1D cells were exposed for 24 hr to non-cytotoxic (50, 100, or 200 µM) or cytotoxic (400, 800, or 1600 µM) Ni^{2+} concentrations. Cytotoxicity was assessed by loss of cell adhesion in 70% confluent cultures after 24 hr Ni-exposure. The data set comprising 868 genes was filtered to select only those 113 genes, which showed a ≥ 2-fold change in expression at one or more of the three nontoxic nickel concentrations. Most of the genes impacted by low nickel concentrations were related to gene transcription, protein synthesis and stability, cytoskeleton, signaling, metabolism, cell membrane, and extracellular matrix.

Gazel et al. (2008) evaluated transcriptional profiles in Ni(II) treated human epidermal keratinocytes using DNA microarrays. Reconstructed human epidermis (RHE) was exposed to 11 µM $NiSO_4$ for 30 min or 6 hr. Microarray analysis showed that 134 genes were affected by Ni(II) exposure: 97 genes were induced and 37 genes were suppressed. The functional categories of affected genes indicated that Ni(II) inhibits apoptosis, promotes cell cycle and induces synthesis of extracellular matrix proteins and proteases. Ni also regulates secreted signaling proteins, inducing vascular endothelial growth factor (VEGF), amphiregulin (AREG), placental growth factor (PGF), prostate differentiation factor (GDF15), and bone marrow stromal cell antigen 2 (BST2), while suppressing IL-18, galectin-3 (LGALS3), and lipopolysaccharide-induced TNF-α Factor (LITAF). Interestingly no Ni(II) effects were seen in epidermal differentiation genes.

Ouyang et al. (2009) studied the effect of nickel compounds on the cell cycle in human lung carcinoma A549 cells in vitro. $NiCl_2$ at doses from 0.25 to 1.0 mM were found equivalent to 0.25 to 2 µg NiS/cm^2 in the activation of transcription factor NFkB and HIF-1α, and induction of TNF-α and CAP43 gene expression. Growth of A549 cells was significantly inhibited by 0.25 mM $NiCl_2$ but only marginally inhibited by NiS at 2.0 µg/cm^2. Nickel sulfide also failed to significantly inhibit human bronchial epithelial cell line HCCBE-3 or mouse skin epidermal cell line C141. Exposure to $NiCl_2$, but not NiS, caused a significant inhibition of cell growth and G1/G0 cell cycle arrest concomitant with a marked down-regulation of cyclin D1 in A549 cells. The down-regulation is due to protein degradation rather than inhibition of transcription. The degradation of cyclin D1 is a ubiquitination- and proteosome-dependent process, but how soluble nickel initiates or regulates this process is unknown. Effects on other cell cycle regulatory proteins were also evaluated, namely cyclin E and p21. Nickel had no effect on cyclin E while both nickel compounds increased the amounts of p21.

Rossman (2009) has criticized the use of dyes, particularly Trypan Blue in the assessment of cytotoxicity when used close to the time of exposure. These methods give better results (close to results with clonal survival) when used about three days after exposure; otherwise cytotoxicity may be significantly underestimated.

TABLE 17. SUMMARY OF STUDIES WITH HUMAN CELLS *IN VITRO*

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Au *et al.*, 2006	Ni^{2+}	Human T-lymphocytes Jurkat cells in vitro: 0, 1, 10, 100 µg Ni/mL for 24 hr.	Cell viability ↓ 35% at 100 µg/mL; caspase-3 ↑ at 10 µg/mL; fragmented nuclei at 100 µg/mL.	16% of cells induced to undergo apoptosis at 100 µg Ni/mL.
M'Bemba-Meka *et al.*, 2006	Ni_3S_2	Isolated human lymphocytes in vitro: 0, 0.25, 0.50, 0.75, 1.0, 1.5, or 2.0 mM $Ni_3S_2$for 30 min to 6 hr	Concentration and time-dependent lymphocyte death. Significant death increases at 0.75 mM for 4 hr and 1.0 mM for 2hr ($P < 0.05$)	At 1.0 mM Ni_3S_2: H_2O_2 ↑; O_2^-↑, lipid peroxidation ↑; cellular sulfhydryl ↓.
Guan *et al.*, 2007	$NiCl_2$	Human T-lymphocytes Jurkat cells in vitro: 0, 20, 40, 60, or 80 µg Ni/mL for 0, 6, 12, 24 hr.	Viability < 10% at 80 µg/mL-24 hr. After 6 hr Ni treatment NO increased from 0.9 (0) to 3.7 µM(80 µg Ni/mL)	Morphological changes and chromosome condensation indicative of apoptosis in Ni-treated cells, dose- and time-dependent.
Trombetta *et al.*, 2005	$NiCl_2$	Human oral epithelium model (RHE) from TR-146 cells exposed to 0, 0.05, 0.1, 0.3, 0.7, 1.0, 1.3, 3.3, or 7.6 mM Ni for 72 hr.	Cell viability reduced at >1.3 mM Ni, prostaglandin E2 and IL-6 increased at < 1.3 mM Ni.	No changes in IL-8 noted, GSH decreased but not significantly, GSSG increased at all concentrations, $P< 0.05$ at ≥ 0.7 mM Ni.
Davidson *et al.*, 2005	$^{63}NiCl_2$ $FeSO_4$	Human A549 cells in culture. Cells treated with 1 mM $NiCl_2$, 500 µM $FeSO_4$, 500 µM $FeSO_4$ + 500 µM $NiCl_2$; 500 µM $FeSO_4$ + 1 mM $NiCl_2$ for 24 hr.	Ni^{2+} taken up by cells via divalent metal ion transporter 1 (DMT1). Ni blocked transferrin-dependent and transferrin independent Fe binding and led to increased cellular ferritin accumulation.	Ni decreased binding of Von Hippel-Landau (VHL) protein to HIF-1α, indicating a decrease in prolyl hydroxylase activity, affecting HIF-1α signaling pathway.

TABLE 17. SUMMARY OF STUDIES WITH HUMAN CELLS *IN VITRO*

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Gazel *et al.*, 2008	$NiSO_4$	Human epidermal keratinocytes (RHE) exposed to 11 µM Ni SO_4 for 30 min or 6 hr. cDNA micro array analysis of gene expression.	134 genes affected, 97 induced, 37 suppressed. Apoptosis suppressed, cell cycle and protein synthesis induced.	Factors induced: VEGF, AREG, PGF, GDF-15, BST2. Factors suppressed IL-18, LGALS3, LITAF.
Ouyang et al., 2009	$NiCl_2$ NiS	Human lung carcinoma cells A549 in vitro. 0.25 to 1.0 mM $NiCl_2$, 0.25 to 2.0 µg NiS/cm^2.	Inhibition of cell growth and G1/G0 cell cycle arrest by $NiCl_2$ at 0.25 and 0.5 mM but not NiS at 2 µg/cm^2. $NiCl_2$ also caused a marked decrease in cyclin D1 protein, NiS effect was marginal.	$NiCl_2$ and NiS doses were equivalent in activation of NFκB and HIF-1α and induction of TNF-α and CAP43 gene expression.

Afridi et al. (2010) evaluated the association between trace toxic elements zinc (Zn), cadmium (Cd), nickel (Ni) and lead (Pb) in biological samples of scalp hair, blood, and urine of 457 smoker and nonsmoker hypertensive patients and 369 referent males, residents of Hyderabad, Pakistan. Of the hypertensive subjects 297 were smokers and 160 were nonsmokers. The metal concentrations were measured by atomic absorption spectroscopy. Mean values of Cd, Ni and Pb were significantly higher in hair, blood and urine of both smoker and nonsmoker hypertensive patients than in referents ($P < 0.001$). Zinc was lower in hair and blood but higher in urine of hypertensive subjects versus referents.

The levels of Ni in scalp hair samples of nonsmoker and smoker referents were lower 6.1 ± 1.5 and 7.85 ± 0.95 µg/g, respectively than in hypertensives 12.2 ± 1.48 and 15.7 ± 0.96 µg/g, respectively. The excretion of Ni in hypertensive subjects was higher than in referents ($P < 0.0002$). The amount of nickel in tobacco ranges from 0.64 to 1.15 mg/g and the higher Ni in hair of hypertensive smokers may be due in part to Ni inhaled from smoking. The reduced Zn and higher exposure to toxic metals as a result of smoking may be synergistic with other risk factors associated with hypertension. Chronic Toxicity to Experimental Animals

Studies of chronic toxicity in animals are summarized in Table 18. The principal target site identified in these studies is the lung.

Both chronic RELs for nickel and nickel compounds (except NiO) and for NiO were based on lung toxicity seen in NTP (1994c, $NiSO_4$) and NTP (1994a, NiO). These are large studies involving several interim evaluations and relatively large numbers of mice and rats of both sexes. The critical effect for the 8-hour REL was also based on lung toxicity seen in NTP (1994c). See sections 9.4 amd 9.5 for details of these derivations.

A two-year inhalation study of nickel oxide (MMAD = 2.8 µm, gsd = 1.87, density = 7.45 g/cm^3) in rats and mice (65 per sex, per group) was conducted by the National Toxicology Program (NTP, 1994a). In the first study, rats were exposed to 0, 0.62, 1.25, or 2.5 mg nickel oxide/m^3 (0, 0.5, 1.0, or 2.0 mg Ni/m^3) 6 hours/day, 5 days/week for 104 weeks. In addition to the carcinogenic effects of nickel oxide, a number of non-cancerous lesions were observed, particularly in the lungs. The incidence of inflammatory pigmentation in the alveoli was significantly greater in all exposed groups, compared to controls. The severity of the lesions reportedly increased with increasing exposure. Atypical alveolar hyperplasia was also seen in all exposed groups. Lymphoid hyperplasia in the bronchial lymph nodes was observed in males and females exposed to 1 mg Ni/m^3 or greater at 7 and 15 months and the incidence generally increased with increasing concentration at the end of the 2-year study. Females had an increased incidence of adrenal medullary hyperplasia at all exposures of nickel oxide. Body weights were significantly lower in the groups exposed to 2.0 mg Ni/m^3 for both sexes, and in males exposed to 1.0 mg Ni/m^3.

A companion study on nickel oxide in mice conducted by NTP showed similar lung inflammatory changes as seen in the rats, in addition to pigmentation of the alveolar region at all exposure concentrations, compared with controls (NTP, 1994a). The mice were exposed to 0, 1.0, 2.0, or 3.9 mg Ni/m^3. Bronchial lymph-node hyperplasia was also evident in all nickel-exposed animals. Body weights were slightly but significantly lower in the 3.9 mg Ni/m^3 group, compared with controls.

A continuous exposure of rats (20 - 40 per group) to 0, 60, or 200 μg Ni/m^3 as nickel oxide for two years resulted in severe pulmonary damage and premature mortality so that carcinogenesis could not be evaluated (Glaser *et al.*, 1986). Pulmonary alveolar proteinosis and septal fibrosis were observed in the animals exposed to nickel. Only one rat per group survived the nickel exposures to the end of the experiment.

The NTP (1994c) studied the chronic non-cancer and carcinogenic effects of nickel sulfate hexahydrate (MMAD = 2.50 μm, gsd = 2.38, density = 2.07 g/cm^3) on rats and mice. Rats were exposed to 0, 0.12, 0.25, or 0.5 mg $NiSO_4$/m^3 (0, 0.03, 0.06, or 0.11 mg Ni/m^3) for 6 hours/day, 5 days/week for 16 days to 104 weeks. Interim evaluations were made at 16 days and 13 weeks, and 7 and 15 months. Chronic effects of nickel exposure in rats included inflammatory lesions in the lung, lung macrophage hyperplasia, alveolar proteinosis, and fibrosis, in addition to bronchial lymph node hyperplasia and nasal epithelial atrophy. The above effects were seen at exposures of 0.06 mg Ni/m^3 or greater and at interim evaluations from 13 weeks. Histological details of these effects are quoted from the NTP report:

> "The incidences of chronic active inflammation, macrophage hyperplasia, alveolar proteinosis, and fibrosis were markedly increased in male and female rats exposed to 0.25 and 0.5 mg/m^3. Chronic active inflammation consisted of multifocal, minimal to mild accumulations of macrophages, neutrophils, and cell debris within alveolar spaces, frequently subjacent to pleural surfaces (Plate 1). Macrophage hyperplasia was of minimal to mild severity and consisted of macrophages (usually with abundant pale vacuolated cytoplasm) within alveolar spaces. The source of these macrophages was probably the intravascular pool of circulating monocytes. Proteinosis consisted of minimal to mild amounts of eosinophilic granular or globular homogeneous pale, acellular, proteinaceous material within alveolar spaces (Plate 2). Fibrosis included increased connective tissue and collagen involving alveolar septae within the parenchyma and subjacent to the pleura and focal solid sclerotic areas either subjacent to the pleura or at the tips of the lung lobes. Focal alveolar epithelial hyperplasia was slightly increased in 0.5 mg/m^3 female rats. Focal alveolar epithelial hyperplasia was a discrete cluster of of alveoli lined by low cuboidal or low columnar cells."

Mice were exposed to a similar regimen that included 0, 0.06, 0.11, and 0.22 mg Ni/m^3 as nickel sulfate hexahydrate (NTP, 1994c). Similar pulmonary, lymphatic and nasal changes were observed in the mice as with the rats. Fibrosis was not reported, but an increased incidence of interstitial infiltration and alveolar proteinosis were observed at exposures of 0.11 mg Ni/m^3 or greater. No clinical findings or hematological effects were observed, but body weights were significantly depressed in all groups of nickel-exposed female mice. The body weights of males were reduced only in the group exposed to 0.22 mg Ni/m^3.

A two-year study on the effects of nickel subsulfide (MMAD = 2.54 µm, gsd = 2.1, density = 5.82 g/cm^3) in rats and mice was conducted by NTP (1994b). Rats (52-53 per sex per group) were exposed to 0, 0.15, or 1 mg Ni_3S_2/m^3 (0, 0.11, or 0.73 mg Ni/m^3) for 6 hours/day, 5 days/week for 104 weeks. Body weights were lowered in rats exposed to 0.73 mg Ni/m^3 compared with controls. Lung inflammation, alveolar hyperplasia, macrophage hyperplasia, and pulmonary fibrosis were observed with a significantly increased incidence at both nickel concentrations. Female rats exposed to nickel had significantly increased adrenal medullary hyperplasia. In addition to the pulmonary lesions, nasal inflammation and olfactory epithelial atrophy were observed in both sexes exposed to 0.73 mg Ni/m^3.

In the second phase of the NTP study (NTP, 1994b), mice were exposed to 0, 0.6, or 1.2 mg Ni_3S_2/m^3 (0, 0.44, or 0.88 mg Ni/m^3) for 6 hours/day, 5 days/week for 104 weeks. The same pathological lesions were observed in the lung and nasal passages as in the rats in the above study. These lesions were evident at both the 0.44 mg Ni/m^3 and the 0.88 mg Ni/m^3 concentrations. The adrenal medullary hyperplasia seen in female rats was not observed in the mice.

It should be noted that although the non-neoplastic lung effects seen in the animal studies discussed above were relatively mild similar effects in humans may be serious or even fatal. For example pulmonary alveolar proteinosis (PAP) is a rare clinical condition first described by Rosen et al. (1958) with some 410 cases reported through 2002 (Seymour and Presneill, 2002). The syndrome is characterized by alveolar accumulation of surfactant components with minimal interstitial inflammation or fibrosis. PAP has a variable clinical course from spontaneous resolution to death with pneumonia or respiratory failure (Seymour and Presneill, 2002). Kitamura et al. (1999) have identified idiopathic pulmonary alveolar proteinosis (I-PAP) with an autoimmune disease. Neutralizing antibody against granulocyte/macrophage colony stimulating factor (GM-CSF) was found in all specimens of BALF from 11 I-PAP patients but not in 2 secondary PAP patients, 53 normal subjects and 14 patients with other lung diseases. A possible immunological mechanism in human alveolar proteinosis is consistent with the nickel-induced immunotoxicity and pneumotoxicity seen in the rodent studies.

An exposure of rats to either 0 or 0.97 mg Ni_3S_2/m^3 (0 or 0.71 mg Ni/m^3) for 6 hours/day, 5 days/week for 78-80 weeks resulted in decreased body weight, hyperplasia, metaplasia, and neoplasia in the lungs (Ottolenghi *et al.,* 1974).

Rats and mice (10 per group) were exposed to nickel sulfate, nickel subsulfide, or nickel oxide six hours/day, five days/week, for 13 weeks (Dunnick *et al.*, 1989). Exposure-related increases in lung weight and histological lesions were observed in both species for all nickel exposures. Histological lesions included inflammatory changes, fibrosis, and alveolar macrophage hyperplasia. Nasal lesions were also observed in animals treated with nickel sulfate or nickel subsulfide. Lung weight changes were observed at exposures of 0.05 mg Ni/m^3 or greater in female rats. Macrophage hyperplasia in the alveolar region was observed at concentrations as low as 0.02 mg Ni/m^3. Additional inflammatory lesions in the lungs were observed at 0.1 mg Ni/m^3.

Early studies on the chronic non-cancer effects of metallic nickel dust were complicated by early mortality and cancer in guinea pigs and rats (Hueper, 1958).

Tanaka et al. (1988) exposed male Wistar rats (five/dose group) to green NiO aerosols (MMAD = 0.6 µm) for 7 hr/day, 5 days/week for up to 12 months. The average exposure concentration was either 0.3 mg/m^3 or 1.2 mg/m^3. For histopathological examination, rats were sacrificed at 3, 6, and 12 months of exposure and 8 months following a 12-month exposure. The nickel content of rat lungs was as high as 2.6 mg and 0.6 mg after 12 months exposure at the high and low concentrations, respectively. Higher incidence of lesions in exposed compared to control animals was seen for pneumonia in all exposure durations at low and/or high exposure concentrations and for bronchiolar metaplasia and adenomatosis for 12 months exposure at the low and/or high exposure concentrations.

Obone et al. (1999) evaluated the effects of $NiSO_4 \cdot 6H_2O$ (0, 44.7, 111.75, or 223.5 mg Ni/L) in drinking water of male Sprague-Dawley rats exposed for 13 weeks. Alkaline phosphatase activity in bronchoalveolar lavage fluid (BALF) was significantly decreased at all dose levels compared to the control animals (8/dose group, $P < 0.05$). No significant changes were seen in the activities of alkaline phosphatase, acid phosphatase, or lactate dehydrogenase in lung tissues after 13 weeks exposure. However, a significant increase in BALF proteins was seen at 111.8 and 223.5 mg Ni/L $NiSO_4$ in drinking water ($P<0.05$).

McDowell et al. (2000) exposed C57BL/6 mice to $NiSO_4 \cdot 6H_2O$ aerosol in a steel inhalation chamber. The particulate aerosol had a MMAD of 0.22 µm and a gsd of 1.85 with a chamber concentration of 110 ± 26 $µg/m^3$. The mice were exposed for 0 (control), 3, 8, 24, 48, or 96 hr before sacrifice and assessment of the progression of lung injury by microarray analysis with murine complementary DNAs. Lung polyadenylated mRNA was isolated, reverse transcribed, and fluorescently labeled. Samples from exposed mice (Cy5 labeled) were

competitively hybridized against samples from unexposed, control mice (Cy3 labeled) to microarrays containing 8734 murine cDNAs. Of the > 8700 genes analyzed, 17 were differentially expressed at 3 hr and 255 at 96 hr. The overall pattern of gene expression with increasing lung injury was indicative of oxidative stress, hypoxia, cell proliferation and extracellular matrix repair, followed by a decrease in surfactant proteins.

Oller et al. (2008) evaluated the effects of inhaled nickel metal powder in a chronic study in Wistar rats. The animals (50/sex/dose group) were exposed by whole-body inhalation to 0, 0.1, 0.4 and 1.0 mg Ni/m^3 nickel metal powder (MMAD = 1.8 µm, gsd = 2.4) for six hr/day, five days/week for up to 24 months. High mortality in the 1.0 mg Ni/m^3 dose group resulted in earlier termination of exposures in this group. No NOAEL was observed. Non-respiratory treatment-related histopathological lesions were a granular brown pigment in the kidneys, extramedullary hematopoiesis in the spleen and hypercellularity of sternum and femoral bone marrows, all in both sexes. Respiratory tract lesions included alveolar proteinosis, alveolar histiocytosis, chronic inflammation, bronchiolar-alveolar hyperplasia and bronchial lymph node infiltrate. Nearly all of these effects exhibited dose-responses in both sexes.

A benchmark dose analysis of the data in Oller et al. (2008, their Table 5B) for the sum of moderate and severe incidences of respiratory tract lesions is summarized in Table 19. $BMDL_{05}$ values ranged from 1 to 12 µg Ni/m^3. A similar analysis of non-respiratory tract lesions (not shown) gave $BMDL_{05}$ values ranging from 8 µg Ni/m^3 (female spleen) to 27 µg Ni/m^3 (male kidney). An average dosimetric adjustment factor (DAF) of 0.395 was derived from Multipath Particle Deposition (MPPD) model (v.2) airway deposition calculations for the rat and average of human age groups (3 months to 21 years) exposed continuously to 0.1 mg Ni/m^3. The human equivalent concentration (HEC) is calculated as Rat Concentration x DAF.

At the 78-week evaluation significant increases ($P < 0.01$) were seen in mean red blood cell count (RBC), hemoglobin levels (Hb) and hematocrit values (HCT) at 0.1 and 0.4 mg Ni/m^3 in males and at 0.4 mg Ni/m^3 in females. These findings were suggested by the study authors as possibly resulting from hypoxia secondary to lung injury, however, they note that similar increases were seen in another study of oral nickel sulfate hexahydrate exposure when no lung injury was observed (Heim et al., 2007). Also, a direct effect of nickel on gene expression of erythropoietin has been reported (e.g. Salnikow et al. 2000). A continuous benchmark dose analysis was conducted on the blood effects data (Oller et al., 2008, Table 3). For male rats the $BMDL_{1SD}$ values for RBC, Hb and HCT averaged 1.9 µg/m^3 and, for females, averaged 3.1 µg/m^3. All the individual data sets were well fit visually by the polynomial model although there were insufficient degrees of freedom to do a fitness test (data not shown).

Ogami et al. (2009) evaluated the toxicity of different sizes of nickel oxide particles following intratracheal instillation in rats. Two sizes of NiO were used: a

fine sized NiO with a median diameter of 0.8 µm (nNiOm), and micrometer sized NiO with a median diameter of 4.8 µm (NiO). The particle distributions were bimodal (NiO) or trimodal (nNiOm) with lower or higher peaks than the median, respectively. The pathological effects were compared with crystalline silica (SiO_2, geometric mean diameter 1.6 µm, gsd = 2.0) and TiO_2 (geometric mean diameter 1.5 µm, gsd = 1.8) particles. The particles (2.0 mg) were suspended in 0.4 mL saline and instilled into Wistar rats (10 weeks old, 25 animals/group) along with a saline only control group. Animals were sacrificed at three days, one week, one month, three and six months after particle instillation. At autopsy 50 mL of bronchoalveolar lavage fluid (BALF) were obtained by injecting saline into the right lung of each animal. Total cells and polymorphonuclear leukocytes (PMN) in BALF were recovered and counted.

The number of total cells in BALF in the nNiOm group was significantly higher than the control and the other particle treatments at all time periods except SiO_2 at 6 mo when comparable values were seen (all $P < 0.01$). NiO showed a gradual increase in total cells with a significant difference at 6 mo ($P < 0.05$). The PMN percentages in BALF were significantly higher than controls for nNiOm and SiO_2 for all time periods, although nNiOm decreased over time (40% to10%) while SiO_2 increased (40% to 65%) (all $P < 0.01$). TiO_2 also showed a significant increase at three days only (25%, $P < 0.05$). The inflammation area rate by the point counting method showed a gradual increase for nNiOm with significant increases vs. controls at all time points with a peak at 3 mo ($P < 0.01$). SiO_2 also increased gradually showing the highest value at 6 mo ($P < 0.01$). No significant differences were seen for the NiO or TiO_2 groups. The results suggest that submicrometer nano-nickel oxide is significantly more toxic to the lung than micrometer-sized nickel oxide. The observed effects were similar in qualitative and quantitative respects to those caused by similar administration of crystalline silica but apparently less persistent.

Lu et al. (2009a) evaluated several short-term in vitro assays for predicting the potential of metal oxide nanoparticles including NiO to cause pulmonary inflammation. The assays were intrinsic free radical generation, extracellular oxidative activity, cytotoxicity to lung epithelial cells, hemolysis, and inflammation in rat lungs via intratracheal instillation. Twelve nanoparticle species (NPs) ranging from 2-4 nm (Al_2O_3, alumina 1) to 300 nm (Alumina 3) were included in the study. The nickel oxide was characterized as 10-20 nm in size, 92 m^2/g in surface area, and 5.4 mg/500 cm^2 in mass (their Table 1, we calculate as 0.54 mg/500 cm^2). Intrinsic free radical generation (IFR) was assessed by electron paramagnetic resonance with surface area doses of 1,500 and 3,000 cm^2/mL. Only NiO, CeO_2, Co_3O_4 and carbon black (CB) showed significant increases in IFR over control ($P < 0.05$). Oxidative potential was measured with a cell-free dichlorofluorescein assay and significant fluorescence intensity over control was observed only for NiO, Co_3O_4, and CB ($P< 0.05$). Cytotoxicity was assessed by incubating alveolar A549 cells with NPs at different surface area doses (9.4 – 300 cm^2/mL) for 24 hr and measuring lactate dehydrogenase (LDH) release in cell lysates. There were clear positive LDH dose-responses for NiO, Co_3O_4 and

CB. Linear dose-dependent hemolytic activity in fresh human venous blood was observed for NiO, CeO_2, and alumina 2. Lung inflammation in vivo was assessed by intratracheal instillation of NPs at 500 cm^2/mL in rats and measuring polymorphonuclear neutrophil (PMN) numbers in BALF 24 hr after instillation. Only NiO and alumina 2 were significantly inflammogenic at the dose employed. Of the assays evaluated, only blood hemolysis gave a correct prediction of lung inflammatory activity for 12/13 NPs (CeO_2, false positive). NiO gave the strongest positive response in all five assays and gave the largest inflammation response *in vivo* (total PMN).

TABLE 18. SUMMARY OF CHRONIC NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Tanaka et al., 1988	NiO (green) aerosols MMAD = 0.6 µm	Male Wistar rats 5/dose group: 0, 0.3, 1.2 mg/m^3, 7 hr/d, 5 d/wk, 3, 6, 12 mo.	Ni content of organs and lung histopathology. Lung Ni 0.6 and 2.6 mg, respectively. Lung lesions at 12 mo: pneumonia at 0.3 mg/m^3; bronchitis with atypical gland hyperplasia, bronchiolar metaplasia, adenomatosis at 1.2 mg/m^3.	After an 8 mo clearance period following a 12 mo exposure, no lung lesions were observed in the low dose group. Lower incidences of pneumonia, bronchitis and bronchiolar metaplasia were seen at the high dose. No adenomatosis was seen in this group.
NTP, 1994a	NiO MMAD = 2.8 µm, gsd = 1.87, density = 7.45 g/cm^3	2-Year Inhalation study in rats, 65/sex/dose group 0, 0.62, 1.25, 2.5 mg NiO/m^3 0, 0.5, 1.0, 2.0 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung lesions: dose-dependent atypical alveolar epithelial hyperplasia in males and females. Chronic inflammation of the lung in most animals exposed ≥ 7 mo.	Pigmentation in the alveoli of exposed rats. Pigmentation in bronchial lymph nodes similar to lung except 0.62 mg/m^3 animals at 7 mo.
NTP, 1994a	NiO MMAD = 2.8 µm, gsd = 1.87, density = 7.45 g/cm^3	2-Year Inhalation study in mice 65/sex/dose group: 0, 1.25, 2.5, or 5.0 mg NiO/m^3, 0, 1.0, 2.0, 3.9 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung lesions: Chronic inflammation increased with exposure in males and females at ≥ 7mo. At 2 yr incidences of chronic inflammation, alveolar epithelial hyperplasia and proteinosis most severe in high dose mice.	Pigment in the lungs increased with exposure conc. at ≥ 7 mo. Lymphoid hyperplasia dose- and time-related increases in males and females. Lung Ni burdens at 15 mo 331 to 2258 µg/g lung (dose- and time-dependent)
NTP, 1994b	Ni_3S_2 MMAD = 2.54µm, gsd = 2.1, density = 5.82 g/cm^3	2-Year Inhalation study in rats 52-53/sex/dose group: 0, 0.15, or 1.0 mg Ni_3S_2/m^3, 0, 0.11 or 0.73 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung lesions: inflammation, alveolar hyperplasia, macrophage hyperplasia, pulmonary fibrosis. Body weights lowered at high dose.	Females had significantly increased adrenal medullary hyperplasia. Nasal inflammation and olfactory epithelial atrophy seen in both sexes at 0.73 mg Ni/m^3.

TABLE 18. SUMMARY OF CHRONIC NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
NTP, 1994b	Ni_3S_2 MMAD = 2.54µm, gsd = 2.1, density = 5.82 g/cm^3	2-Year Inhalation study in mice, 52-53/sex/dose group: 0, 0.6, or 1.2 mg Ni_3S_2/m^3, 0, 0.44 or 0.88 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung lesions: inflammation, alveolar hyperplasia, macrophage hyperplasia, pulmonary fibrosis.	Nasal inflammation and olfactory epithelial atrophy seen in both sexes at 0.88 mg Ni/m^3.
NTP, 1994c	$NiSO_4$•$6H_2O$ MMAD = 2.50µm, gsd = 2.38, density = 2.07 g/cm^3	2-Year Inhalation study in rats 52-53/sex/dose group: 0, 0.12, 0.25 or 0.5 mg $NiSO_4$/m^3, 0, 0.03, 0.06 or 0.11 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung, lymph nodes and nasal lesions: active pulmonary inflammation, macrophage hyperplasia, alveolar proteinosis, fibrosis, lymph node hyperplasia, olfactory epithelial atrophy.	
NTP, 1994c	$NiSO_4$•$6H_2O$ MMAD = 2.50µm, gsd = 2.38, density = 2.07 g/cm^3	2-Year Inhalation study in mice 60-61/sex/dose group: 0, 0.25, 0.5 or 1.0 mg $NiSO_4$/m^3, 0, 0.06, 0.11 or 0.22 mg Ni/m^3, 6hr/d, 5d/wk, 104 weeks.	Lung lesions: Chronic active inflammation, bronchialization, macrophage hyperplasia, interstitial infiltration, alveolar proteinosis, at high dose in both sexes and in females at 0.11 mg Ni/m^3.	
Glaser et al., 1986	Ni (form and size unspecified)	2-Year Inhalation Study in rats 20-40/dose group: continuous exposure 0, 60, 200 µg Ni/m^3.	Severe pulmonary damage and mortality. Pulmonary alveolar proteinosis, septal fibrosis.	Only 1 Ni-exposed rat survived for 2 yr.

TABLE 18. SUMMARY OF CHRONIC NICKEL TOXICITY IN ANIMALS

Study	Compound	System	Toxic Endpoint	Comments / other effects observed.
Obone *et al*., 1999	$NiSO_4 \cdot 6H_2O$	13-week drinking water study in rats 8 rats /dose group: 0, 0.02, 0.05, 0.1% or 0, 44.7, 111.75, 223.5 mg Ni/L dw.	Alkaline phosphatase activity in BALF significantly decreased at all dose levels ($P < 0.05$).	Blood: total proteins ↓; plasma albumins ↓; globulins ↓; plasma glutamate-pyruvate transaminase ↓ all $P < 0.05$ at high dose.
Oller et al., 2008	Ni metal powder MMAD = 1.8µm gsd = 2.4	2-Year inhalation study in rats 50/sex/dose group: 0, 0.1, 0.4, 1.0 mg Ni/m^3, 6hr/d, 5 d/wk, 24 mo	Respiratory tract lesions: alveolar proteinosis, alveolar histiocytosis, chronic inflammation, bronchial alveolar hyperplasia, bronchial lymph node infiltrate, most effects in both sexes.	High mortality at 1 mg Ni/m^3, granular brown pigment in kidneys, extramedullary hematopoiesis in spleen, hypercellularity in sternum and femoral bone marrows.
Ogami et al., 2009	NiO 0.8µm MMAD (nNiOm) 4.8 µm MMAD (NiO)	Intratracheal instillation in rats: 5/dose group examined at 3d, 1 wk, 1 mo, 3 mo, 6 mo post treatment, single 2 mg doses.	BALF: significantly increased total cells, % PMN and inflammation at all time points with nNiOm vs. controls ($P < 0.01$) and for total cells at 6 mo with NiO ($P < 0.05$).	

Note: AM = alveolar macrophages; MMAD = mass median aerodynamic diameter; BALF = bronchial alveolar lavage fluid; PMN = polymorphonuclear lymphocytes; ↑ = increase; ↓ = decrease.

TABLE 19. BENCHMARK DOSE ANALYSIS OF RESPIRATORY TRACT LESIONS INDUCED BY NICKEL METAL INHALATION IN WISTAR RATS (DATA OF OLLER ET AL. 2008).*

Lung Lesion Observed	Incidence at 0, 0.1, 0.4 mg/m^3	X^2	P	BMD_{05} mg/m^3	$BMDL_{05}$ mg/m^3	$BMDL_{05}$ $\mu g/m^3$ Continuous*
Male						
Proteinosis	0/50, 19/50, 40/50	0.35	0.83	0.012	0.0095	1.7
Histiocytosis	0/50, 7/50, 17/50	0.69	0.71	0.045	0.0326	5.8
Inflammation	0/50, 1/50, 22/50	0.34	0.84	0.12	0.07	12.5
Hyperplasia	1/50, 3/50, 9/50	0	1.0	0.12	0.069	12.3
Lymph node infiltrate	0/34, 4/37, 9/42	1.16	0.56	0.073	0.0475	8.5
Female						
Proteinosis	0/50, 22/50, 38/54	0	1.0	0.0077	0.0053	0.95
Inflammation	0/50, 10/50, 23/54	0	1.0	0.021	0.012	2.1
Lymph node infiltrate	0/39, 4/42, 9/44	0.88	0.64	0.078	0.051	9.1

*Note: All dose responses fit with the multistage-quadratic model of BMDS v 1.4.1c; values are for rats adjusted for continuous exposure (values multiplied by 6/24 x 5/7) but not for human equivalent concentrations. X^2 and P are the goodness of fit statistics. An acceptable fit has a P value ≥ 0.1)

Morimoto et al. (1995) studied the effects of nickel oxide (green) (MMAD = 2.7 µm, gsd = 2.3) on the production of tumor necrosis factor (TNF) by alveolar macrophages of rats exposed in vitro and in vivo. For in vivo exposure five male Wistar rats (nine weeks old) were exposed to 11.7 ± 2.0 mg NiO/m^3 for 8 hr/day, 5days/week, for 4 weeks along with five unexposed control animals. Bronchoalveolar lavage was performed and recovered alveolar macrophages were assayed for TNF production. Nickel oxide exposure produced a three-fold higher concentration of TNF produced by macrophages from exposed animals compared to controls ($P < 0.01$). In addition acid phosphatase and lactate dehydrogenase (LDH) release from macrophages were also significantly greater ($P<0.01$) than controls, both indicators of cytotoxicity.

Shiao et al. (1998) investigated the effects of nickel acetate on cell cycle, apoptosis and p53 expression in Chinese hamster ovary (CHO) cells in vitro. CHO cells were grown for 72 hours in medium containing 0, 40, 80, 160, 240, 320, 480, or 640 µM nickel(II) acetate. DNA fragmentation, representative of

apoptosis, was examined by gel electrophoresis. The distribution of cells in various stages of the cell cycle was determined by DNA flow cytometry and p53 expression by the Western blotting technique. DNA fragmentation was seen at nickel concentrations ≥ 160 µM. The proportion of cells at S-phase declined in a Ni^{2+} concentration-dependent manner above 160 µM (33% to 12%). The decline was accompanied by an increase in the proportion of G_2/M phase cells (9% to 26%). Expression of p53 was not affected by nickel exposure. The authors conclude that these cellular responses were most likely induced by a common effector(s) that cause G_2/M arrest and concurrent apoptosis. P53 protein is apparently not responsible for the effects seen but nickel(II) up-regulates other proteins, which may be involved.

Gurley et al. (1983) studied the toxicity to CHO cells in vitro of particulate Ni_5As_2, one of a number of nickel arsenides formed during oil shale retorting. The Ni_5As_2 particles (examined by electron microscopy) ranged in size from 0.14 to 9.40 µm with 1.8% >2µm, 75% 0.23 to 1.0 µm, and 94% 0.18 to 1.40µm. The insoluble Ni_5As_2 powder was suspended in culture medium with the cells at concentrations of 0, 10, 25, 50, and 100 µM Ni_5As_2 (assuming complete solubility of the powder). At 10 µM Ni_5As_2 the growth rate doubling time was increased from 16.5 hr (control) to 40 hr. At 100 µM Ni_5As_2 growth was completely inhibited. Cell cycle analysis showed that at Ni_5As_2 concentrations ≥ 50µM cells accumulated in the G2 +M phases. Cells treated for 24 hr with 25 µM Ni_5As_2 and transferred to nickel arsenide free medium completely recovered viability but grew at a slower than control rate. Cells similarly treated at 50 or 75 µM nickel arsenide had survivals of only 61% and 25%, respectively.

Takahashi et al. (1999) studied the cytotoxicity of two types of NiO (black and green) and five intermediate types prepared by calcinations of black NiO at 600-1000ºC. The NiO forms varied in Ni and O content, color and X-ray diffractometric pattern. They also varied in water solubility from NiO(B) at 6-7µg/mL to 1-3 µg/mL for calcined forms and 0.5-1.5 for NiO(G). Cytotoxicity was assessed with rat alveolar macrophages obtained from female Sprague-Dawley rats aged 12-16 weeks and CHO cells cultured in vitro. The viability of rat alveolar macrophages exposed to NiO at 800 µg/mL for 18, 42 and 72 hr showed the greatest toxicity for NiO(B) followed by NiO(600ºC) and NiO(800ºC). CHO cells exposed to 50, 100, or 200 µg/mL of each nickel oxide for 24 hr exhibited a dose and compound related decrease in cell proliferation from NiO(B) to NiO(G) with the calcined forms in order of temperature. The authors conclude that water solubility, which is inversely related to calcination temperature, modulates the cytotoxicity of NiO particles.

Clemens and Landolph (2003) evaluated the cytotoxicity and cell transformation of mouse embryo cells by samples of nickel refinery dust containing different concentrations of nickel arsenide and pure nickel arsenide. Mouse embryo C3H/T101/2 cells (200/dose) were treated with 0, 0.5, 1.0, 2.5, 5.0 or 7.5 µg/mL. The dust samples were composed largely of NiO and $Cu_2Ni_8O_{10}$ with 25% Ni_5As_2 in dust sample 1 and 2.5% Ni_5As_2 in dust sample 2. After treatment for 48 hr the

cells were recovered and assayed for survival. For each treatment the average survival fraction was plotted to determine the 50 percent lethal concentration (LC_{50}) value. Dust sample 1 and nickel arsenide gave an identical LC_{50} value of 2.4 µg/mL, whereas dust sample 2 with less Ni_5As_2 gave a slightly lower LC_{50} of 1.7 µg/mL. Although the dust sample appeared to be more cytotoxic than the other samples, the reverse was true in parallel chromosome aberration and cell transformation assays.

Nickel chloride induced lactate dehydrogenase (LDH) release and lipid peroxidation (LPO) in rat renal cortical slices in vitro in a concentration- (0 to 2.0 mM) and time- (0 to 4 hr) dependent manner (Chakrabarti and Bai, 1999). Both $NiCl_2$-induced LDH release and LPO were significantly prevented by glutathione and dithiothreitol, suggesting that $NiCl_2$-induced renal cell injury is partially dependent on thiols. Superoxide dismutase partially reduced the $NiCl_2$-induced LDH release without affecting LPO and glutathione, whereas catalase did not affect such LDH release and LPO. Dimethylthiourea and DMSO completely prevented $NiCl_2$-induced LPO, but only partially reduced LDH release. Deferoxamine prevented $NiCl_2$-induced renal cell injury without affecting LPO and without significantly reducing Ni^{2+} uptake by the renal cortex, suggesting that nickel chelation is not important in prevention of cell injury. $NiCl_2$-induced loss of cellular glutathione was significantly prevented by thiols and deferoxamine, but not by superoxide dismutase or dimethylthiourea. The results suggest that LPO was not related to $NiCl_2$-induced lethal renal cell injury. Renal cell injury was more likely the result of the induction of the Fenton reaction, generating hydroxyl radicals.

The effects of nickel chloride on the expression patterns of stress proteins in rat organs and human and monkey cell lines was studied by Hfaiedh et al. (2005). Three-month old female Wistar rats were injected i.p. with 4 mg $NiCl_2$/kg bw for 1, 3, 5, or 10 days. Rat kidneys, liver and ovaries were cut into small pieces, sonicated briefly in lysis buffer, and 5000 x g (30 min) supernatants collected and frozen until use. Relative protein expression in total organ extracts was measured for three proteins, namely, cytosolic Hsp72 and Hsp73, and the reticulum-associated GRP94. In kidney, nickel induced significant increases ($P < 0.01$) in GRP96 and Hsp73 at ≥ 3 days of treatment (GRP96) and at 3 and 5 days (Hsp73). Hsp72 was significantly suppressed at all days of treatment ($P < 0.05$). Few effects were noted in liver or ovary. Dietary restriction (1 month 50%) did not significantly alter the results. The authors infer that Ni-induced GRP94 over-expression in kidney and in cell lines could be mediated by hypoxic stress at the cellular level.

The effects of nickel ions on reductive amination and oxidative deamination activities of bovine liver glutamate dehydrogenase (GDH) were studied kinetically by UV spectroscopy (Ghobadi et al., 2007). The fact that Ni^{2+} ions have the capacity to enhance binding of NADH (reduced nicotinamide adenine dinucleotide) to the enzyme was confirmed by an electrochemical method. Ni^{2+} decreased the K_m for NADH from 0.083 mM (control) to 0.053 mM at 200 µM

$NiCl_2$. The NADPH (reduced nicotinamide adenine dinucleotide phosphate) K_m was similarly decreased (0.077 to 0.036 mM, respectively). Lineweaver-Burk plots with respect to alpha-ketoglutarate and ammonium ions indicated substrate and competitive inhibition patterns in the presence of nickel ion, respectively. Adenosine diphosphate (ADP) at 0.2 mM protected inhibition caused by nickel. The observations are explained by the authors in terms of formation of a nickel-NADH complex with a higher affinity for binding to the regulatory site in GDH, than in the absence of nickel. (The K_m is the Michaelis or affinity constant for Michaelis-Menten enzyme kinetics defined by the rectangular hyperbola, reaction velocity $V = V_{max} \times S/(K_m + S)$ where V_{max} is the maximum reaction rate (e.g., mg/hr), S is the substrate concentration (mg/L) and K_m is the concentration at $V_{max}/2$.)

Lu et al. (2009b) studied the mechanisms of cytotoxicity of Ni(II) ions based on gene expression profiles. Mouse fibroblast cells (L-929) were cultured in medium with 0, 100, 200, 300, 400, or 500 µM $NiCl_2 \cdot 6H_2O$ for 24, 48, or 72 hours. Cytotoxicity was assessed by methylthiazoltetrazolium (MTT) assay. Ni-induced cytotoxicity was dose- and time-dependent. After 72 hr, cell viability was reduced from 100% (control) to 36.1% at 500 µM. Gene expression was assessed by cDNA microarray analysis of cells treated with 200 µM Ni(II) for 24, 48, or 72 hr. Twenty up-regulated and 19 down-regulated genes were differentially expressed in all three exposure periods. Gene ontology analysis showed that the Ni-affected genes represented biological processes (e.g., development- 7%, cellular process-36%, physiological process-38%), molecular function (e.g., binding-52%, catalytic activity-24%, signal transducer-6%), and cellular components (cell-48%, protein complex-8%, organelle-36%). Specifically the down-regulation of the *Hsp90aa1* gene affected the processes associated with cell adhesion, cell morphogenesis, regulation of cell proliferation, and regulation of cell migration. Overall the results showed broad effects on gene expression even when no obvious cytotoxicity was evident (i.e., 91.5% viability at 200 µM Ni(II), 24 hr). Ni(II) has extensive effects on cells by inhibiting cell proliferation and differentiation, through inducing cell apoptosis, affecting cell development and influencing cholesterol metabolism.

Rubanyi and Kovach (1980) observed the effects of $NiCl_2$ on contractility, NADH-fluorescence, O_2-consumption and total coronary resistance (TCR) of isolated perfused rat hearts. Ni^{2+} at 1 mM abolished contractability, reduced O_2 consumption, increased TCR and caused a biphasic NADH-fluorescence response. Inhibition of cardiac contractability was dose-dependent in the Ni^{2+} concentration range 10^{-7} to 10^{-3} M, in the presence of 1.3 mM Ca^{2+}. The amplitude of TCR elevation reached its maximum at 10^{-6} M Ni^{2+}. Koller et al. (1982) reported Ni-induced coronary vasoconstriction in dog heart in situ in the presence of the selective Ca-antagonist verapamil. Verapamil abolished the coronary blood flow (CBF) and basal conductance (BC) decreasing the effect of low doses of Ni^{2+} (0.02-0.2 mg/kg). Higher doses of $NiCl_2$ increased CBF and BC in the presence of verapamil. The authors conclude that trace amounts of exogenous $NiCl_2$ induce coronary vasoconstriction in the dog heart in situ by enhancing Ca^{2+} influx into vascular smooth muscle cells.

Golovko et al. (2003) studied the possible role of the Na-Ca exchange (NCX) in arrhythmogenesis in isolated rat heart atrial preparations using microelectrodes. In preparations with low beating frequency (~48/min) a partial inhibition of NCX by 0.3 mM Ni(II) was observed to cause a single early afterdepolarization (EAD) at 15 min. In preparations with a high beating frequency (~84/min) 0.3 mM Ni(II) did not cause EAD, but at a higher concentration of 0.5 mM a single EAD was observed. The authors conclude that Ca2+ overload due to partial block of NCX may contribute to the development of atrial tachyarrhythmias.

Wellenius et al. (2002) studied the effects of Boston residual oil fly ash (ROFA, 3 mg/m^3) in a rat model for myocardial infarction. The ROFA was reported to produce arrhythmias, ECG abnormalities, and decreases in heart rate variability (HRV). Increased arrhythmias, decreased heart rates, and hypothermia were seen in monocrotaline-treated Sprague-Dawley rats exposed to 15 mg/m^3 ROFA (Watkinson et al., 2000). The same concentration of ROFA in spontaneously hypertensive (SH) rats caused cardiomyopathy, monocytic cell infiltration, and increased expression of cardiac cytokines IL-6 and TGF-β. ROFA-exposed SH rats also exhibited ECG abnormalities compared to air-exposed rats. Inhalation of 50 µg/m^3 of oxides or sulfates of Ni or V for 3 hr/d for 3 consecutive days in old dogs with preexisting cardiac abnormalities showed no acute changes in cardiovascular function (Muggenburg et al. 2003). However, in a different study $NiSO_4$ (>1.2 mg/m^3, 6hr/d, for 4 days) caused delayed bradycardia, hypothermia, and arrhythmogenesis in rats (Campen et al., 2001).

Lippmann et al. (2009) evaluated the cardiovascular effects of nickel in ambient air in a mouse model of atherosclerosis. Six week old *ApoE*$^{-/-}$ mice were implanted with electrocardiograph (ECG) transmitters three weeks prior to the initiation of exposure. Ten-second ECG, heart rate (HR), activity, and body temperature were sampled every 5 minutes. Six mice were exposed to 10 times concentrated air particulate matter (CAPs, with 43 to 174 ng Ni/m^3) or filtered air for 6 hr/d, 5 days/ week, for 6 months. Six control mice were sham exposed to the same protocol. To estimate the effects of exposure on HR and heart rate

variability (HRV), generalized additive models (GAMs) were used to fit the nonlinear trends of chronic and acute effects. Of the four metals evaluated in the GAM for acute HR effect only nickel was a significant CAP component (β = 3.321 ± 1.628SE, P = 0.041). Similarly for acute HRV only nickel was significant (β = 0.044 ± 0.016SE, P = 0.005). The authors note the paucity of mechanistic studies on the cardiovascular effects of Ni but also note nickel's effects on signaling pathways that may have an adverse cumulative effect on vascular function.

Kang et al. (2011) found that inhaled nickel hydroxide nanoparticles exacerbated atherosclerosis in hyperlipidemic, apoprotein E-deficient (ApoE-/-) mice exposed to 0 or 79 μg Ni/m^3, via whole body inhalation, for 5 hr/day, for either 1 week or 5 months. The nanoparticles of $Ni(OH)_2$ induced significant oxidative stress and inflammation in the pulmonary and extrapulmonary regions. These effects were indicated by up-regulated levels of antioxidant enzyme and inflammatory cytokine genes, increased mitochondrial DNA damage in the aorta, significant signs of inflammation in BALF, and alterations in lung histopathology. After 5 month's exposure the nickel nanoparticles exacerbated the progression of atherosclerosis in the ApoE-/- mouse model.

8 Immunotoxicity

8.1 Immunotoxicity Summary

Contact dermatitis is a widespread disease and, in the western hemisphere, nickel sensitization is the most common single cause of contact allergy (Lisby, 1999b). The mechanism underlying nickel-induced allergy is still incompletely understood. As noted in the papers described below most research has focused on T cell activation in Ni-allergic patients. Systemic contact dermatitis in humans has been used to study inflammatory skin disease occasionally seen as a flare-up of previous dermatitis or as de novo dermatitis when sensitized individuals are exposed to the hapten orally, transcutaneously, intravenously or by inhalation. Studies of immunological mechanism of Ni-induced disease have tried to determine if effects are elicited primarily via activation of CD4+ and/or CD8+ T cells of the type 1 or type 2 or even type 0 cytokine profile subsets (Jensen et al., 2004). The likely involvement of MAPK and possibly other signaling pathways in the disease process has added another level of complexity. The potential role of nickel in airborne particulate matter (PM2.5)-induced human respiratory disease may also have an immunological mechanism.

8.2 Human Immunotoxicity Studies

Dermal exposure to nickel and nickel alloys has long been known to cause dermatitis in both nickel workers and the general population. A number of studies indicated that oral exposure of nickel could aggravate nickel dermatitis in people who are sensitive to nickel. Christensen and Möller (1975) found that oral administration of nickel (approximately 5 mg) in diet worsen hand eczema in nickel-allergic patients. In a clinical trial, Kaaber et al. (1978) reduced the nickel dose to 2.5 mg and observed flaring of hand dermatitis in 13 of the 28 patients with chronic nickel dermatitis. A similar finding was reported by Veien et al. (1983); they observed that 26 patients had flare-ups following oral challenge with nickel compounds (2.5 mg nickel in a capsule). The conditions of some of the patients improved when they were placed on a low-metal allergen diet for four to six weeks (Kaaber et al., 1978; Veien et al., 1983).

Cronin et al. (1980) gave groups of five fasting female patients that had hand eczema a gelatin lactose capsule containing nickel, together with 100 ml of water. Three doses were used, 2.5 mg, 1.25 mg, and 0.6 mg nickel as nickel sulfate. After administration of nickel, the fast was continued for a further hour, at which time the patient was given a cup of coffee; thereafter, normal meals were taken. Assuming a female body weight of 62 kg (OEHHA, 2000b, p10-4) and the lowest dose that aggravated nickel dermatitis of 0.6 mg, we estimate a LOAEL of 9.7 µg Ni/kg bw.

Nielsen et al. (1999) studied the aggravation of nickel dermatitis in people by giving them an oral dose of soluble nickel. Twenty nickel-sensitized women and

20 age-matched controls, both groups having vesicular hand eczema of the pompholyx type, were given a single dose of nickel in drinking water (3 µg/mL or 12 µg Ni/kg bw). All patients fasted overnight and fasting was maintained for another 4 hours after the nickel administration. Nielsen et al. (1999) reported that nine of 20 nickel-allergic eczema patients experienced aggravation of hand eczema after nickel administration, and three also developed a maculopapular exanthema. No exacerbation was seen in the control group. From the results of this study, we identified a LOAEL of 12 µg Ni/kg bw for the nickel-sensitized women.

A number of human studies have shown that oral administration of low levels of soluble nickel over a long period of time may reduce nickel contact dermatitis. Sjovall et al. (1987) orally administered 0, 5 or 0.5 mg nickel per day to a group of patients allergic to nickel. After six weeks, they found evidence of reduced sensitization in patients exposed to 5 mg/day but not to 0.5 mg/day. Santucci et al. (1988) gave a single oral dose of 2.2 mg Ni to 25 nickel-sensitized women and found that 22 reacted to the treatment. After a 15-day rest period, the subjects were given gradually increasing doses under the following schedule: 0.67 mg Ni/day for one month, 1.34 mg Ni/day for the second month, and 2.2 mg Ni/day for the third month. In the last phase of the testing, 3/17 of the subjects had flare-ups even at the lowest dose. The other 14 subjects, however, did not respond to the highest dose, even though they had responded to that dose in the initial testing.

Boscolo et al. (1999) evaluated systemic effects of ingested nickel on the immune system of nickel-sensitized women. Twenty-eight women were administered 10 mg of $NiSO_4$. Group A consisted of 19 non-atopic Ni-sensitized or nine non-allergic women. After Ni ingestion non-allergic and 12 Ni-sensitized women were asymptomatic (non-responders, group B) while seven Ni-sensitized women showed a flare up of urticaria and/or eczema (responders, group C). Before Ni treatment, groups B and C showed higher values of blood CD19+ (280 for both groups, vs. 150 pg/mL for Group A, $P < 0.05$) and CD5--CD19+ (235 for B,183 for C, vs. 113 pg/mL for A, $P < 0.05$). Group C also showed higher serum interleukin (IL) 2 (538 vs. 483) and lower serum IL-5 (296 vs. 445, $P < 0.05$) than Group A. Four hours after Ni ingestion, group C showed a significant increase in serum IL-5 (+53.7%, $P <0.05$). Twenty-four hours after treatment, group A showed a significant reduction in blood CD4+-CD45RO- “virgin” cells and an increase of CD8+ lymphocytes, while group C showed a marked decrease in total blood lymphocytes and CD3+(-41.5%), CD4+-CD45RO-(-46.5%), CD4+-CD45RO+(-35.6%), CD8+(-34.6%), CD19+(-28.8%), and CD-CD19+(-20.8%) cell subsets (all $P <0.05$ by Kruskall-Wallis test and/or Wilcoxon matched-pairs signed-rank test). Overall the results suggest that Ni ingestion induces a change in immune response from a TH-1 like pattern to a TH-0 like pattern in responder patients with systemic symptoms, as indicated by elevated serum IL-2 and IL-5 during the test.

Rietschel et al. (2008) studied trends in nickel sensitivity in 25,626 North American subjects over the period 1992 to 2004. The data exhibited a steady increase in nickel sensitivity indicated by patch test from 14.5% in 1992 to 18.8% in 2004 ($P < 0.0001$). Females were 1.1 to 1.2 times more likely to be allergic in the late (2001-2004) group compared to the early group (1992-1995) with a relative risk (RR) = 1.2, 95% C.I. 1.10-1.28, $P < 0.0001$, or the middle group (1996-2000) $P = 0.0011$. Younger males and females (≤ 18 yr) showed significantly higher sensitivity compared to older subjects, i.e. 14.1% (55/389) vs. 6.1% (536/8839) in males and 32.4% (177/546) vs. 21.4% (3385/15,821) in females. The cause of increased sensitivity is unclear but seems indicative of increased population exposures to nickel possibly related to body piercing (Nielsen et al., 1993; Meijer et al., 1995).

Mann et al. (2010) conducted a cross-sectional study of airborne nickel exposure and nickel sensitization in 309 6-year old children from three towns in North Rhine Westphalia, Germany (about 100 subjects from each town). Two of the towns were in the proximity of steel mills (Duisburg and Dortmund) and one was in a rural area (Borken). Ambient air quality data and Lagrangian dispersion modeling were used to estimate individual annual average air concentrations. Assessment of internal nickel exposure was accomplished by analysis of morning urine samples by electro-thermal atomic absorption spectroscopy. Nickel content of drinking water was also analysed as a potential confounder. Nickel sensitization was measured with a dermatological patch test. A weak but significant correlation ($r = 0.256$, 95% CI = 0.137-0.375, $P < 0.001$) was observed between nickel concentration in ambient air and urine using Pearson correlation of log-transformed values. A comparison of the nickel concentrations in ambient air between sensitized and non-sensitized children shows an association of nickel sensitization prevalence with exposure to nickel for Duisburg (Mann-Whitney test: $P = 0.094$). A similar association was not seen in Dortmund. Overall, nickel levels in urine of sensitized children were higher than non-sensitized children ($P < 0.001$). Children who had urinary Ni or ambient air Ni below the median showed a higher prevalence of Ni sensitization than children with both levels below the median (X^2-test: $P = 0.109$). The authors conclude that nickel in ambient air might be a risk factor for nickel sensitization, but a larger study is necessary.

Lisby et al. (1999a) observed nickel-induced activation of T cells in individuals with negative patch test to nickel sulfate. Eighteen subjects (8 males and 10 females, aged 27-54 years) were included in the study. Maximum T cell proliferation was seen after seven days of in vitro stimulation of isolated peripheral blood mononuclear cells (PBMC) with $NiSO_4$. Nickel sulfate concentrations above 1.0 mM were toxic to the cells by trypan blue exclusion. At concentrations between 0.1 and 100 µM a dose-dependent stimulation of PBMC was seen in 16 of the 18 subjects. Maximum stimulation occurred between 1 and 100 µM $NiSO_4$ with the mean maximum stimulation index (SI) of 7.1, range 1.4-21.8 ($P < 0.0005$). Similar results were obtained with $NiCl_2$ (N = 3, mean SI = 13, range 8.0-20.2). The functional capacity of Ni-inducible T cells was assessed

by cytokine release from PBMC from Ni-allergic and Ni-nonallergic individuals. T cells from both allergic and nonallergic subjects released interferon-γ (IFN-γ) but no significant difference was observed between the two groups in the concentrations of IFN-γ released after 72 hr stimulation with $NiSO_4$. Umbilical cord mononuclear cells (UCMC) were used as a model for unexposed individuals. When incubated with 10^{-10} to 10^{-4} M $NiSO_4$ these cells showed no cell proliferation compared to controls. The authors note that: "even if the observed T cell reactivity towards Ni by itself does not result in the development of clinical disease, such a T cell reactivity may add to the reactivity of other T cells with other allergen specificity resulting in the development of overt clinical disease."

In a follow-up study, Lisby et al. (1999b) found that the proliferative response in Ni-nonallergic individuals was mainly confined to T cells within the CD4+ subset. Also in contrast to the conventional recall antigen tetanus toxoid, $NiSO_4$ stimulated both naïve and memory CD4+ T cells. Preincubation of monocytes/macrophages but not T cells with $NiSO_4$ resulted in subsequent T cell proliferation. The results suggest that T cells in Ni-nonallergic individuals are capable of recognizing nickel or nickel-modified peptides.

Buchvald and Lundeberg (2004) investigated the in vitro responses of peripheral blood mononuclear cells (PBMCs) to nickel stimulation in groups of atopic and nonatopic patients with nickel allergic contact dermatitis (ACD). ACD is dependent on cell-mediated immune responses mediated by type-1 T lymphocytes whereas atopic dermatitis (AD) occurs via sustained activation of type-2 subsets of T cells. Ten subjects each with nonatopic nickel ACD, nickel ACD + concomitant AD, AD but no contact allergy, and healthy controls provided PBMCs that were stimulated with $NiSO_4$, phytohemagglutinin (PHA), or tetanus toxoid (TT). Ni-induced lymphocyte DNA synthesis in PBMC cultures was measured with [^{3}H] thymidine incorporation and expressed as a stimulation index (SI). The SI for controls averaged about one, for AD about two, for ACD about 20 and for ACD+AD about two. IL-2 secretion (pg/mL) averaged about 1, 1, 50, and 10, respectively. IL-5 secretion (pg/mL) averaged about 10, 10, 175, and 25, respectively. The results indicated that PBMCs of nickel-allergic subjects with concomitant AD exhibited impaired in vitro proliferative and secretory responses to nickel but not to the mitogen PHA or the recall antigen TT. There was a statistically significant correlation between the amounts of IL-2 and IL-5 secreted by Ni-stimulated lymphocytes of the ACD+AD subjects. The authors speculate that IL-5 may play a role in the development of ACD.

Moed et al. (2004) determined the identity of nickel-responding T cell subsets in five nickel-allergic subjects and four controls. The T cell subsets were isolated from peripheral blood mononuclear cells (PBMCs) and their proliferative capacity, type-1 or type-2, measured by IFN-γ or IL-5 release, and phenotypical marker expression were assessed after nickel treatment with 50 µM $NiSO_4$. The authors found that only CD4+ CLA+ CD45RO+ and not CD8+ T cells proliferated and produced both type-1 and type-2 cytokines in response to nickel. Cells with the

marker CLA in combination with CD4+, CD45RO+, or CD69 are increased after nickel stimulation. Analysis of nickel-reactive cells for expression of distinct chemokine receptors showed that proliferative capacity and cytokine production were confined to subsets expressing CXCR3 and CCR4 but not CCR6. A subset of T cells expressing CLA+ and CXCR3, CCR4 and CCR10 increased in response to allergen. The authors conclude that Ni-reactive T cells are characterized as CD4+ CLA+ memory cells, which express chemokine receptors CXCR3, CCR4, and CCR10, but not CCR6. The lack of Ni-induced IFN-γ or IL-5 release from CD8+ T-cell fractions suggests that they play no significant role in nickel allergy.

Jensen et al. (2004) similarly characterized lymphocyte subpopulations and cytokine profiles in PBMCs of Ni-sensitive individuals after nickel exposure. Thirty-three Ni-sensitive individuals were randomly divided into four groups of 7-10 each and orally challenged with 0, 0.3, 1.0, or 4.0 mg nickel given as $NiSO_4 \cdot 6H_2O$. Nineteen healthy controls were randomly divided into two groups and orally challenged with 0 or 4.0 mg Ni. Blood samples were obtained 24 hr after Ni-exposure and PBMCs isolated for analysis. Ni-sensitive individuals had significantly higher fractions of lymphocytes in their peripheral blood than the healthy controls (mean percent): $CD3^+$ $CD45RO^+$ CLA^+ cells (12.5 vs. 8.5, P = 0.0035); $CD4^+$ $CD45RO^+$ CLA^+ cells (21.2 vs. 12.2, P = 0.000095); and $CD8^+$ $CD45RO^+$ CLA^+ cells (6.1 vs. 1.6, P = 0.000007).

The Ni-sensitive subjects were divided into two groups based on cutaneous response following oral exposure (responders N = 13, non-responders N = 20). A dose-response reaction was observed among nickel-sensitive subjects. Both responders and non-responders had significantly higher fractions of $CD3^+$ $CD45RO^+$ CLA^+ lymphocytes before challenge than the healthy controls (P = 0.014 and 0.049, respectively). After challenge this was significant only for the non-responders (P = 0.025). Both Ni-sensitive groups showed significantly higher fractions of $CD4^+$ $CD45RO^+$ CLA^+ cells before and after Ni-challenge (P < 0.001). Responders had the highest fraction of $CD8^+$ $CD45RO^+$ CLA^+ before and after Ni-challenge [7.7 vs. 1.6 (P = 0.022) and 6.5 vs. 1.6 (P = 0.0014), respectively]. Only those individuals that responded to Ni-challenge with 4 mg Ni had significantly elevated levels of IL-5 in the serum (P = 0.025) and a smaller non-significant increase in IL-10. No differences in the levels of IL-2, IL-4, IFN-γ, or TNF-α were observed before or after challenge. Overall the results indicate that $CD8^+$ $CD45RO^+$ CLA^+ T-lymphocytes and T lymphocytes with the type 2 cytokine profile are involved in systemic contact dermatitis associated with nickel exposure.

Minang et al. (2006a) investigated the effect of IL-10 on Ni-induced Th-1(IFN-γ) and Th-2-type (IL-4 and IL-13) cytokine responses in human peripheral blood mononuclear cells (PBMC). PBMC from 15 Ni-allergic and 8 control donors were stimulated with nickel and the frequency of cytokine-producing cells and cytokine concentrations analyzed by enzyme-linked immunospot (ELISpot) and enzyme-linked immunosorbent assay (ELISA). PBMC suspensions of 2.5×10^5 cells with

or without 50 µM $NiCl_2$•$6H_2O$ were incubated with different concentrations of recombinant rIL-10 (0 to 25 ng/mL). Nickel-PBMC showed significantly higher levels of endogenous IL-10 compared to control PBMC. The mean increase in IL-10 induced by Ni(II) was 33.1 pg/mL and 2.2 pg/mL in the Ni-PBMC and control PBMC, respectively. Addition of rIL-10 to Ni-PBMC reduced the levels of Ni-induced IL-13, and IFN-γ. The mean levels of IFN-γ were reduced by 40% to 71% using 0.2 and 1 ng/mL of rIL-10. No effects of rIL-10 were seen in the control PBMC. The results suggest that IL-10 may play a role in vivo in counteracting the allergic reactions mediated by Th-1-type reactions. In a follow-up study the authors observed similar mixed Th1- and Th2-type cytokine profiles in allergic subjects with cobalt(II), chromium(Cr III and VI), palladium(Pd II) and gold(Au I and III). In terms of the optimal dose for induction of cytokines IL-2, IL-4 and IL-13 the order of effectiveness was: Cr(VI), 0.5 µM > Au(III), 2 µM > Au(I), 25 µM > Ni(II) ~ Co(II), 50 µM > Cr(III) ~ Pd(II), 100 µM.

8.3 Studies on Cells in vitro.

Zeromski et al. (1995) measured the effects of Ni_3S_2 (median particle size ≥ 30 µm) or $NiSO_4$ on human lymphocytes in vitro. Blood was obtained from a blood bank and peripheral mononuclear cells (PBMCs) from normal donors were cultured for 24 hr at 0, 0.01, 0.02, or 0.04 mM Ni. Following culture, the immuno-phenotype of the cells was determined by indirect immunofluorescence, using monoclonal antibodies to major differentiation antigens of PBMCs, and their natural killer (NK) activity toward K562 target cells. Ni_3S_2 had a marked inhibitory effect on the PBMCs consisting of a decreased number of CD4-positive cells at 0.02 and 0.04 mM Ni and a fall of NK (CD56-positive) cell number at all concentrations tested. $NiSO_4$ induced a significant 30 percent decrease in the CD4 phenotype of T cells at 0.04 mM ($P < 0.05$ vs. control). The inhibitory effects noted by both nickel compounds could be prevented by co-treatment with magnesium acetate. Ni or Mg salts did not affect CD3, CD8, CD20, or CD11a cell populations.

Caicedo et al. (2007) investigated the metal ion-induced DNA damage, apoptosis, necrosis and proliferation in a human CD4+ T-helper lymphocyte (Jurkat) cell line. Cell suspensions with 1×10^6 cells were incubated for 48 hr with 0, 0.05, 0.5, 1.0, or 5.0 mM metal ion as chlorides. The results indicated that the metal ions did not preferentially induce Jurkat T-lymphocyte DNA damage prior to other forms of toxicity indicated by apoptosis and/or necrosis. In terms of the average concentration (of the four endpoints) required to induce a significant adverse effect, the metals were ranked as follows: V(III), 0.29 mM; Ni(II), 1.41 mM; Co(II), 2.65 mM; Cu(II), >2.65 mM; Nb(V), >2.75 mM; Mo(V), >2.87 mM; Zr(II), >3.875 mM; Be(II), >4 mM; Cr(III), >5 mM; Al(III), >5 mM; and Fe(III), >5 mM. Vanadium (III) and nickel (II) stand out as the more toxic of the metal ions surveyed on average. In terms of cytotoxicity only cobalt (II) and niobium (V) were more toxic (0.5 mM) than vanadium (1.0 mM) and nickel (5.0 mM).

Miyazawa et al. (2008) studied the role of the mitogen-activated protein kinase (MAPK) signaling pathway in the activation of dendritic-type THP-1 cells by nickel sulfate. Nickel and other low molecular weight allergens induce contact hypersensitivity via a cell-mediated delayed-type immune response. In the induction phase these compounds or haptens first make contact with dendritic cells (DCs) in the skin, including Langerhans cells (LCs). Activated DCs migrate to regional lymph nodes and trigger the allergen-specific T-cell response with expression of stimulatory molecules (e.g., CD86 and CD54) and the production of several stimulatory cytokines (e.g., IL-1β). Human myeloid cell lines (THP-1, U937 and MUTZ-3) are good surrogates of DCs and have a high capacity to induce tumor necrosis factor (TNF-ά) release and CD86, CD54 and CD40 expression following allergen treatment. THP-1 cells (1×10^6) were cultured for one hour in one mL of culture medium with either 170 µg/mL $NiSO_4$ or 5 µg/mL 2,4-dinitrochlorobenzene (DNCB). Some experiments included 0.03 to 3 µM of the p38 MAPK inhibitor SB203580. Nickel sulfate and DNCB induced phosphorylation of p38 and extracellular signal-regulated kinase (ERK). Inhibition of p38 MAPK activation selectively blocked DNCB-induced TNF-ά release, but not $NiSO_4$. Alternatively, inhibition of ERK pathways selectively suppressed $NiSO_4$-induced TNF-ά but not DNCB-induced release. The authors conclude that the two allergens activate p38 MAPK and ERK, and stimulate TNF-ά release via different signal transduction pathways.

Boisleve et al. (2005) demonstrated that in immature human $CD34^+$-derived DC, three MAPK pathways (ERK, p38MAPK, and JNK) participated in the expression of CD83, CD86 and CCR7 molecules induced by $NiSO_4$. In contrast, following TNF-α stimulation, only p38 MAPK was involved in CD83 and CCR7 expression. ERK inhibited DC maturation while JNK had no effect. The authors also demonstrated that inhibition of the MAPK pathways did not suppress $NiSO_4$-induced down-regulation of the adhesion molecule E-cadherin and the specific LC protein, langerin, suggesting that other signaling pathways may be involved.

Goebeler et al. (1993) evaluated the effects of sensitizing agents (2,4-dinitro-benzenesulfonic acid, metal salt haptens) on endothelial adhesion molecule expression. Endothelial surface molecules play a role in leukocyte recruitment to sites of inflammation. Using flow cytometry and an enzyme-linked immunosorbent assay, $NiCl_2$ and to a lesser extent $CoCl_2$ were observed to up-regulate intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1(ELAM-1, E-selectin) expression on cultured human umbilical vein endothelium. The other substances tested showed no effects including $AlCl_3$, $CrCl_3$, $K_2Cr_2O_7$, $MnCl_2$, $CuCl_2$, $ZnCl_2$ and dinitrobenzenesulfonate. Induction of adhesion molecules by $NiCl_2$ required de novo mRNA and protein synthesis and could be blocked by kinase inhibitor H-7. Neutralizing antibodies to IL-1 did not block Ni(II) up-regulation indicating independence of an IL-1-dependent autocrine mechanism. In a separate analysis of foreskin specimens in organ culture, $NiCl_2$ up-regulated microvascular ELAM-1 expression (2.06 ± 0.31SEM in control *vs*. 3.25 ± 0.27SEM

with 0.7mM $NiCl_2$: $P < 0.01$). The authors speculate on the importance of the findings with regard to nickel induced contact allergies.

Schmidt et al. (2010) reported that Ni(II) (form not specified) triggered an inflammatory response by directly activating human Toll-like receptor 4 (TLR4). The response was specific to humans and absent in mouse TLR4. Studies with mutant TLR4 proteins showed that the non-conserved histidines 456 and 458 of human TLR4 are required for Ni(II) activation but not by the natural ligand polysaccharide. Transgenic expression of human TLR4 in TLR4 deficient mice allowed efficient sensitization to Ni(II). The results suggest site-specific human TLR4 inhibition as a potential therapy for contact hypersensitivity.

Gao et al. (2010) studied the interaction of microbial stimuli and nickel to amplify the release of inflammatory and immune-modulating cytokines in cultured human lung fibroblasts (HLF). $NiSO_4$ and MALP-2(*M. fermentans*-derived macrophage-activating lipopeptide-2) induced synergistic increases in IL-6 gene expression. HLF were exposed to 200 µM $NiSO_4$ and/or 600 pg/mL MALP-2. The combined treatment increase in IL-6 mRNA was about 20-fold versus 5-fold for individual treatments over 30 hr. Nickel and MALP-2, alone or together, led to rapid and transient phosphorylations of $ERK_{1/2}$ and JNK/SAPK. P38 phosphorylation was seen only after prolonged treatment with both agents together. PI3K-dependent Akt phosphorylation was unchanged by Ni and/or MALP-2 treatment. IL-6 induced by Ni/MALP-2 was partially dependent on the activity of HIF-1α and COX-2. IL-6 was also partially sensitive to the inhibition of $ERK_{1/2}$, p38, and PI3K signaling. Protein kinase inhibitors had little or no effect on Ni/MALP-2-induced accumulation of HIF-1α protein, however, COX-2 expression and, especially, PGE_2 production were suppressed. The authors conclude that Ni/MALP-2 interactions involve multiple protein kinase pathways ($ERK_{1/2}$, p38, PI3K) that modulate events downstream from early accumulation of HIF-1α gene expression to COX-2 derived autocrine products like PGE_2.

Fugitive fly ash derived from the combustion of residual fuel oil (ROFA) containing nickel has been used to study the effects of metal-containing PM. The toxicity of ROFA and other PM involves initiation of inflammatory cascades within the lung (Gao et al., 2010). It is possible that these effects may play a role in human disease caused by nickel bearing PM.

Carter et al. (1997) exposed normal human bronchial epithelial (NHBE) cells for 2 or 24 hr to 0, 5, 50, or 200 µg/mL residual oil fly ash (ROFA). The ionizable metal content of the ROFA was mainly vanadium (185 mg/g), nickel (37.5 mg/g) and iron (35.5 mg/g). Concentrations of inflammatory cytokines IL-8, IL-6 and TNF-α, as well as mRNA coding for these cytokines were measured using ELISA and RT-PCR methods. Incubation of cells for 2 hr stimulated the accumulation of IL-8 protein and mRNA in a dose-dependent manner. Significant increase of IL-8 mRNA was seen in 2 hr with 5 µg/mL ROFA. ROFA induction of IL-6 was similar to that of IL-8. ROFA induction of TNF-α was not as marked, with cells requiring 50 or 200 µg/mL for 2 hr to elicit a significant increase. Cytokine induction by

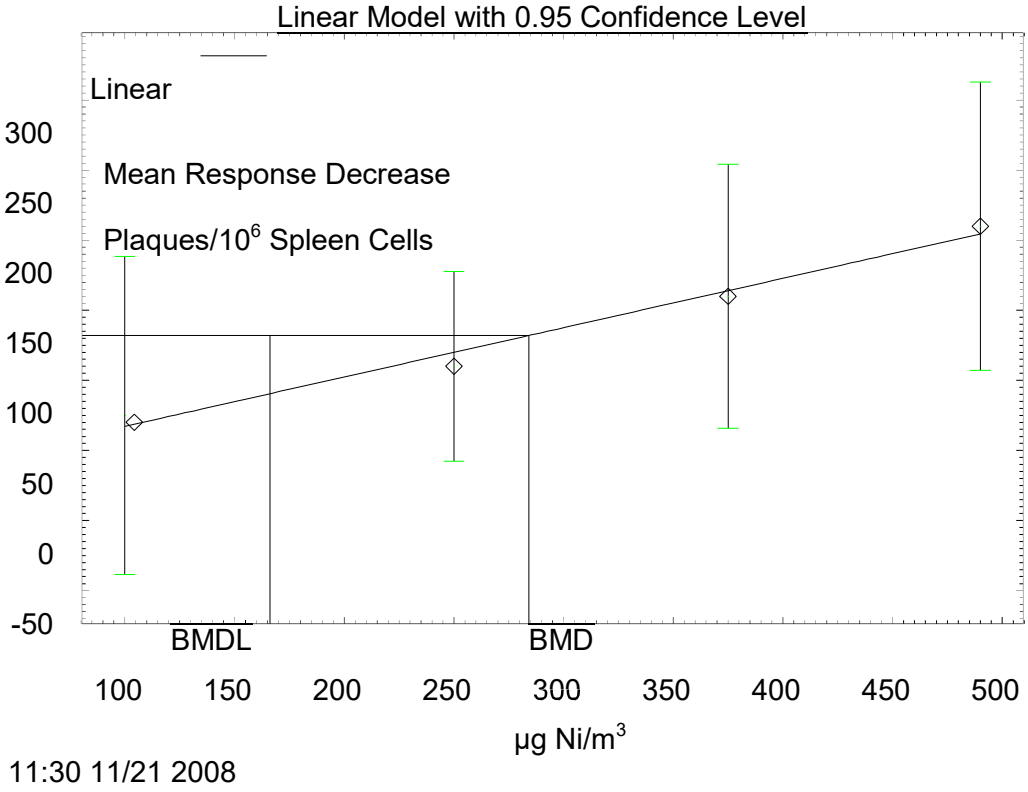
ROFA was inhibited by inclusion of either the metal chelator deferoxamine (1.0 mM) or the free radical scavenger dimethylthiourea (1.0 mM). On this basis the authors concluded that the ROFA-induced cytokine production by the human airway cells was metal-dependent.

8.4 Immunotoxicity Studies in Experimental Animals

Both the critical study and the supporting study for the derivation of the acute REL for nickel compounds exhibited immunotoxicity endpoints in experimental animals. The study of Graham et al. (1978) on inhibition of antibody production was the critical study for the aREL and was a supporting study for the 8-hour REL. Adkins et al. (1979) showing increased mortality in nickel-treated animals subjected to experimental infection was the supporting study for the aREL. The details of the derivations are given in sections 9.3 and 9.4 below.

Studies by Graham et al. (1975, 1978) indicate that the immune system is a sensitive target for acute nickel toxicity showing inhibition of antibody production against sheep erythrocytes. These authors used a hemolytic plaque technique to determine the number of specific antibody-producing spleen cells. Six-week old SPF female Swiss mice (14-29 per group) were exposed by inhalation to 0, 100, 250, 375, or 490 μg Ni/m³ as $NiCl_2$ (99% of particles were ≤ 3μm in diameter, exposure values were estimated from their Fig. 3) for two hours. The exposed animals showed a significant decrease in splenic antibody-forming cells following a challenge with a T-lymphocyte dependent antigen (Graham *et al.*, 1978). A linear dose-response was observed with a negative linear regression of Y = -34.9 - 0.347X, where Y is the number of hemolytic plaques formed/10^6 spleen cells and X is the exposure concentration in μg Ni/m^3. The results indicate a LOAEL of 250 μg Ni/m^3 and a potential NOAEL of 100 μg Ni/m^3. Unfortunately this study is short on details and the NOAEL is not considered as reliable as the LOAEL (no control values are given). We analyzed the data in the Graham et al. (1978, Figure 3) with a continuous benchmark dose approach. The extrapolated background from their Fig. 3 is approximately -40 plaques/10^6 cells. Using a criterion of -100 plaques/10^6 cells as a significant effect (a reduction of more than double the background), we obtained a good fit to a linear model (P = 0.95) with a benchmark dose (BMD) for a 100 plaque loss of 284 μg Ni/m^3 and a 95% lower confidence limit on BMD (BMDL) of 164.6 μg Ni/m^3 (Figure 6). The latter value is used as the point of departure in the derivation of a potential 8-hour REL (Section 9.4).

FIGURE 6. CONTINUOUS BENCHMARK DOSE ANALYSIS OF DECREASE IN PLAQUES/10^6 SPLEEN CELLS VS. µG NI/M^3, 2 HOURS EXPOSURE OF FEMALE SWISS MICE. BMD AND BMDL ARE FOR A 100 PLAQUE DECREASE (DATA FROM GRAHAM ET AL. 1978, THEIR FIG. 3).



A host-resistance study by Adkins *et al*. (1979) showed that mice (80-120 per group) exposed to inhaled soluble nickel aerosols for two hours in the form of $NiCl_2$ or $NiSO_4$ (particle sizes 86 to 96% <1.4µm, 99% <3.0µm) were significantly more susceptible to mortality from streptococcal bacterial infection. The concentrations of nickel that showed these effects were 499 µg Ni/m³ ($NiCl_2$) and 455 µg Ni/m³ ($NiSO_4$). No significant change in mortality was seen with exposure to 369 µg Ni/m³ as $NiCl_2$. The data for percentage mortality difference from control for the post $NiCl_2$ treatment infection interval of 24 hr (their Table 1) was analyzed by the benchmark dose method. Using a doubling of the mortality percentage as the benchmark (i.e., 3.74 to 7.5%) a BMDL of 365 µg Ni/m^3 was obtained with the power model and unequal variances (doses of 0, 289, 369, and 499 µg Ni/m^3). This value is about twice the BMDL obtained with the Graham et al. (1978) data shown above but for a more severe endpoint.

Some of the immunologic effects of nickel in exposed rodents in vivo are summarized in Table 20.

TABLE 20. IMMUNOLOGIC EFFECTS OF NICKEL COMPOUNDS OBSERVED IN RODENT STUDIES (NTP, 1996A)

Nickel Compound	Species/Route	Chemical treatment	Response	Reference
Cell-mediated immunity				
Nickel chloride	CBA/J mice, intramuscular	Single injection, 18 mg/kg bw	Reduced T-lymphocyte proliferation	Smialowicz et al., 1984
Nickel sulfate	B6C3F1 mice female, oral	Up to 4,000 mg/kg-d for 23 weeks	Depressed spleen lymphoproliferative response to LPS (no effect on NK activity; PFC assay; mitogen response in spleen cells; resistance to *Listeria* challenge)	Dieter et al., 1988
Nickel sulfate	Sprague-Dawley rats, oral, drinking water 13 weeks	0, 0.02, 0.05, 0.1%$NiSO_4$•$6H_2O$, or 0, 44.7, 11.75, 223.5 mg Ni/L	Increase of CD4+ and CD8+ T-cells and decrease of CD4/CD8 ratio	Obone et al. 1999.
Humoral immunity				
Nickel chloride	CBA/J mice, intramuscular	Single injection, 18 mg/kg bw	Reduced antibody response to T-cell dependent sheep red blood cells	Smialowicz et al., 1984
	Swiss albino mice, intramuscular	3-12 µg Ni/kg bw followed by immunization with sheep red blood cells	Depressed antibody formation	Graham et al., 1975
	Swiss mice, inhalation	2-hour inhalation exposure at 250 µg/m^3	Depressed antibody response to sheep red blood cells	Graham et al., 1978
Nickel acetate	Sprague-Dawley rats, intraperitoneal	11 mg/kg bw immunized with *E. coli* bacteriophage	Depressed circulating antibody response	Figoni and Treagan, 1975
Macrophage function				
Nickel chloride	CBA/J mice, intramuscular	Single injection, 18 mg/kg bw	No effect on phagocytic capacity of peritoneal macrophages	Smialowicz et al., 1984

TABLE 20. IMMUNOLOGIC EFFECTS OF NICKEL COMPOUNDS OBSERVED IN RODENT STUDIES (NTP, 1996A)

Nickel Compound	Species/Route	Chemical treatment	Response	Reference
Natural killer cell activity				
Nickel chloride	CBA/J and C57BL/6J mice, intramuscular	Single injection, 18 mg/kg bw	Depressed NK activity against Yac-1 murine lymphoma cells	Smialowicz et al., 1984, 1985, 1986
Host resistance				
Nickel chloride and nickel oxide	CD mice and Sprague-Dawley rats, inhalation	0.5 mg/m^3 for 2 hours	Enhanced respiratory infection by *Streptococcus*	Adkins et al., 1979

A similar suppression in antibody-forming cells was seen in mice (10-12/dose group) exposed intramuscularly to 0, 3.09, 6.17, 9.25, or 12.34 μg Ni/g body weight as $NiCl_2$ or $NiSO_4$ (Graham *et al*., 1975, 1978). Statistically significant decreases in plaque production ($P < 0.05$ vs. control by William's test) were seen at 9.25 μg Ni/m^3 with $NiCl_2$ and at 3.09 μg Ni/m^3 with $NiSO_4$ (Graham et al., 1975). Similar exposures with NiO showed no decreases at any dose. A linear dose-response was given for $NiCl_2$ of $Y = -2.64 – 0.028X$, where Y is the log10 of plaques/10^6 cells and X is the i.m. dose of μg Ni/g bw.

Condevaux et al. (2001) compared the effects of morphine and nickel chloride on natural killer (NK) cell activity in vitro in rats and in the cynomolgus monkey. The NK cells were exposed to either $NiCl_2$ at 0, 1, 10, or 100 μg/mL or morphine at 0, 0.01, 1, or 1000 nM. There were statistically significant decreases in NK cell activity at the highest concentrations of nickel or morphine. The magnitudes of the decreases were greater in the monkey than in the rat, i.e. for $NiCl_2$ the decreases were 34.4-42.2% in monkey and 21.6-24.3% in rat. Morphine hydrochloride induced decreases of 59.1-68% in the monkey and 23.7-34.7% in the rat.

Haley *et al*. (1987) showed that male cynomolgus monkeys, exposed to intratracheal Ni_3S_2 (particle size not stated) at a delivered dose of 0.06 μmol Ni/g lung tissue, had impaired pulmonary macrophage phagocytic function and increased NK cell activity. Mice also exhibited impairment of pulmonary macrophage function in addition to decreases in antibody-forming spleen cells with inhalation exposure to Ni_3S_2 or NiO (Haley *et al*., 1990). Natural killer cell activity measured by splenic cytotoxic activity to tumor cells as well as by clearance of melanoma tumors *in vivo* was suppressed in two strains of mice exposed to intramuscular injections of 18.3 mg Ni/kg as $NiCl_2$ as compared to controls (Smialowicz *et al*., 1985).

Smialowicz et al. (1984, 1985) injected nickel chloride i.m. in mice and found a significant reduction in a variety of T-lymphocytes and natural killer cell-mediated immune functions. They also demonstrated that suppression of natural killer cell activity could be detected with *in vitro* and *in vivo* assays and that reduction of natural killer cell activity was not associated with either a reduction in spleen cellularity or the production of suppressor cells. Their findings confirmed those reported by other investigators on the immunosuppressive effects of nickel compounds on circulating antibody titers to T_1 phage in rats (Figoni and Treagan, 1975), on antibody response to sheep erythrocytes (Graham et al., 1975), on interferon production in vivo in mice (Grainer et al., 1977), and on the susceptibility to induced pulmonary infection in mice following inhalation of nickel chloride (Adkins et al., 1979).

Haley *et al.* (1990) found that exposure of mice to nickel sulfate, nickel subsulfide, or nickel oxide resulted in various immunological effects. Mice were exposed to 0, 0.11, 0.45, or 1.8 mg Ni/m^3 as Ni_3S_2 (MMAD = 2.4 µm, gsd = 2.2); 0.47, 2.0, or 7.9 mg Ni/m^3 as NiO (MMAD = 2.8 µm, gsd = 1.8); and 0.027, 0.11, and 0.45 mg Ni/m^3 as $NiSO_4$ (MMAD = 2.3 µm, gsd = 2.4) for 6 hours/day, 5 days/week for 13 weeks. Nickel exposures consistently decreased splenic antibody-forming cell (AFC) responses, with significant decreases occurring at 1.8 mg Ni/m^3 as nickel subsulfide. In contrast, AFC responses in the lung-associated lymph nodes were consistently increased, indicating a possible indirect influence of inflammatory mediators released in the lung on local lymph nodes.

Rabbits (8 nickel exposed and 8 controls) exposed to 0.24 mg Ni/m^3 as nickel chloride (MMAD = 0.5-1.0 µm, cut off at ≤7.0µm) 6 hours/day, 5 days/week for 4 weeks exhibited significantly decreased macrophage lysozyme activity in pulmonary lavage fluid and in macrophage cultures, compared with control animals (Lundborg and Camner, 1984). Similar exposures of rabbits to chlorides of cadmium, cobalt, or copper did not reduce lysozyme activity.

Obone et al. (1999) evaluated the bioaccumulation and toxicity of nickel sulfate in rats following 13 weeks of oral exposure. Adult male Sprague-Dawley rats (8/dose group) were given 0, 0.02%, 0.05% and 0.1% nickel sulfate, i.e. 0, 44.7, 111.75, and 223.5 mg Ni/L, in their drinking water for 13 weeks. Measurements of splenic lymphocyte subpopulations following exposure to 0.05% $NiSO_4$ showed significant increases in absolute numbers of T-cells, CD4+ and CD8+. Statistically significant increases in CD8+ and decrease in the ratio of CD4/CD8 were observed at all dose levels. Significant increases in both the absolute number and percentage of thymocyte CD8+ cell populations were also seen at all dose levels. The findings indicate a LOAEL of approximately 7.0 mg/kg-d for immunotoxicity ($C = 0.1*W^{0.7377}$ L/d, W = 0.185 kg rats; U.S. EPA, 1988).

Harkin et al. (2003) studied immunosuppression in Sprague-Dawley rats following i.p. administration of 0 (vehicle), 0.12, 0.36, 1.1, or 3.3 mg $NiCl_2$/kg bw. Nickel chloride suppressed T-lymphocyte proliferation and Th-1 (IFN-γ) and Th-2

(IL-10) cytokine production in a dose- and time-dependent manner. In addition, $NiCl_2$ inhibited production of the pro-inflammatory cytokine TNF-ά and increased the production of the anti-inflammatory cytokine IL-10 from lipopolysaccharide (LPS) stimulated cultures. Three of the cytokine data sets from Harkin et al. (2003) were subjected to continuous benchmark dose analysis (their Figure 2 (a), (b), and (c)). All the data sets were fit by the Hill model with P values greater than 0.22 (P ≥ 0.1 adequacy of fit criterion). For concanavalin-A (Con-A) stimulated Th1:IFN-γ, the $BMDL_{1SD}$ was 0.18 mg Ni^{2+}/kg bw. For Con A-stimulated Th2:IL-10, the $BMDL_{1SD}$ was 0.14 mg Ni^{2+}/kg bw. LPS-stimulated TNF-ά gave a $BMDL_{1SD}$ of 0.17 mg Ni^{2+}/kg bw. The similarity of the quantitative dose responses for nickel-induced cytokine suppression may indicate a common mode of action. The authors reported that the minimum plasma concentrations of nickel required to provoke immunosuppression are in the range 209 to 585 ng/mL. In the kinetic portion of the study a 3.3 mg/kg $NiCl_2$ dose provoked immunological changes that were maximal one hour following administration. The data demonstrate that $NiCl_2$ suppresses T-cell function and promotes an immunosuppressive macrophage phenotype in rats.

Roberts et al. (2009) studied the metal components of residual oil fly ash (ROFA) on pulmonary host defense in rats. The soluble fraction of ROFA contained Ni, Fe, Al and Zn. Sprague-Dawley rats were intratracheally instilled with 55.7 µg/rat ($NiCl_2$), 32.7 µg/rat ($FeSO_4$), 46.6 µg/rat ($Al_3(SO_4)_2$), 8.69 µg/rat ($ZnCl_2$), or a combination of all metals. Rats were also instilled with mixtures without a specific metal e.g., Mix-No Ni. Prior to infection with *Listeria monocytogenes* (5 x 10^4 cells) soluble nickel alone or in metal mixture produced no more lung injury than saline controls. Following infection nickel-treated animals had increased bacterial lung burden and body weight decrease. Ni alone and in mixtures increased reactive oxidants in the lung and was most important in suppressing T-cell activity following infection. Weight decreases in the mixes without Fe or Al indicate that iron and aluminum may act antagonistically to nickel. Overall the authors conclude that soluble Ni is the primary metal involved in the increased susceptibility to infection observed in rats exposed to the soluble metals of ROFA.

9 Derivation of Reference Exposure Levels

9.1 Introduction

The toxic effects of chemicals are of varying types and degrees of severity. Toxic effects from airborne substances may be due to exposure via the skin, eyes, and upper and lower respiratory tract. Systemic effects, such as hemolysis or central nervous system injury, may result from absorption of material through the lungs, and, to a lesser extent, through the skin. For a toxic endpoint to be considered due to acute exposure, the effects do not have to be observed immediately. Rather, the effects may be observed hours to days following the acute exposure. OEHHA has chosen to adopt U.S.EPA's general definition of adverse effects as "a biochemical change, functional impairment, or pathologic lesion that negatively affects the performance of the whole organism, or that reduce an organism's ability to respond to an additional challenge" (U.S.EPA, 2007). In assessing the dose-response relationship for non-cancer toxicological endpoints and developing RELs, the objective is to define concentrations of chemicals at or below which no adverse health effects are anticipated in the general human population, including sensitive subpopulations, over the specified exposure duration (1 hour, eight hours or chronic).

In selecting the critical and supporting studies upon which to base the RELs a number of factors are considered. Firstly, human studies are preferred if they are of sufficient quality in terms of endpoint relevance, numbers of subjects, dose response, study design etc. Most often we rely on animal studies, which generally are more available and have better dosimetry data than human studies. Here we look for the most sensitive effect in the most sensitive sex and species. We favor studies that provide a dose response that we can analyze with either quantal or continuous data yielding a BMDL or 95% lower confidence bound on a specific response level, usually 5%. This approach uses all the available data and is generally superior to the traditional approach of identification of a NOAEL or LOAEL, which is more influenced by dose selection (spacing), does not consider sample size and does not use information from the higher doses. When a BMD analysis is not possible, the NOAEL/LOAEL approach is used. Both approaches employ uncertainty factors to address shortcomings in available toxicity data when deriving the RELs.

9.2 Selection of Critical Studies

The available studies of acute lung toxicity in humans and animals were unsuitable for the derivation of an acute REL. Human data were limited to case reports and small occupational clinical or epidemiological studies with limited reporting and inadequate exposure data. Animal studies in many cases are complicated by less relevant exposure routes (e.g. subcutaneous injection, intratracheal installation), or the endpoints examined were not the most sensitive. Instead, it was found that acute or short-term studies of immunotoxicity provided

a better basis for this derivation. In the derivations for the acute REL we have selected critical studies based on two related toxic endpoints, namely immunotoxicity and pneumotoxicity. The acute REL critical study (Graham et al., 1978) and its supporting study (Adkins et al., 1979) are both based on immunotoxicity and give values of 0.2 and 0.7 µg Ni/m^3, respectively. Another study we considered was that of Ishihara et al. (2002) on bronchial inflammatory responses and mucus secretion in rats but the exposure of 5 hr/day x 5 days/week was too extensive for the 1 hour aREL.

The 8-Hour REL uses the NTP (1994c) $NiSO_4$ inhalation study in rats as the critical study and the Graham et al. (1978) as a supporting study. In this case we used a NOAEL approach but for a very large study with several time intervals up to 2 years. We also considered two other studies for the 8-hour REL (see Table 21). The chronic RELs for nickel compounds and for NiO also use NTP studies for $NiSO_4$ in rats, and NiO in mice. Both studies show similar effects of lung toxicity (e.g., alveolar proteinosis) but the derivation of the cRELs differ somewhat in that the rat data could be analyzed using a computer program for particle deposition in rats and humans (MPPD2) whereas the mouse used published data on deposition calculations since the MPPD2 model does not analyze deposition in the mouse lung. Both data sets were analyzed for dose response (i.e. $BMDL_{05}$). For the oral REL we adopted a study previously used in our drinking water program to set the public health goal (PHG). In all cases we apply uncertainty factors according to our published guidance (OEHHA, 2008) and the sufficiency of the data available in deriving the final REL proposals.

9.3 Acute Reference Exposure Level (aREL)

Study	Graham et al., 1978; supported by Adkins et al. (1979)
Study population	Immunotoxicity in mice,
Exposure method	Inhalation of 100 to 490 µg/m³ $NiCl_2$
Critical effects	Depressed antibody response
BMDL	165 µg Ni/m^3 (-100 plaques/10^6 cells)
Exposure duration	2 hours
Extrapolated 1 hour concentration	233 µg Ni/m³ (usingC^n x T = K, with n =2)
BMR uncertainty factor	√10 (clear response at BMR)
Interspecies uncertainty factor	10(default)
Intraspecies uncertainty factor	(√10PD * 10PK)
Cumulative uncertainty factor	1000
Reference Exposure Level	0.2 µg Ni/m³

An acute REL of 0.2 µg Ni/m³for mild effects following a 1-hour exposure was derived using the study of Graham *et al*. (1978) as the basis. This study is discussed above in section 8.4 and a dose response analysis is shown in Figure 6. The study gives a clear linear dose response. It involved an adequate number of animals per dose group (14-29) and each group was compared with its own controls. An extrapolation from the BMDL of 165 µg Ni/m^3 to that of a 1-

hour exposure was made using the time adjustment formula $C^n * T = K$, where n = 2. This yielded a 1-hour value of 233 μg/m^3. An overall uncertainty factor of 1000 was applied. This included a factor of √10 to allow for the fact that the BMDL was calculated for a benchmark response rate (BMR) which was considered to be a clearly measurable and biologically significant response. Interspecies and individual variabilities were represented by the usual defaults of 10 and 30, respectively. This results in a 1-hour REL of 0.2 μg Ni/m³.

The data of Graham et al. are supported by Adkins et al. (1979), who demonstrated increased mortality in mice exposed to $NiCl_2$ aerosol followed by streptococcal infection. In this case a BMDL of 365 μg Ni/m^3 for a doubling of mortality (from 3.74 to 7.5%) was obtained with the continuous power model. Other acute studies, particularly Ishihara et al. (2002) on lung toxicity, are less suitable to deriving a one-hour value. This aREL value should be reevaluated if human immunotoxicity or other human data become available. The aREL specifically does not apply to nickel carbonyl, which releases both nickel and carbon monoxide.

9.4 8-Hour Reference Exposure Level (8-hour REL):

Study	NTP, 1994c (supported by Graham *et al*., 1978)
Study population	*Female and male rats*
Exposure method	inhalation of 0.12 to 0.5 mg $NiSO_4$/m³ 6.2hr/d x 5d/wk, 16 days to 24 months
Critical effects	alveolar macrophage hyperplasia, alveolar proteinosis, chronic active inflammation
NOAEL	*0.03 mg/Ni/m3*
Exposure duration	*6.2 hours/day x 5/7 days/week) for 13 weeks*
Extrapolated 8 hour concentration	*5.7 μg Ni/m³ (30 μg/m3 x 0.264 DAF)*
Interspecies uncertainty factor	*√10 (default)*
Intraspecies uncertainty factor	*30*
Cumulative uncertainty factor	*100*
Reference Exposure Level	*0.06 μg Ni/m³*

The studies and endpoints considered in deriving the 8-hour REL are summarized in Table 21. The 8-hour REL proposed is based on the NTP (1994c) bioassay results on non-neoplastic lung lesions. This study provides daily exposures of 6.2 hours for five days/week for durations of 16 days to 24 months(Table 22). The data were unsuitable for benchmark dose analysis. The most consistent value presented was a NOAEL of 0.03 mg Ni/m^3 for alveolar macrophage hyperplasia in female rats (Table 22). This would give a daily value of 5.7 μg Ni/m^3 (30 μg Ni/m^3 x 0.264DAF x 5/7 days/wk). A value of 1 for UF_L

was used since an acceptable NOAEL was identified. Determination of the DAF in this study is described below in the section on derivation of the chronic REL. A model was used to account for rat to human differences in upper and lower airway deposition of nickel particles and it seems likely that deposition is the key event leading to subsequent lung toxicity. Therefore, a UF_{A-k} subfactor of 1 was applied to pharmacokinetic differences and $UF_{A-d} = \sqrt{10}$ for pharmacodynamic differences, for a total $UF_A = \sqrt{10}$. An intraspecies uncertainty factor (UF_H) of 30 was used incorporating a subfactor of 10 for pharmacodynamic differences and $\sqrt{10}$ for pharmacokinetic differences. The value of UF_{H-d} of 10 addresses potential increased sensitivity of infants and children vs. adults to continuous exposures to airborne nickel particles. There is also pharmacokinetic uncertainty, but this is somewhat lessened by the deposition model which was also appled to several child lung structures. With a cumulative uncertainty factor of 100 ($\sqrt{10}$ x 30) the calculated 8-hour REL would be 0.06 μg Ni/m^3. The experimental exposures were 6.2 hours and repeated daily exposures were made over a period of 13 weeks.

A suitable supporting study for the 8 hour REL is the Graham et al. (1978) study, the immunotoxicity endpoint and the 2 hr BMDL of 165 μg Ni/m^3. Where the 1-hour extrapolation yielded a value of 233 μg/m^3 the 8-hour value was 82 μg/m^3. In this derivation we used an uncertainty factor (UF_L) of $\sqrt{10}$ for the BMDL, which replaces the LOAEL. The BMDL has the advantage over the LOAEL of using all the dose-response data, although in this case the benchmark response was considered to represent a measurable non-zero response rate. However, since a dose-response model was used, a smaller UF than would be applied for a LOAEL is adequate. There was insufficient confidence in the reported NOAEL to base a REL on that value. For interspecies uncertainty (UF_A) we adopted the usual value of 10 which can be considered to account equally for pharmacokinetic and pharmacodynamic differences between mice and humans. For intraspecies uncertainty (UF_H) we used a value of 30, which includes a subfactor of 10 for pharmacodynamic differences (i.e., child sensitivity) and $\sqrt{10}$ for pharmacokinetic differences. Using the cumulative uncertainty factor of 1000 yields an 8-hour REL of 0.08 μg/m^3. Repeated exposures to airborne nickel may have a greater impact on infants and children than on adults due to its targeting of the immune system and lung function, and its asthma inducing capability. Thus, following our approved guidelines, we have used a full UF_H of 30.

The advantage of the NTP study is multiple doses in two species and both sexes with extended durations of exposure. Daily exposures are close to eight hours and approximate the type of repeated exposures the 8-hour REL is intended to address. However, the Graham et al. (1978) study addresses an alternate toxic endpoint albeit with greater uncertainty due to study design limitations. The Ishihara et al. (2002) data on lung inflammation and mucus secretion endpoints generally fall in between the Graham et al. and the NTP studies in severity and duration of exposure, however the derived REL values appear to be consistent with the more severe lung and immunotoxicity effects evaluated.

TABLE 21. STUDIES AND TOXIC ENDPOINTS CONSIDERED FOR THE 8-HOUR REL

Study	Endpoint	Criterion	Duration	8 hr Adjusted Value	Cumulative uncertainty factor	Proposed REL µg/m^3
Graham et al., 1978	Immunotoxicity	BMDL = 165 µg/m^3 (BMD_{100} = 284 µg/m^3)	2hr (single inhalation exposure)	82.3 µg/m^3	1000	0.082
NTP 1994c	Lung toxicity in rats	NOAEL = 0.03 mg/m^3	6.2 hr/d x 5 d/wk, 16 d, ≤ 24 mo	5.7 µg/m^3	100	0.06
Ishihara et al. 2002	Lung inflammation, total cells/µL in BALF	$BMDL_{1SD}$ = 5.5 µg (BMD_{1SD} = 9.8 µg)	5 hr/d x 5 d/wk x 1wk	19.6 µg/m^3	300	0.065
"	Lung inflammation, total protein in BALF, mg/mL	$BMDL_{1SD}$ = 18.6 µg (BMD_{1SD} = 26.9 µg)	5 hr/d x 5 d/wk x 1 wk	66.4 µg/m^3	300	0.22
"	Lung inflammation, total elastolytic activity in BALF	$BMDL_{1SD}$ = 50.0 µg (BMD_{1SD} = 53.0 µg)	5 hr/d x 5 d/wk x 1 wk	178 µg/m^3	300	0.60
"	Mucus secretion, sialic acid in BALF, µg/mL	$BMDL_{1SD}$ = 13.5 µg (BMD_{1SD} = 23.0 µg)	5 hr/d x 5 d/wk x 1wk	48.2 µg/m^3	300	0.16
Pandey & Srivastava, 2000	Decreased sperm motility percent	$BMDL_{1SD}$ = 2.91 mg $NiSO_4$/kg	1 oral dose/d x 5 d/wk x 5 wk	0.47 mg Ni/kg-d	1000	3.3
"	Increased Sperm Abnormalities percent	$BMDL_{1SD}$ = 0.46 mg $NiSO_4$/kg	1 oral dose/d x 5 d/wk x 5 wk	0.074 mg Ni/kg	1000	0.52
"	Increased Sperm Abnormalities percent	$BMDL_{1SD}$ = 0.34mg $NiCl_2$/kg	1 oral dose/d x 5 d/wk x 5 wk	0.060 mg Ni/kg	1000	0.42

Note: BALF = bronchoalveolar lavage fluid; for spermatotoxicity it was assumed that the hexahydrate salts were used, for the inhalation equivalent level it was assumed that only 50% of nickel would be absorbed via the inhalation route in addition to a 70 kg body weight and a 20 m^3/d inhalation rate (i.e. mouse µg/kg/d x 70 kg/20 m^3/d/0.5 = human µg/m^3.

TABLE 22. NON-NEOPLASTIC LUNG TOXICITY OBSERVED WITH INHALATION OF NICKEL SULFATE (NTP, 1994C).

Effect	16 days (animals/dose group)*	13 weeks	7 months	15 months	24 months
		(N)OAEL or (L)OAEL mg Ni/m^3			
Male Mice					
Lung Inflammation	0.77L (5)	0.44N(10)	0.22N(5)	0.11N(5)	0.056N(61)
Alveolar Macrophage Hyperplasia		0.056N(10)	0.11N(5)	0.056N(5)	0.056N(61)
Fibrosis		0.22N(10)			
Female Mice					
Lung Inflammation	0.77L(5)	0.22N(10)	0.22N(5)	0.11N(5)	0.056L(60)
Alveolar Macrophage Hyperplasia		0.056N(10)	0.11N(5)	0.11N(5)	0.056L(60)
Fibrosis		0.22N(10)			
Male Rats					
Lung Inflammation	0.7L(5)	0.11N(10)	0.03L(5)	0.06N(5)	0.03N(53)
Alveolar Macrophage Hyperplasia		0.03L(10)	0.03N(5)	0.06N(5)	0.03N(53)
Fibrosis				0.11N(5)	0.03N(53
Female Rats					
Lung Inflammation	0.7L(5)	0.06N(10)	0.03N(5)	0.06N(5)	0.03N(53)
Alveolar Macrophage Hyperplasia		0.03L(10)	0.03N(5)	0.06N(5)	0.03N(53)
Fibrosis				0.11N(5)	0.03N(53)

*Note: animals exposed to $NiSO_4$ aerosol for 6.2 hr/day, 5days/week.

9.5 Derivation of Chronic Reference Exposure Levels (cRELS)

The studies conducted by NTP (1994a & c) were used as the bases for the chronic RELs. These studies all showed similar non-carcinogenic effects in rats and mice, regardless of the form of nickel administered. It therefore appears that soluble and insoluble forms of nickel cause similar effects in rodents. For nickel sulfate the NOAELs for alveolar proteinosis are virtually identical for male or female rats (Table 22). The data set for exposures of 24 months duration was used in the development of the cREL for nickel and nickel compounds other than nickel oxide. Benchmark dose analysis was undertaken with the results shown in Table 23. A benchmark concentration of 0.0305 mg Ni/m^3, which is the average of the values obtained for alveolar proteinosis in male and female rats, was selected.

TABLE 23. BENCHMARK DOSE ANALYSIS OF LUNG EFFECTS INDUCED BY $NISO_4$ IN TWO-YEAR STUDIES (NTP, 1994C)

Species, Sex, Endpoint, Quantal Response	**Model**	**Goodness of Fit, X^2, p**	**BMD_{05} mg Ni/m^3**	**$BMDL_{05}$ mg Ni/m^3**
Rats, Male				
Macrophage Hyperplasia, 7/54,9/53,35/53,48/53	Log logistic	1.30, 0.25	0.024	0.016
Alveolar proteinosis 0/54,0/53,12/53,41/53	**Multistage**	**1.68, 0.64**	**0.036**	**0.029**
Rats, Female				
Macrophage Hyperplasia, 9/53,10/53,32/53,45/54	Multistage	3.94, 0.14	0.018	0.007
Alveolar proteinosis 1/52,0/53,22/53,49/54	**Log probit**	**2.02, 0.16**	**0.038**	**0.032**

For extrapolation to humans the multiple-path particle dosimetry model (MPPD) version two was used to derive a dosimetric adjustment factor (DAF) to calculate a human equivalent concentration (HEC), see Table 24.

TABLE 24. LUNG DEPOSITION OF $NiSO_4 \cdot 6H_2O$ AND NIO PARTICLES PREDICTED BY THE HSIEH ET AL. (1999A, C) AND THE AGE-SPECIFIC MPPD MODEL (VERSION 2)*

Age Distribu-tion	$NiSO_4$ Hsieh et al. 1999a		NiO Hseih et al. 1999c		$NiSO_4$ MPPD2		NiO MPPD2	
MMAD, µm	2.33		2.80		2.50		2.46	
gsd	2.20		1.87		2.38		1.87	
Density, g/cm^3	2.07		7.45		2.07		6.67	
Concn. mg/m^3	0.12, 0.2, 0.50		1.25, 2.5, 5.0		0.12		1.25	
Species	Rat		Mouse		Rat		Rat	
TB + ALV	**ADF**	**DAF**	**ADF**	**DAF**	**ADF**	**DAF**	**ADF**	**DAF**
Rat, adult	0.0769	1.00	0.0354	1.00	0.089	1.00	0.1289	1.00
Human 3 months	0.3982	0.193	0.4491	0.0788	0.4008	0.2225	0.4329	0.30
Human 3 years	0.3246	0.237	0.3674	0.0964	0.3245	0.274	0.3552	0.36
Human 9+ years	0.4086	0.188	0.4631	0.0764	0.4047	0.2199	0.4502	0.29
Human 14 years	0.3653	0.21	0.3209	0.1102	0.3600	0.2472	0.4039	0.32
Human 21 years	0.2643	0.291	0.2957	0.1197	0.2479	0.3597	0.3026	0.43
Human mean		0.224		0.096		0.264		0.338

*Note: MPPD = Multi-Pathway Particle Dosimetry model run with particle concentration of 1 $\mu g/m^3$, rat nasal breathing and human oronasal normal augmenter, ADF = airway deposition fraction (tracheobronchial plus alveolar), DAF = dosimetric adjustment factor (Human Equivalent Concentration = DAF x Animal Concentration);The MPPD model was developed by the CIIT Center for Health Research, The National Institute of Public Health and the Environment, The Netherlands (RIVM), the Ministry of Housing Spatial Planning and the Environment, The Netherlands, and the National Institute for Occupational Safety and Health (NIOSH). See Brown et al. (2005) for model comparisons.

In using the ratio of animal to human deposition fractions $(Fr)_A/(Fr)_H$ as the DAF, our approach differs from that of U.S.EPA (1994). In their regional deposited dose rate ratio (RDDRr) approach they would multiply the deposition ratio by the ratios of adult minute volumes $(V_E)_A/(V_E)_H$ and regional surface areas $(SA)_H/(SA)_A$ to estimate a deposited dose. In our case this adjustment would approximately double the DAF to 0.554 from 0.264. We have chosen not to apply this adjustment since our human fractional deposition in the above ratio is the average of several age-specific MPPD2 model predictions. We believe that this ratio would be significantly discounted by the RDDRr approach, which does not include deposition predictions for children. Note that in Table 17 all of the child models show higher airway deposition fractions than adult (0.32 to 0.4 vs. 0.25 for adult).

We have investigated the use of the MPPD2 model in deposition and clearance simulations to estimate alveolar dosimetry in units of µg Ni retained/day/m^2 alveolar surface area (TB clearance is very rapid and doesn't figure in the retention rates) for the various age-specific models. The results indicate an average retention ratio $(R)_A/(R)_H$ of 0.61 leading to a DAF of about 2/3 the value we are currently using. For the present time we propose to continue using the simple deposition fraction ratio as providing the most direct and unmanaged value without additional assumptions about clearance rates and adult values etc.

With a DAF of 0.26 the HEC was calculated as 1.4 µg/m^3. The uncertainty factors applied to this value were $UF_L = 1$ since a NOAEL was identified. The interspecies uncertainty factor $UF_A = \sqrt{10}$ was used since the MPPD2 model accounted for rat to human differences in upper and lower airway deposition of nickel particles and it seems likely that deposition is the key event leading to subsequent lung toxicity (e.g., alveolar proteinosis). Therefore, a UF_A subfactor of 1 would then apply to pharmacokinetic differences and $\sqrt{10}$ for pharmacodynamic differences. The default intraspecies uncertainty factor (UF_H) of 30 was used, incorporating a subfactor of 10 for pharmacodynamic differences and $\sqrt{10}$ for pharmacokinetic differences. The value of 10 addresses potential increased sensitivity of infants and children vs. adults to continuous exposures to airborne nickel particles. There is also pharmacokinetic uncertainty but this is somewhat lessened by the MPPD2 model which was also applied to several child lung structures. A cumulative uncertainty factor of 100 was then used to derive a chronic REL of 0.014 µg/m^3.

9.6 cREL for Nickel and Nickel Compounds (except nickel oxide)

Study	National Toxicology Program, 1994c
Study population	Male and female F344/N rats (52-53 per group)
Exposure method	Discontinuous inhalation
Critical effects	Pathological changes in lung, lymph nodes, and nasal epithelium: (1) active pulmonary inflammation, (2) macrophage hyperplasia, (3) alveolar proteinosis, (4) fibrosis, (5) lymph node hyperplasia, (6) olfactory epithelial atrophy
$BMDL_{05}$	30.5 µg/m^3 (alveolar proteinosis, male and female mean)
Exposure continuity	6 hours/day, 5 days/week
Exposure duration	104 weeks
Average experimental exposure	5.4 µg Ni/m^3 for NOAEL group (30 x 6/24 x 5/7)
Human equivalent concentration	1.4 µg Ni/m^3 for NOAEL group males (particulate with respiratory effects, DAF = 0.26 based on MMAD = 2.50 µm, gsd = 2.38 µm, density = 2.07 g/cm^3 by MPPD2 model)
LOAEL uncertainty factor	1(default)
Subchronic uncertainty factor	1(default)
Interspecies uncertainty factor	√10 (√10 PD * 1 PK)
Intraspecies uncertainty factor	30 (10 PD * √10 PK)
Cumulative uncertainty factor	100
Inhalation reference exposure level	0.014 µg Ni/m^3

A supporting study is that of Berge and Skyberg (2003) measuring pulmonary fibrosis in nickel refinery workers over a 22 year period. The authors found a weak but positive dose response for pulmonary fibrosis and cumulative nickel exposure expressed as (mg Ni/m^3)-yr. The best model fit to the data was obtained with the unadjusted data on soluble nickel of 0.35 (mg/m^3)-yr for the $BMDL_{01}$ (1% excess risk, multistage model) (Table 25). Converting this value to a lifetime continuous value (8/24 hr x 5/7 days x 1/70 yr) gives 1.2 µg/m^3 equivalent and applying a 30-fold UF_H would give a supporting value for the cREL of 0.04 µg/m^3. The respiratory lesions observed in the Oller et al. (2008) chronic rat study with nickel metal powder give lower cREL values, particularly for alveolar proteinosis (0.004 µg Ni/m^3 female and 0.007 µg Ni/m^3 male), but the material is probably atypical of ambient air exposures.

TABLE 25. BENCHMARK DOSE ANALYSIS OF PULMONARY FIBROSIS IN NICKEL REFINERY WORKERS (DATA FROM BERGE & SKYBERG, 2003)

Nickel type, cumulative dose	**Quantal response**	**Adjustment, goodness of fit χ^2, P Multistage Model**	**BMD_{01}** (mg/m^3)-yr	**$BMDL_{01}$** (mg/m^3)-yr
Soluble Ni: 0.03, 0.27, 1.03, and 4.32 (mg/m^3)-yr	6/254, 3/246, 13/283, 25/263	None, 2.21, 0.33	0.51	0.35
	6/254, 4/246, 12/283, 13/263	Age, smoking, asbestos, sulfidic Ni, 2.21, 0.33	1.38	0.69
	6/254, 4/246, 12/283, 16/263	Age, smoking, asbestos, 1.72, 0.42	0.98	0.56
Sulfidic Ni: 0.01, 0.08, 0.33, 1.73 (mg/m^3)-yr	4/264, 9/237, 15/282, 19/263	None, 3.91, 0.14	0.33	0.19
	4/264, 9/237, 11/282, (8/263)	Age, smoking, asbestos, soluble Ni, 3.27, 0.20; (1.87, 0.17)	No Value for full data set; (0.15 without top dose)	No Value for full data set; (0.063 without top dose)
	4/267, 10/237, 13/282, 12/263	Age, smoking, asbestos, 4.16, 0.125	0.95	0.34

9.7 Nickel Oxide

For nickel oxide the benchmark dose analysis of the lung lesion data from NTP (1994a) gives an improved value of 117 µg Ni/m^3 for the $BMDL_{05}$. The results of the analysis are summarized in Table 26. The derivation of the chronic REL for NiO is similar to that for other nickel compounds shown above with only a slightly different DAF resulting in a proposed cREL for NiO of 0.06 µg/m^3 based on pulmonary inflammation in male and female mice.

TABLE 26. BENCHMARK DOSE ANALYSIS OF LUNG EFFECTS INDUCED BY NIO IN TWO-YEAR STUDIES (NTP, 1994A)*

Species, Sex, Endpoint, Quantal Response	Model	Goodness of Fit, X^2, p	BMD_{05} mg Ni/m^3 (see note)	$BMDL_{05}$ mg Ni/m^3 (see note)
Rats, Male				
Bronchiolar hyperplasia 0/52,7/51,10/53,18/52	Quantal Linear	0.22, 0.89	0.15	0.004
Mice, Male				
Lung inflammation 0/57,21/67,34/66,55/69	Quantal Linear	0.09, 0.95	0.16	0.052
Alveolar proteinosis 0/57,12/67,22/66,43/69	Quantal Linear	0.09, 0.96	0.33	0.13
Mice, Female				
Lung inflammation 7/64,43/66,53/63,52/64	Multistage Cubic	0, 1.0	0.056	0.028
Alveolar proteinosis 0/64,8/66,17/63,29/64	Quantal Linear	0.14, 0.93	0.40	0.12

*Note: BMD and BMDL values are in mg Ni/m^3 continuous

Note that since the MPPD2 model does not calculate airway deposition fractions for the mouse we have included airway deposition fractions from Hsieh et al. (1999c) in Table 24. These authors used the following values for NiO: MMAD = 2.8 µm; gsd = 1.87; density = 7.45 g/cm^3; and concentrations from 1.25 to 5.0 mg NiO/m^3. Predicted mouse deposition fraction for the tracheobronchial region was 0.0096 and for the alveoli was 0.0258 with a total (TB + Alv) of 0.0354. This is much lower than the MPPD2 rat deposition fraction of 0.1289 (OEHHA) or 0.0801 in Hsieh et al. (1999a). Applying this mouse deposition from Hsieh gives a lower DAF of 0.096 and consequently lower HEC of 2.0 µg Ni/m^3. We applied the following uncertainty factors in the derivation of the cREL summarized below. Since an adequate chronic BMDL was available, the UF_L is 1. For interspecies uncertainty we used the same UF_A and rationale as for nickel (above). We assumed that alveolar deposition was the key event leading to subsequent lung toxic effects (e.g., alveolar proteinosis) and that the dosimetric adjustment factor (DAF) would adequately account for the interspecies differences. We applied a factor of √10 for pharmacodynamic differences between mice and humans. For intraspecies differences we applied a UF_H of 30 using the same rationale as with the values derived above. A subfactor of 10 was used to account for the anticipated greater sentitivity of infants and children to continuous exposure to airborne nickel oxide particles. A subfactor of √10 was applied for pharmacokinetic differences between children and adults. The cumulative UF of

100 (√10 x 30) was applied to the HEC of 2.0 µg Ni/m^3 to derive the cREL of 0.02 µg Ni/m^3. This derivation is summarized below.

Study	National Toxicology Program, 1994a
Study population	Male and female B6C3F_1 mice (57-69 per group)
Exposure method	Discontinuous inhalation
Critical effects	Pathological changes in lung: (1) active pulmonary inflammation, (2) alveolar proteinosis
$BMDL_{05}$	117 µg Ni/m^3 (alveolar proteinosis)
Exposure continuity	6 hours/day, 5 days/week
Exposure duration	104 weeks
Average experimental exposure	20.9 µg Ni/m^3 for LOAEL group (117 x 6/24 x 5/7)
Human equivalent concentration	2.0 µg Ni/m^3 for $BMDL_{05}$ for female mice (particulate with respiratory effects, DAF = 0.096 based on MMAD = 2.80 µm, gsd = 1.87, density = 7.45 g/cm^3, from Hsieh et al. 1999c)
LOAEL uncertainty factor	1(default)
Subchronic uncertainty factor	1(default)
Interspecies uncertainty factor	√10 (√10PD * 1PK)
Intraspecies uncertainty factor	30 (10 PD * √10 PK)
Cumulative uncertainty factor	100
Inhalation reference exposure level	0.02 µg Ni/m^3 as NiO

The human epidemiological literature predominantly describes cancer mortality rates from occupational exposures to nickel compounds, but does not specifically examine non-cancer effects. However, it is clear from many case reports that allergies and dermatitis can occur in exposed workers. Hypersensitive reactions to nickel have not been quantitatively studied in humans or animals; therefore it is not possible to develop an REL based on immunological hypersensitivity at the present time. A host of subacute and subchronic animal studies have shown nickel to affect certain immunological responses unrelated to hypersensitivity, but the applicability of these results to chronic human exposures and responses involves considerable uncertainty. Furthermore, data show that nickel may precipitate onset of asthma in occupational settings.

The results of the NTP studies and these dose response analyses support the speciation of nickel oxide for noncancer effects. The health effects data for nickel oxide indicate that its adverse pulmonary effects were less severe (absence of fibrosis, lower chronic lung inflammation severity scores) at higher doses than the pulmonary effects observed for nickel sulfate and nickel subsulfide. The higher chronic REL value for nickel oxide of 0.06 µg/m^3 reflects

these dose response differences. OEHHA therefore concludes that 0.06 $\mu g/m^3$ is an appropriate REL for nickel oxide. However, in setting inhalation exposure RELs for groups of compounds, OEHHA uses the most sensitive strain, species, sex, chronic endpoint, and agent for each group of substances. Therefore, as the pulmonary toxicity of the relatively insoluble nickel subsulfide is greater than that of nickel oxide and closer to that of nickel sulfate, OEHHA proposes to use the chronic REL derived from nickel sulfate for all other nickel compounds.

It should be noted tha although the non-neoplastic lung effects seen in the animal studies discussed above were relatively mild, similar effects in humans may be serious or even fatal.

9.8 Data Strengths and Limitations for Development of the Chronic RELs

The strengths of the inhalation REL include the availability of controlled lifetime exposure inhalation studies in multiple species at multiple exposure concentrations and with adequate histopathological analysis and the observation of a NOAEL. The major areas of uncertainty are the lack of adequate human exposure data and the lack of lifetime toxicity studies in any non-rodent species. The toxicological response to various inhaled nickel compounds in children compared to adults is also an area of uncertainty addressed by a larger uncertainty factor for intra-individual variation (UF_H). Nickel targets the immune system and the lung, which are likely a more susceptible system and organ in exposed infants and children.

9.9 Oral Chronic Reference Level

Study	NiPERA (2000a,b) supported by Smith *et al*., 1993
Study population	Rats (Sprague-Dawley)
Exposure method	Aqueous gavage
Critical effects	Perinatal mortality in two generation study
LOAEL	2.23 mg Ni/kg-d
NOAEL	1.12 mg Ni/kg-d
Exposure continuity	Continuous
Exposure duration	Chronic (70 weeks)
Average exposure	1.12 mg/kg-day
Human equivalent concentration	1.12 mg/kg-day
LOAEL uncertainty factor	1(default)
Subchronic uncertainty factor	1(default)
Interspecies uncertainty factor	10(default)
Intraspecies uncertainty factor	10(default)
Cumulative uncertainty factor	100
Oral reference exposure level	0.0112 mg/kg-day

In addition to being inhaled, airborne nickel can settle onto crops and soil and enter the body by ingestion. Thus an oral chronic REL for nickel is also required.

The proposed oral REL for nickel uses the same three studies used to support OEHHA's Public Health Goal for nickel in drinking water. OEHHA (2000) identified the oral dose of 1.12 mg/kg-d from the lower dose-range of (NiPERA, 2000b) as the appropriate NOAEL value. This NOAEL is lower than the doses at which early pup mortality was observed (LOAEL of 2.23 mg/kg-d) in the preliminary study (NiPERA. 2000a) and the LOAEL of 1.3 mg Ni/kg-d reported by Smith et al. (1993). The oral REL derivation summarized above used uncertainty factors of 10 each for interspecies, and intraspecies extrapolations. The final value is 0.0112 mg Ni/kg-d or 11.0 µg Ni/kg-d. Haber et al. (2000) have proposed an oral reference dose of 8 µg Ni/kg-d based on albuminuria seen in female Wistar rats exposed to $NiSO_4$ for six months (Vsykocil et al., 1994). In our view the limitations of the Vsykocil et al. study, particularly the lack of a clear dose response, render it less acceptable than the NiPERA studies as the basis for a chronic oral REL. All of the inhalation-based RELs derived above give much lower intake values than the oral chronic REL and are considered sufficiently protective of nickel-mediated developmental or reproductive toxicity.

10 Nickel as a Toxic Air Contaminant that Disproportionately Impacts Children

There is a potential for exposure to nickel and nickel compounds in view of its widespread occurrence and numerous uses (see section 3). Nickel is a minor component of airborne particulate matter (PM) and may play a role in the toxicity of PM. It also occurs in tobacco smoke. The adverse impacts of nickel compounds on the respiratory and immune systems (including asthma), and also the increased perinatal mortality and reduced birth weight observed in animal studies of reproductive toxicity (see Section 6), are among the types of effect leading to the potential for differential impacts on infants and children. OEHHA therefore recommends that nickel be identified as a toxic air contaminant, which may disproportionately impact children, pursuant to Health and Safety Code, Section 39669.5(c).

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Appendix A: Additional Toxicological Data on Nickel and its Compounds.

A1 Air Pollution Studies: Nickel as a Component of Particulate Matter

Inhalation exposure to airborne particulate matter (PM) has been linked to multiple adverse respiratory and cardiovascular effects including premature deaths (Englert, 2004). PM of 2.5 µm or less is considered more hazardous since a larger percentage of fine particles are retained in the lung compared with larger particles. $PM_{2.5}$ contains a variety of heavy metals such as iron (Fe), vanadium (V) and nickel (Ni). Several studies in the past several years have found associations between nickel as a metal constituent of $PM_{2.5}$ or PM_{10} and both mortality and morbidity. In a study of daily mortality in 60 National Mortality and Morbidity Air Pollution Study (NMMAPS) cities in the United States Lippmann et al. (2006) found that the association between PM_{10} and mortality was significantly higher in cities where the nickel component level was high (95^{th} percentile) versus when it was low (5^{th} percentile). The difference was 0.6 percent per 10 µg/m^3 increase in PM_{10}. A subsequent reanalysis of the NMMAPS data found that when counties included in the New York community were excluded the effect modification by nickel was much weaker and no longer statistically significant (Dominici et al., 2007). Another study of mortality in 25 U.S. cities found that the effect of $PM_{2.5}$ on mortality increased significantly (0.37%) when $PM_{2.5}$ mass contained a higher proportion of nickel (Franklin et al., 2008). In a study of mortality and sources of $PM_{2.5}$ in six U.S. cities, Laden et al. (2000) found that an increase in nickel from the 5^{th} to 95^{th} percentile of exposure (10.3 ng/m^3) was associated with a significant 1.5% increase in daily mortality. Burnett et al. (2000) studied mortality and fine particulate matter components in 8 Canadian cities. Nickel was significantly associated with mortality in both single pollutant models and multi-pollutant models, which included ozone. A study of mortality and fine particulate components in nine California counties failed to find any association for nickel (Ostro et al., 2007).

Patel et al. (2009) investigated associations between respiratory symptoms in the first 24 months of age and specific components of $PM_{2.5}$ including elemental carbon (EC), Ni, V, and Zn. The study included 653 children. Twenty-four-hour average ambient concentrations of $PM_{2.5}$ and $PM_{2.5}$ fractions of Ni, V, Zn, and EC were measured every third day by the New York State Department of Environmental Conservation. Data on subject characteristics, residence, ETS exposure, and respiratory symptoms were collected by questionnaires administered to mothers every three months. Associations between metals, EC and $PM_{2.5}$ and the presence of wheeze and cough were analyzed using generalized additive mixed effects models. In single pollutant models each pollutant was analyzed as a parametric continuous variable. For each subject, 3-month moving average concentrations of Ni, V, Zn, EC, and $PM_{2.5}$ were

calculated for each symptom-reporting period. Significant positive associations were observed between metals and wheeze but not cough. The analysis was conducted using general additive mixed models adjusted for sex, ethnicity, postnatal ETS exposure and calendar time. The authors found that an increase in interquartile range concentration of ambient nickel (0.014 μg/m^3) was associated with a 28% increased probability of wheeze (p = 0.0006). The findings were robust to the inclusion of co-pollutants EC, NO_2, copper and iron.

The largest effect estimates were seen with nickel. In models that adjusted for sex, ethnicity, postnatal ETS exposure, and calendar time, an increase of 0.014 μg Ni/m^3 was associated with a 28% increased probability of wheeze (P = 0.0006). The authors conclude that exposure to $PM_{2.5}$ associated metals (particularly Ni) and EC may be associated with asthma morbidity in urban children as young as 2 years of age. Perhaps the biggest limitation of the study is that exposure estimates were based on two monitoring stations in the general residential area, which exhibited significant differences in Ni and EC between them. These may not represent true exposures as accurately as personal or residential measurements. Alternatively the exposed population is one of specific concern to OEHHA and the study involves realistic exposure conditions.

In a recent study of birth weight and constituents of $PM_{2.5}$ in three Connecticut counties and one Massachusetts county from 2000 to 2004, Bell et al (2010) found that an interquartile range increase in nickel resulted in an 11% increase in term low birth weight. The analysis was adjusted for tobacco use, alcohol use, marital status, age, race and education of the mother. Looking at change in birth weight, the authors found a significant decrease in birth weight associated with third trimester exposure to nickel. A study of 106 U.S. counties estimated county and season specific relative risks of cardiovascular and respiratory hospital admissions associated with $PM_{2.5}$ chemical components (Bell et al 2009). The authors found that the effect of $PM_{2.5}$ on both respiratory and cardiovascular admissions was significantly modified by the fraction of nickel in the $PM_{2.5}$ mass. An interquartile range increase in nickel resulted in 19% increase in the association between $PM_{2.5}$ and cardiovascular admissions and a 223% increase for respiratory admissions. These increases were robust to adjustment for elemental carbon or vanadium for the cardiovascular but not for the respiratory hospital admissions. Lippmann et al. (2006) and Chen and Lippmann (2009) analyzed and reviewed the data on health-related effects caused by inhalation of airborne particulate matter (PM) and metals within PM in the National Morbidity, Mortality, and Air Pollution Study (NMMAPS). Based on human and laboratory animal studies of concentrated PM and human population studies for which health effects and PM composition data were available, they reached the following conclusions: (1) residual oil fly ash (ROFA) was the most toxic source-related mixture, and (2) Ni and V, which are characteristic of ROFA, were the most influential components for acute cardiac function changes and excess short-term mortality. The difference in PM_{10} mortality risk estimates (in percent/10-μg/m^3 increase in PM_{10}) per 5^{th} to 95^{th} percentile difference in the the PM component across 60 metropolitan areas for which speciation data were

available showed Ni and V with high risk coefficients of 0.6 (their Fig. 1). Dominici et al. (2007) analyzed the same data and more or less came to the same conclusion.

Franklin et al. (2008) investigated the role of particle composition on the association between $PM_{2.5}$ and mortality in 25 communities including six in California. The study sites included $PM_{2.5}$ mass concentration and daily mortality data for at least two years between 2000 and 2005. The data were obtained from the U.S. EPA's Technology Transfer Network Air Quality System and the National Center for Health Statistics. Meteorologic data were obtained form the National Climatic Data Center. 1,313,983 nonaccidental deaths were examined. Thirty-one percent of deaths were due to cardiovascular, 10% were due to respiratory disease, and 7% were due to stroke. The average number of PM2.5 days examined per community was 1451 and the number of speciation days was 321. Seasonally averaged PM2.5 concentrations ranged from well below the National Ambient Air Quality Standard of 15 $\mu g/m^3$ in Sacramento, CA in spring (6.7 $\mu g/m^3$) to over twice the standard in Bakersfield and Fresno, CA in winter (34.4 and 33.4 $\mu g/m^3$, respectively). There was a 0.74% (95% CI = 0.41-1.07%) increase in nonaccidental deaths associated with a 10 $\mu g/m^3$ increase in 2-day averaged $PM_{2.5}$ mass concentration. The association was smaller in the west than in the east and was highest in spring. It was increased when $PM_{2.5}$ mass contained a higher proportion of aluminum, arsenic, sulfate, silicon, and nickel. The combination of aluminum, sulfate and nickel also modified the effect. The results support the concept that mass alone is an insufficient metric when evaluating the health effects of PM exposure and that metal ions, specifically nickel may play a role in the toxic mechanism.

In summary it appears that nickel is a component of ambient PM, which contributes to the overall toxicity, but the available data are not consistent as to the extent of this effect. This and the fact that the studies all involve mixed exposures where the overall effects are dominated by other components and properties of PM make these data unsuitable for consideration as the basis for an REL.

A2 Genetic Toxicity

While genetic toxicology generally provides key supporting documentation for cancer risk assessment rather than the present noncancer assessment, we believe that mutagenicity and other genetox effects, particularly oxidative DNA damage, may contribute to chronic diseases such as heart disease, neurodegenerative diseases, diabetes mellitus, rheumatoid arthritis and aging, irrespective of their role in initiation and promotion of tumors (Burnet, 1974; Cooke et al., 2006; Kelly et al., 2007). In particular nickel's effects on the epigenome and gene expression indicate the probability that nickel's genetic toxicity is relevant to its noncancer effects.

The International Agency for Cancer Research (IARC, 1990), the International Program on Chemical Safety (IPCS, 1991), and NTP (1998) have reviewed the genotoxicity of nickel and nickel compounds in humans. Waksvik and Boysen (1982) studied groups of nickel refinery workers (9-11 workers in each group) and observed increases in chromosomal aberrations compared to controls. Deng et al. (1988) found elevated levels of both sister chromatid exchanges and chromosome aberrations (gaps, breaks, fragments) in seven electroplating workers exposed to nickel and chromium. Kiilunen et al. (1997) found that the frequency of micronucleated epithelial cells in the buccal mucosa of nickel refinery workers in the Helsinki area was not significantly elevated versus controls. The significance of these study results is somewhat limited due to the small sample sizes and the possibility that some workers were exposed to genotoxic compounds other than nickel. We summarize genetic toxicity findings in human test systems in Table 27.

Chen et al. (2003) evaluated the effects of nickel chloride on genotoxicity in human lymphocytes in vitro. Peripheral blood mononuclear cells (PBMC, primarily lymphocytes) were collected from five randomly selected healthy individuals (aged 18 to 23). Isolated lymphocytes (2×10^6 cells/µL) were incubated in saline solution with 0, 0.5, 1.0, 2.5, 5.0, or 10.0 mM $NiCl_2$ for one hour at 37ºC with continuous shaking in the dark. The levels of intracellular reactive oxygen species (ROS), lipid peroxidation, hydroxyl radical (•OH), and DNA damage via the Comet assay were evaluated.

The viability of the lymphocytes based on either trypan blue or neutral red exclusion decreased in a dose-dependent manner (neutral red control 92.3 % vs. 69.7% at 10 mM $NiCl_2$). Intracellular oxidants measured by dichlorofluorescin (DFC) increased in a dose-dependent manner (control 4.8% vs. 59.9% fluorescence intensity at 10 mM $NiCl_2$) with all dose levels significantly greater than the control. 2-Thiobarbituric acid reactant substances (TBARS) were also significantly increased compared to control at all $NiCl_2$ levels (control 156.5 vs. 553.7 nmol/10^6 cells at 10 mM $NiCl_2$). Lipid peroxidation in lymphocytes was significantly increased by three-fold with 10 mM $NiCl_2$.

Hydroxy radical production was measured by the hydroxylation of salicylate to 2,3-dihydroxybenzoate (2,3-DHB) and 2,5-dihydroxybenzoate (2, 5-DHB) byproducts. Both byproducts were significantly increased by $NiCl_2$ in a dose-dependent manner. The greater increase was seen with 2, 3-DHB (control 33.3 vs. 80.5 nM/10^6 cells at 10 mM $NiCl_2$). DNA damage as assessed by the extent of cell tailing in the Comet assay was increased in a dose-dependent manner (control 60 vs. 260 arbitrary units at 10 mM $NiCl_2$). The authors conclude that the generation of •OH radical was responsible for the $NiCl_2$-induced DNA strand breakage as evidenced by the dose-dependent association with •OH radical generation and comet tailing. The high correlation of DNA damage and DHB byproducts ($r^2 = 0.9519$) indicates that ROS in Ni-treated lymphocytes are responsible for Ni-induced oxidative stress. The generation of Ni-induced •OH radical may play an important role in genotoxicity in human cells.

TABLE 27. GENOTOXICITY OF NICKEL COMPOUNDS IN HUMAN TEST SYSTEMS
(adapted from ATSDR, 2005)

Compound	Test System	End point	Result	Reference
Nickel chloride	Human diploid fibroblasts	DNA damage	-	Hamilton-Koch et al., 1986
Nickel sulfate	Human gastric mucosal cells	DNA damage	-	Pool-Zobel et al., 1994
Nickel chloride	Human HeLa cells	DNA replication	+	Chin et al., 1994
Nickel sulfate Nickel sulfide	Human lymphocytes	Sister chromatid exchange	+	Andersen, 1983; Larremendy et al., 1981; Ohno et al., 1982; Saxholm et al., 1981
Nickel sulfate	Human lymphocytes	Chromosome aberration	+	Larremendy et al., 1981
Nickel subsulfide	Human lymphocytes	Sister chromatid exchange, metaphase analysis, micronuclei formation	+ + +	Arrouijal et al., 1982
Nickel sulfate	Human bronchial epithelial cells	Chromosome aberration	+	Lechner et al., 1984
Nickel subsulfide Nickel oxide Nickel sulfate Nickel acetate	Human foreskin cells	Cell transformation	+	Bidermann and Landolph,1987
Nickel oxide Nickel subsulfide Nickel carbonate hydroxide nickel sulfate	Human lymphocytes	Sister chromatid exchange	- +	Waksvik and Boysen, 1982; M'Bemba-Meka et al. 2007
Nickel chloride	Human lymphocytes	DNA strand breakage, Comet assay	+ +	Chen et al., 2003
Nickel containing particles	Human A549 lung cells	Cytotoxicity, DNA repair capacity, mutation frequency	+ + +	Mehta et al., 2008

Broday et al. (2000) observed nickel-induced inhibition of histone H4 acetylation in yeast and human cells in vitro. *Saccharomyces cerevisiae* cells were grown in medium with 0, 0.2 or 0.5 mM $NiCl_2$ for 1, 3, or 6 cell generations. Histones were isolated and analyzed with antibodies specific for H4 acetyl-lysine 5, 8, 12, or 16. The addition of 0.5 mM $NiCl_2$ suppressed the growth-related accumulation of lysine acetylation at all four lysine residues compared with the control cells. The effect of nickel on the levels of histone acetylation was also examined in human lung carcinoma A549 cells treated with soluble $NiCl_2$ and insoluble Ni_3S_2. The soluble nickel treatment of 0 or 3 mM $NiCl_2$ did not change the level of H4 acetylation. Nickel subsulfide treatment at 0, 0.5, 1.0 µg/cm^2 for two days (40 to 80% confluent growth) resulted in a concentration-dependent decrease in H4 acetylation at Lys-12. The concentrations used were reported as nontoxic. What toxic effects may result from altered histone acetylation patterns in vivo, particularly when coupled with Ni-induced DNA methylation, are unknown.

Jia and Chen (2008) studied nickel-induced DNA damage and cell death in human leukemia HL-60 cells and the protecting role of antioxidants. Cells were treated for up to 96 hr with 0, 0.5, 1.0, or 10.0 mM Ni^{2+}. Ten mM Ni^{2+} was rapidly fatal to cells along with a concomitant increase in DNA fragmentation as measured by flow cytometry with propidium iodide. Lower concentrations of Ni^{2+} also resulted in DNA fragmentation and death but at lower levels and after much longer exposures, i.e. no less than 48 or 72 hr at 1.0 or 0.5 mM, respectively. Nickel treatment of HL-60 cells also resulted in a release of malondialdehyde (MDA) in a dose- and time-dependent manner. The antioxidants ascorbic acid and *N*-acetyl-cysteine significantly reduced the Ni-induced generation of MDA and DNA fragmentation in a dose-dependent manner. Alternatively, H_2O_2 increased both Ni-induced MDA generation and DNA fragmentation also in a dose-dependent manner. Similar results were obtained for the cell death endpoint.

Mehta et al. (2008) evaluated the effects of particulate matter containing nickel and chromium on nucleotide excision repair capacity (NER) in human lung cells in vitro. They observed that human A549 cells exposed to 100 µg/mL of urban particulate matter (collected in the Washington DC area) for 24 hr had only a 10% reduction in viability, but a 35% reduction in repair capacity, and a five-fold increase in mutation frequency. The authors interpret their results with a view to three potential mechanisms: (1) particle components such as heavy metals and aldehydes directly modify repair proteins and DNA; (2) ROS and secondary products of ROS modify repair proteins and DNA; and (3) direct modification of DNA replication proteins by heavy metals and aldehydes reduce the fidelity of DNA replication. Specifically “Ni and cadmium can induce repair protein-DNA damage complex formation. Aldehydes, Cr, and Ni are known to have a high affinity towards thiol groups and histones and, therefore, their potential targets could be zinc finger structures in DNA binding motifs.”

The Agency for Toxic Substances and Disease Registry (ATSDR, 2005), NTP (1998), Snow (1992), Kasprzak (1991), IPCS (1991), Costa (1991), IARC (1990), the California Air Resources Board (CARB, 1991), and Sunderman (1989) have reviewed the genotoxicity data and mode of action of nickel and nickel compounds. In Table 28 are summarized the *in vitro* and *in vivo* genotoxicity data of nickel compounds in microbial and mammalian test systems. In general the data suggest that nickel does not alter the frequency of gene mutations in non-mammalian systems although some studies have found gene mutations (ATSDR, 2005). The results in mammalian systems are stronger with increased gene mutations found at the HGPRT locus in Chinese hamster V79 cells (Hartwig and Beyermann, 1989; Miyaki et al., 1979) but not in Chinese hamster ovary (CHO) cells (Hsie et al., 1979). Increased gene mutations were also seen in CHO AS52 cells (*grp* locus) (Fletcher et al., 1994), mouse lymphoma cells (Amacher and Paillet, 1980; McGregor et al., 1988), and virus-infected mouse sarcoma cells (Biggart and Murphy, 1988; Biggart et al., 1987).

TABLE 28. GENOTOXICITY OF NICKEL IN MICROBIAL AND MAMMALIAN TEST SYSTEMS (UPDATED FROM ATSDR, 2005)

Compound	Test System	End point	Result	Reference
Microbial systems				
Nickel chloride Nickel nitrate Nickel sulfate	*Salmonella typhimurium*	Gene mutation	-	Arlauskas et al., 1985; Biggart and Costa, 1986; Marzin and Phi, 1985;Wong, 1988
Nickel chloride	*Escherichia coli*	Gene mutation	-	Green et al., 1976
Nickel chloride	*Escherichia coli*	DNA replication	+	Chin et al., 1976
Nickel chloride	*Corynebacter-ium* sp.	Gene mutation	+	Pikalek and Necasek, 1983
Nickel oxide Nickel trioxide	*Bacillus subtilis*	DNA damage	-	Kanematsu et al., 1980
Nickel chloride	*Saccharomyces cerevisiae*	Histone H4 acetylation decreases at Lys5,8,12,16	+	Broday et al., 2000

TABLE 28. GENOTOXICITY OF NICKEL IN MICROBIAL AND MAMMALIAN TEST SYSTEMS (UPDATED FROM ATSDR, 2005)

Compound	Test System	End point	Result	Reference
Mammalian systems				
Nickel chloride	CHO cells	Gene mutation at the HGPRT locus	-	Hsie et al., 1979
Nickel chloride	Virus-infected mouse cells	Gene mutation	+	Biggart and Murphy, 1988; Biggart et al., 1987
Nickel chloride Nickel sulfate	Mouse lymphoma cells	Gene mutation	+	Amacher and Paillet, 1980; McGregor et al., 1988
Nickel chloride	Chinese hamster V79 cells	Gene mutation	+	Hartwig and Beyersmann, 1989; Miyaki et al., 1979
Nickel chloride Crystalline NiS	CHO cells	DNA damage	+	Hamilton-Koch et al., 1986; Patierno and Costa, 1985
NiO (black and green, <10 µm)) NiS (amorphous, <10 µm) Nickel subsulfide (< 10µm) Nickel chloride Nickel sulfate Nickel acetate	CHO AS52 cells	Gene mutation (*grp* locus)	+	Fletcher et al., 1994
Nickel chloride Nickel sulfate NiS (crystalline)	Hamster cells	SCE	+	Andersen, 1983; Larremendy et al., 1981; Ohno et al., 1982; Saxholm et al., 1981
Nickel sulfate Nickel chloride NiS	Hamster cells	Chromosome aberration	+	Conway and Costa, 1989; Larremendy et al., 1981; Sen and Costa, 1986b; Sen et al., 1987

TABLE 28. GENOTOXICITY OF NICKEL IN MICROBIAL AND MAMMALIAN TEST SYSTEMS (UPDATED FROM ATSDR, 2005)

Compound	Test System	End point	Result	Reference
Nickel sulfate	Rat bone marrow and spermatogonia cells	Chromosome aberration	-	Mathur et al., 1978
Nickel chloride Nickel sulfate Nickel nitrate	Mouse bone marrow cells	Micronucleus test (oral)	+	Sobti and Gill, 1989
Nickel chloride	Mouse bone marrow cells	Chromosome aberrations (i.p.)	-	Dhir et al., 1991
Nickel chloride	Mouse bone marrow cells	Micronucleus test (i.p.)	-	Deknudt and Leonard, 1982
Nickel acetate	Mouse	Dominant lethal test (i.p.)	-	Deknudt and Leonard, 1982
Nickel subsulfide (< 10 µm)	Human lung fibroblast MRC-5 cells	DNA strand breaks, PADPRP activation	+ +	Zhuang et al., 1996
Nickel chloride	CHO Cells	DNA repair inhibition	+	Lynn et al. 1997; Iwitzki et al. 1998
Nickel subsulfide (97% < 10 µm, 70% < 5 µm)	Transgenic mouse	Gene mutation (inhalation)	-	Mayer et al., 1998
Nickel subsulfide (97% < 10 µm, 70% < 5 µm)	Rat	Gene mutation respiratory tissue (inhalation)	-	Mayer et al., 1998
Nickel sulfide, (0.5 µg/cm^2) Nickel chloride, (50 µmol/L) Nickel sulfate, (100 µmol/L)	BALB/c-3T3 Ni-transformed cells in vitro	DNA strand breaks (comet), DNA-protein crosslinks, Telomerase	+ + +	Lei et al. 2001
Nickel sulfate	Chinese hamster V79 cells	Gene mutation, Chromosome aberrations, Aneuploidy, Polyploidy	+ + + +	Ohshima, 2003

TABLE 28. GENOTOXICITY OF NICKEL IN MICROBIAL AND MAMMALIAN TEST SYSTEMS (UPDATED FROM ATSDR, 2005)

Compound	Test System	End point	Result	Reference
Nickel sulfate	Human lung tumor cell lines, HCC15, NCI-H2009, A427	Induction of microsatellite mutations	+ + +	Zienolddiny et al., 2000
Nickel subsulfide (particle size not stated)	Human lung carcinoma A549 cells	Histone H4 acetylation decrease at Lys 12	+	Broday et al., 2000
Nickel chloride	Male Mice	Dominant lethal mutation	+	Doreswamy et al., 2004
Nickel chloride	Male Mice	DNA fragmentation	+	Danadevi et al., 2004
Nickel chloride	Human lung carcinoma A549 cells	Histone H4 acetylation	-	Broday et al., 2000
Nickel sulfate	Male Rats	Micronuclei formation oral	-	Oller and Erexson, 2007
Nickel chloride	Human leukemia HL-60 cells	DNA fragmentation, cell death	+ +	Jia and Chen, 2008
Nickel arsenide	Mouse embryo C3H/10T1/2 Cl 8 cells	Cell transformation Chromosome aberrations	+ +	Clemens and Landolph, 2003
Tungsten-nickel-cobalt alloy 91-6-3 particles	Cultured L6-C11 rat muscle cells	DNA damage, Caspase-3 inhibition, hypoxia, cyto-toxicity	+ + + +	Harris et al. (2011)
$Ni(OH)_2$ nanoparticles (size not specified)	Hyperlipidemic(ApoE -/-) Mice, 79 µg Ni/m^3	Mitochondrial DNA damage in the aorta	+	Kang et al. (2011)

A2.2.1 Studies *in vitro*

Examination of the genotoxicity database for soluble nickel compounds indicated that they generally did not cause mutation in bacterial test systems. Positive results have been observed (1) in tests for single and double DNA strand breaks and/or crosslinks in both human and animal cells, (2) in tests for cell transformation, (3) in tests for sister chromatid exchanges and chromosomal aberrations in hamster and human cells, and (4) in tests for mutation at the HGPRT locus in animal cells (IARC, 1990).

Several studies reported that nickel compounds have the ability to enhance the cytotoxicity and mutagenicity of other DNA damaging agents such as ultra-violet light, benzo(a)pyrene, cis-platinum, and mitomycin C (Hartwig and Beyersmann, 1989; Christie, 1989; Rivedal and Sanner, 1980). Hartwig et al. (1994) showed that Ni^{2+} inhibited the removal of pyrimidine dimers and repair of DNA strand break in HeLa cells after exposure to ultra-violet light or X-rays. Hartmann and Hartwig (1998) demonstrated that the inhibition of DNA repair was effective at a relatively low concentration, 50 µM Ni^{2+}, and partly reversible by the addition of Mg^{2+}. Based on these observations, they suggested that Ni^{2+} disturbed DNA protein interactions essential for the DNA repair process by the displacement of essential metal ions.

Soluble nickel compounds can inhibit the normal DNA synthesis, impair or reduce the fidelity of DNA repair, and transform initiated cells in vitro. Basrur and Gilman (1967) and Swierenga and McLean (1985) showed that nickel chloride inhibited DNA synthesis in primary rat embryo cells and in rat liver epithelial cells. Costa et al. (1982) found that nickel chloride at 40-120 µM selectively blocked cell cycle progression in the S phase in Chinese hamster ovary cells.

Abbracchio et al. (1982) demonstrated that Chinese hamster ovary cells maintained in a minimal salts/glucose medium accumulated 10-fold more ^{63}Ni than did cells maintained in a minimal salts/glucose medium with 5 mM cysteine. The results were obtained after the removal of surface-associated radioactivity by treating the cells with trypsin. They also showed that supplementation of the salts/glucose medium with fetal bovine serum decreased in a concentration dependent fashion both the Ni^{2+} uptake and cytotoxicity.

Nieborer et al. (1984) demonstrated that chelation of Ni^{2+} by amino acids and proteins has a significant effect on the cellular uptake of Ni^{2+} in human B-lymphoblasts, human erythrocytes, and rabbit alveolar macrophages. They observed that addition of L-histidine or human serum albumin at physiological concentrations to the cell cultures reduced Ni^{2+} uptake by 70% -90%. The concentration of nickel used in the study was $7x10^{-8}$ M (or 4.1 µg/L); it was comparable to serum nickel levels observed in workers occupationally exposed to nickel.

Findings of Nieborer et al. (1984) and Abbracchio et al. (1982) indicate the important role of specific amino acids and proteins in regulating the uptake and cytotoxicity of Ni^{2+}. For this reason, when in vitro genotoxicity test results are compared, it is important to standardize the concentration of these chelating agents.

Zhuang et al. (1996) treated MRC-5 human lung fibroblast cells with crystalline Ni_3S_2 (0, 2.5, 5.0, 10.0, or 20 µg/cm^2) for four hours and DNA strand breaks measured by single cell electrophoresis (comet assay). All Ni-treated cells gave significantly increased tail lengths compared to the control ($P < 0.01$). A linear dose-response was observed up to 10 µg Ni/cm^2 (their Fig 2a). Significant leakage of lactate dehydrogenase was seen at 10 and 20 µg/cm^2 and increased activity of poly (ADP-ribose) polymerase (PADPRP) at 5.0 µg/cm^2 and above ($P < 0.01$). PADPRP is a nuclear enzyme associated with DNA damage and repair. PADPRP activity (pmol/µg DNA) was directly correlated with tail length (µm) in the comet assay ($R = 0.971$).

Lynn et al. (1997) studied the role of Ni^{2+} and ROS on enzymes of DNA repair in CHO cells in vitro. Nickel chloride exposure increased cellular oxidant levels in CHO cells in a dose-dependent manner between two and eight mM. When inhibitors of glutathione (BSO, buthione sulfoximine) or catalase (3ATA, 3-aminotriazole) were included with nickel chloride the cytotoxicity of Ni^{2+} was significantly enhanced. The effect was more pronounced in UV-irradiated cultures indicating that ROS were involved in the cytotoxic effect of nickel as well as the enhancing effect of nickel on UV cytotoxicity. The authors tested the effect of H_2O_2 on Ni inhibition of DNA polymerase and ligation. In the presence of 0.1 mM $NiCl_2$ or 1.0 mM H_2O_2, the activities of DNA ligation were about 85% and 50% of control, respectively. The activity of DNA ligation decreased to 9.3% when cell extracts were treated with 0.1 mM $NiCl_2$ and then with 1.0 mM H_2O_2. This level was significantly lower than expected by simple additivity (χ^2 analysis).

This synergistic inhibition induced by Ni plus H_2O_2 was also observed in DNA polymerization in which activity fell to 46.5% after treatment with 0.1 mM $NiCl_2$ and 2.0 mM H_2O_2. The results indicate that DNA ligation is more sensitive to oxidant enhanced Ni inhibition than DNA polymerase. A 30-minute incubation with glutathione could completely remove the inhibition of Ni or recover ligation activity to 80% of control following H_2O_2 treatment or only 45% of control following Ni plus H_2O_2. Ni has a high binding affinity with cellular proteins ($K = 10^9\ M^{-1}$). The redox potential of Ni^{2+} is very high but can be lowered by binding to suitable ligands, such as the imidazole nitrogen of histidine. In the presence of oxidants such as H_2O_2, Ni^{2+}/Ni^{3+} redox cycling can occur leading to the formation of free radicals such as •OH. Radical formation can lead to irreversible damage to proteins involved in DNA repair, replication, recombination and transcription and contribute to the toxic effects of nickel.

Mayer et al. (1998) tested Ni_3S_2 in a *lacI* transgenic BigBlue Rat 2 embryonic fibroblast cell line exposed for two hours to 0, 0.01, 0.04, or 0.17 mM Ni_3S_2. The

mutation frequencies were 4(control), 7.2, 10.4, and 34.1 (x 10^{-5}), respectively. However, molecular analysis in one-third of the mutants did not show DNA sequence change in the *lacI* gene despite loss of function. DNA damage as indicated by fragmentation in the comet assay was also seen in lung and nasal mucosa cells at 0.04 and 0.3 mM Ni_3S_2. Transgenic mice and rats were also exposed by inhalation for two hours (nose only) to 24-352 mg Ni_3S_2/m^3. Control animals were exposed to 8-126 mg $CaCO_3/m^3$and sacrificed immediately after exposure. Transgenic test animals were sacrificed after an expression time of 14 days. Nasal mucosa and lung tissues were removed and frozen until analysis. The spontaneous mutation frequencies of the *lacZ* in mice or the *lacI* in rats was not significantly increased compared to controls in these tissues by exposure to 10 mg Ni_3S_2/kg bw and 6 mg Ni_3S_2/kg bw, respectively.

Iwitzki et al. (1998) studied the effect of nickel chloride on the induction and repair of O^6-methylguanine and N^7-methylguanine after treatment with N-methyl-N-nitrosourea (MNU) in Chinese hamster ovary cells. The CHO cells were transfected with human O^6-methylguanine-DNA methyltransferase (MGMT) cDNA, and compared with MGMT-deficient parental cells. For N^7-methylguanine repair, there was no marked difference in the kinetics of lesion removal with or without nickel. However, nickel (II) led to a significant decrease in repair of O^6-methylguanine lesions. Seventy-eight percent of O^6-methylguanine was repaired in 24 hours in the absence of nickel, while this was reduced to 48% with 250 µ*M* Ni^{2+}. Nickel-induced inhibition of repair exhibited a dose-dependence in the 50-250 µM range. Repair inhibition was accompanied by an increase in MNU-induced cytotoxicity in nickel-treated cells but not in MGMT-deficient controls.

Kawanishi et al. (2001, 2002) described two separate mechanisms of oxidative DNA damage induced by 20 µM $NiSO_4$ in studies with calf thymus DNA, 10 µg/mL of various Ni compounds in cultured HeLa cells, or rats exposed intratracheally. With calf thymus DNA treated with Ni(II) and H_2O_2 they observed a time- and peroxide-dependent increase in 8-hydroxydeoxyguanosine (8-OH-dG). Ni(II) or H_2O_2 alone gave little or no increase in 8-OH-dG. With HeLa cells, incubation with Ni_3S_2 (10 µg/mL) for 24 hr significantly increased 8-OH-dG in extracted cellular DNA. Similar incubations (10 µg/mL) with Ni_2O_3 (black), NiO (green), or $NiSO_4$ did not induce 8-OH-dG formation. A significant increase in of 8-OH-dG was found in DNA extracted from lungs of 3 to 5 rats treated with 1.0 mg each of the nickel compounds intratracheally. The mean 8-OH-dG formation was Ni_3S_2 (2.57±0.87), Ni_2O_3 (black, 2.33±0.55), NiO (green, 2.33±0.61), $NiSO_4$ (1.65±0.97), and control (0.78±0.51) in units of 8-OH-dG/dG x 10^5. All mean increases were significantly greater than the control mean ($P < 0.05$). The results were interpreted by the authors as supporting a direct mode of DNA damage whereby Ni(II) enters the cells and then interacts with endogenous and/or Ni_3S_2-produced H_2O_2 to give reactive oxygen species that cause DNA damage. Additionally an indirect mode of oxidative DNA damage via inflammation is also supported. In this mode the sources of endogenous oxygen radicals are phagocytic cells such as neutrophils and macrophages. All of the

nickel compounds can operate via the indirect mode while nickel subsulfide can also act directly.

Lei et al. (2001) measured DNA strand breaks, DNA-protein crosslinks, and telomerase activity in nickel-transformed BALB/c-3T3 cells in vitro. The transformed loci were induced by insoluble crystalline NiS (particle size not specified, 0.5 μg/cm^2), soluble $NiCl_2$ (50 μM) and $NiSO_4$ (100 μM). All three compounds showed statistically significant DNA strand breaks by the comet assay (single cell electrophoresis). The mean tail lengths of 100 comets were control 13.4, NiS 51.9, $NiCl_2$ 48.3, and $NiSO_4$ 42.2 μm, (all $P < 0.01$ vs. control). DNA-protein crosslinks were measured by ^{125}I-postlabelling techniques. Again all three nickel compounds gave significantly increased crosslinks compared to the control non-transformed cells 618, NiS 2414, $NiCl_2$ 1127, and $NiSO_4$ 988 cpm/μgDNA (all $P < 0.05$). In this case NiS was clearly much more active than the soluble nickel compounds. Telomerase activities were detected in all three nickel-transformed cells but the activity was much higher with NiS and $NiCl_2$ than with $NiSO_4$.

Ohshima (2003) studied genetic instability induced by nickel sulfate in V79 Chinese hamster cells. The cells were treated with 320 μM $NiSO_4$ for 24 hr at low cell density of 100 cells/100 mm diameter dish and clones selected from single surviving cells. When post-treatment cells were grown to 23-25 population doublings, the mutation frequency at the hypoxanthine phosphoribosyltransferase (HPRT) locus and chromosome aberration frequency of each clone were measured. Five out of 37 clones from Ni-treated cells showed increased frequencies of HPRT mutations ($\geq 1 \times 10^{-4}$), while only 1/37 control clones showed a mutation rate this high. Also, 17/37 clones from treated cells showed structural chromosomal aberrations vs. 3/37 for the controls. These included chromatid gaps and breaks, chromosome gaps and breaks, exchange, ring, and dicentric aberrations. The frequencies of chromosome gaps, ring, and dicentric aberrations were statistically significantly increased compared to controls, as was mean frequency of all aberrations ($P < 0.05$, *t*-test). Numerical aberrations were also observed in clones from Ni-treated cells: 8/37 for aneuploidy and 11/37 for polyploidy. Only a few control clones showed such numerical aberrations. The authors conclude that nickel sulfate can induce genetic and chromosomal instability in V79 cells.

Oxidative DNA damage has been implicated as a contributing factor in neurodegeneration and heart disease as well as cancer and may figure in many degenerative diseases. Several studies to date have focused on the formation of the primary products of DNA oxidation: 7, 8-dihydro-8-oxoguanine (8-oxoG) and 8-hydroxy-2'-deoxyguanosine (8-OH-dG). Kelly et al. (2007) studied the oxidation of guanine, 8-oxoG and DNA by a Ni(II)/H_2O_2 system in vitro. They observed erratic oscillatory-like formation of 8-oxoG from free guanine and from DNA. Oxidation of 8-oxoG by Ni(II)/H_2O_2 led to guanidinohydantoin (GH) or its oxidized analog (oxGH). The authors conclude that the instability of 8-oxoG (and presumably 8-OH-dG) in this system and its further oxidation products indicate a

complex oxidative mechanism for guanine and unsuitability as a biomarker of DNA damage. However, it's not yet clear how quantitatively significant these "further" oxidative steps are under usual exposure scenarios.

Another problem with interpreting DNA adduct data is revealed by the study of Kaur and Dani (2003) on the relative nickel binding to RNA versus DNA. Female Sprague-Dawley rats (3 x 0.15 kg) were administered i.p. injections of $^{63}NiCl_2$. After 24 hr the animals were sacrificed and selected tissues removed for analysis. The subcellular distribution of ^{63}Ni in the liver, kidney, spleen and lungs was highest in the nucleus. About 10% to 50% of the nuclear radioactivity level was seen in the mitochondria, lysosomes, and microsomes. Further analysis of the nuclear fraction showed that in each tissue the large majority of ^{63}Ni label was associated with RNA rather than with DNA or nucleoproteins. The highest association observed was with kidney RNA. In vitro binding of $^{63}NiCl_2$ to DNA, denatured DNA, highly polymerized (HP) DNA, and RNA showed the maximum binding to RNA and HP DNA. Binding to DNA and denatured DNA was less than 25% of these values. Significant differences were observed between the infrared (IR) spectra of RNA and DNA incubated in vitro with $NiCl_2$, which also support the radiolabel findings. The authors postulate that Ni(II) may act by controlling gene expression post-transcriptionally via interaction with mRNA. Loss of mRNA has been reported in nickel-transformed cells (Salnikow et al., 1994).

Deng et al. (2006) observed that treatment of V79 cells with $NiCl_2$ after, but not before, exposure to benzo[a]pyrene (BaP) or its diol-epoxide (BPDE) metabolite led to significant enhancements of chromosome damage compared to control cells. Treatment of V79 cell for two hours with 0, 1, 5, 10, or 20 µg/mL of $NiCl_2$ resulted in proportions of aberrant cells of 0.75%, 0.75%, 1.0%, 1.3%, and 1.8 %, respectively. A similar value, 1.3% was obtained with 0.5 µg/mL BaP. Treatment of $NiCl_2$ at 5, 10, or 20 µg/mL after BaP exposure gave 9.3%, 12%, or 13% aberrant cells (all $P < 0.05$). The large majority of aberrations were chromosome breaks. The authors interpret the Ni-mediated potentiation of BaP genetic toxicity as a result of nickel inhibition of nucleotide excision repair (NER).

A2.2.2 Studies *in vivo*

The clastogenic potential of soluble nickel compounds has been shown in many in vivo studies. Sobti and Gill (1989) reported that oral administration of nickel sulfate (28 mg Ni/kg bw), nickel nitrate (23 mg Ni/kg bw), or nickel chloride (43 mg Ni/kg bw) to mice increased the frequency of micronuclei in the bone marrow at 6 and 30 hours after treatment. Details of the study were not reported and it was not clear how many animals were used in each experiment. Mohanty (1987) reported that intraperitoneal injections of nickel chloride at 6, 12, or 24 mg/kg bw increased the frequency of chromosomal aberrations in bone-marrow cells of Chinese hamsters. However, Mathur et al. (1978) observed that intraperitoneal injections of nickel sulfate at 3 and 6 mg/kg bw did not induce chromosomal aberrations in bone-marrow cells and spermatogonia of male albino rats. Saplakoglu et al. (1997) administered 44.4 mg nickel chloride/kg bw to rats via

subcutaneous injections and did not observe increased levels of single-strand breaks in cultured lung, liver, or kidney cells.

Similarly, Deknudt and Leonard (1982) administered 25 mg/kg bw nickel chloride and 56 mg/kg nickel nitrate (about 50% of the LD_{50} in both cases) to mice by intraperitoneal injection and did not detect a significant increase of micronuclei in the bone marrow of the animals after 30 hours. Inhibition of DNA synthesis has been observed in vivo. Amlacher and Rudolph (1981) observed that intraperitoneal injections of nickel sulfate at 15 - 30% of the LD_{50} to CBA mice suppressed DNA synthesis in hepatic epithelial cells and in the kidney. Hui and Sunderman (1980) also reported that intramuscular injections of nickel chloride to rats at 20 mg Ni/kg bw inhibited DNA synthesis in the kidney.

Danadevi et al. (2004) administered $NiCl_2$ to 4-week old male Swiss mice. Eight groups of five animals each were given 0, 3.4, 6.8, 13.6, 27.2, 54.4, or 108.8 mg $NiCl_2$/kg bw by gavage. One group was given 25 mg cyclophosphamide/kg bw i.p. as a positive control. Blood was collected from each animal at 24, 48, and 72 hr, one week and two weeks post-treatment. DNA damage was assessed by single cell electrophoresis of leucocytes (comet assay). All doses produced significant dose-dependent DNA damage ($P < 0.05$) when compared to controls at 24, 48, 72 hr and one week. Clinical signs included loss in weight and feed intake at doses ≥ 13.6 mg $NiCl_2$/kg bw. From 72 hr post-treatment the mean comet lengths of all doses gradually decreased and after two weeks the lower doses (≤13.6 mg/kg) were not significantly different from the negative controls.

Oller and Erexson (2007) found a lack of micronuclei formation in 6 male Sprague-Dawley rats/dose group exposed to 0, 125, 250, or 500 mg $NiSO_4 \cdot 6H_2O$/kg-d for 3 days. At least 2000 polychromatic erythrocytes (PCEs) per animal were analyzed for micronuclei. Average micronuclei (2000/animal) found were 0.07, 0.01, 0.07, 0.06%, respectively. Nickel concentrations found in plasma and bone marrow were significantly higher in all dose groups than in the control animals.

Jia and Chen (2008) extended their study of antioxidant protection against nickel-induced DNA fragmentation to 40 male C57 mice and ascorbic acid (ASA) as antioxidant. Five groups of eight mice each were treated with a single daily i.p. injection for two weeks with 0, 2.0, 20.0 mg/kg-d $NiCl_2$, 2.0 + 5.0 mg/kg-d ASA, or 20.0 + 5.0 mg/kg-d ASA. DNA fragmentation and malondialdehyde (MDA) generation were measured in peripheral blood mononuclear cells (PBMC) and serum, respectively. Without ASA significant dose-dependent DNA fragmentation and MDA generation was observed. For DNA fragmentation the mean (± SD, N = 8) for 0, 2, and 20 mg Ni/kg-d were 4.68 ± 0.89%, 9.83 ± 1.16%* and 15.25(1.91) %*, respectively (*$P < 0.01$). MDA in serum also showed a significant but shallower increase. Treatment of Ni + ASA showed slight, non-statistically significant, increases of MDA and DNA fragmentation. For the latter the values were 4.68(0.89), 6.16(0.88), and 7.85(1.1), respectively. MDA values gave a shallower response. No trend tests were provided. The

authors suggest the use of ascorbic acid to ameliorate the chronic toxic effects in individuals occupationally exposed to nickel compounds.

A number of hypotheses have been proposed about the mechanisms that can explain the observed genotoxicity and transformation potential of soluble nickel compounds. Costa et al. (1982) and Sahu et al. (1995) showed that soluble nickel compounds affected cell growth by selectively blocking the S-phase of the cell cycle. Kasprzak (1991) and Sunderman (1989) suggested that most of the genotoxic characteristics of Ni^{2+} including DNA strand breaks, DNA-protein crosslinks, and chromosomal damage could be explained by the ability of Ni^{2+} to generate oxygen free radicals. While Ni^{2+} in the presence of inorganic ligands is resistant to oxidation, Ni^{2+} chelated with peptides has been shown to be able to catalyze reduction-oxidation reactions. Andrews et al. (1988) observed that certain peptides and proteins (especially those containing a histidine residue) form coordination complexes with Ni^{2+}. Many of these complexes have been shown to react with O_2 and/or H_2O_2 and generate oxygen free radicals (such as •OH) *in vitro* (Bossu et al., 1978; Inoue and Kawanishi, 1989; Torreilles and Guerin, 1990; Nieboer et al., 1984 and 1988). It is important to note that the major substrates for nickel mediated oxygen activation, O_2 and H_2O_2, are found in mammalian cells, including the nucleus (Peskin and Shlyahova, 1986).

Tkeshelashvili et al. (1993) showed that mutagenesis of Ni^{2+}in a bacterial test system could not only be enhanced by the addition of both hydrogen peroxide and a tripeptide glycyl-glycyl-L-histidine but also could be reduced by the addition of oxygen radical scavengers. Huang et al. (1993) treated Chinese hamster ovary cells with 0 to 5 mM nickel chloride and the precursor of fluorescence dye, 2, 7-dichlorofluorescin diacetate, and observed a significant increase of fluorescence in intact cells around the nuclear membranes. The effect was related to the concentration of the nickel chloride and was detectable at or below 1 mM. Since only strong oxidants, such as hydrogen peroxide and other organic hydroperoxides, can oxidize the nonfluorescent precursor to a fluorescent product, Huang et al. (1993) suggested that Ni^{2+} increased the level of such oxidants in intact cells.

Evidence of oxidative damage to cellular and genetic materials as a result of nickel administration has also been obtained from a number of *in vivo* studies. There are data indicating lipid peroxidation participates in the pathogenesis of acute nickel poisoning (Sunderman et al., 1985; Donskoy et al., 1986; Knight et al., 1986; Kasprzak et al., 1986 and Sunderman et al., 1987). Stinson et al. (1992) subcutaneously dosed rats with nickel chloride and observed increased DNA strand breaks and lipid peroxidation in the liver 4-13 hours after the treatment. Kasprzak et al. (1992) administered nickel acetate (5.3 mg Ni/kg bw) to pregnant rats by a single or two intraperitoneal injections and identified eleven oxidized purine and pyrimidine bases from the maternal and fetal liver and kidney tissues. Most of the products identified were typical hydroxyl radical-produced derivatives of DNA bases, suggesting a role for hydroxyl radical in the induction of their formation by Ni^{2+}. In two other animal studies, Kasprzak et al. (1990 and

1992) also observed elevated levels of 8-hydroxy-2'-deoxyguanosine (8-OH-dG) in the kidneys of rodents administered a single intraperitoneal injection of nickel acetate. Formation of 8-OH-dG is often recognized as one of the many characteristics of •OH attack on DNA.

Besides generating oxygen free radicals, Ni^{2+} can also weaken cellular defense against oxidative stresses. Donskoy et al. (1986) demonstrated that administration of soluble nickel compounds depleted free-radical scavengers (e.g., glutathione) or catalase, superoxide dismutase, glutathione peroxidase, or other enzymes that protect against free-radical injury in the treated animals.

Insoluble crystalline nickel compounds are generally found to be more potent in genetic toxicity assays than the soluble or amorphous forms of nickel. To find out the reason for this phenomenon, Harnett et al. (1982) compared the binding of ^{63}Ni to DNA, RNA, and protein isolated from cultured Chinese hamster ovary cells treated with either crystalline nickel sulfide (^{63}NiS) or a soluble nickel compound, $^{63}NiCl_2$ (both at 10 µg/mL). They reported that in the case of $^{63}NiCl_2$ treatment, cellular proteins contained about 100 times more bound ^{63}Ni than the respective RNA or DNA fractions; whereas in cells treated with crystalline ^{63}NiS, equivalent levels of nickel were associated with RNA, DNA, and protein. In absolute terms, RNA or DNA had 300 to 2,000 times more bound nickel following crystalline ^{63}NiS treatment compared to cells treated with $^{63}NiCl_2$. Fletcher et al. (1994) reported similar findings. Chinese hamster ovary cells were exposed to either water-soluble or slightly water-soluble salts. They observed relatively high nickel concentrations in the cytosol and very low concentrations in the nuclei of the cells exposed to the water-soluble salts. In contrast, they found relatively high concentrations of nickel in both the cytosol and the nuclei of the cells exposed to the slightly water-soluble salts.

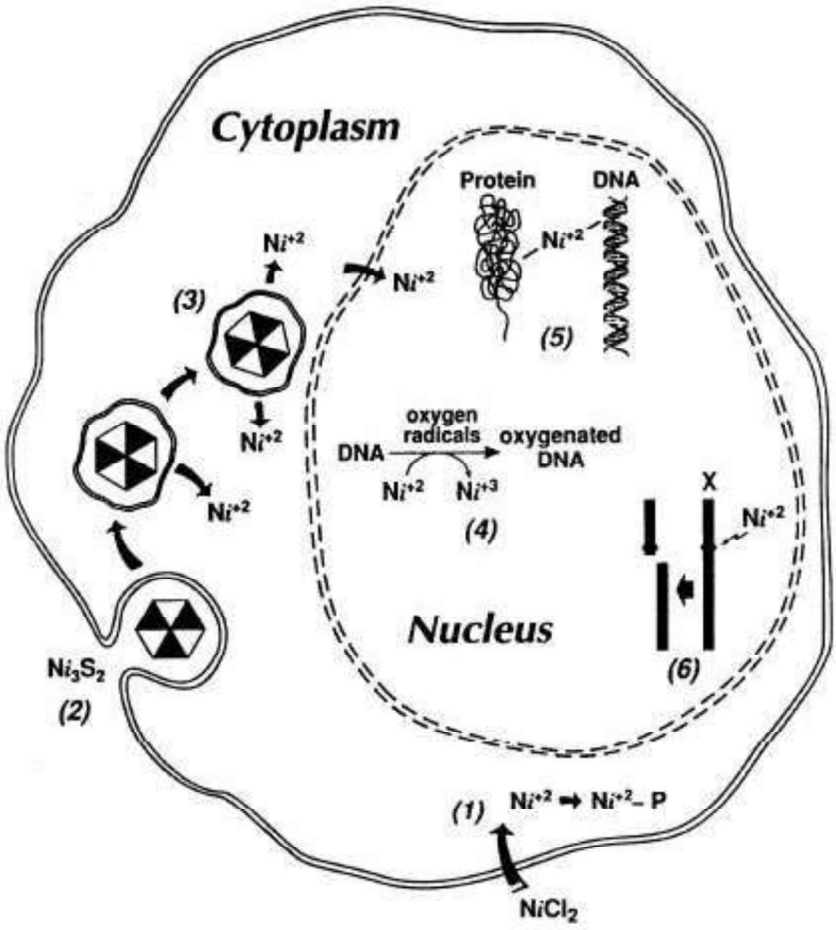
Sen and Costa (1986) and Costa et al. (1994) theorized that this is because NiS and $NiCl_2$ are taken up by cells through different mechanisms. Ni^{2+} has a high affinity for protein relative to DNA; treatment of cells with soluble nickel compounds resulted in substantial binding of the metal ion to cytoplasmic proteins, with a small portion of the metal ion eventually reaching the nucleus. When cells are treated with crystalline nickel sulfide, the nickel containing particles were phagocytosed and delivered to sites near the nucleus. This mode of intracellular transport reduces the interaction of Ni^{2+} with cytoplasmic proteins and peptides.

To support their theory, Sen and Costa (1986) exposed Chinese hamster ovary cells to nickel chloride alone, nickel chloride-albumin complexes, nickel chloride-liposomes, and nickel chloride-albumin complexes encapsulated in liposomes. They found that at a given concentration (between 100 and 1,000 µM), cellular uptakes of nickel were 2-4 fold higher when the ovary cells were exposed to nickel chloride-liposomes or nickel chloride-albumin complexes encapsulated in liposomes than to nickel chloride alone or nickel chloride-albumin complexes. Even at comparable levels of cellular nickel (approximately 300 pmole Ni/10^6

cells), fragmentation of the heterochromatic long arm of the X chromosome was only observed in cells treated with nickel encapsulated in liposomes and not in those exposed to nickel or nickel-albumin. Based on these data, they suggested that the higher genotoxic potency of crystalline nickel sulfide and nickel encapsulated in liposomes was not primarily due to the higher cellular nickel concentration, but rather to the way nickel ion was delivered into cells.

IARC (1980) suggested that cellular binding and uptake of nickel depend on the hydro- and lipophilic properties of the nickel complexes to which the cells are exposed. Nickel-complexing ligands, L-histidine, human serum albumin, D-penicillamine, and ethylenediaminetetraacetic acid, which form hydrophilic nickel complexes, inhibited the uptake of nickel by rabbit alveolar macrophages, human B-lymphoblasts, and human erythrocytes. Diethyldithiocarbamate and sodium pyridinethione, however, which form lipophilic nickel complexes, enhanced the cellular uptake of nickel. Several ideas and findings bearing on the mode of action of nickel genotoxicity have been integrated into a scheme proposed by NTP (1996a) and reproduced in Figure 7.

FIGURE 7. POSSIBLE MECHANISMS OF NICKEL-INDUCED GENOTOXICITY (FROM NTP, 1996A).



1) Soluble nickel compounds such as nickel chloride diffuse into the cell; Ni^{2+} ions are rapidly bound to cytoplasmic proteins (P) (Lee et al., 1993).
2) Insoluble nickel compounds such as nickel subsulfide are phagocytized into the cell and move toward the nucleus (Costa et al., 1982).
3) Lysosomal breakdown of insoluble nickel compounds releases large quantities of Ni^{2+} ions that concentrate adjacent to the nuclear membrane (Costa and Heck, 1983).
4) Oxidative damage is induced in DNA by nickel ions bound to nuclear proteins ($Ni^{2+} \rightarrow Ni^{3+}$), releasing active oxygen species (Tkeshelashvili et al., 1993; Sugiyama, 1994).
5) DNA-protein crosslinks are produced by Ni^{2+} ions binding to heterochromatin (Lee et al., 1982; Patierno and Costa, 1985; Sen and Costa, 1986).
6) Binding of nickel ions to the heterochromatic regions of the long arm of the X chromosome, which may contain a senescence gene and a tumor suppressor gene, can cause deletion of all or part of this region, leading to an immortalization of the cell and clonal expansion (Conway and Costa, 1989; Klein et al., 1991).

In general nickel genotoxicity is the result of indirect mechanisms. Three mechanisms predominate: (1) interference with cellular redox regulation and induction of oxidative stress and possible oxidative DNA damage; (2) inhibition of major DNA repair systems resulting in genomic instability and accumulation of mutations; and (3) deregulation of cell proliferation by induction of signaling pathways or inactivation of growth controls including tumor suppressor genes (Beyersmann and Hartwig, 2008).

A3 Effects on Gene Expression and the Epigenome

The effects of nickel on the epigenome are summarized in Table 29. Effects on DNA methylation and/or histone methylation, acetylation, or ubiquitination may influence the initiation and/or progression of chronic diseases in addition to cancer. In their review of metal epigenetics Arita and Costa (2009) conclude :

> "Taken together, numerous data suggest that epigenetic changes contribute more to nickel-induced toxic and carcinogenic effects than mutagenic effects."

Yan et al. (2003) studied histone modifications and gene silencing in nickel-treated *gpt* (guanine phophoribosyl transferase gene) transgenic G12 Chinese hamster cells. Four nickel-induced *gpt*-silenced G12 clones (N24, N37, N96, N97) obtained by treatment with NiS or Ni_3S_2 were used (particle sizes not specified). These clones were readily reverted to wild type (gpt^+) by treatment with 5-azacytidine. Analysis of chromatin proteins associated with Ni-silenced *gpt* gene was by chromosome immunoprecipitation assay (ChIP). The results showed hypoacetylation of both histones H3 and H4 in all four silenced G12 cell clones. Histone H4 acetylation of N24 was higher than the other clones but much lower than G12 control cells. The ChIP assay also showed hypoacetylation of histone H3-K9 in all four silenced clones. Alternatively, methylation was higher than controls in three of four silenced clones. Overall the results indicate that gene silencing induced by nickel involved the loss of histone acetylation and the activation of histone methylation. Silenced clones exhibited an increase in the methylation of the lysine 9 in histone H3.

Zhang et al. (2003) observed inhibition and reversal of nickel-induced transformation by the histone deacetylase inhibitor trichostatin A (TSA). Human T85 osteoblastic cells (HOS) were exposed to 0, 0.15, or 0.30 μg/cm^2 Ni_3S_2 or 0, 1, 2 mM $NiCl_2$ for 24 hr. The cells were rinsed, allowed to grow for 48 hr and the Ni treatment repeated. This procedure was repeated nine times. Either 5.0 ng/mL or 25 ng/mL TSA were added to the cells four hr before each exposure. Ni treated HOS cells exhibited dose-dependent increases in anchorage-independent colonies with both nickel compounds (ca. 500-750/10^5 cells vs. 250/10^5 cells in controls). Similar exposure to mouse PW cells showed 150 - 250/10^5 cells for $NiCl_2$ and 1500-2200/10^5 cells for Ni_3S_2 vs. 0 for controls. TSA treatment caused a dose-dependent suppression of Ni-induced transformation of HOS and PW cells. For HOS cells treated with 2 mM $NiCl_2$ the extent of

transformation at 0, 5.0, and 25.0 ng/mL TSA was 100%, 59.5% ($P < 0.05$), and 51.0% ($P < 0.01$), respectively. For HOS cells treated with 0.30 μg/cm^2 Ni_3S_2 the extent of transformation was 100%, 93.3% and 78.9% ($P<0.05$), respectively. Suppression was greater in the mouse PW cells (range 67 to 39%). Isolated Ni-transformed clones of mouse PW cells were reverted to normal by treatment with 5.0 ng/mL or 25.0 ng/mL TSA. Transformed cells ranged from 33 to 65% at 5 ng TSA/mL, 16 to 36% at 25.0 ng TSA/mL vs. 100% in untreated Ni-transformed clones.

Costa et al. (2005) found that exposure of human lung A540 cells to NiS particles for 48 to 72 hours resulted in most of the nickel bound in the cell nuclei. In contrast cells exposed to soluble $NiCl_2$ resulted in Ni ions localized in the cytoplasm. This result is consistent with reports that short-term (1-3 days) exposure to crystalline nickel particles can epigenetically silence target genes near heterochromatin, while similar short-term exposure to soluble nickel does not silence the genes. However, longer term (3 weeks) exposure to soluble nickel is also able to induce gene silencing. Nickel compounds were also found to activate hypoxia-signaling pathways. This probably results from nickel compounds blocking iron uptake leading to cellular iron depletion, affecting iron-containing enzymes. The inhibition of iron-dependent enzymes, such as aconitase and HIF proline hydroxylases may stabilize HIF protein and activate hypoxic signaling. Nickel and hypoxia decrease histone acetylation and increase methylation of H3 lysine 9. The loss of histone acetylation and methylation of lysine 9 in H3 results in global silencing of gene expression. Costa et al. also observed increases in the ubiquitination of histones of H2A and H2B in A549 cells after only 8 hours exposure to 1 mM $NiCl_2$. No changes were seen in ubiqitinated H4 as a result of similar exposures for up to 72hr.

Ke et al. (2006) studied alterations of histone modifications and transgene silencing by $NiCl_2$. Human lung bronchoepithelial A549 cells in culture were exposed to 0, 0.25, 0.50, or 1.0 mM $NiCl_2$ for 24 hr. Using pan-acetylated histone antibodies, the global levels of histone acetylation on histones H2A, H2B, H3 and H4 were measured following nickel exposure. The nickel doses had no effect on cell viability whereas histone acetylation was decreased in all four-core histones. A similar loss of histone acetylation was also observed in human hepatoma Hep3B cells, mouse epidermal C141 cells and *gpt* transgenic Chinese hamster G12 cells. Nickel treatment also resulted in increases of ubiquitination of H2A and H2B in a dose-dependent manner. The G12 *gpt* transgenic cell line was used to measure Ni-induced gene silencing in cells treated for 7 to 21 days with 50 or 100 μM $NiCl_2$ or 1 μg/cm^2 NiS. Treatments of three days or longer, resulted in increased frequency of 6-thioguanine (6-TG) resistant colonies, suggesting silencing of the *gpt* transgene in a time-dependent manner. After Ni-treatment the cells were placed in normal medium for either one or five weeks. The mRNA levels of the *gpt* transgene, which were very low after Ni treatment, returned to basal level after five weeks recovery. The data suggest that the nickel-induced effects were epigenetic.

Chen et al. (2006) reported that $NiCl_2$ treatment of human lung carcinoma A549 cells induced increases in histone H3 lysine 9 dimethylation and transgene silencing. Nickel(II) ions were found to increase global histone H3K9 mono- and dimethylation but not trimethylation. Increases in dimethylation occurred at ≥ 250 µM Ni(II) in a time-dependent manner. Nickel exposure decreased the activity of histone H3K9 methyltransferase G9a thus interfering with the histone dimethylation process. Cultured transgenic *gpt*$^+$ *hprt*$^-$ G12 cells were used to study Ni-induced gene silencing. Both acute and chronic nickel exposures decreased the expression of the *gpt* transgene in G12 cells. The cells were exposed to Ni(II) for 3 to 25 days to 50 or 100 µM $NiCl_2$ then selected for the *gpt*$^-$ phenotype by growing cells in the presence of 6-thioguanine (6-TG). Nickel exposure increased the frequency of 6-TG^r variants in a dose- and time-dependent manner. The variants were treated with 5-aza-2'-deoxycytidine resulting in a very high percentage reversion from *gpt*$^-$ to *gpt*$^+$ phenotype. Such a high frequency of reversion indicates that Ni(II) silenced the *gpt* transgene via an epigenetic rather than a genetic mechanism involving mutations or deletions. Overall the results indicated that the increase in H3K3 dimethylation played a key role in the *gpt* transgene silencing due to Ni(II) exposure.

Karaczyn et al. (2006) observed that human lung cells treated with Ni(II) resulted in a stimulation of mono-ubiquitination of H2A and H2B histones. Cultured 1HAEo and HPL1D human diploid lung cells were treated for 1 to 5 days with 0.05 to 0.5 mM Ni(II) acetate. Cell viability, assessed by Trypan blue exclusion, ranged from 90% at the low nickel concentration to 55-65% at the high concentration. Maximum stimulation of ubiquitination of H2B histone was reached in 24 hr at 0.25 mM Ni(II) in both cell lines. The authors note: "covalent modifications of core histones in chromatin, such as acetylation, methylation, phosphorylation, ribosylation, ubiquitination, sumoylation, and possibly others (e.g. deimination and biotinylation) serve as regulatory mechanisms of gene transcription." Usually increased ubiquitination of histone H2B is associated with gene silencing and decreased ubiquitination with gene activation, although this may depend on gene location. The authors interpret their results on Ni-induced histone ubiquitination as part of nickel's adverse effects on gene expression and DNA repair.

Ji et al. (2007) investigated epigenetic alterations in a set of DNA repair genes in NiS-treated 16HBE human bronchial epithelial cells (0, 0.25, 0.5, 1.0, or 2.0 µg Ni/cm^2 for 24 hr). The silencing of the O^6-methylguanine DNA methyltransferase (MGMT) gene locus and upregulation of DNA methyltransferase 1 (DNMT1) expression was observed in treated cells. Other epigenetic alterations included DNA hypermethylation, reduced histone H4 acetylation and a decrease in the ratio of Lys-9 acetylated/methylated histone H3 at the MGMT CpG island in NiS-transformed 16HBE cells. It is likely that Ni-induced alterations in DNA and histones contribute to altered gene expression, cytotoxicity and tumorigenicity.

Ke et al. (2008) demonstrated the both water-soluble and insoluble nickel compounds induce histone ubiquitination (uH2A and uH2B) in a variety of cell lines. Human A529 lung cells were treated with $NiCl_2$ (0.25, 0.5, and 1.0 mM) or Ni_3S_2 (0.5 and 1.0 μg/cm^2) for 24 hr. After exposures histones were isolated and Western blots performed using antibody against uH2A. $NiCl_2$ and Ni_3S_2 exposures resulted in increased levels of uH2A in a dose-dependent manner. Other mouse and human cell lines tested were C141, Beas-2B, HeLa, and Hep3B. In each case $NiCl_2$ treatment resulted in increased levels of uH2A. In vitro assays indicated that the presence of nickel did not affect the levels of ubiquinated histones through increased synthesis; instead nickel significantly prevented loss of uH2A and uH2B presumably inhibiting putative deubiquitinating enzyme(s). The study indicates that nickel ions may alter epigenetic homeostasis in cells.

Li et al. (2009) studied signaling pathways induced by nickel in non-tumorigenic human bronchial epithelial Beas-2B cells. Both 0.25 mM and 1.0 mM $NiSO_4$ exposures for 24 hr significantly up-regulated *c-Myc* protein in Beas-2B cells in a time-dependent manner. Because of the central role of *c-Myc* in cell growth regulation, cell apoptosis was also studied. Beas-2B cells were treated with $NiSO_4$ and whole cell lysates to determine poly (ADP-ribose) polymerase (PARP) cleavage, a marker for cell apoptosis. Nickel ions at 0.5 and 1.0 mM significantly induced PARP cleavage, indicating $NiSO_4$- induced apoptosis in the Beas-2B cells. Knockout of *c-Myc* and its restoration in a rat cell system confirmed the role of *c-Myc* in Ni(II)-induced apoptosis. Ni(II) ions increased the *c-Myc* mRNA concentration and *c-Myc* promoter activity but not *c-Myc* mRNA and protein stability. By the use of pathway specific inhibitors the investigators concluded that Ni(II) induced *c-Myc* in Beas-2B cells via the *Ras/ERK* signaling pathway. The study suggests possible roles for *c-Myc* in Ni-induced toxicity.

Ellen et al. (2009) observed that nickel ion Ni^{2+} condenses chromatin to a greater extent than the natural divalent cation in the cell, the magnesium ion Mg^{2+}. The authors found a significant difference in circular dichroism spectropolarimetry (CD) of oliginucleosomes exposed to the divalent cations. The maximum molar ellipticity at 272 nm decreased from ~6000 in the absence of cations to ~5000 with 0.6mM Mg^{2+}. In the presence of 0.6mM Ni^{2+} the molar ellipticity was reduced to ~3000. The authors note that this condensation or heterochromatinization of chromatin within a region containing a target gene would inhibit further molecular interactions essentially silencing the gene. In addition they used a model system that incorporated a transgene, the bacterial xanthine guanine phophoribosyl transferase gene (*gpt*) near and far from a heterochromatic region of the genome in two cell lines of Chinese hamster V79-derived cells. The model demonstrated by a Dnase I protection assay that nickel treatment protected the *gpt* gene sequence from Dnase I exonuclease degradation. The authors propose Ni-induced condensation of chromatin as a mechanism of nickel-mediated gene regulation.

The effects of nickel, chromate, and arsenite on histone 3 lysine 4 (H3K4) methylation in human A549 cells was evaluated by Zhou et al. (2009). Treatment of human lung carcinoma A549 cells with $NiCl_2$ (1.0 mM), Cr(VI) (10 µM), or As(III) (1.0 µM) significantly increased tri-methyl H3K4 after 24 hr exposure. Seven days exposure to lower levels (e.g., 50 µM Ni(II)) also increased tri-methyl H3K4. The results indicate that the metals studied alter various histone tail modifications, which can affect the expression of genes that may cause cell transformation or other cytotoxic effects. The specific genes that may be affected by these alterations are unknown. Other relevant DNA methylation and mapping of post-translational modifications of histones in the promoter regions of target genes warrant further investigation.

TABLE 29. EFFECTS OF NICKEL ON THE EPIGENOME*

Study	Compound	Gene or factor affected	Effect	Cell Type	Comments or other effects
Li et al., 2009	$NiSO_4$	c-Myc c-Myc	↑ ↑	BEAS-2B HaCaT	Apoptosis induced.
Guan et al., 2007	$NiCl_2$	bcl-2	↓	T cells Jurkat	Apoptosis induced, NO ↑.
Andrew & Barchowsky, 2000	Ni_3S_2	PAI-1	↑	BEAS-2B	Fibrinolysis inhibited. Particle sizes < 2.5μm
Andrew et al., 2001	Ni_3S_2	PAI-1 c-Jun c-Fos	↑ ↑ ↑	BEAS-2B	Fibrinolysis inhibited. Particle sizes < 2.5μm
Salnikow et al., 2002	$NiCl_2$	HIF-1α *Cap43* *Nip3* *Prolyl-4-hydroxylase* *HSP70* *GADD45* *p21* *p53*	↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑	Mouse fibroblasts HIF-1α knockout	Hypoxia, *Nip3* and prolyl-4-hydroxylase are HIF-1 dependent; *HSP70*, *GADD45*, *p21* and *p53* are HIF-1 independent; *ATM, GADD153*, *Jun B* and *MDR-1* are mixed.

*Note: BEAS, human bronchial epithelial cells; HaCaT, human keratinocyte cells; NO, nitric oxide generation; PAI-1, plasminogen activator inhibitor-1; HIF-1α, hypoxia-inducible transcription factor-1; AhR, aryl hydrocarbon receptor; A549, human lung bronchoepithelial cells; H3B, human hepatoma cells; H3K9, histone H3 lysine 9; HOS, human osteoblastic cell line; PW, mouse embryo fibroblasts; *MGMT*, O^6-methylguanine DNA methyltransferase gene locus; *DNMT1*, DNA methyltransferase 1 gene; 16HBE, Ni-transformed human bronchial epithelial cells; H3K9ac, histone H3 lys-9 acetylation; H4ac, histone H4 acetylation; H3K9me2, histone H3 Lys-9 methylation; NHBE, normal human bronchial epithelial cells; ↑, enhanced activity; ↓, reduced activity.

TABLE 29. EFFECTS OF NICKEL ON THE EPIGENOME*

Study	Compound	Gene or factor affected	Effect	Cell Type	Comments or other effects
Salnikow et al., 2003	$NiCl_2$	HIF-1α *Cap43* *Bcl-2* *Nip3* *EGLN1* *HIG1* *Prolyl-4-hydroxylase* *Focal adhesion kinase*	↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑	Mouse fibroblasts HIF-1α knockout	HIF-1 independent genes up-regulated *GADD45, p21, ATM, p53, Jun B;* genes up-regulated in HiF-1α deficient cells *HSP70, NGFb, IP-10, CD44 antigen, melanocortin 1 receptor, heparin-binding EGF-like, SGK kinase, BCL-2-like, E-MAP-115.*
Davidson et al., 2003	$NiCl_2$	HIF-1α AhR *CYP1B1* *NQO1* *UDP glucuronyl-transferase 1A6*	↑ ↓ ↓ ↓ ↓	Mouse fibroblasts HIF-1α knockout	All genes suppressed were HIF-independent including *prostaglandin endoperoxide synthase I* and *glutathione S –transferases μ, α3,* and *α Ya*
Li et al., 2004	$NiCl_2$ Ni_3S_2	HIF-1α *Cap43* protein expression	↑	Mouse C141 epidermal cells and PI-3K and Akt deficient mutants	Activation of phosphatidylinositol 3-kinase (PI-3L), Akt, and p70S6 kinase ($p70^{S6k}$). Particle sizes of Ni_3S_2 not specified.
Broday et al., 2000	$NiCl_2$ Ni_3S_2	Histone H4 acetylation	↓	A549 lung carcinoma cells, yeast cells	Lysine 12 acetylation in H4 inhibited in A549 cells and at Lys 12, 16, 5, and 8 in yeast. Particle sizes of Ni_3S_2 not specified.

*Note: BEAS, human bronchial epithelial cells; HaCaT, human keratinocyte cells; NO, nitric oxide generation; PAI-1, plasminogen activator inhibitor-1; HIF-1α, hypoxia-inducible transcription factor-1; AhR, aryl hydrocarbon receptor; A549, human lung bronchoepithelial cells; H3B, human hepatoma cells; H3K9, histone H3 lysine 9; HOS, human osteoblastic cell line; PW, mouse embryo fibroblasts; *MGMT*, O^6-methylguanine DNA methyltransferase gene locus; *DNMT1*, DNA methyltransferase 1 gene; 16HBE, Ni-transformed human bronchial epithelial cells; H3K9ac, histone H3 lys-9 acetylation; H4ac, histone H4 acetylation; H3K9me2, histone H3 Lys-9 methylation; NHBE, normal human bronchial epithelial cells; ↑, enhanced activity; ↓, reduced activity.

TABLE 29. EFFECTS OF NICKEL ON THE EPIGENOME*

Study	Compound	Gene or factor affected	Effect	Cell Type	Comments or other effects
Yan et al., 2003	Ni_3S_2 NiS	*gpt*+ gene silencing	↓	G12 Chinese hamster transgenic *gpt*+ cells	Histones H3 and H4 hypoacetylated,H3K9 methylated, H3K9 deacetylated. Particle sizes of Ni_3S_2 not specified.
Ke et al., 2006; 2008	$NiCl_2$ NiS	*gpt*+ *gpt*-	↓	A549 cells, Hep3B cells, G12 Chinese hamster transgenic *gpt*+ cells, and *gpt*- clones N24, N37, N96	Histones H2A, H2B, H3 and H4 deacetylated, increases of H3K9 dimethylation, increases of H2A and H2B ubiquitination, minimal cytotoxicity. Ni acts by inhibiting deubiquitination. Particle sizes of NiS not specified.
Chen et al., 2006	$NiCl_2$	*gpt*+ gene silencing	↓	G12 Chinese hamster transgenic *gpt*+ cells, A549 cells	Increased mono- and dimethylation of histone H3K9, decreased H3K9 methyltransferase G9a. gpt silencing reversed by dimethylation of H3K9 with 5-aza-2'-deoxycytidine.
Zhang et al., 2003	Ni_3S_2 $NiCl_2$	Reversion of Ni-induced cell transformation	↑	Human HOS TE85 cells, mouse PW cells	Cells treated with histone deacetylase inhibitor trichostatin A (TSA) had increased frequency of revertants in transformed cells. Particle sizes of Ni_3S_2 not specified.
Ji et al., 2008	NiS	*MGMT* *DNMT1*	↓ ↑	NiS-transformed human 16HBE cells	Silencing of *MGMT* associated with DNA hypermethylation, altered histones H3K9me2, H4ac and H3K9ac, and *DNMT1* upregulation. Particle sizes of NiS not specified.
Karaczyn et al., 2006	Ni(II) counter ion unspecified	Dysregulation of H2B ubiquitination	↑	1HAEo- and HPL1D human lung cells	Histone H2B and H2A ubiquitination stimulated by Ni(II) exposure. H2B was monoubiquinated and H2A mono- and diubiquinated.

*Note: BEAS, human bronchial epithelial cells; HaCaT, human keratinocyte cells; NO, nitric oxide generation; PAI-1, plasminogen activator inhibitor-1; HIF-1α, hypoxia-inducible transcription factor-1; AhR, aryl hydrocarbon receptor; A549, human lung bronchoepithelial cells; H3B, human hepatoma cells; H3K9, histone H3 lysine 9; HOS, human osteoblastic cell line; PW, mouse embryo fibroblasts; *MGMT*, O^6-methylguanine DNA methyltransferase gene locus; *DNMT1*, DNA methyltransferase 1 gene; 16HBE, Ni-transformed human bronchial epithelial cells; H3K9ac, histone H3 lys-9 acetylation; H4ac, histone H4 acetylation; H3K9me2, histone H3 Lys-9 methylation; NHBE, normal human bronchial epithelial cells; ↑, enhanced activity; ↓, reduced activity.

TABLE 29. EFFECTS OF NICKEL ON THE EPIGENOME*

Study	Compound	Gene or factor affected	Effect	Cell Type	Comments or other effects
Kang et al., 2003	$NiCl_2$	Histone acetylation Reactive oxygen species (ROS)	↓	Human Hep3B hepatoma cells	Dose- and time-dependent decrease in H4 acetylation. Ni(II) inhibited histone acetyltransferase (HAT) but not histone deacetylase (HDAC). ROS involved in MOA.
Zhou et al., 2009	$NiCl_2$	Histone methylation	↓ ↓	A549 cells NHBE cells	H3K4 increased di- and tri-methylation but not mono-methylation.

*Note: BEAS, human bronchial epithelial cells; HaCaT, human keratinocyte cells; NO, nitric oxide generation; PAI-1, plasminogen activator inhibitor-1; HIF-1α, hypoxia-inducible transcription factor-1; AhR, aryl hydrocarbon receptor; A549, human lung bronchoepithelial cells; H3B, human hepatoma cells; H3K9, histone H3 lysine 9; HOS, human osteoblastic cell line; PW, mouse embryo fibroblasts; *MGMT*, O^6-methylguanine DNA methyltransferase gene locus; *DNMT1*, DNA methyltransferase 1 gene; 16HBE, Ni-transformed human bronchial epithelial cells; H3K9ac, histone H3 lys-9 acetylation; H4ac, histone H4 acetylation; H3K9me2, histone H3 Lys-9 methylation; NHBE, normal human bronchial epithelial cells; ↑, enhanced activity; ↓, reduced activity.

Salnikow et al. (2002) studied gene expression in nickel(II) treated mouse embryo fibroblasts with and without the hypoxia-inducible transcription factor-1 (HIF -1α $^{+/+}$, HIF-1α $^{-/-}$). HIF-1α strongly induces hypoxia-inducible genes, including the tumor marker gene *Cap43*. The wild type and knockout cells were exposed to 1.0 mM $NiCl_2$ for 20 hr and gene expression assessed by cRNA hybridization and GeneChip microarray analysis. Nickel exposure induced genes involved in glucose metabolism in HIF-1α-proficient cells. Of 12 glycolytic enzyme genes studied by microarray 10 were induced by Ni(II) exposure in proficient but not in HIF-1α deficient cells. Glucose-6 phosphate dehydrogenase and hexokinase I were the only unaffected genes. Nickel(II) was also found to induce some genes in HIF-1α proficient and deficient cells (*HSP70, GADD45, p21, p53, ATM, GADD, JunB,* and *MDR-1).*

In a subsequent study, Salnikow et al. (2003) found a number of genes induced by Ni(II) in HIF-1α deficient but not in proficient cells. Among these genes are *NGF-β*, *SGK*, *IP10*, *CD44*, heparin binding EGF-like, melanocortin 1 receptor, *Grg1*, *BCL-2*-like, and tubulin-binding protein *E-Map-115*. IFN-inducible protein 10 (IP10) is a chemokine that targets T cells and NK cells. The elevation of *IP10* expression has been demonstrated in human diseases including chronic cirrhosis and biliary atresia (Koniaris et al., 2001). Most of the nickel-induced genes appear to be related to stress response. A number of genes were significantly suppressed by nickel exposure in an HIF-1-dependent manner (i.e. suppression was greater in HIF-1α proficient cells compared with HIF-1α deficient cells) including monocytes chemoattractant protein 1 (*MCP-1*) and the tumor suppressor gene *Zac1*. *Zac1* induces apoptosis and cell cycle arrest and was not suppressed in HIF-1α deficient cells. Neuropilin-1 (*Npn-1*) was also suppressed by nickel in an HIF-1α-dependent manner. Neuropilin is a transmembrane receptor in endothelial and other cells. The effects of nickel on gene expression after 20 hr exposure were transient and disappeared after nickel removal, although chronic nickel exposure can lead to selection of cells in which these changes persist.

Salnikow et al. (2003) evaluated the modulation of gene expression by $NiCl_2$ and Ni_3S_2 in two mouse and one human cell lines. Mouse embryo fibroblast cell lines MEF-HIF1α and PW were exposed to 0, 0.03, 0.1, 0.3, 1.0, or 2.0 µg Ni_3S_2/cm^2 or 0, 0.125, 0.25, 0.5, 1.0, or 2.0 mM $NiCl_2$ for 20 hr. Total RNA was isolated from Ni-exposed and control cells and cDNA prepared for GeneChip analysis. Both soluble and insoluble nickel compounds induced similar signaling pathways in the mouse cell lines. The microarray data indicated increases in expression of genes involved in glucose metabolism including glucose transporter I and glycolytic enzymes such as hexokinase II, phosphofructokinase, pyruvate kinase, and triosephosphate and glucose phosphate isomerases and lactate dehydrogenase. All of these genes are induced by hypoxia, suggesting that nickel similarly induces the HIF-1 transcription factor, which regulates these genes. Other HIF-1 genes induced included Tdd5, Egln I, Nip3, Est and Gly96. The results indicate that the form of nickel has little effect on the Ni-induced alterations of gene expression and is therefore expected to have little effect on carcinogenic or other toxic potential *in vivo*.

Davidson et al. (2003) studied the interaction of the aryl hydrocarbon receptor (AhR) pathway and the hypoxia inducible factor-1α (HIF-1α) pathway in nickel-exposed cells. HIF-1α knockout and wild type cells were derived from C57B mice. Mouse cells exposed to1.0 mM $NiCl_2$ for 24 hr exhibited the suppression of several AhR-regulated genes including CYP1B1, NQO1, UDP-glucuronyltransferase 1A6, and glutathione *S*-transferase Ya. All of the observed AhR-dependent genes except glutathione *S*-transferase θ1 were down regulated in the HIF-1α knockout cells. The most suppressed gene was CYP1B1, which was reduced 22.9-fold in wild type cells and 29.7-fold in knockout cells. Desferrioxamine and hypoxia were also able to suppress basal and inducible expression levels of AhR genes. Dimethyloxalylglycine, an inhibitor of Fe(II)- and 2-oxoglutarate (2-OG)-dependent dioxygenases also inhibited AhR-dependent gene expression in an HIF-1α-dependent manner. The authors conclude that an Fe(II)-, 2-OG- or oxygen-dependent enzyme may be involved in the regulation of AhR-dependent transcriptional activity by nickel(II).

Lee (2006) studied differential gene expression in nickel(II)-treated normal rat kidney cells. NRK-52E cells were exposed for two months to 0, 160 and 240 µM Ni^{2+} (acetate). cDNAs corresponding to mRNAs for which expression levels were altered by nickel were isolated, sequenced and followed by GenBank Blast homology search. Specificity of differential expression of cDNAs was determined by reverse transcriptase-polymerase chain reaction. Two of the nickel(II) responsive differential display clones were down regulated: SH3 glutamic acid-rich protein (SH3BGRL3) and fragile histidine triad (FHIT). One clone was up-regulated, metallothionein. The expression of these mRNAs was nickel concentration-dependent. The author notes that SH3BGRL3 probably belongs to the thioredoxin-like superfamily. These small disulfide-reducing enzymes act as hydrogen donors and are thought to be involved in regenerating glutathionated proteins. Down-regulation of SH3BGRL3 may be related to apoptotic death of NRK-52E cells induced by nickel (e.g., as noted by Shiao et al., 1998). Metallothionein is involved in the regulation of physiologically important trace metals such as copper and the detoxification of toxic metals. Since the kidney is a target organ of nickel toxicity the observed up-regulation of metallothionein is not surprising.

Prows et al. (2003) used cDNA microarray analysis in nickel sensitive (A/J) and resistant (C57BL/6J) mouse strains. The mice were exposed continuously to $NiSO_4$ 150 µg Ni/m^3 (MMAD = 0.22 µm, gsd = 1.85) for 3, 8, 24, or 48 hr. Significant expression changes were identified in one or both strains for more than 100 known genes. The results indicated a temporal pattern of increased cell proliferation, extracellular matrix repair, hypoxia, and oxidative stress, followed by reduced surfactant proteins. Fifteen functional candidate genes were associated with expression ratio differences of two-fold or greater between strains for at least one exposure time. Of these two genes—metallothionein-1 (*Mt1*) on chromosome 8 and SP-B (*Sftpb*) on chromosome 6—map to QTL intervals linked to nickel-induced acute lung injury survival.

A4 Mechanisms of Toxicity

It is possible that the effects of nickel on the various elements of the immune system and its ability to induce lung injury are related on a mechanistic level. This may involve increased levels of oxidative stress, both directly via Ni-induced formation of reactive oxygen species (ROS) and by modulation of signaling pathways promoting inflammatory processes. This section is not meant to be a comprehensice review of mechanistic studies. Rather, we provide a synopsis of several mechanistic studies examining potential mechanisms of action of nickel compounds.

Inhalation of nickel dust has been associated with increased incidence of pulmonary fibrosis. A potential mechanism is via inactivation of the pulmonary fibrinolytic cascade (Andrew and Barchowsky, 2000). Andrew et al. (2001) studied the effect of nickel subsulfide on activator protein-1 (AP-1) induction of plasminogen activator inhibitor-1 (PAI-1). Addition of 2.34 µg Ni/cm^2 Ni_3S_2 (<2.5µm) to a layer of cultured BEAS-2B human airway epithelial cells stimulated intracellular oxidation, induced c-Jun and c-Fos mRNA levels, increased phospho- and total c-Jun levels, and increased PAI-1 mRNA levels over a 24-hr treatment period. No cytotoxicity was observed with nickel treatment. Pretreatment with the antioxidants N-acetyl-L-cysteine and ascorbic acid blocked the nickel-induced increases in reactive oxygen species (ROS) but did not affect the nickel induction of PAI-1. The results indicate that the potential effect of nickel on fibrinolytic activity is independent of its participation in redox cycling.

Barchowsky et al. (2002) exposed BEAS-2B human airway epithelial cells in culture to non-cytotoxic levels (based on cell survival assays) of Ni_3S_2 (< 2.5 µm diameter) and observed increased expression of the inflammatory cytokine interleukin-8 (IL-8). Confluent layers of cultured cells were treated with 2.34 µg Ni/cm^2 nickel subsulfide for 24 or 48 hr. After 48 hr there was a statistically significant increase in IL-8 protein in the culture medium compared to the control (ca. 2.3 vs. 0.9 ng/mL, $P < 0.001$, their Fig. 1). No increase was seen after 24 hr. IL-8 mRNA levels preceded the increase in IL-8 protein. Transient exposure to soluble nickel sulfate failed to increase IL-8 mRNA. Further study revealed that nickel induced IL-8 transcription through a novel pathway that requires both AP-1 and non-traditional transcription factors, Fos and cJun. The authors note that the protracted course of particulate nickel-stimulated IL-8 production observed in the study contrasts with the immediate IL-8 induction in response to cytokines, hypoxia, and many inhaled toxicants. Thus the study indicates "particulate Ni_3S_2 activates specific signaling cascades following uptake by pulmonary epithelial cells. These activated cascades stimulate parallel pathways for inducing transcription of both inflammatory and profibrotic genes."

Mongan et al. (2008) studied the role of mitogen activated protein kinase kinase kinase 1 (MAK3K1) in nickel-induced acute lung injury in mice. Wild type mice and MAK3K1 deficient mutants were exposed to $NiSO_4 \cdot 6H_2O$ aerosol (MMAD = 0.2 µm) at 150 µg/m^3 continuously and survival times recorded. Inactivation of

one functional allele in *Map3k1*$^{+/\Delta KD}$ heterozygous mutants did not alter survival; however, *Map3k1* homozygous mutants died significantly sooner than wild type control mice. Wild type and heterozygous mutants showed 20% survival at 110 hr compared to 20% survival at 80 hr for the homozygous mutants (N = 6 mice/group, $P < 0.01$ by *t*-test). During exposure, the mice developed severe dyspnea, with gross lung pathology showing air trapping and extensive hemorrhagic edema indicative of acute lung injury. Other experiments carried out in vitro with mouse embryo fibroblast cells indicate that MAK3K1 protects against lung injury by inhibiting the Ni-induced activation of c-jun N-terminal kinases (JNKs).

Carter et al. (1997) noted that the induction of inflammatory cytokines in human airway epithelial cells by airborne particulate pollution was dependent on particle metal content, particularly vanadium and nickel. Miyazawa et al. (2008) concluded that $NiSO_4$ could activate p38 MAPK and ERK and stimulate the release of TNF-α in THP-1 cells.

Li et al. (2009) concluded that nickel sulfate induced *c-Myc* in human bronchial epithelial cells via the *Ras/ERK* signaling pathway. Freitas et al. (2010) found that Ni(II) as nickel nitrate induced oxidative burst in human neutrophils where significant increases in chemiluminescence were seen at ≥250 µM Ni(II) and a clear dose response extended down to 7.8 µM Ni(II). Forti et al. (2011) evaluated the effects of $NiCl_2$ and Ni metal particles (0.5-1.0 µm diameter) on Calu-3 human bronchial epithelial cells in vitro. Exposure to $NiCl_2$ or Ni metal particles resulted in disruption of epithelial cell barrier function as demonstrated by transepithelial electrical resistance and increased oxidative stress as indicated by Ni-induced ROS and upregulation of stress-inducible genes (i.e., *MT1X, HSP70*, *HMOX-1*, and *γGCS*). The effects were partially attributed to an increase in intracellular levels of Ni^{2+} ions.

Horie et al. (2009) evaluated uptake and subsequent Ni^{2+} release in A549 human lung cells exposed to ultrafine NiO particles (black NiO = 20 nm; green NiO = 100 nm). Ultrafine NiO particles showed higher cytotoxicity than fine NiO particles (600-2000 nm) and up to 150-fold higher degree of dissolution in the cell culture medium than fine particles. The authors conclude that intracellular Ni^{2+} release may be a key factor determining the cytotoxicity of NiO and that ultrafine particles release more Ni^{2+} than fine particles.

Nickel metal nano particles (Ni NP, <100 nm in diameter) induce a number of toxic responses in human lung epithelial A549 cells (Ahamed, 2011). The cells were exposed to Ni NP (0, 1, 2, 5, 10, 25 µg/mL) for 24 hr or 48 hr. Cell viability decreased linearly with dose for both 24 and 48 hr Ni metal NP exposures, by up to 80 and 90% , respectively. Significant increases ($P < 0.05$) were seen in LDH leakage, ROS generation, and lipid peroxidation at ≥2 µg/mL. Significant decreases in cellular GSH at ≥2 µg/mL were also seen. The authors concluded that Ni metal NP toxicity to human lung cells in vitro was mediated by oxidative stress. Horie et al. (2011) evaluated the acute oxidative stress induced by NiO

nanoparticles in vivo and in vitro. Black NiO nanoparticles (20 nm) were evaluated with human A549 cells in vitro, and responses in vivo were examined by intratracheal instillation of nanoparticles in rats. The levels of intracellular ROS and lipid peroxidation in A549 cell increased with increasing exposure to NiO nanoparticles. Increased gene expression of lipid peroxide heme oxygenase-1 (HO-1) and surfactant protein-D (SP-D) were also seen in A549 cells. The lipid peroxide level in BALF significantly increased after 24 hr instillation. LDH leakage was also observed in BALF of exposed rats. The authors concluded that NiO nanoparticles induced oxidative stress-related lung injury.

Ahamed et al. (2011) studied the toxicity of nickel ferrite nanoparticles (26 nm) in A549 human lung cells. The $NiFe_2O_4$ particles at doses of 1 to 100 µg/mL induced dose-dependent cytotoxicity as demonstrated by MTT, NRU and LDH assays. Nickel ferrite nanoparticles were also seen to induce oxidative stress by ROS generation and GSH depletion. Quantitative real-time PCR analysis showed that following exposure, the level of mRNA expression of cell cycle checkpoint protein p53 and apoptotic proteins (bax, caspase-3 and caspase-9) were significantly up-regulated, whereas expression of anti-apoptotic proteins (survivin and bcl-2) were down-regulated. The authors concluded that nickel ferrite nanoparticles induced apoptosis in A549 cells through ROS generation and oxidative stress via p53, survivin, bax/bcl-2, and caspase pathways.

Long-term exposure of hyperlipidemic apoprotein E-deficient mice to $Ni(OH)_2$ nanoparticles (5 nm diameter, count median diameter of agglomerates = 40 nm, gsd = 1.50) resulted in significant oxidative stress and inflammation in the lung and extrapulmonary organs (Kang et al., 2011). The $ApoE^{-/-}$ mice were exposed to 0 or 79 µg Ni/m^3 for 5 hr/day, 5 days/week for 1 week (6 mice/group) or 5 months (16 mice/group). Pulmonary responses included significant increases in the number of cells, number of neutrophils and total protein in BALF of Ni exposed mice compared to controls at either exposure duration ($P < 0.01$). Relative increases in proinflammatory genes (mRNA) *Ccl-2* and *Il-6* were seen in the lung at 1 week ($P < 0.01$) and *Ccl-2*, *Il-6*, and *Tnf-α* at 5 months ($P < 0.05$). Significantly, increases in expression of *Ccl-2* and *Il-6* ($P < 0.05$) were also seen after 5 months Ni exposure in the heart and of *Ccl-2*, *Il-6*, and *Tnf-α* ($P<0.01$) in the spleen. Also relative mRNA levels of *Ccl-2*, *Vcam-1* and *Cd68* were all increased in aortas from 5 months Ni-exposed mice ($P <0.01$). After 5 months exposure to Ni nanoparticles relative *Ho-1* mRNA levels, indicative of oxidative stress, were significantly increased in lung > heart > spleen > aorta (all $P < 0.05$). Mitochondrial DNA damage in the aorta was also observed after 5 months exposure ($P < 0.01$) as were relative increases in plaque area in four regions of the aorta (all $P < 0.01$). This paper demonstrates that inhaled $Ni(OH)_2$ nanoparticles can induce oxidative stress and inflammation, not only in the lung but systemically in the cardiovascular system and can ultimately contribute to the progression of atherosclerosis in an $ApoE^{-/-}$ mouse system.

A possible mechanism leading to nickel pneumotoxicity may involve Ni-induced reactive oxygen species (ROS) and electrophiles initiating prooxidant activity, which in turn activates signaling pathways, including MAPK and multiple proteins involved in the pathway (p38, JNK, ERK). This leads to activation of transcription factors that initiate inflammatory processes and subsequent immunological effects leading to respiratory effects such as alveolar proteinosis. That is, the mechanism of respiratory effects derives from activation/inactivation of signaling pathways. A similar scheme was described by Pan et al. (2010) for Ni-induced apoptosis in human Beas-2B cells via the Akt/ASK1/p38 signaling pathway.

Appendix B

B.1 Berkeley Madonna Code for Sunderman et al. Human Oral Nickel Model.

METHOD RK4 {integration routine}

STARTTIME = 0

STOPTIME=24 {hours}

DT = 0.02 {step time or integration interval, i.e. 1200 steps total}

{Nickel biokinetic model of Sunderman et al. 1989; model units µg, hr}

{Nickel compartments, µg Ni initial values}

init Agi = 50*BW {Ni dose given in water 50 µg/kg body weight}

init Aserum = 0

init Aurine = 0

init Atissues = 0

{Model parameters, /hr unless otherwise specified}

Kf = 0.092 {zero-order rate constant for dietary absorption of nickel}

K01 = 0.28 {first-order rate constant for intestinal absorption of oral NiSO4 in water}

K10 = 0.21 {first-order rate constant for nickel excretion in urine}

K12 = 0.38 {first-order rate constant for nickel transfer from serum to tissues}

K21 = 0.08 {first-order rate constant for nickel transfer from tissues to serum}

BW = 70 {kg}

{Model differential equations calculate masses of nickel in respective compartments over 24 hours}

d/dt(Agi) = -Kf - K01*Agi

d/dt(Aserum) = Kf + K01*Agi - K10*Aserum - K12*Aserum + K21*Atissues

d/dt(Atissues) = K12*Aserum - K21*Atissues

d/dt(Aurine) = K10*Aserum

Massbal = Agi + Aurine+ Aserum + Atissues {sum of model compartments equals dose input}

B.2 Berkeley Madonna Code for Nickel Keratinocyte Model of Franks et al.

METHOD RK4 {integration routine}

STARTTIME = 0

STOPTIME=24

DT = 0.02

{Model parameters}

dni = 2.62E-5 {rate of cell death due to nickel ions, /µM/hr}

bci = 0 {/hr, rate of cytokine release by nickel affected cells}

kn = 13.3 {/hr, rate of ion exchange}

un = 2.2 {unitless, partition coefficient}

dn = 0.00875 {/hr, rate of natural wastage of cells}

dc = 0.133 {/hr, rate of natural decay of cytokines within the media}

bcn = 6.25E-5 {µM/hr, rate of cytokine release by nickel affected cells}

n0 = 0.0165 {volume of cells, mL}

A0 = 100 {µM}

cpg = c*1.77E4*1000 {IL-1ά, pg/mL}

init c = 0 {initial concentration IL-1ά}

init Ai = 0 {initial intracellular Ni concentration}

init n = n0 {initial volume of keratinocytes}

init Ac = A0 {initial extracellular concentration of Ni}

{model differential equations}

d/dt(n) = -kd*n {volume fraction of keratinocytes}

kd = dni*Ai + dn

d/dt(Ac) = -kn*n*(un*Ac - Ai) + kd*n*Ai {extracellular nickel}

d/dt(Ai) = kn*n*(un*Ac - Ai) - Kd*n*Ai {intracellular nickel}

d/dt(c) = bcn*n + bci*n*Ai - dc*(1-n)*c {IL-1ά cytokine release}

B.3 Intracellular Dosimetry Model of Inhaled Nickel Subsulfide.

METHOD RK4 {integration routine}

STARTTIME = 0

STOPTIME= 168 {hours}

DT = 0.01

DTOUT = 0.5

{Nickel mass μmoles Ni_3S_2}

init Agi = 0

init Asurf = Concn*Vmuc*0.23/MW

init Aionic = Concn*Vmuc*0.10/MW

init Aven = 0

init Avacuol = 0

init Acyto = 0

init Acytprot = 0

init Aperinuc = 0

init Aperinucytprot = 0

init Anucl = 0

init Anucprot = 0

{Concentrations, µmol/mL}

Csurf = Asurf/Vsurf

Cionic = Aionic/Vmuc

Ccyto = Acyto/Vcyto

Cperinuc = Aperinuc/Vperinuc

Cven = Aven/Vven

Cnucl = Anucl/Vnucl

Cnuni = 3*Cnucl

{Volumes, mL}

Vcyto = 0.54*Vtb

Vnucl = 0.06*Vtb

Vperinuc = 0.1*Vtb

Vtb =0.07*Vlu

Vlu = 0.014*BW

Vsurf = Vtb

Vionic = Vtb

Vven = 0.04*BW

Vmuc = 100 {mL}

{Model parameters}

VmiC = 10 {µmol/hr/μm^2}

Vmi = VmiC*2.4E11

Kmi = 1E9 {µmol/mL}

VmeC = 0.001 {µmol/hr/μm^2}

Vme = VmeC*2.4E11

Kme = 1E9{µmol/mL}

Kdm = 0.0001{/h}

Kdv = 0.0106 {/h}

PAcpC = 0.011{μm^2/hr}

PAcp = PAcpC

PApnC = 1.5

PApn = PApnC

ClpC = 1E-8 {mL/hr/cell}

Clp = ClpC*1E9 {/1E9 cells}

ClmC = 1.0E-11{mL/hr/cell}

Clm = ClmC*1E9 {/1E9 cells}

AbcC = 1E3{µmol/mL}

Abc = AbcC

AbpC = 1E3

Abp = AbpC

AbnC = 1E4

Abn = AbnC

Kbc = 1E9 {µmol/mL}

Kbn = 1E9

Kbp = 1E9

Frac = 0.08

Md = 0.1*MMAD

MMAD = 3.75 {µm}

Concn = 10 {µg/mL}

MW = 234.19

BW = 7E4

Protmg = 161{mg/1E9 cells}

Acytomg = Acyto/Protmg {µmol Ni/mg cytosol protein}

{Differential equations, µmol/hr}

d/dt(Agi) = Asurf*Clmc + Aionic*Clmc

d/dt(Asurf) = - Asurf*Kdm - Csurf*Clmc - Csurf*Clp

d/dt(Aionic) = Asurf*Kdm - Cionic*Vmi/(Kmi + Cionic) - Cionic*Clm

d/dt(Aven) = Ccyto*Vme/(Kme + Ccyto)

d/dt(Acyto) = Cionic*Vmi/(Kmi + Cionic) - Ccyto*Vme/(Kme + Ccyto) + Avacuol*Kdv*Frac - Ccyto*Abc/(Kbc + Ccyto) - Acyto*PAcp

d/dt(Avacuol) = Csurf*Clp - Avacuol*Kdv*Frac - Avacuol*Kdv*(1-Frac)

d/dt(Acytprot) = Ccyto*Abc/(Kbc + Ccyto)

d/dt(Aperinuc) = Avacuol*Kdv*(1-Frac) + Acyto*PAcp - Cperinuc*Abp/(Kbp + Cperinuc) - Aperinuc*PApn

d/dt(Aperinucytprot) = Cperinuc*Abp/(Kbc + Cperinuc)

d/dt(Anucl) = Aperinuc*PApn - Cnucl*Abn/(Kbn + Cnucl)

d/dt(Anucprot) = Cnucl*Abn/(Kbn + Cnucl)

B.4 PBPK Rat Model for NiO Inhalation Based on Teeguarden et al.

METHOD Stiff {integration routine}

STARTTIME = 0

STOPTIME= 8640 (12 months}

DT = 0.001

DTOUT = 0.25

{Draft PBPK model for nickel inhaled as nickel oxide; model loosely based on Teeguarden et al. 2007 Mn model w/ Pi's based on Ishimatsu et al.1995 and lung clearance based on Benson et al. 1994 and Tanaka et al. 1985}

{NiO in tissues, µg}

init Aart =0 {arterial blood}

init Aven = 0 {venous blood}

init Amusc = 0 {muscle shallow}

init Amuscdeep = 0 {muscle deep}

init Abone = 0

init Abonedeep =0

init Akid = 0 {kidney shallow}

init Akiddeep = 0 {kidney deep}

init Aliv = 0 {liver shallow}

init Alivdeep = 0 {liver deep}

init Alu = 0 {lung shallow}

init Alungdeep = 0 {lung deep}

init Alungdep = 0 {lung surface deposition}

init Anpdeep = 0 {nasopharynx deep}

init Anpdep = 0 {nasopharynx surface deposition}

init Anp = 0 {nasopharynx shallow}

init Agi = 0 {gastro-intestinal tract}

init Afeces = 0

init Aurine = 0

{Cardiac output, alveolar ventilation, body weight L/hr, kg}

BW = 0.325 {body weight}

Qtot = 14.6*BW^0.74 {cardiac output}

Qalv = 1.2*Qtot {alveolar ventilation}

{Blood flows, L/hr}

Qmusc = 0.534*Qtot

Qbone = 0.122*Qtot

Qkid = 0.141*Qtot

Qliv = 0.183*Qtot

Qnp = 0.01*Qtot

{Tissue volumes, L}

Vart = 0.0224*BW

Vblood = 0.0676*BW

Vmusc = 0.738*BW

Vbone = 0.021*BW

Vbonedeep = 0.052*BW

Vkid = 0.007*BW

Vliv = 0.034*BW

Vlu = 0.007*BW

Vnp = 0.0038*BW

Vtb = 0.01107*BW

Vpu = 0.01107*BW

Vven = 0.0452*BW

Vdeplu = Vtb + Vpu

{Concentrations µg Ni/L}

Cart = Cvlung {arterial concentration}

Cvmusc = Amusc/(Vmusc * Pmusc) {concentration leaving the muscle shallow compartment}

Cmusc = (Amuscdeep+Amusc)/Vmusc {total concentration in muscle}

Cvbone = Abone/(Vbone*Pbone)

Cbone = (Abonedeep + Abone)/Vbone

Cvkid = Akid/(Vkid*Pkid)

Ckid = (Akiddeep + Akid)/Vkid

Cvliv = Aliv/(Vliv*Pliv)

Cliv = (Alivdeep + Aliv)/Vliv

Cvnp = Anp/(Vnp*Pnp)

Cnp = (Anpdeep + Anp)/Vnp

Cvlung = Alu/(Vlu*Plung)

Clung = (Alungdeep + Alu)/Vlu

Cven = Aven/Vven {venous concentration}

Cvtot = (Qmusc*Cvmusc + Qkid*Cvkid + Qliv*Cvliv + Qbone*Cvbone + Qnp*Cvnp)/Qtot {mixed venous concentration}

Cair = IF TIME <= 140 THEN 600 ELSE 0 {140 hr exposure to 600 µg/m3}

Tvol = Qalv/0.6 {tidal volume}

{tissue/blood partition coefficients, unitless}

Pmusc = 0.8

Pbone = 1.0

Pkid = 16.0

Pliv = 2.0

Plung = 4.0

Pnp = 0.3

{Clearance rates, /hr}

Kf = 0.0001*BW^-0.25

Kinmusc = 0.017*BW^-0.25 {rate constants for nickel moving into and out of deep tissue compartments}

Kinbone = 0.105*BW^-0.25

Kinkid = 0.146*BW^-0.25

Kinliv = 0.621*BW^-0.25

Kinnp = 0.035*BW^-0.25

Kinlung = 0.035*BW^-0.25

Koutmusc = 0.0035*BW^-0.25

Koutbone = 0.085*BW^-0.25

Koutkid = 0.007*BW^-0.25

Koutliv = 0.015*BW^-0.25

Koutnp = 0.035*BW^-0.25

Koutlung = 0.0002*BW^-0.25

Kurine = 0.15 {kidney shallow to urine}

Kfeces = 0.5 {GI tract to feces}

Kai = 0.25 {GI tract to liver shallow}

Kbile = 0.05 {Liver to GI tract}

Kgi = 0.1 {respiratory tract to GI tract, i.e. swallowed particles mechanically removed from lung}

{rate constants for uptake from respiratory tract surface into shallow and deep compartments for lung and nasopharynx}

KdepSL = 2.0*BW^-0.25

KdepDL = 0.0*BW^-0.25

KdepSN = 0.2*BW^-0.25

KdepDN = 0.0*BW^-0.25

{fractional coeffs for deposited particles}

fdepNP = 0.2 {nasopharnyx}

fdepTB = 0.08 {tracheobroncheal}

fdepPu = 0.05 {pulmonary}

fdepLu = fdepTB + fdepPu

{differential equations}

d/dt(Abone) = Qbone*(Cart - Cvbone) - Kinbone*Cvbone*Vbone + Koutbone*Abonedeep

d/dt(Abonedeep) = Kinbone*Cvbone*Vbone - Koutbone*Abonedeep

d/dt(Amusc) = Qmusc*(Cart - Cvmusc) - Kinmusc*Cvmusc*Vmusc + Koutmusc*Amuscdeep

d/dt(Amuscdeep) = Kinmusc*Cvmusc*Vmusc - Koutmusc*Amuscdeep

d/dt(Akid) = Qkid*(Cart - Cvkid) - Kinkid*Cvkid*Vkid + Koutkid*Akiddeep

d/dt(Akiddeep) = Kinkid*Cvkid*Vkid - Koutkid*Akiddeep

d/dt(Alu) = Qtot*(Cvtot - Cvlung) - Kinlung*Cvlung*Vlu + Koutlung*Alungdeep + kdepSL*Alungdep

d/dt(Alungdeep) = Kinlung*Cvlung*Vlu - Koutlung*Alungdeep + kdepDL*Alungdep

d/dt(Alungdep) = fdepLu*Cair*Tvol - kdepDL*Alungdep - kdepSL*Alungdep - Alungdep*Kgi

d/dt(Aven) = Qmusc*Cvmusc + Qbone*Cvbone + Qkid*Cvkid + Qliv*Cvliv + Qnp*Cvnp - Qtot*Cven

d/dt(Aart) = Qtot*(Cvlung - Cart)

d/dt(Aliv) = Qliv*(Cart - Cvliv) - Kbile*Cvliv*Vliv - Kinliv*Cvliv*Vliv + Koutliv*Alivdeep - Aliv*Kbile

d/dt(Alivdeep) = Kinliv*Cvliv*Vliv - Koutliv*Alivdeep

d/dt(Anp) = Qnp*(Cart - Cvnp) - Kinnp*Cvnp*Vnp + Koutnp*Anpdeep + kdepSN*Anpdep

d/dt(Anpdeep) = kdepDN*Anpdep - Koutnp*Anpdeep + Kinnp*Cvnp*Vnp

d/dt(Anpdep) = fdepNP*Cair*Tvol - kdepDN*Anpdep - kdepSN*Anpdep - Anpdep*Kgi

d/dt(Agi) = Anpdep*Kgi + Alungdep*Kgi - Kai*Agi - Kfeces*Agi + Aliv*Kbile

d/dt(Afeces) = Kfeces*Agi

d/dt(Aurine) = Akid*Kurine

MASSBAL1 = Abone + Akid + Aliv + Anp + Amusc + Alu

MASSBAL2 = Abonedeep + Akiddeep + Alivdeep + Anpdeep + Amuscdeep + Alungdeep

MASSBAL3 = Anpdep + Alungdep

MASSBAL4 = Aurine + Afeces + Agi

MASSTOT = MASSBAL1 + MASSBAL2 + MASSBAL3 + MASSBAL4

TABLE 30. COMPARISON OF PREDICTED AND OBSERVED NICKEL TISSUE CONCENTRATIONS TWELVE MONTHS AFTER A 140 HOURS EXPOSURE TO NIO AEROSOL.*

Tissue µg/L	8.0 mg/m^3 Model	Observed	O/P	0.6 mg/m^3 Model	Observed	O/P
Bone	5.95	ND		0.45	ND	
Kidneys	99.62	100 ± 90	1.00	7.47	80 ± 30	10.7
Liver	116.72	110 ± 70	0.94	8.75	50 ± 20	5.7
Nasopharynx	3.47	ND		0.26	ND	
Muscle	15.82	ND		1.19	ND	
Lung	285826	277000 ± 98000	0.97	21437	17000 ± 4000	0.79

*Note: NiO aerosol MADD = 1.2 µm, gsd = 2.2. Model exposure was continuous for 140 hr, actual exposure was discontinuous over a one month period (not specified but probably about 6 hr/day x 5 days/week x 30days).

B.5 Biokinetic Model of Uthus (1999) for Oral $NiCl_2$ in the Rat.

METHOD Stiff

STARTTIME = 0

STOPTIME= 10000 {minutes}

DT = 0.02

DTOUT = 10

{Uthus biokinetic model for 63Ni in the rat, Proc ND Acad Sci, 53:92-96(1999)}

{model compartments, ug Ni}

init GI_1 = 0.84 {ug at 12.7 uCi/ug Ni}

init GI_2 = 0

init GI_11 = 0

init Feces_3 = 0

init Blood_16 = 0

init Blood_15 = 0

init Blood_10 = 0

init Blood_4 = 0

init Liver_5 = 0

init Liver_6 = 0

init Liver_12 = 0

init Urine_9 = 0

init Urine_13 = 0

init Body_7 = 0

init Body_8 = 0

init Body_14 = 0

{mass transfer rate constants, /min}

K2_1 = 0.975

K3_11 = 0.000543

K4_1 = 0.025

K4_5 = 0.14

K4_7 = 0.3

K4_15 = 0.02

K5_4 = 0.155

K5_6 = 0.055

K6_5 = 0.05

K6_12 = 0.00003

K7_4 = 1.0

K7_8 = 0.005

K8_7 = 0.05

K8_14 = 0.0004

K9_13 = 0.0007

K10_4 = 0.0525

K11_2 = 0.001

K12_6 = 0.00175

K13_4 = 1.05

K14_8 = 0.0075

K15_10 = 0.066667

K15_16 = 0.0015

K16_15 = 0.01

{model differential equations, ug/min}

d/dt(GI_1) = -GI_1*K2_1 - GI_1*K4_1

d/dt(GI_2) = GI_1*K2_1 - GI_2*K11_2

d/dt(GI_11) = GI_2*K11_2 - GI_11*K3_11

d/dt(Feces_3) = GI_11*K3_11

d/dt(Blood_4) = GI_1*K4_1 - Blood_4*K5_4 + Liver_5*K4_5 - Blood_4*K10_4 + Blood_15*K4_15 - Blood_4*K13_4 - Blood_4*K7_4 + Body_7*K4_7

d/dt(Blood_10) = Blood_4*K10_4 - Blood_10*K15_10

d/dt(Blood_15) = Blood_10*K15_10 - Blood_15*K4_15 + Blood_16*K15_16

d/dt(Blood_16) = -Blood_16*K15_16 + Blood_15*K16_15

d/dt(Liver_5) = Blood_4*K5_4 - Liver_5*K4_5 -Liver_5*K6_5 + Liver_6*K5_6

d/dt(Liver_6) = Liver_5*K6_5 - Liver_6*K5_6 - Liver_6*K12_6 + Liver_12*K6_12

d/dt(Liver_12) = Liver_6*K12_6 - Liver_12*K6_12

d/dt(Urine_13) = Blood_4*K13_4 - Urine_13*K9_13

d/dt(Urine_9) = Urine_13*K9_13

d/dt(Body_7) = Blood_4*K7_4 - Body_7*K4_7 - Body_7*K8_7 + Body_8*K7_8

d/dt(Body_8) = Body_7*K8_7 - Body_8*K7_8 + Body_14*K8_14 - Body_8*K14_8

d/dt(Body_14) = Body_8*K14_8 - Body_14*K8_14

{Mass balance}

Mass_1 = GI_1 + GI_2 + GI_11 + Feces_3

Mass_2 = Blood_4 + Blood_10 + Blood_15 + Blood_16

Mass_3 = Liver_5 + Liver_6 + Liver_12

Mass_4 = Body_7 + Body_8 + Body_14

Mass_5 = Urine_13 + Urine_9

Mass_total = Mass_1 + Mass_2 + Mass_3 + Mass_4 + Mass_5

PCRECOV = Mass_total*100/0.84 {percent recovery of administered Ni}

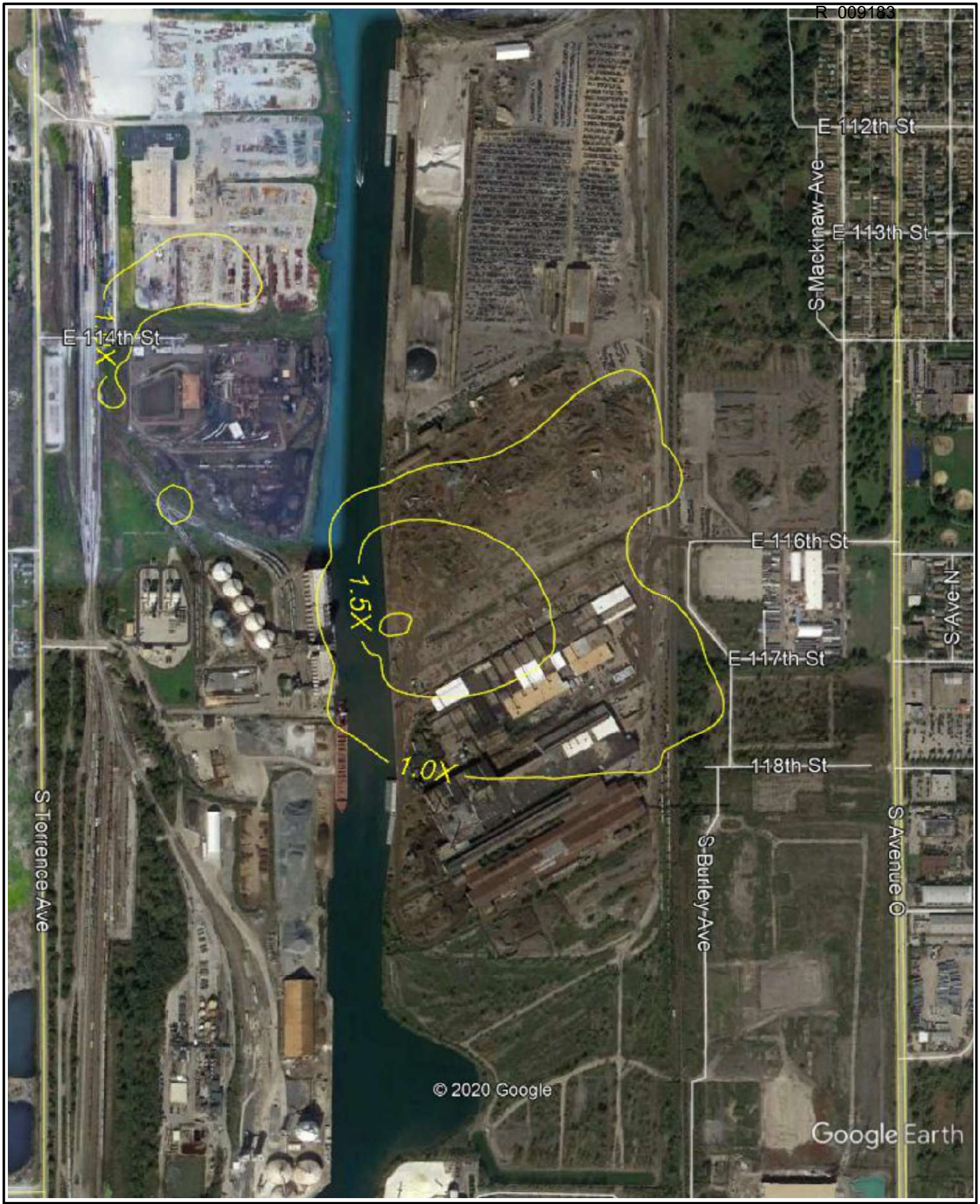


Figure 1 *Mn Impact Contour Plot*

1X = 0.17 ug/m3
8-hour average

Figure 2 *PM10 Impact Contour Plot*

NAAQS = 150 ug/m3
24-hour average

48217 COMMUNITY AIR MONITORING PROJECT

September 2016 – September 2017

April 27, 2018

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Air Quality Division
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P.O. Box 30260
Lansing, Michigan 48909-7760

Table of Contents

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Michigan's Environmental Justice Policy promotes the fair, non-discriminatory treatment and meaningful involvement of Michigan's residents regarding the development, implementation, and enforcement of environmental laws, regulations, and policies by this state. Fair, non-discriminatory treatment intends that no group of people, including racial, ethnic, or low-income populations, will bear a disproportionately greater burden resulting from environmental laws, regulations, policies, and decision-making. Meaningful involvement of residents ensures an appropriate opportunity to participate in decisions about a proposed activity that will affect their environment and/or health.

Background

For many years, residents of the 48217 ZIP code in Southwest Detroit have voiced concerns about impacts from industry and traffic on their air quality and health. These concerns are a subgroup of related concerns, including environmental injustice, health disparities, odors, lack of notification during environmental emergencies, noise, and cumulative impacts.

This outdoor air study was community led in collaboration with state, federal, and academic partners. This project was done to answer the following questions:

- What is the air quality in the 48217 ZIP code?
    - How might the air quality in this ZIP code affect someone's health?
    - How does the air quality compare to other locations?

- How can information about the air quality be used to help this community?

How the Project Started

- In June 2015, MDEQ's Southeast Michigan staff invited MDEQ Director Wyant to speak to local activists. At this meeting he asked for proposals on how the MDEQ could help them.
- In the summer of 2015, community leader, Dr. Dolores Leonard submitted a proposal for air monitoring, which was accepted and funded by the MDEQ.
- In the fall of 2015, Dr. Leonard selected four individuals to represent various 48217 neighborhoods along with a resident with prior science and engineering experience. A member of the Sierra Club also helped facilitate efforts.
- In December 2015, a project kick-off meeting was held with community representatives, MDEQ-AQD staff, University of Michigan researchers, and the United States Environmental Protection Agency (USEPA).

The community stakeholder group identified pollutants that should be measured and provided recommendations to the MDEQ on possible station locations. The stakeholders' goal for The Community Air Monitoring Project was to evaluate the air quality in the neighborhood, not to target a specific facility. To select the pollutants, the stakeholder group worked with two University of Michigan researchers who helped identify major emission sources and the pollutants of interest.

The stakeholder group identified a list of 12 possible locations for the monitoring station. The MDEQ-AQD staff evaluated these locations and provided the stakeholder group with the top four that would meet air monitoring siting criteria. Two location owners declined the request for the monitoring station and one did not respond. The New Mount Hermon Missionary Baptist Church, located at 3225 South Deacon Street, agreed to host the air monitoring site.

Pollutants Monitored in the Project

The 1-year monitoring study began in September 2016 for the following compounds:

Sampled once every six days (sent to laboratories):

- Acids: hydrochloric acid, sulfuric acid, and hydrogen cyanide
- Polyaromatic hydrocarbons (PAHs): 66 different compounds
- Volatile organic compounds (VOCs): 67 different compounds
- Metals: 13 different compounds

Sampled continuously (reported in real-time to website, http://www.deqmiair.org/):

- Fine particulate matter ($PM_{2.5}$)
- Sulfur dioxide (SO_2)

Community Outreach

Open community meetings were held to present and discuss findings from the monitoring project. Meetings were held in the evening at the New Mount Hermon Missionary Baptist Church on February 13, June 27, and November 20, 2017, and May 3, 2018.

Summary and Conclusions

Air Quality and Health Risk Results

Air monitoring results were compared to pollutant levels that are used to protect the public, including sensitive groups like asthmatics and children. For the purposes of this report, these health-protective levels are referred to as “health limits”.

- SO_2, lead, and $PM_{2.5}$ were compared to federal health limits: primary National Ambient Air Quality Standards (NAAQS). Monitored levels were below the level of the NAAQS. See Appendix A for a discussion of the NAAQS.

- Other pollutants were compared to state limits, which are the MDEQ-AQD screening levels.
    - Except for sulfuric acid, all pollutants were below the screening levels for noncancer-related health protection.
    - Two out of 53 sulfuric acid samples were above the screening level. Breathing a high level of sulfuric acid can impair lung function, and people with lung disease like asthma are more susceptible to these health problems.
    - For pollutants that can cause cancer, the additional risk of developing cancer over a person’s entire lifetime was considered. The pollutants of potential concern in this study were arsenic, naphthalene, and hexavalent chromium.

- Some pollutants, like benzene, are also likely to be of potential concern. However, these pollutants were rarely or never detected due to limitations at the laboratory. Therefore, some pollutant levels are not known.

To consider cumulative impacts, concentration levels from different pollutants were combined when they had a common health effect. For example, the pollutants that cause irritation were combined, and pollutants that may cause cancer were combined.

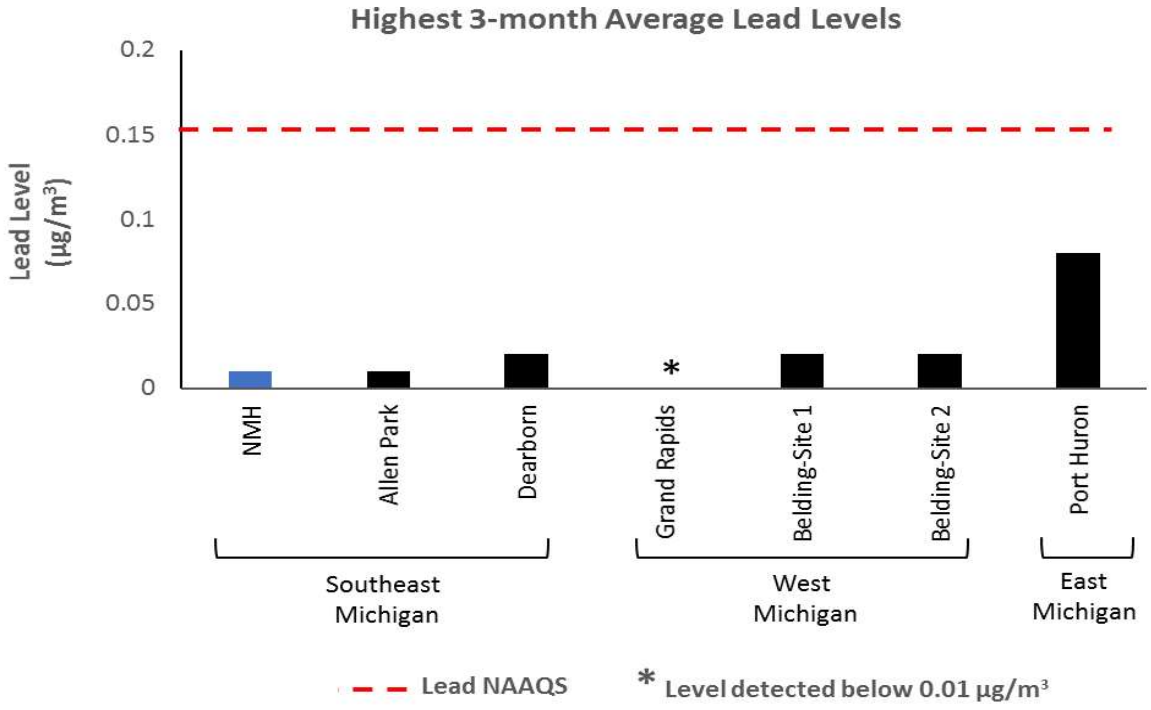
- For noncancer-related risks, the combined risks did not reach a level of a health concern, except for the two occasions when sulfuric acid reached a level of concern by itself.
  - The high levels occurred about a year apart from each other. Attempts were made to identify the source for the two high sulfuric acid levels, but the source was not able to be identified. Since these high levels were not frequent, it is suspected that the source (or sources) is not regularly emitting sulfuric acid to the outdoor air. The AQD is continuing to investigate and is exploring other technologies and opportunities for identifying the source of sulfuric acid.

- For pollutants that can cause cancer, there was a cumulative lifetime additional risk of about eight in one million.
  - This additional risk was mostly due to arsenic, naphthalene and hexavalent chromium. Similar levels for these pollutants are also seen in other urban areas, like the Dearborn air monitoring site.

Air Quality at this Site Compared to Other Sites

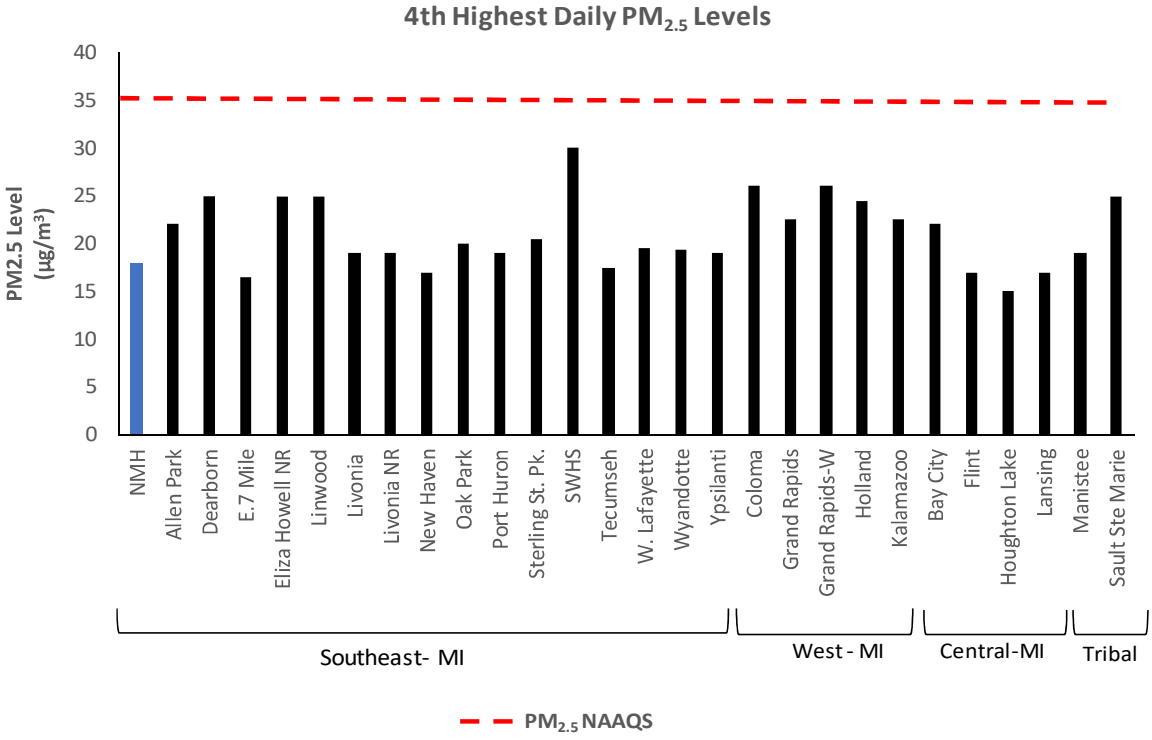
Overall, the pollutant levels at the New Mount Hermon (NMH) site were similar to other monitoring sites in metro Detroit. Other Michigan monitoring sites are monitoring for fewer pollutants, so it's difficult to compare to these other sites.

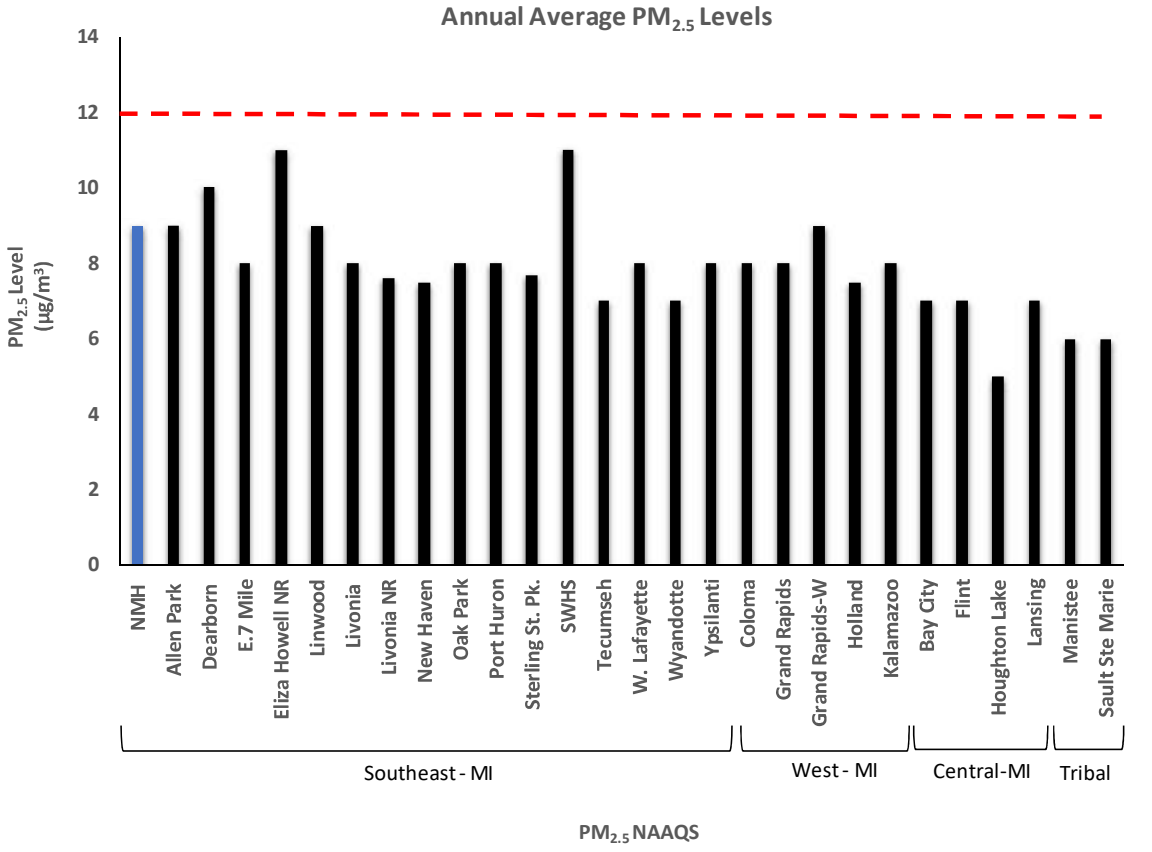
Air monitoring for lead is also a good example of the different purposes for air monitoring across the state. Lead levels at the NMH site were similar to current levels at most Michigan sites. The NMH site is monitoring for lead because it was a recommendation from the community stakeholder group. The Allen Park and Grand Rapids sites are monitoring for lead as a part of the National Core Network. The Dearborn site is a part of the National Air Toxics Trends Stations. Both programs are used to monitor long-term trends. The Belding sites and the Port Huron site are used for source-oriented monitoring of sources that may emit especially high levels of lead. The Houghton Lake site is a remote background site, where there is relatively little manmade air pollution. The Houghton Lake site previously monitored for lead as well, and it showed levels similar to the levels currently seen at the Grand Rapids site. Lead is used here as an example of a pollutant that is monitored more extensively throughout the state. There is no absolute safe exposure to lead, but the lead NAAQS provides a level of health protection for at-risk groups. Lead levels at the NMH site were similar to current levels at most Michigan sites.



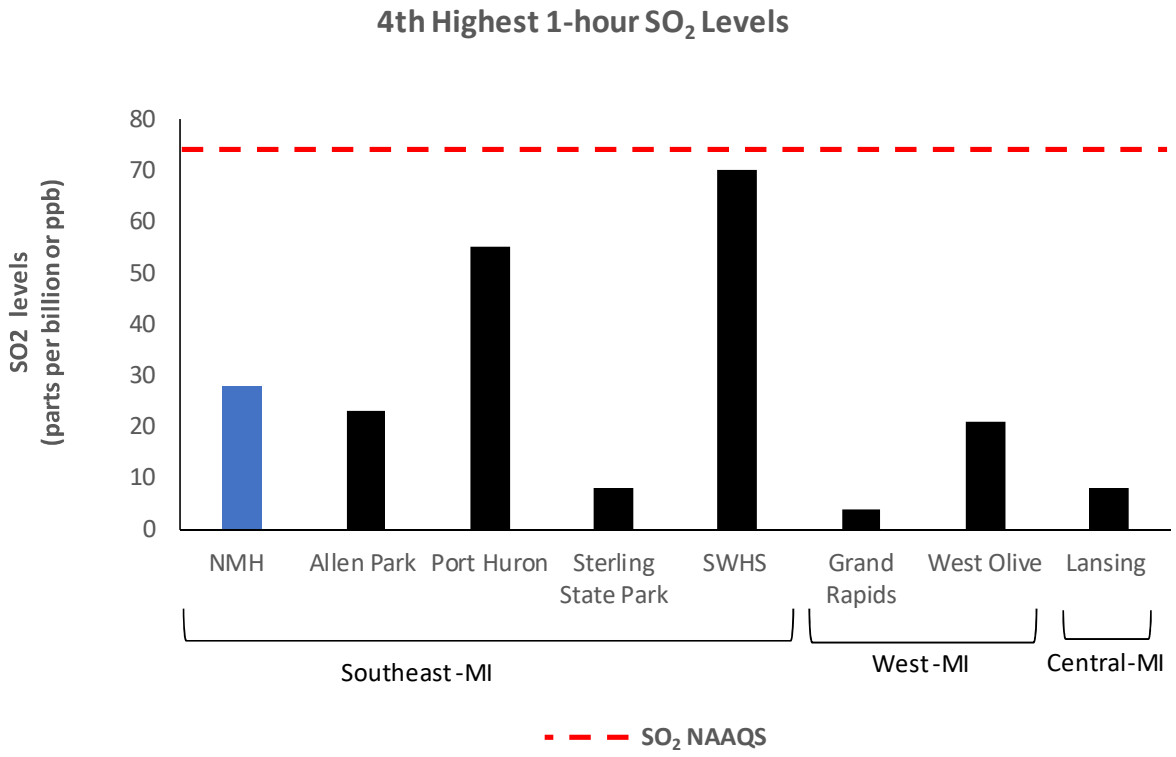
$PM_{2.5}$, SO_2, and lead are used here as examples of pollutants that are monitored more extensively throughout the state. Just as important, they are all significant in terms of health risk. For example, health can be impacted at levels even below the $PM_{2.5}$ NAAQS. While breathing lead in the outside air is usually not the main way that people are exposed, there is also no absolute safe exposure to lead. The NAAQS for both $PM_{2.5}$ and lead provide a level of health protection for at-risk groups.

$PM_{2.5}$ is a mixture of pollutants, and it is one of the main health risk concerns with air pollution. When averaged over the year-long study (the annual average level), $PM_{2.5}$ levels at the NMH site are similar to levels at other sites in Michigan. The annual average level at the NMH site is slightly higher than most levels at sites in West Michigan, Central Michigan and on Tribal lands. With the average over each day (the daily level), levels at the NMH site were similar to other sites in Michigan as well.


4th Highest Daily PM2.5 Levels
PM2.5 Level (µg/m³)
40
35
30
25
20
15
10
5
0
NMH
Allen Park
Dearborn
E.7 Mile
Eliza Howell NR
Linwood
Livonia
Livonia NR
New Haven
Oak Park
Port Huron
Sterling St. Pk.
SWHS
Tecumseh
W. Lafayette
Wyandotte
Ypsilanti
Coloma
Grand Rapids
Grand Rapids-W
Holland
Kalamazoo
Bay City
Flint
Houghton Lake
Lansing
Manistee
Sault Ste Marie
Southeast- MI
West - MI
Central-MI
Tribal
PM2.5 NAAQS


Annual Average PM2.5 Levels
PM2.5 Level (µg/m³)
14
12
10
8
6
4
2
0
NMH
Allen Park
Dearborn
E.7 Mile
Eliza Howell NR
Linwood
Livonia
Livonia NR
New Haven
Oak Park
Port Huron
Sterling St. Pk.
SWHS
Tecumseh
W. Lafayette
Wyandotte
Ypsilanti
Coloma
Grand Rapids
Grand Rapids-W
Holland
Kalamazoo
Bay City
Flint
Houghton Lake
Lansing
Manistee
Sault Ste Marie
Southeast - MI
West - MI
Central-MI
Tribal
PM2.5 NAAQS

SO_2 is also an important example here, because the 48217 ZIP Code is currently in an SO_2 non-attainment area, which means that the area is not meeting the health standards based on 3 years of data. SO_2 levels at the NMH site are like some other sites in Michigan, but SO_2 levels greatly depend on local pollution sources. The Allen Park and Grand Rapids sites monitor for SO_2 as part of the National Core Network and the other sites are monitoring to meet federal requirements.



Benefits and Limitations of this Study

This benefits and limitations list identifies ways that this study may be helpful to the community. A limitation, for example, may be an avenue for the community to focus future efforts.

Benefits:

- The community has additional information about air quality in the 48217 ZIP code.
- The NMH site is now a part of the state ambient air monitoring network, which is used to help measure compliance with environmental regulations. The MDEQ anticipates retaining this site for several years.

- One year of monitoring samples were collected and compared to health standards and nearby sites using nationally accepted methods.
- Health risks were studied using well established health-based limits designed to protect the most sensitive populations; cumulative impacts of breathing these pollutant levels were included.
- This study included monitoring for acids, which are not routinely monitored in outdoor air by any state monitoring network.
- Sampling results were shared with the community throughout the study and the community's comments were used to improve the project. For example, the USEPA was recruited to use their mobile air monitor in other areas of the ZIP code.
- The results of this study can be used by others (including other scientists, health professionals, and community members) for future research and projects.

Limitations:

- The monitoring site selection was dependent on siting criteria and property owner cooperation, which limited options for where the monitor could be located.
- There could be other pollutants of concern that were not monitored, do not have reliable monitoring methods, do not have health limits, or have health limits based on very limited information.
- While health effects of some pollutants have no known threshold below which health effects do not occur, this study did not focus on possible risks at levels below established heath limits.
- Of all the potential health impacts this community may face, there was only a risk assessment for the monitored air pollutants.
- Health statistics of this community were not included in the health assessments.
- Interactions between mixtures of pollutants may increase health risks, but all the potential interactions between pollutants are not known.

Next Steps for New Mount Hermon Monitoring Station

The sampling for PAHs, acids, VOCs, and some metals has concluded. MDEQ plans to sample for $PM_{2.5}$, SO_2, and five metals, which include lead, arsenic, cadmium, nickel, and manganese in 2018.

Other Resources for the 48217 ZIP Code Community

Information on Air Quality

Reporting outdoor air complaints
Contact the MDEQ-AQD Detroit Field Office: 313-456-4700

Information on current air quality
MIair: http://www.deqmiair.org/

Air NOW: https://www.airnow.gov/

Tutorial on how to get involved in the air permitting process
http://www.epaejtraining.org/OAQPS/past-trainings/clean-air-act-rulemaking-and-permitting-training-detroit-mi/

Public health action plan to address air quality in Detroit
University of Michigan's Community Action to Promote Healthy Environments:
http://caphedetroit.sph.umich.edu/

Information on Detroit's Anti-Idling Ordinance
http://www.sdevweb.org/issues/anti-idling/

Information on Other Environmental Issues

City of Detroit Emergency Management
www.detroitmi.gov/dhsem (313) 596-2590

USEPA's MyEnvironment Tool
https://www3.epa.gov/myem/envmap/find.html

USEPA's Environmental Justice Screening Tool
https://www.epa.gov/ejscreen

USEPA's Environmental Justice Screening Tool
https://www.epa.gov/ejscreen

State and Federal Contacts on Vapor Intrusion and Soil Issues
MDEQ Remediation and Redevelopment Division and Waste Management and Radiological Protection Division, Southeast Michigan District Office: 586-753-3700

USEPA Grosse Ile Office
Emergency Response: 734-692-7600

Information on Health Statistics

Asthma Hospitalization Rates in 2012-2014
http://www.michigan.gov/documents/mdch/Michigan-and-Detroit-Asthma-Hosp-Rates_498682_7.pdf

Childhood Lead Testing in 2013
http://www.michigan.gov/documents/mdhhs/2013_Child_Lead_Testing_and_Elevated_Levels_Report_515288_7.pdf

Cancer Rates from 1999-2009
http://www.michigan.gov/documents/mdch/Southwest_Detroit_Cancer_Incidence_and_Mortality_Report10_18_12_402088_7.pdf

Global Burden of Disease, including state of Michigan results
https://vizhub.healthdata.org

Appendix A. Pollutants and Health Risk Assessment Methods

Monitored Pollutants

1. Sulfur Dioxide (SO_2)

Sulfur dioxide (SO_2) is a gas formed by the burning of sulfur-containing materials. Sources of SO_2 include coal-burning power plants, petroleum refineries, pulp and paper mills, steel mills, and other transportation sources. Sulfur dioxide is classified as a criteria pollutant and has a National Ambient Air Quality Standard (NAAQS) that is based on the 4th highest daily 1-hour value for each year, averaged over 3 years. Exposure to elevated levels can affect breathing, cause respiratory distress, aggravate existing cardiovascular and pulmonary disease, and alter the body's immune system. SO_2 was measured continuously using a Federal Reference Method analyzer: Thermo Environmental 43I-Pulsed Fluorescence analyzer.

2. Fine Particulate Matter ($PM_{2.5}$)

Particulate matter (PM) is a general term used for a mixture of solid particles and liquid droplets found in the air. These are further categorized according to size. $PM_{2.5}$ consists of tiny particles with a diameter of 2.5 microns or less. $PM_{2.5}$ is a mixture of very small particles and liquid droplets that are created during combustion when coal, gasoline, and other fuels are burned. Sources of $PM_{2.5}$ include industrial sources and motor vehicles (especially diesel trucks and buses). $PM_{2.5}$ can also be formed in the air by chemical reactions between other pollutants. Because of their small size, fine particles can be inhaled into the lungs. Fine particulate matter is classified as a criteria pollutant and has a NAAQS based on both a 24-hour value of 35 micrograms per cubic meter (ug/m^3) which is based on the 4th highest daily value for each year, averaged over 3 years and an annual 3-year average of 12 ug/m^3. The Exposure to fine particulate matter can affect breathing and cause cardiovascular problems. The fine particulate matter was measured continuously using a Tapered Element Oscillating Microbalance (TEOM) analyzer.

3. Lead (Pb)

Lead (Pb) is a metal found in coal, oil, and other fuels. It is also found in older paints, dusts, soil, and is sometimes released from industrial sources. Lead is classified as a criteria pollutant and has a NAAQS based on a rolling 3-month average. Exposure occurs through the inhalation or ingestion of lead in food, water, soil, or dust particles. Lead primarily accumulates in the body's blood, bones, and soft tissues, and adversely affects the kidneys, liver, nervous system, and other organs. Lead sampling was conducted using a high-volume total suspended particulate sampler. Outside air is pulled into the sampler and material is collected on a filter that is placed in the sampler. The sampler operated every 6 days for a 24-hour period. The filter was removed and sent to the MDEQ Laboratory for metals analysis.

4. Air Toxics

Air toxic pollutants are those chemicals known or suspected to cause human health effects or adverse environmental effects. The 48217 monitoring project measured a large list of compounds classified as air toxics. Some of the air toxics measured included trace metals, volatile organic compounds (VOCs), and poly aromatic hydrocarbons (PAHs). Air toxics can come from a variety of sources such as vehicles, industrial sources, man-made materials such as paints and cleaning products, and natural sources. Air toxics can have a wide range of potential health effects such as the aggravation of asthma; irritation to the eyes, nose, and throat; nervous system effects; and, some could cause cancer. The metals were collected using a high-volume total suspended particulate sampler. Outside air is pulled into the sampler and material is collected on a filter that is placed in the sampler. The sampler operated every 6 days for a 24-hour period. The filter was removed and sent to the MDEQ Laboratory for analysis. The VOCs were collected in a 6-liter, metal, summa-type canister. The programmable sampler operated once every 6 days for a 24-hour period and pulled outside air into the canister. The canister was then sent to a laboratory where it was analyzed using Toxic Organic (TO) Method 15. The PAH compounds were collected using a polyurethane foam (PUF) high-volume sampler. The outside air was pulled into the sampler and collected on an internal cartridge once every 6 days for a 24-hour period. The cartridge is removed and sent to a contract laboratory where it is analyzed using TO-Method 13 for PAH compounds.

The monitoring project also conducted sampling for air toxics that are not routinely being measured in the national air toxics network. These air toxics are sulfuric acid, hydrochloric acid, and hydrogen cyanide.

- Sulfuric acid can be released directly and can be formed from SO_2 released when coal, oil, and gas are burned. The released SO_2 reacts in the atmosphere to form sulfuric acid.
- Hydrogen chloride is used in the manufacture of a variety of industrial chemicals, fertilizers, and dyes. Hydrogen chloride is also known as hydrochloric acid.
- Cyanide enters water, soil, and air from both natural processes and industrial activities. In air, cyanide is present mainly as the gas hydrogen cyanide.

Sampling of the acids was conducted using a programmable Gillian pump. Outside air was pulled through two sorbent tubes. One tube containing silica gel was analyzed for hydrochloric acid and sulfuric acid, and the other tube containing soda lime was analyzed for hydrogen cyanide. Sampling was conducted once every 6 days for an 8-hour period. The tubes were sent to a contract laboratory and analyzed using the National Institute of Occupational Health (NIOSH) method 7903 for hydrochloric and sulfuric acid, and the NIOSH Method 6010 for hydrogen cyanide.

Health Risk Assessment Methods

Evaluation of Pollutants That Can Cause Health Effects Other than Cancer

The monitored pollutant concentrations from this study were compared to health limits when they were available. The health-based limits used in this assessment were either the NAAQS for the USEPA criteria pollutants (SO_2, $PM_{2.5}$, and lead), the USEPA's Air Quality Index (AQI) or the Initial Threshold Screening Levels (ITSLs) developed for toxic air contaminants according to the procedure given in AQD Rule 336.1232. The lead NAAQS is based on a 3-month rolling average, but SO_2 and $PM_{2.5}$ are based on a 3-year calculation. Because 3 years of results are needed for the SO_2 and $PM_{2.5}$ NAAQS, direct comparison to the SO_2 and $PM_{2.5}$ NAAQS cannot be made with a 1-year study. The AQI was used to evaluate how daily SO_2 and $PM_{2.5}$ levels may affect health. ITSLs are utilized in the AQD's permitting program as health limits protective for potential noncancer effects. For this study, some health-based limits were assigned to pollutants that do not currently have specific health-based limits based on structurally similar pollutants and the most toxic component they have in common. This is noted when done.

After the appropriate health limits were identified, a hazard quotient (HQ) approach was used to determine if pollutants other than the criteria pollutants were at a level of concern for noncancer (see results in Appendix B-2). The HQ is the pollutant estimate divided by the appropriate long-term or short-term health limit. Long-term describes an exposure that lasts for a year or longer. Short-term describes an exposure that lasts for an hour or one day.

For a given pollutant, pollutant estimates at or below the health limit indicate that adverse noncancer effects are not likely to occur. In Appendix B-2, HQs are described as percentages. Pollutant concentrations found above their respective health limits indicate a potential health hazard; these instances were further evaluated to estimate the health risk.

Risks of health effects from short periods of exposure to a given pollutant were evaluated by comparing the respective health limit to the highest 8-hour concentrations of the acid or the highest 24-hour concentrations of all other pollutants. A two-step process, similar to the one described in the Detroit Air Toxics Initiative (Simon et al, 2005) was used. In the first step, maximum pollutant levels were compared to the short-term health limits without considering whether their averaging times were the same. If a pollutant's maximum detected level was above the health limit, the results were reviewed again to consider averaging times.

Risks of noncancer health effects from long periods of exposure to a given pollutant were evaluated by comparing the respective health limit to the 95% Upper Confidence Limit (UCL) on the mean when that pollutant was measured at levels above the method detection limit or reporting limit more than 15% of the time (USEPA, 2004). When virtually synonymous pollutants are present (e.g., xylene isomers), the measured

concentrations for each of the pollutants were added together before comparison to the group's respective health-based limits.

The method detection limit (MDL) is the lowest amount of a chemical that can reliably be observed (with 99% confidence) above the normal, random noise of an analytical instrument or method. Pollutant levels below the MDL are called non-detects. The reporting limit (RL) is the minimum value below which the data are documented as non-detects. When provided by the laboratory, the MDL is used to generate estimates of the pollutant level measured. When the MDL is not available from the laboratory, the RL is used. ProUCL (USEPA, 2015) was used to generate the 95% UCL and average estimates of the mean to account for non-detects.

Evaluation of Pollutants That Can Cause Cancer

For carcinogenic air pollutants, the annual average measured concentrations were compared to health limits associated with specific cancer risk levels. Cancer risk levels characterize the potential cancer risk based upon a lifetime (70 years) of exposure at the annual averaged monitored concentrations. The average level of hexavalent chromium was calculated from total chromium levels using previous estimates of hexavalent chromium in the Detroit area (Simon et al, 2005). The unit risk estimates were used to derive Initial Risk Screening Levels (IRSLs) for the AQD's permitting program. IRSLs are ambient air concentrations associated with an upper-bound lifetime cancer risk estimate of 1 in one million (1×10^{-6}). The IRSLs were used to characterize the potential cancer risk from exposure to the annual average concentration of each individual carcinogenic chemical found at each monitoring site. It should be noted that there is no USEPA or MDEQ ambient air quality standard for an acceptable level of carcinogens in ambient air, for individual substances or cumulatively for multiple collocated carcinogens. However, the 1 in ten thousand (1×10^{-4}) risk level was also presented, since this level is used by the USEPA as an upper limit of the presumptive acceptable risk level for the Clean Air Act Section 112(f) Risk and Technology Reviews (RTRs) for industrial source categories. The USEPA has also used a risk level of 1 in ten thousand or greater to denote high risk facilities for the National Scale Air Toxics Assessment (NATA).

Evaluation of Cumulative Impacts

Exposure to air pollutants generally occurs as a complex mixture, and the potential for interactive effects should be characterized when possible. USEPA guidance for the risk assessment of complex mixtures recommends that dose additivity be assumed for evaluating noncancer risks for a complex mixture that lacks adequate toxicity data on the specific mixture or a similar mixture (Hertzberg et al., 2000). The resulting hazard indices (HIs) are called "Target Organ Specific Hazard Indices," or TOSHIs. For TOSHIs with a value of 1 or less, a lack of adverse effects may be presumed. For TOSHIs exceeding a value of 1, harmful effects should not be presumed, but safety also cannot be presumed without further evaluation. The risk assessment in that situation proceeds with a more extensive assessment of the HQs which contribute the most to the TOSHI.

USEPA guidance also supports a “risk additivity” assumption for characterizing total cancer risk by summing the individual chemical’s cancer risk estimates at each site (Hertzberg et al., 2000). For short-term TOSHIs, a tiered system similar to that as described in the Detroit Air Toxics Initiative was used to consider potential health effects from exposure to the multiple pollutants (Simon et al., 2005). TOSHIs were developed from HQs for detected pollutants with short-term health limits, and then the corresponding time frame during which a spike occurred was also considered. It is important to note that this cumulative impact evaluation focuses on the potential health effects of breathing the multiple pollutants that were detected.

Appendix B. Results

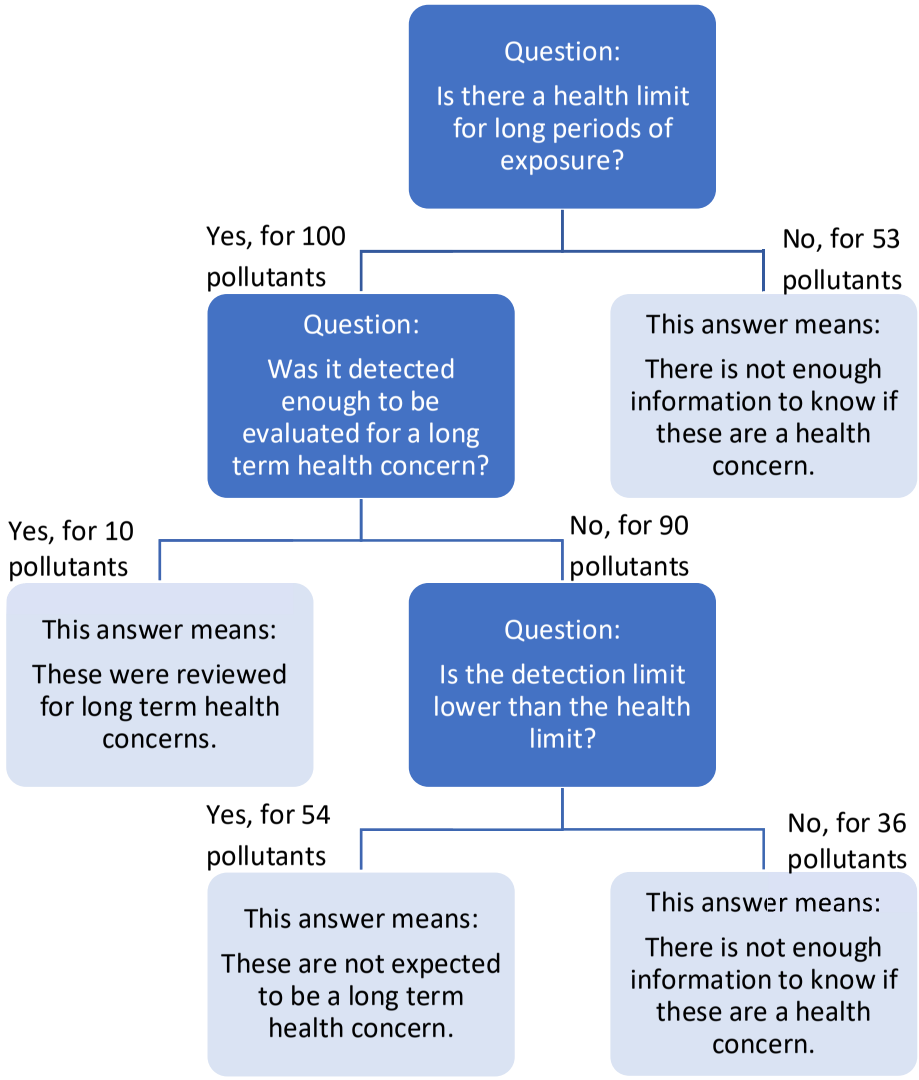
Pollutant levels measured at the New Mount Hermon (NMH) site are shown in comparison to their individual health limits. In cases where it is known that multiple pollutants health-based limits were derived using the same health effect, a cumulative exposure risk analysis was performed.

Pollutant levels are also shown as compared to pollutant levels measured at other sites in Michigan, especially the Marathon-sponsored air monitors in the 48217 ZIP code, the MDEQ-Dearborn site, and the MDEQ-SWHS site. These specific sites were a focus for comparison because they are the only other sites in Michigan that were measuring volatile organic compounds or polyaromatic hydrocarbons that were quality assured and uploaded to the USEPA's Air Quality System at the time of the study. Regional site data for SO_2 and $PM_{2.5}$ are also shown. Since there is such diversity in which pollutants are measured at each site, cumulative impact analysis was only performed for levels measured at the NMH site.

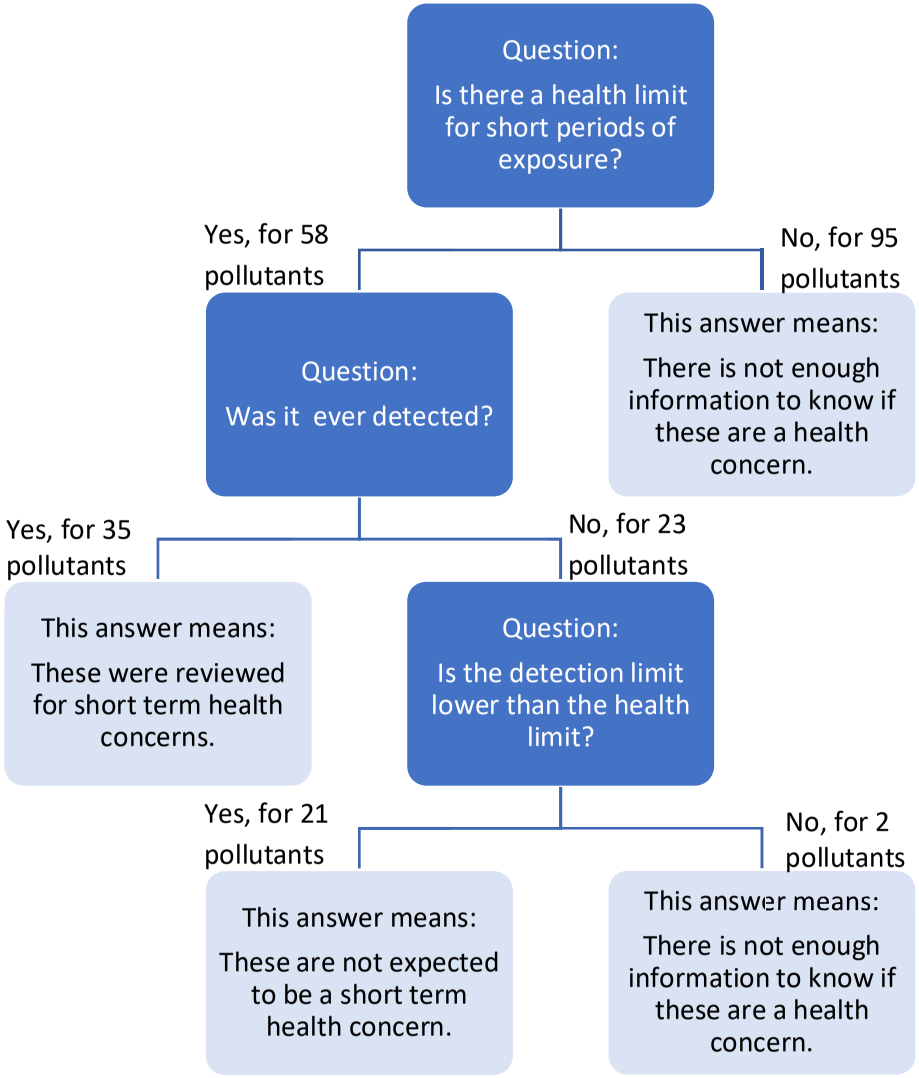
Air Monitoring Site	Corresponding Symbol in Graphs	Types of Pollutants Monitored
NMH		**$PM_{2.5}$; SO_2; 13 metals; acids; PAHs; and VOCs**
Marathon-North		**SO_2; VOCs;** PM_{10}; CO; total reduced sulfur compounds
Marathon-West		**SO_2; VOCs;** PM_{10}; CO; total reduced sulfur compounds
Marathon-East		**SO_2; VOCs;** PM_{10}; CO; total reduced sulfur compounds
Marathon-MTMS		**SO_2; VOCs;** PM_{10}; CO; total reduced sulfur compounds
Dearborn		**$PM_{2.5}$; SO_2; 14 metals; PAHs; VOCs;** PM_{10}; and carbonyls
SWHS		**$PM_{2.}$; SO_2; 4 metals, specifically manganese, arsenic, cadmium and nickel; VOCs;** $PM_{10;}$ and carbonyls

Comparison of Pollutant Levels to Health Limits

Questions to determine if the results may indicate a concern for health effects from long periods of exposure:



Questions to determine if the results may indicate a concern for health effects from short periods of exposure:



B-1. Air Quality Index Summary for SO_2 and $PM_{2.5}$

The Air Quality Index (AQI) allows for review of potential health effects from SO_2 and $PM_{2.5}$ below the federal health limits. The categories and descriptions were developed by the USEPA.

Using the AQI, there were no days when SO_2 or $PM_{2.5}$ reached levels expected to be unhealthy for sensitive groups or the general population. There were 70 days when the $PM_{2.5}$ level might have been a health concern for unusually sensitive individuals. There was only one day when the SO_2 level reached a level that might have affected unusually sensitive individuals. The AQD traditionally does not consider Moderate days as unhealthy days because the range for this category is below the health protective NAAQS values.

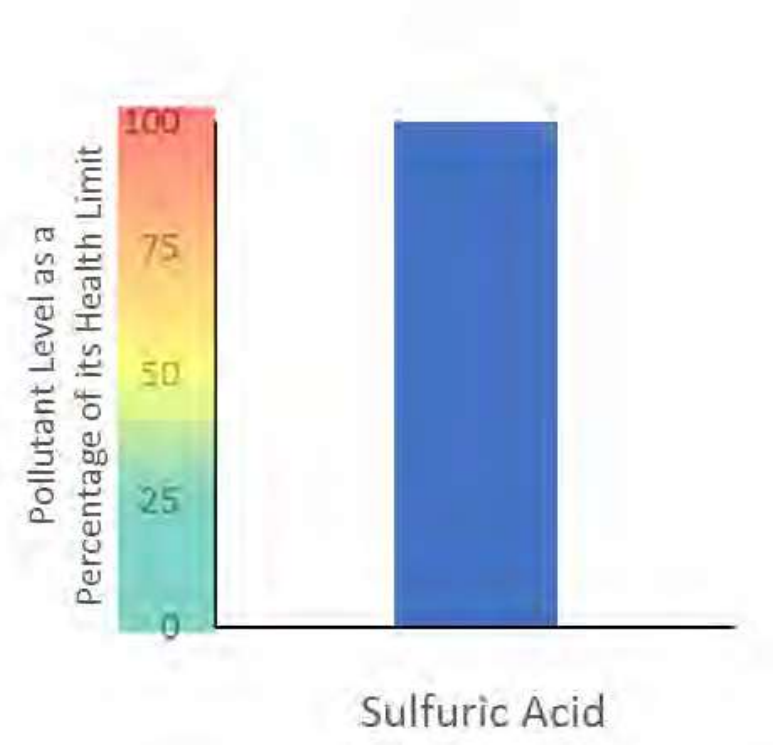
Air Quality Index Category	Number of Days When $PM_{2.5}$ Level was in Each Category	Number of Days When SO_2 Level was in Each Category
Good: Not expected to be a health risk	325	392
Moderate: May be a health concern for unusually sensitive individuals	70	1
Unhealthy for Sensitive Groups: May be a health concern for sensitive groups	0	0
Unhealthy: May be a health concern for everyone and sensitive groups may have more serious health effects	0	0
Very Unhealthy: Everyone may have more serious health effects	0	0
Hazardous: The entire population is likely to be affected	0	0

B-2. Measured Pollutant Levels as a Percentage of the Noncancer-Related Health Limit

In this section, pollutants are described in comparison to their short-term and long-term noncancer health limits using a color scale from 0 to 100%. The pollutant level is the same as the health limit when the pollutant level is 100%. When the pollutant level is 100% or more, it's important to further evaluate those health risks. The sulfuric acid level measured was higher than 100% of the health limit. The health risks of SO2 are further evaluated in Appendix C. Besides sulfuric acid, none of the pollutants that were detected at the NMH site and have noncancer-related health limits reached higher than 20% of the health limit. As a result, they were not considered a health concern.

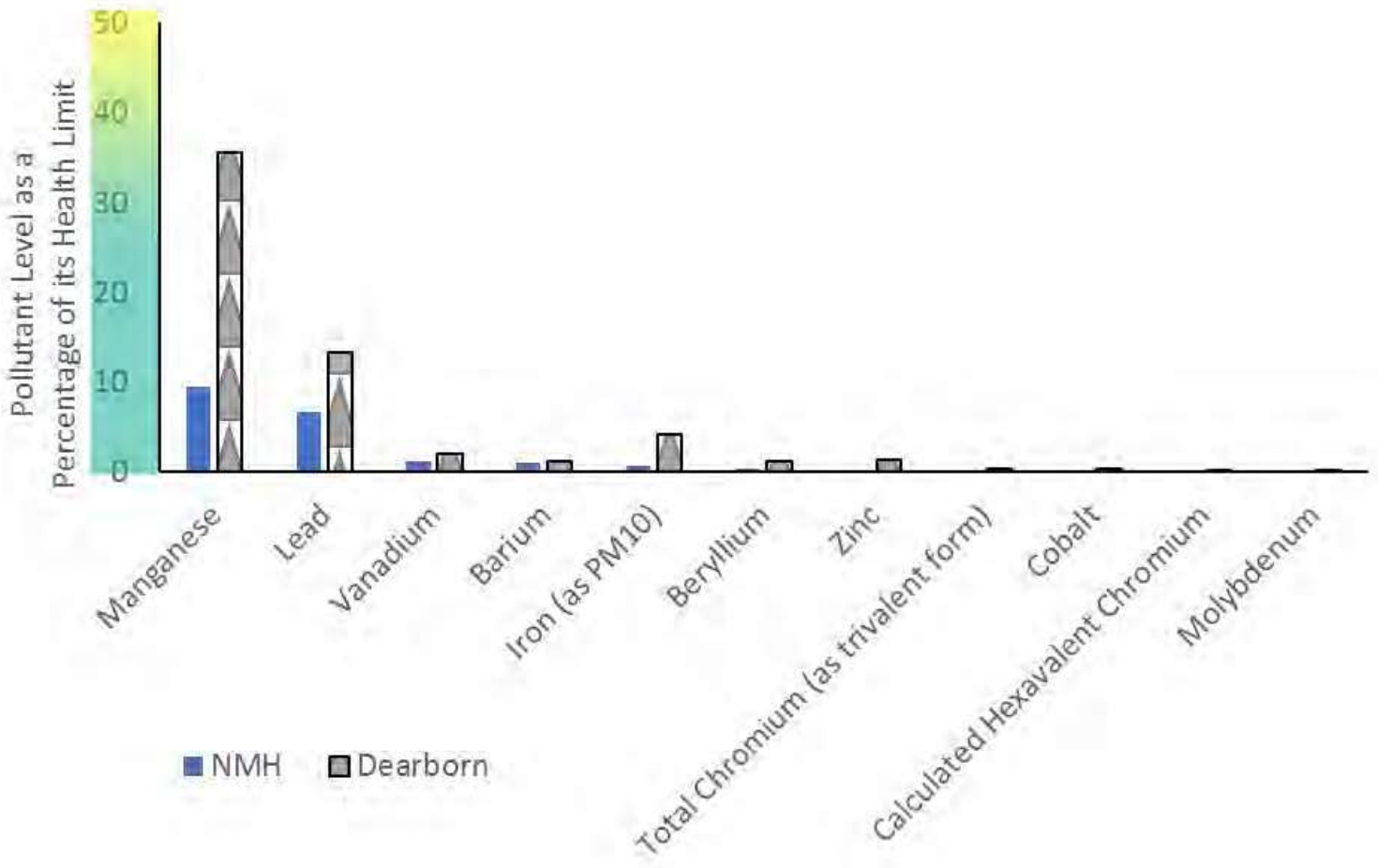
Some pollutants have two noncancer health limits, but the graphs show the comparison that gave the highest percentage. For example, if a pollutant level compared to its short-term health limit is 10% and compared to its long-term noncancer health limit is 20%, then the 20% comparison is shown on the graph.

Pollutant results at the NMH site are also compared to other sites in the 48217 ZIP code (the Marathon-sponsored air monitors) or in metro Detroit.



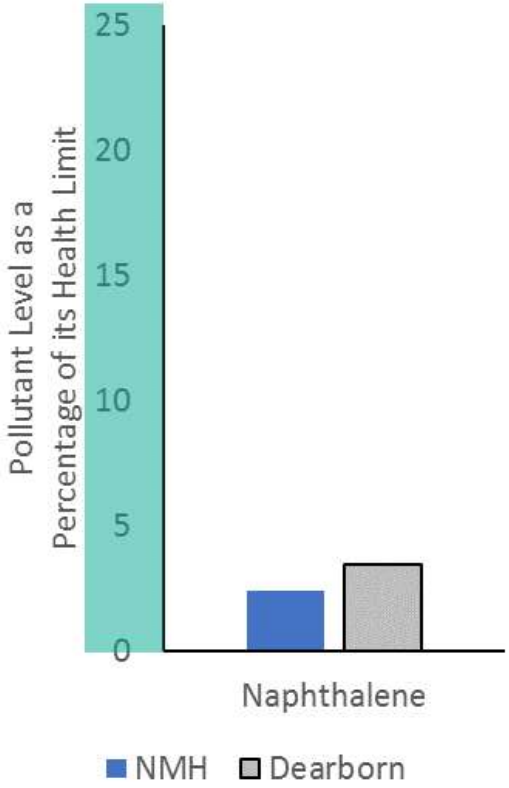
Metals monitored at NMH site compared to Dearborn site

This graph includes metals that were detected at the NMH site and were also detected at the MDEQ-Dearborn site. Manganese and hexavalent chromium are compared to health limits for long-term exposure, and all the other metals shown are compared to health limits for short-term exposure.



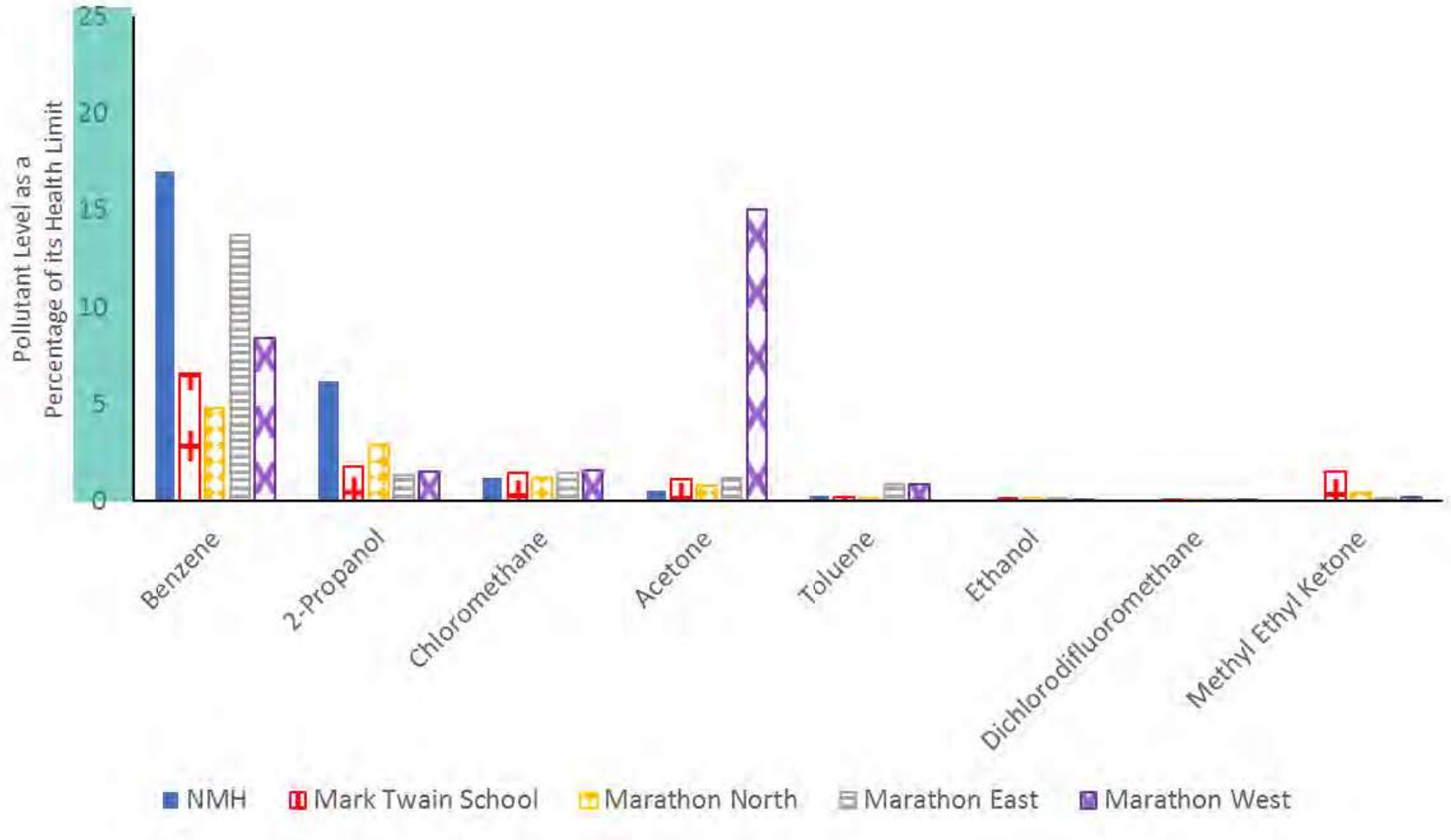
PAH Monitored at NMH Site Compared to Dearborn Site

Naphthalene was the only PAH detected at the NMH site, and also monitored at the Dearborn site. Naphthalene has two noncancer health limits, and the graph shows the comparison to the long-term health limit because it gave the highest percentage.



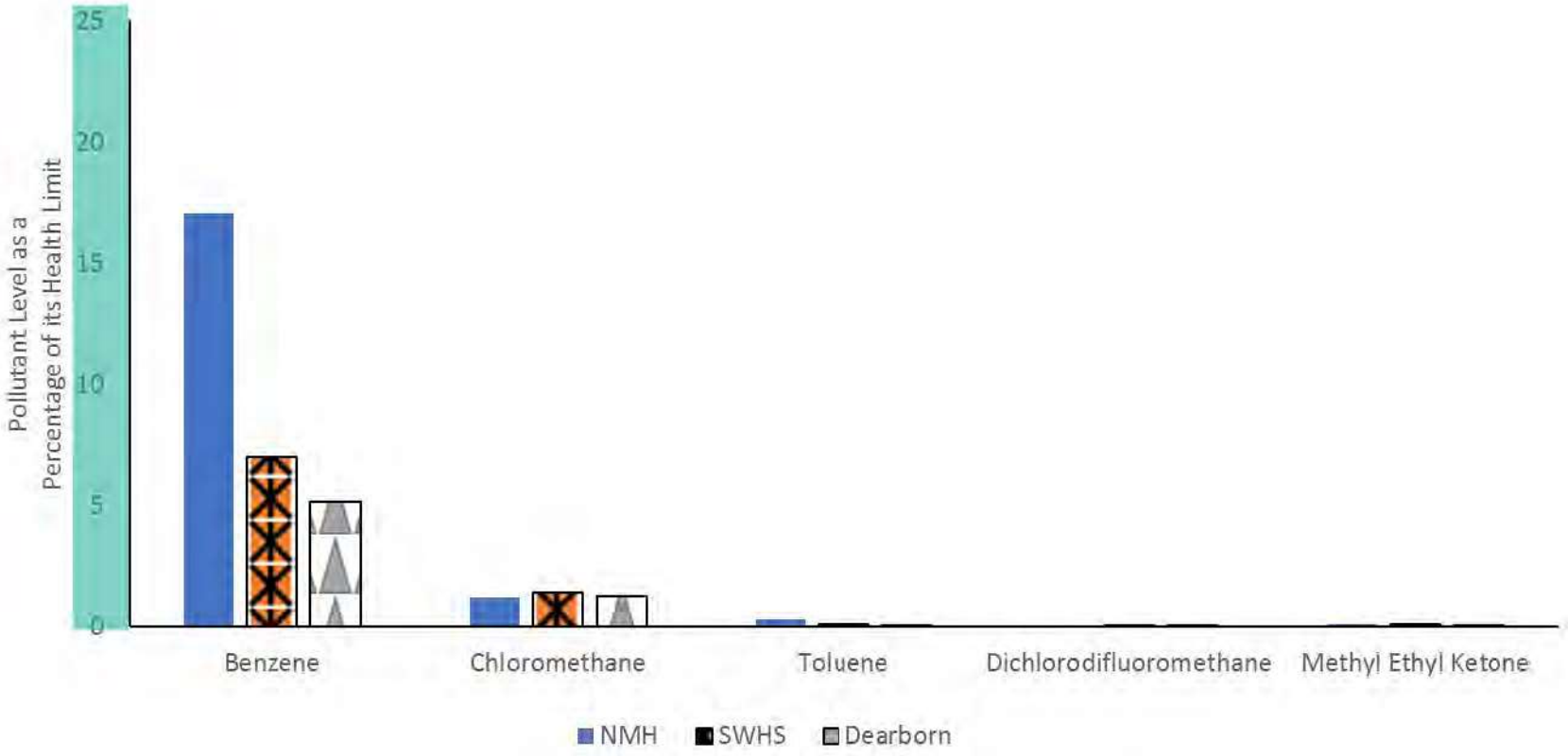
VOCs monitored at NMH and Marathon-sponsored sites in 48217 ZIP code

This graph includes VOCs that were detected at the NMH site and were also detected at the Marathon-sponsored sites in the 48217 ZIP code. Benzene levels were compared to the short-term health limit because it was not detected enough at the NMH site to compare it to the long-term health limit. 2-Propanol and chloromethane levels were compared to long-term health limits. All the other pollutants shown were compared to their respective short-term health limits.



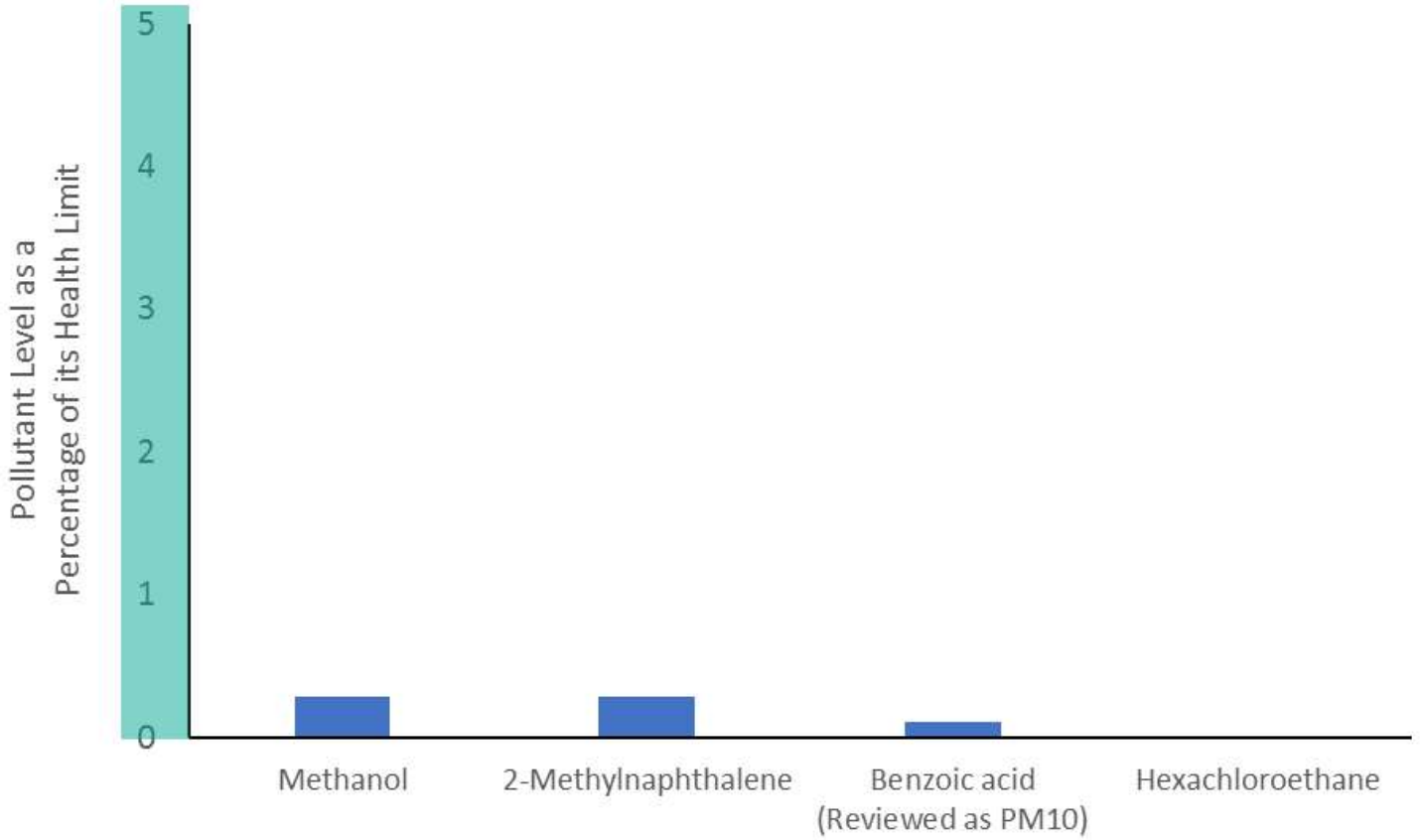
VOCs monitored at NMH and other metro Detroit monitors

This graph includes VOCs that were detected at the NMH site and were also detected at the MDEQ-SWHS and MDEQ-Dearborn sites. Benzene levels were compared to the short-term health limit because it was not detected enough at the NMH site to compare it to the long-term health limit. Chloromethane levels were compared the chloromethane long-term health limit. All the other pollutants shown were compared to their respective short-term health limits.



Pollutants Monitored and Detected Only at NMH Site

This graph includes pollutants that were only monitored and detected at the NMH site. Methanol was compared to its short-term limits, and the comparison that gave the highest percentage is shown below. 2-Methylnaphthalene was compared to its long-term health limit, and benzoic acid and hexachloroethane were compared to short-term health limits since they were only detected once.



B-3. Cumulative Impact Assessment

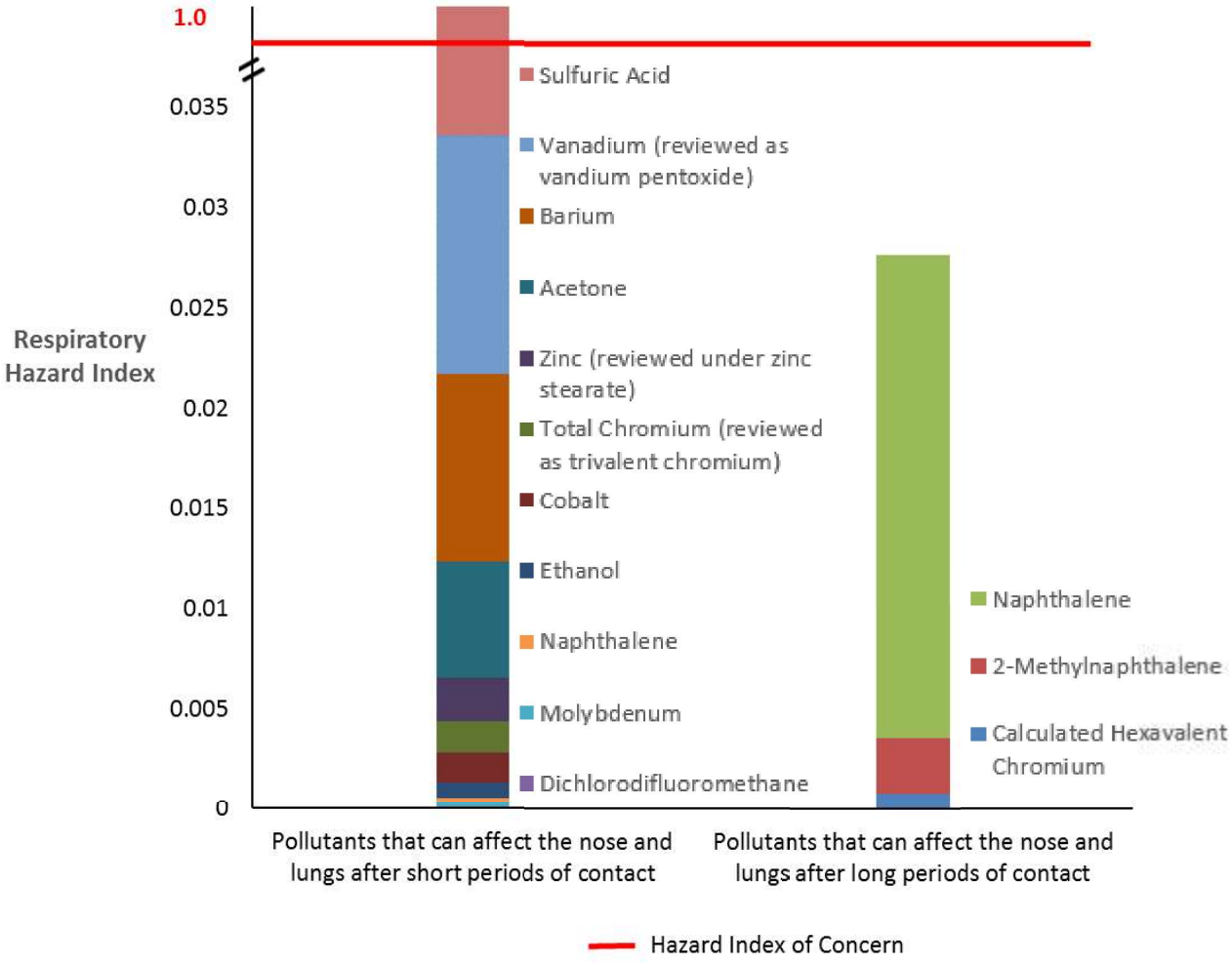
The cumulative impacts of breathing the multiple pollutants that were detected at the NMH site are described for pollutants that affect the respiratory system (nose and lungs), the nervous system (brain and nerves), and pollutants that can cause cancer. Most of the pollutants that were detected are known to affect the respiratory and nervous system, therefore these systems were a focus for this study.

When combined impacts for noncancer effects are less than one on the hazard index scale, the combined impacts do not reach a level of a health concern. When combined impacts are more than one, it's important to review which pollutants are driving the high combined risk and try to understand why the levels for those pollutants are high.

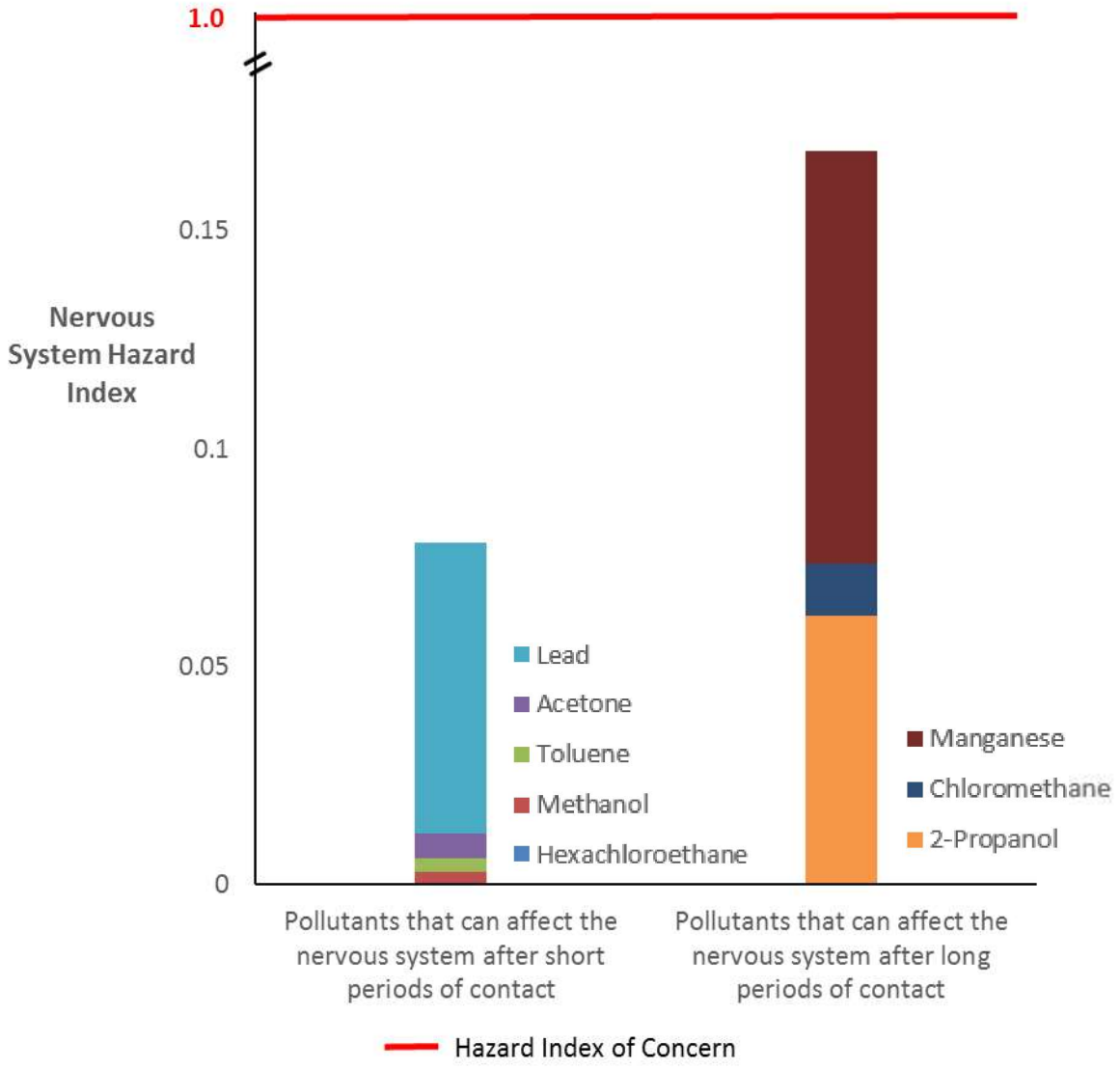
For the cumulative impact of the pollutants that have long-term noncancer health effects, the combined impact of the pollutants detected did not reach a level of concern. Besides sulfuric acid, which reached a level of health concern by itself, the cumulative impact of the pollutants that have short-term health effects did not reach a level where they are expected to be a health concern. Since this evaluation began with the conservative consideration of the combined impact of the maximum sample collected at any time during the one-year study, and a level of concern was not reached outside of the impact of sulfuric acid alone, further analysis into whether timeframes corresponded was not considered.

The combined impact of the pollutants detected that may cause cancer were evaluated and found to have an incremental cancer risk of 8 in one million if a person was exposed to those pollutant levels over their entire lifetime (see Appendix A, page A3 for details).

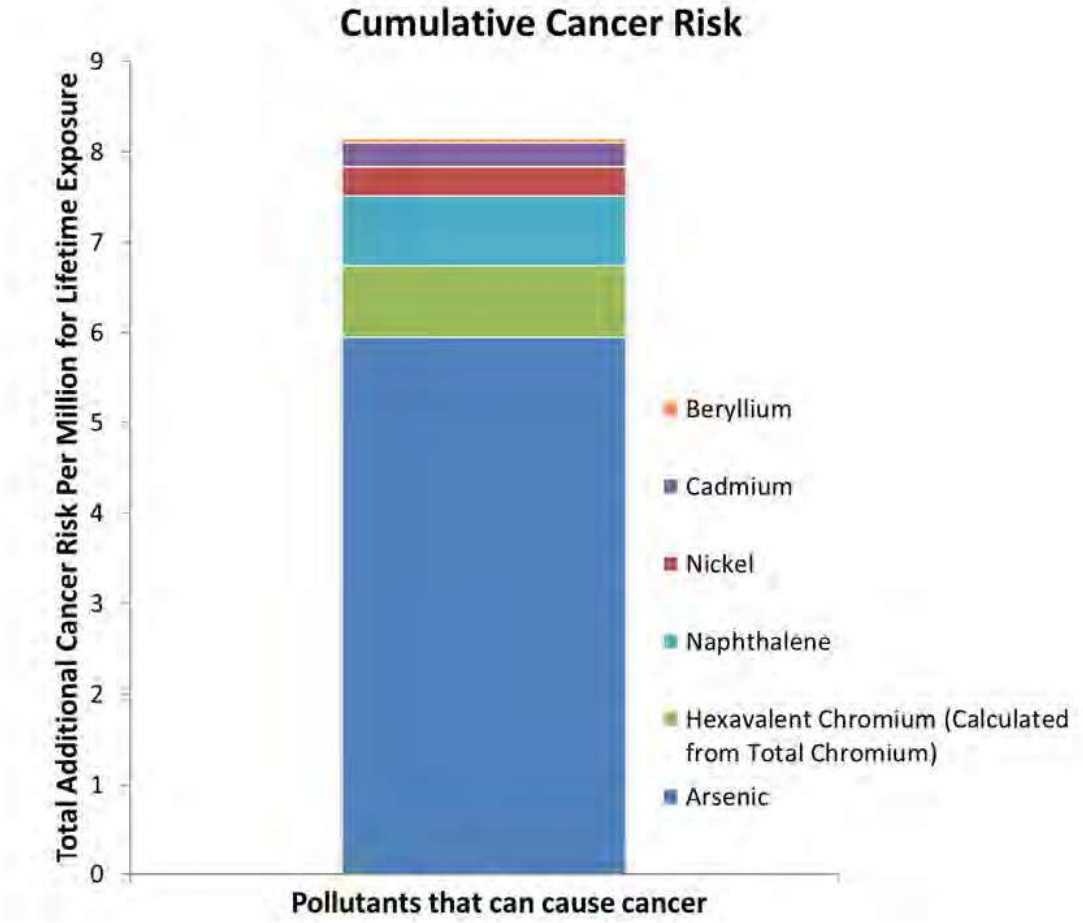
Cumulative Impact: Pollutants that can affect the respiratory system (nose and lungs)



Cumulative Impact: Pollutants that can affect the nervous system (brain and nerves)



Cumulative Impact: Sum of Cancer Risk



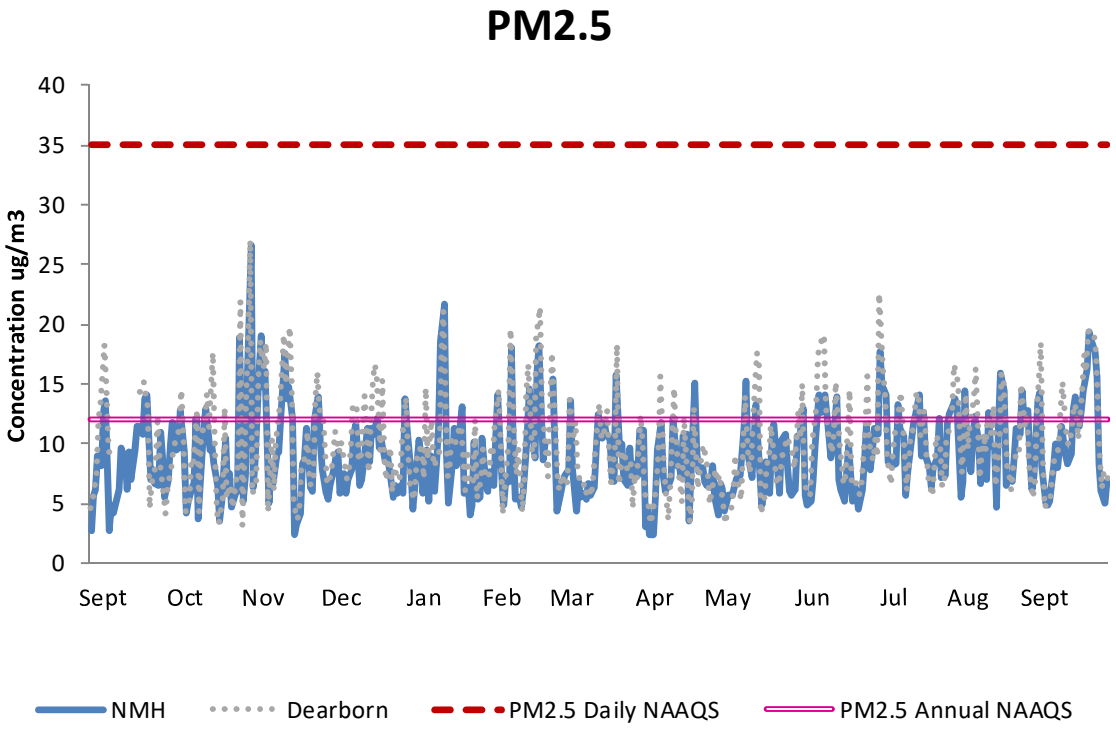
B-4. Time series

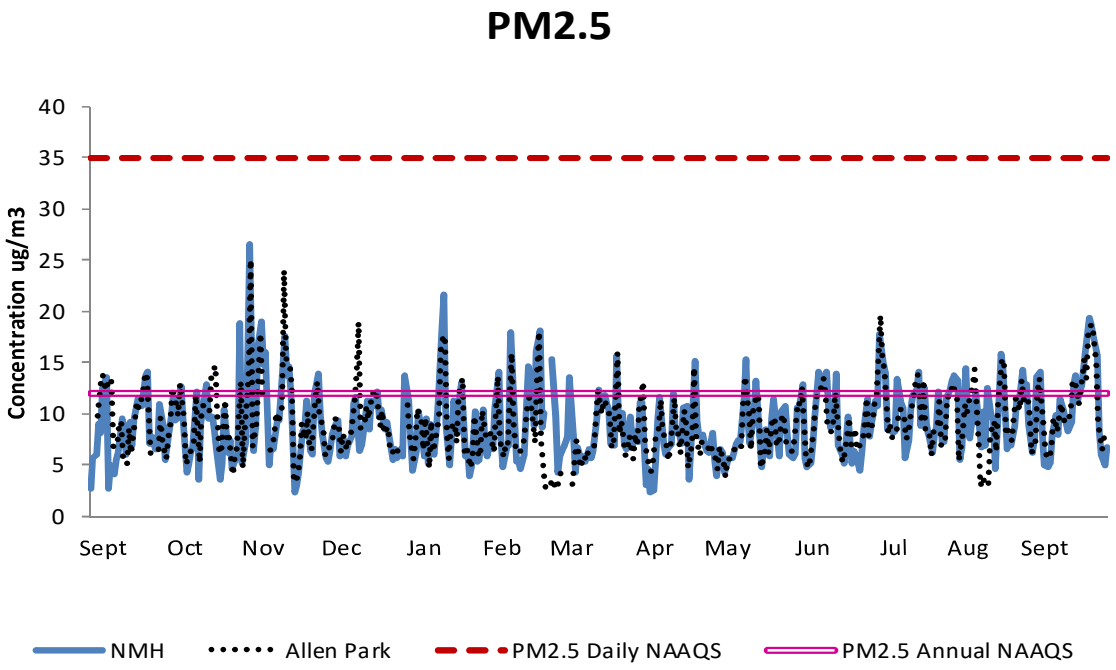
Results from the NMH site are shown in time series graphs so that each sample over the one-year study can be seen. This was done for all pollutants except $PM_{2.5}$ and SO_2. The daily average level is shown for $PM_{2.5}$ and the daily, 1-hour maximum is shown for SO_2. When a sample was collected, but the pollutant level was too low to detect, it is represented as a dark gray symbol on the graph. The results from the NMH site are shown in comparison to other sites in the region and health limits. For some of the parameters, the graphs became difficult to read when all the sites were put on one graph. Therefore, we provided multiple graphs for a single pollutant.

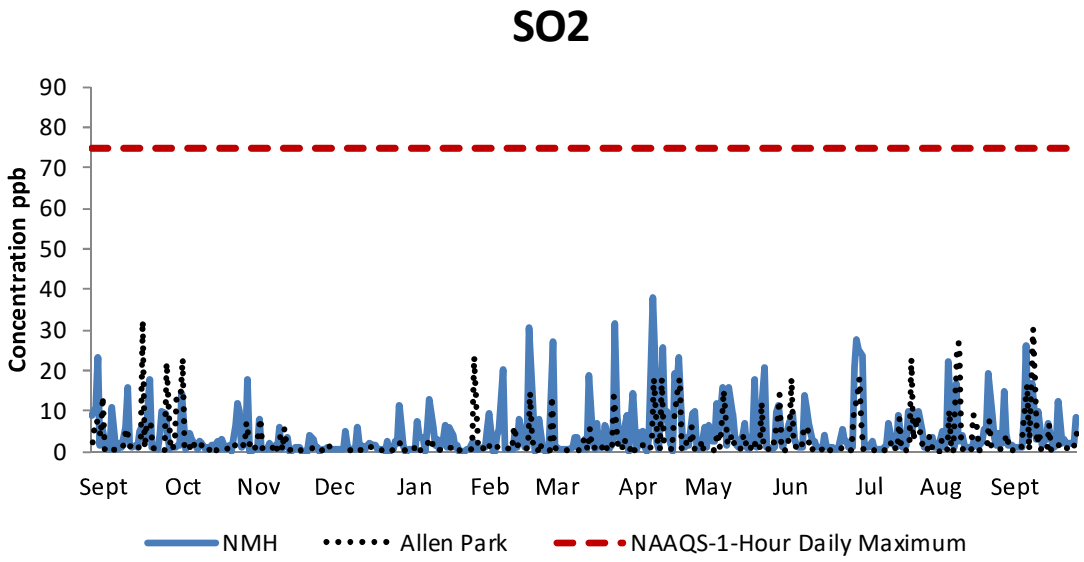
Pollutant levels at the NMH site were below noncancer-related health limits, except for 2 samples of sulfuric acid. For arsenic, naphthalene, and a calculation of hexavalent chromium, pollutant levels reached the one in one million cancer risk level. However, none of these pollutants reached the 1 in 10,000 cancer risk level (the risk level used by the USEPA for RTR and NATA analyses). Both risk levels are used in regulatory processes to identify pollutants and facilities of concern, but it should be noted that there is no USEPA or MDEQ health limit for an acceptable ambient air level for pollutants that can cause cancer.

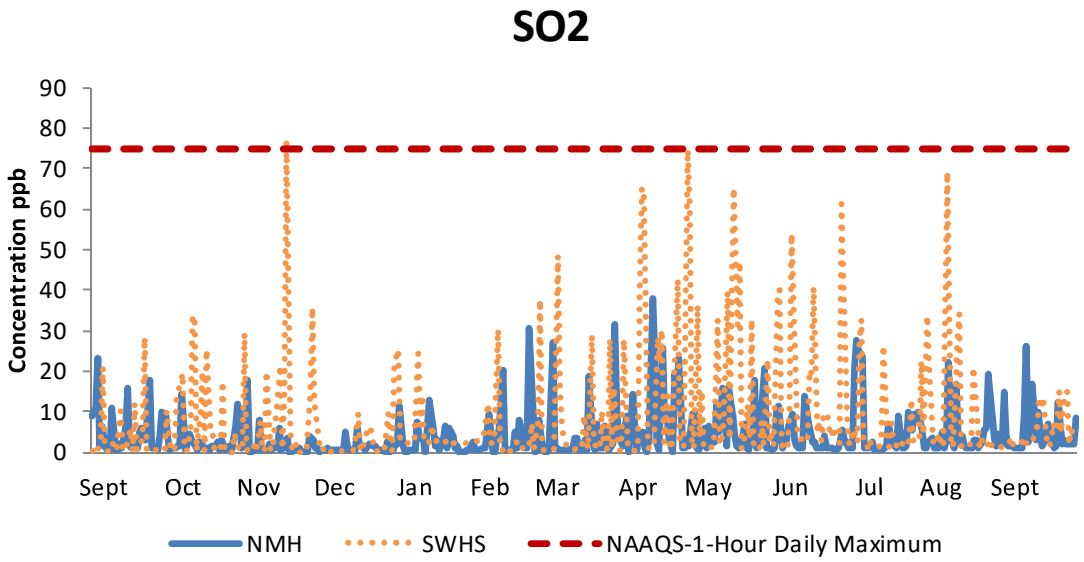
With few exceptions, the time series plots of pollutant concentration levels monitored at the NMH site were like that of other sites in metro-Detroit. Noted exceptions are higher 2-propanol levels at the NMH site, higher SO_2 levels at SWHS, and higher levels of acetone and toluene on the west side of Marathon's property.

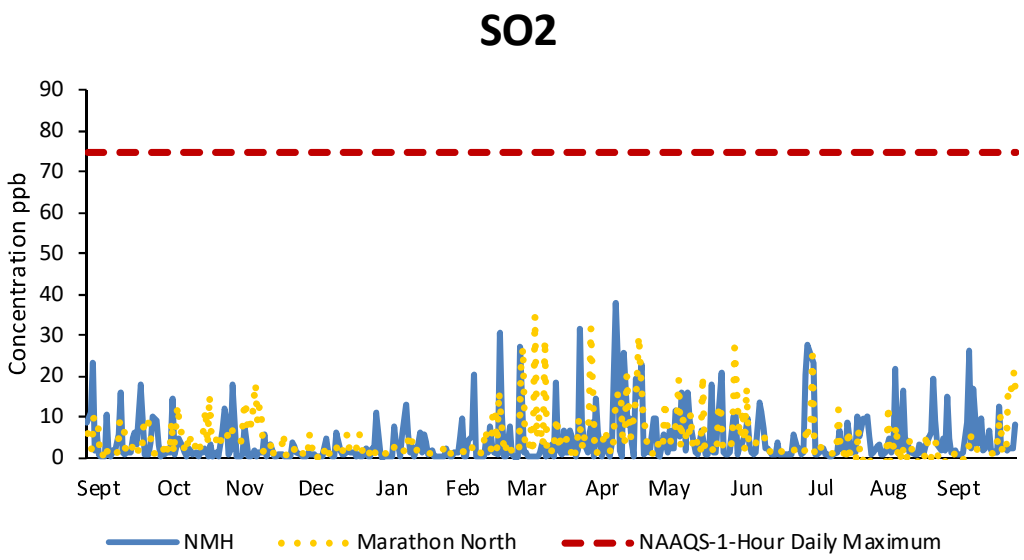
Criteria Pollutants: $PM_{2.5}$, SO_2, and Lead (Pb)

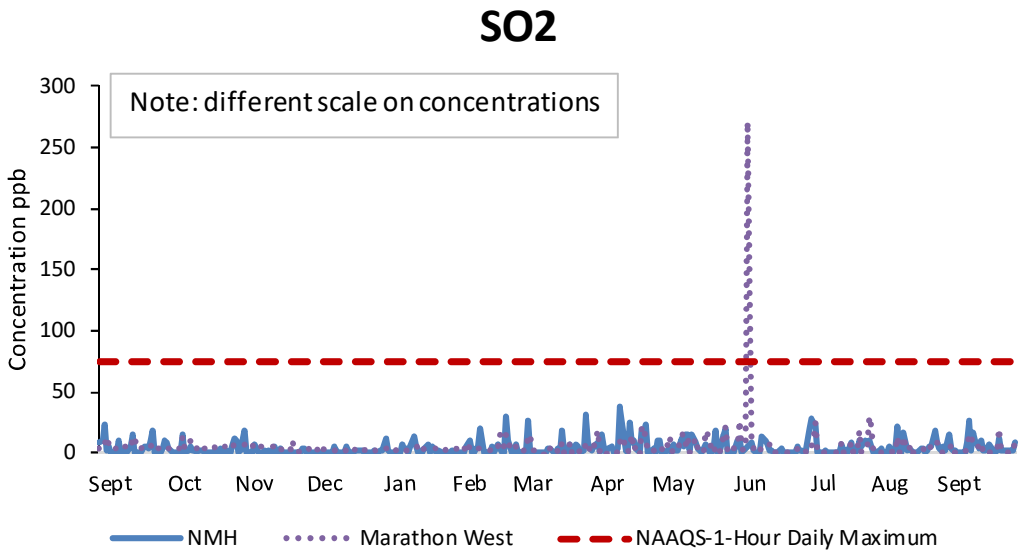


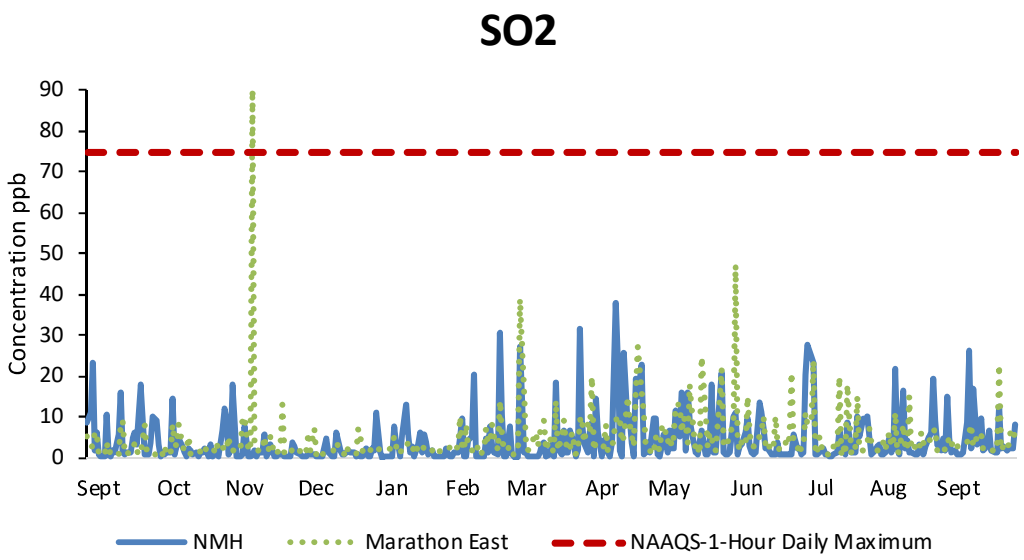


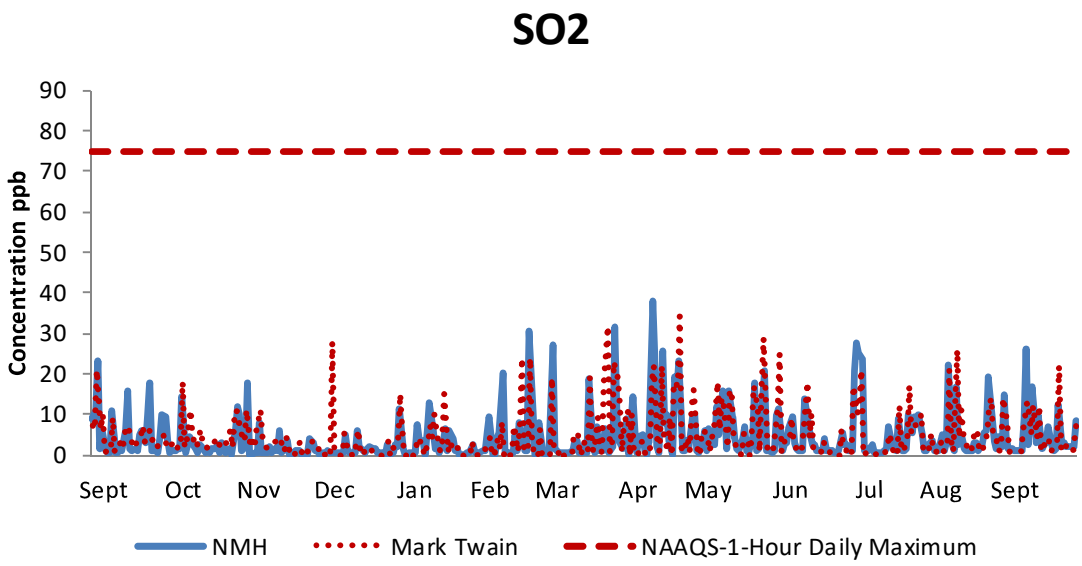

SO2
Concentration ppb
90
80
70
60
50
40
30
20
10
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Allen Park
NAAQS-1-Hour Daily Maximum

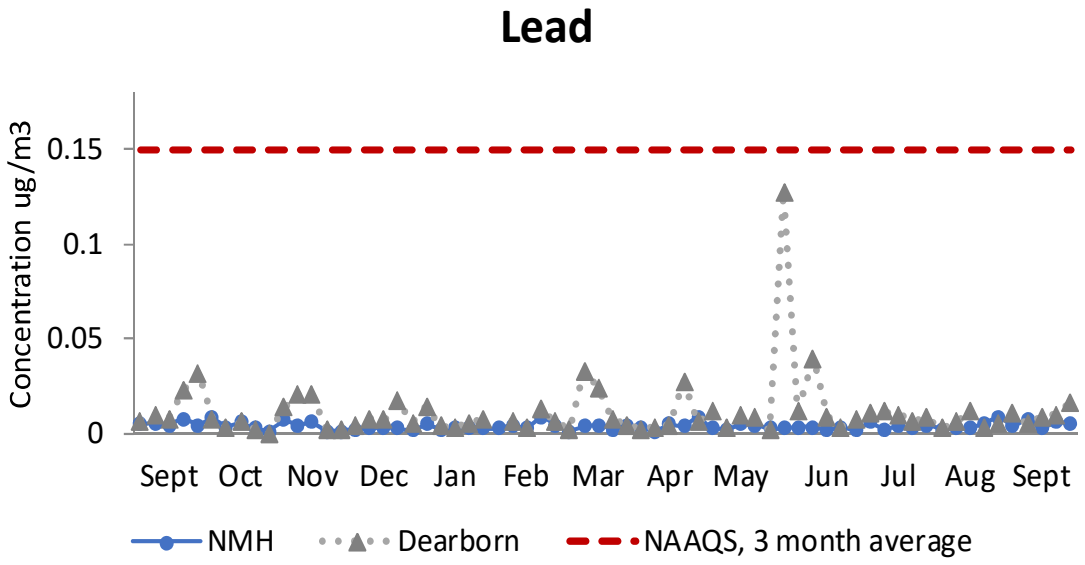

SO2
Concentration ppb
90
80
70
60
50
40
30
20
10
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
SWHS
NAAQS-1-Hour Daily Maximum


SO2
Concentration ppb
90
80
70
60
50
40
30
20
10
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Marathon North
NAAQS-1-Hour Daily Maximum

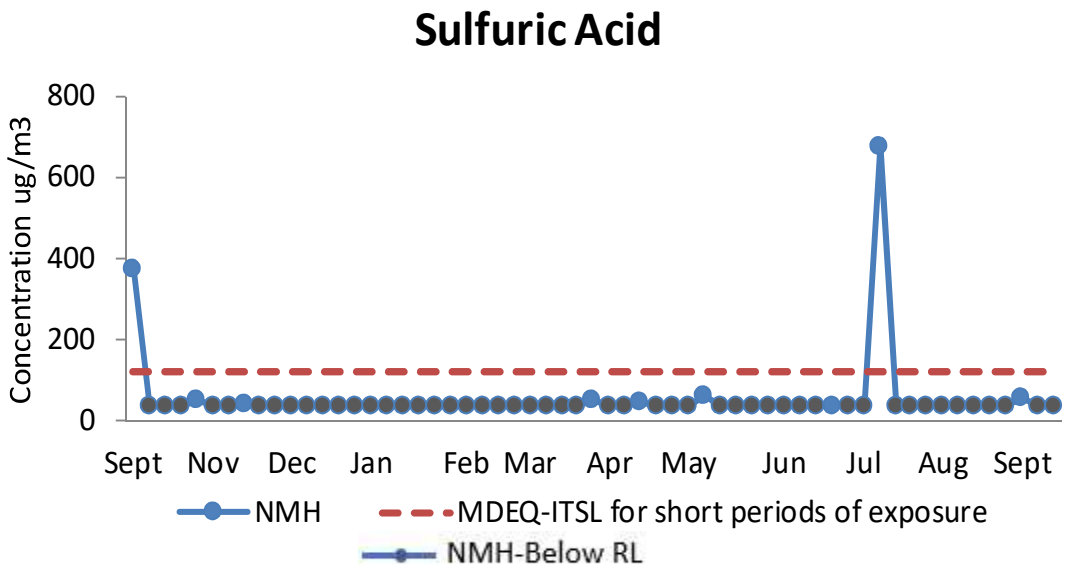

SO2
Note: different scale on concentrations
Concentration ppb
300
250
200
150
100
50
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Marathon West
NAAQS-1-Hour Daily Maximum


SO2
Concentration ppb
90
80
70
60
50
40
30
20
10
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Marathon East
NAAQS-1-Hour Daily Maximum

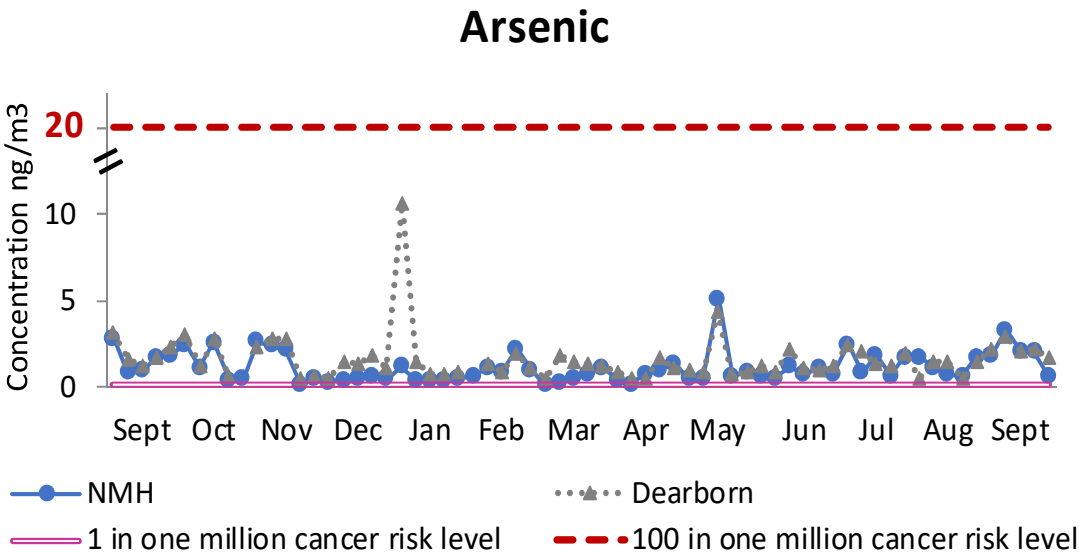

SO2
Concentration ppb
90
80
70
60
50
40
30
20
10
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Mark Twain
NAAQS-1-Hour Daily Maximum

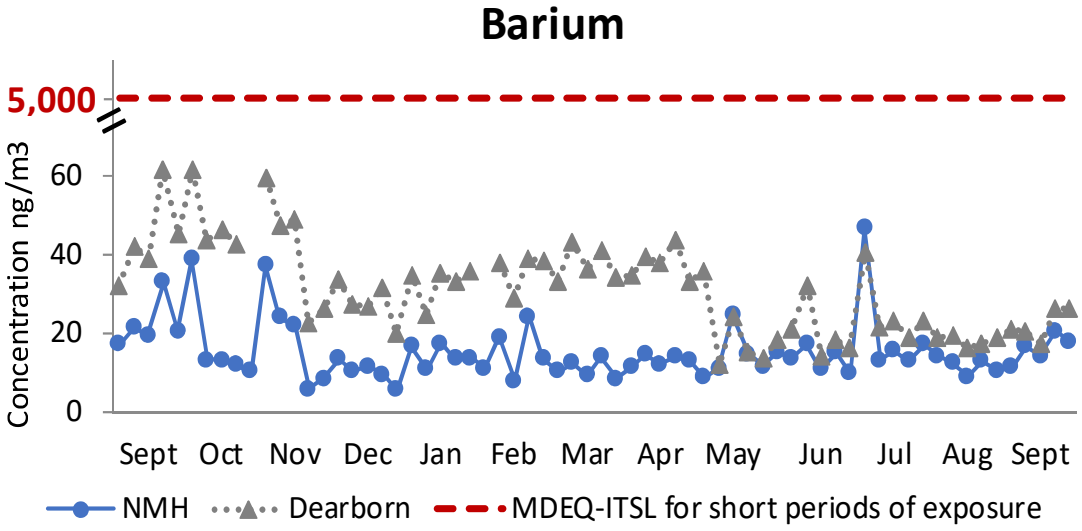

Lead
Concentration ug/m3
0.15
0.1
0.05
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
Dearborn
NAAQS, 3 month average

ACIDS:

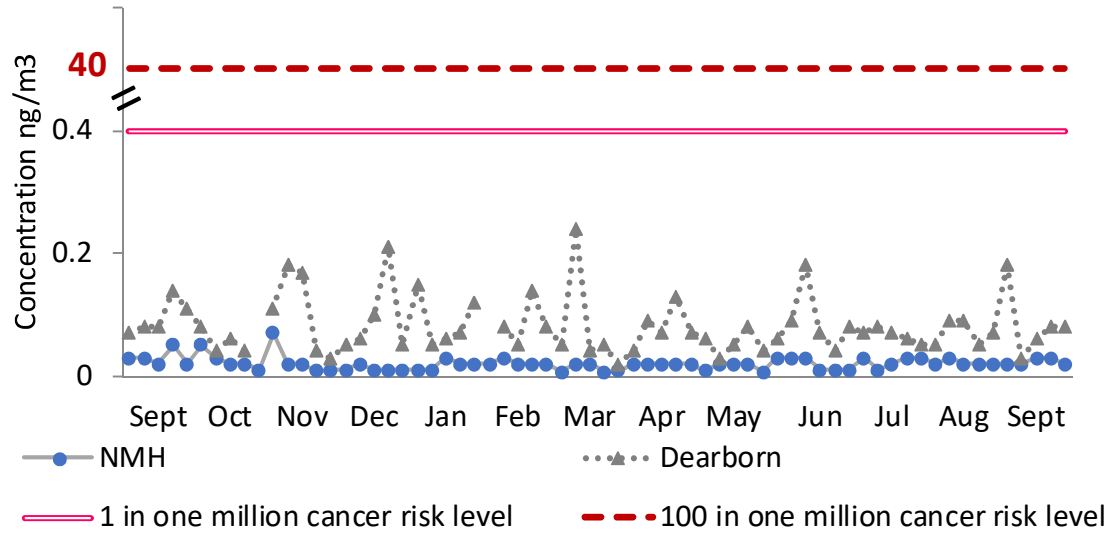

Sulfuric Acid
Concentration ug/m3
800
600
400
200
0
Sept Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
MDEQ-ITSL for short periods of exposure
NMH-Below RL

Air Toxics: Metals

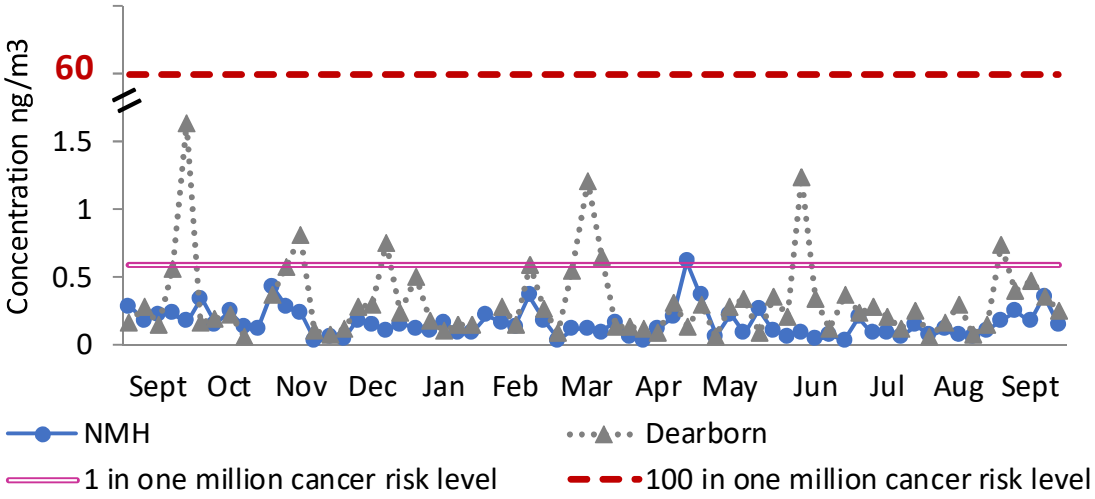




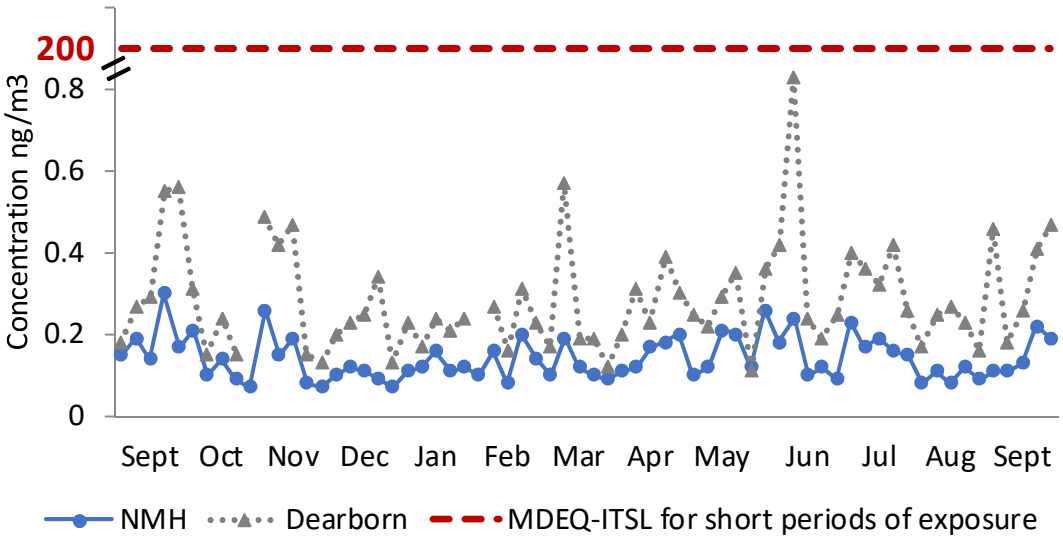
Beryllium



Cadmium

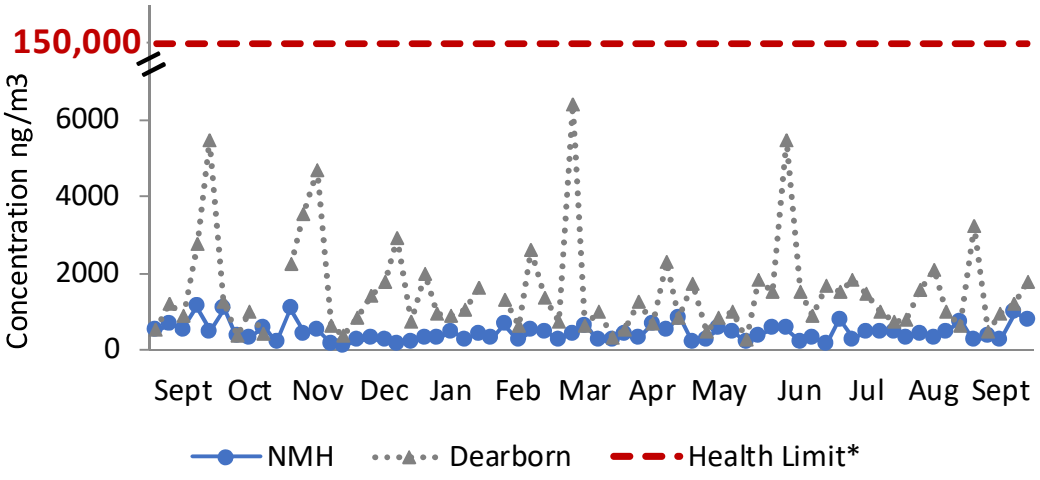


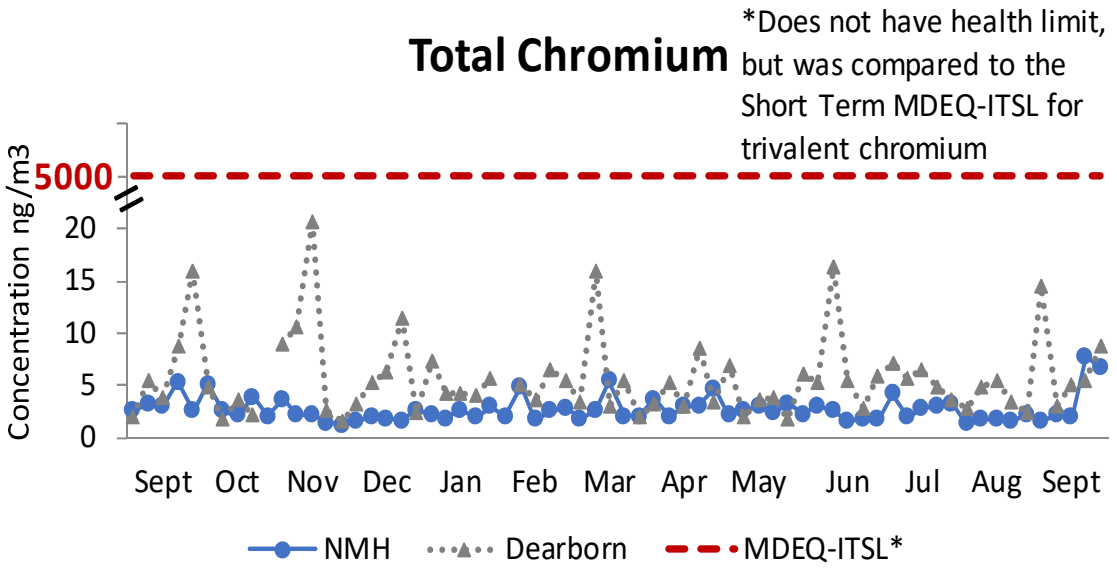
Cobolt

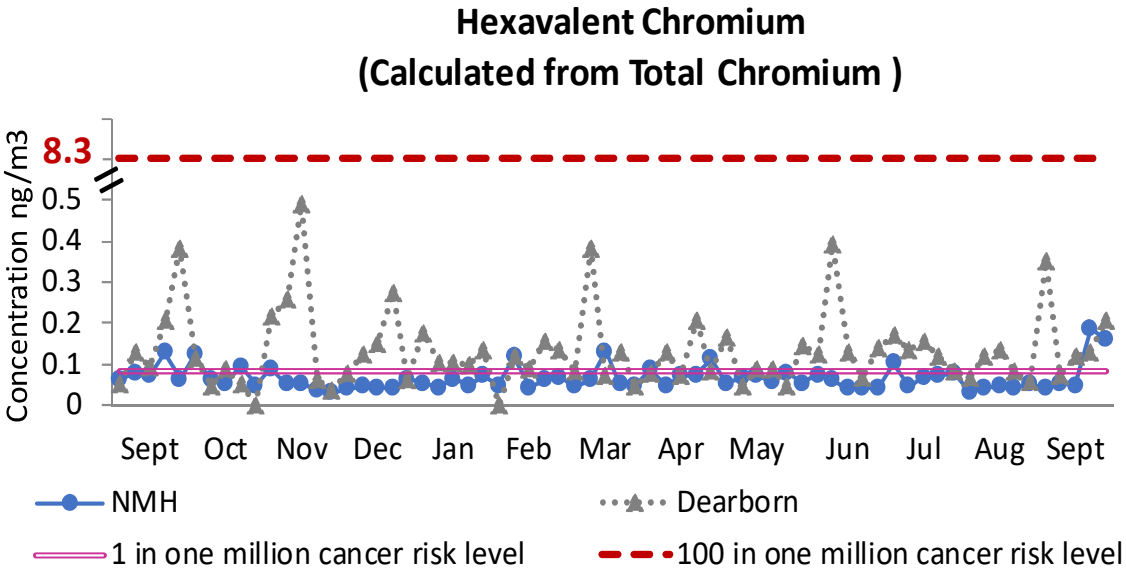


Iron

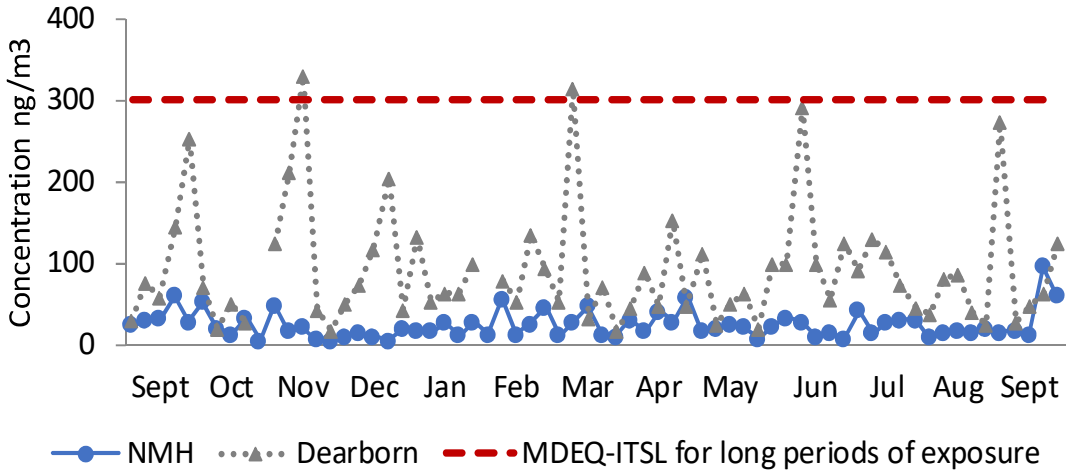
*Does not have health limit, but was compared to the Daily PM10 NAAQS



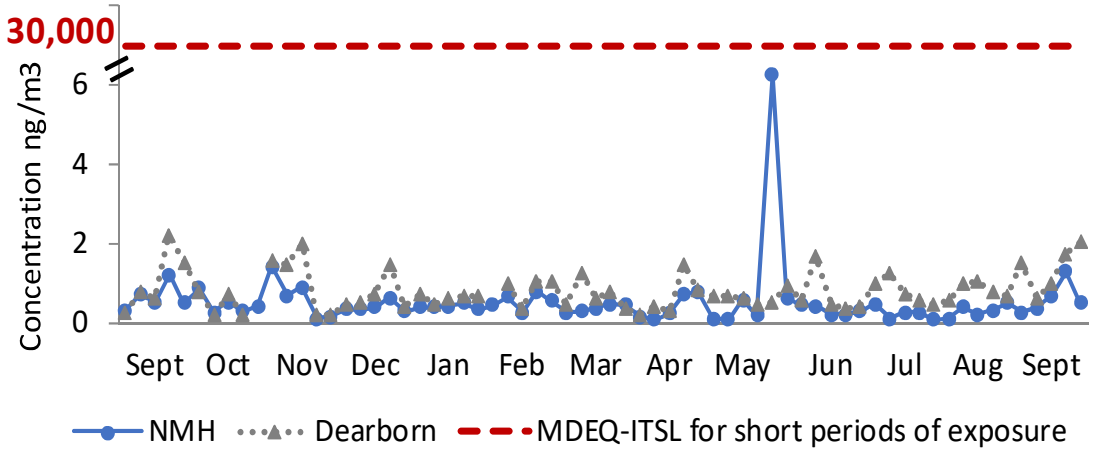

Total Chromium
*Does not have health limit, but was compared to the Short Term MDEQ-ITSL for trivalent chromium
Concentration ng/m3
5000
20
15
10
5
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
Dearborn
MDEQ-ITSL*


Hexavalent Chromium
(Calculated from Total Chromium)
Concentration ng/m3
8.3
0.5
0.4
0.3
0.2
0.1
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
Dearborn
1 in one million cancer risk level
100 in one million cancer risk level

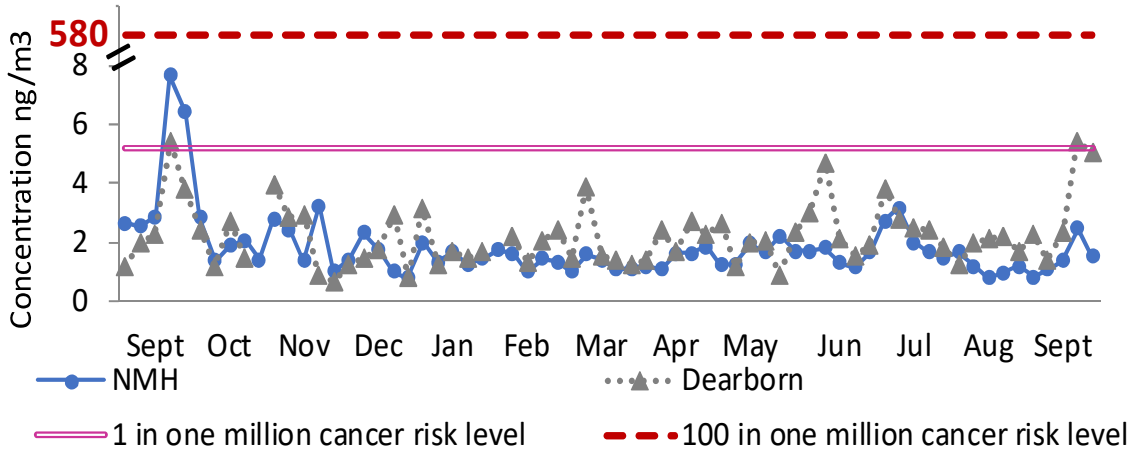
Manganese



Molybdenum

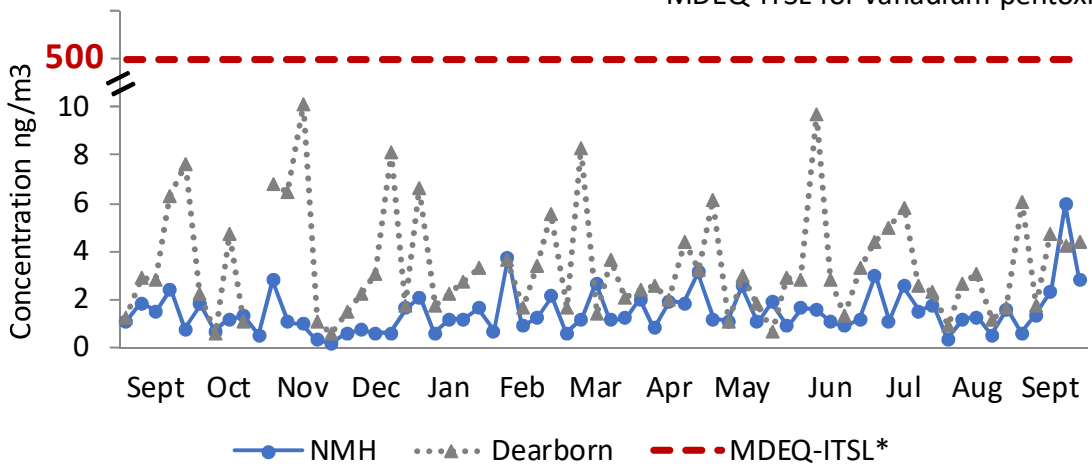


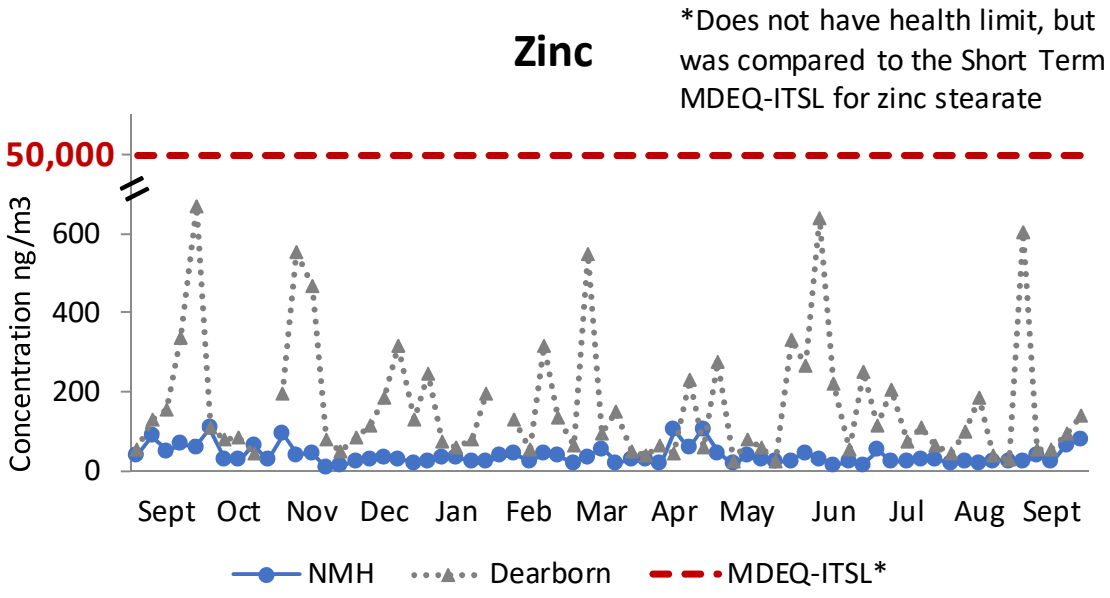
Nickel



Vanadium

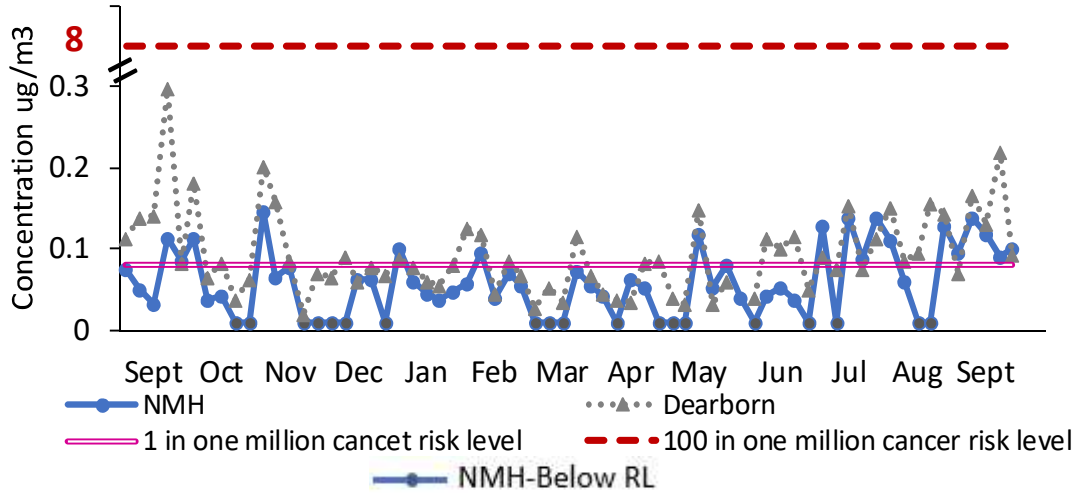
*Does not have health limit, but was compared to the Short Term MDEQ-ITSL for vanadium pentoxide



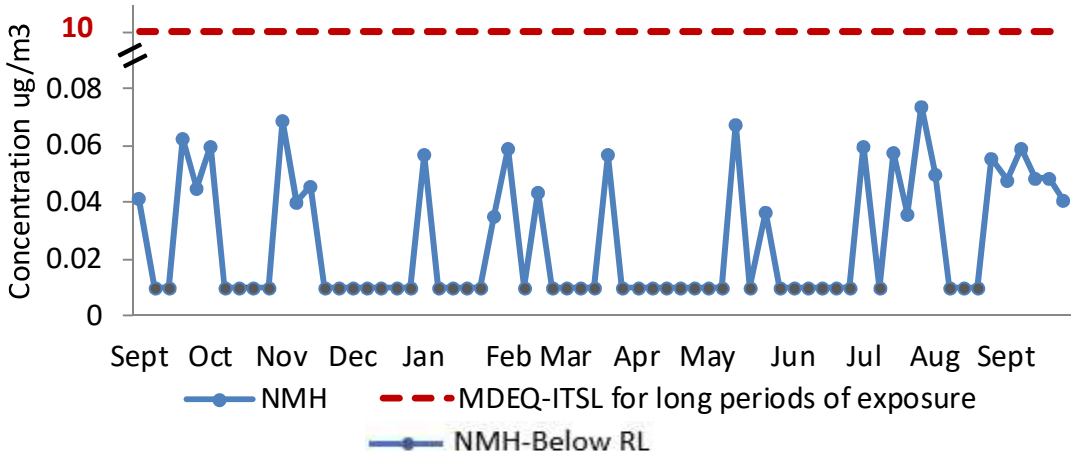

Zinc
*Does not have health limit, but was compared to the Short Term MDEQ-ITSL for zinc stearate
50,000
600
400
200
0
Concentration ng/m3
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Dearborn
MDEQ-ITSL*

Air Toxics: Polyaromatic Hydrocarbons (PAHs)

Naphthalene

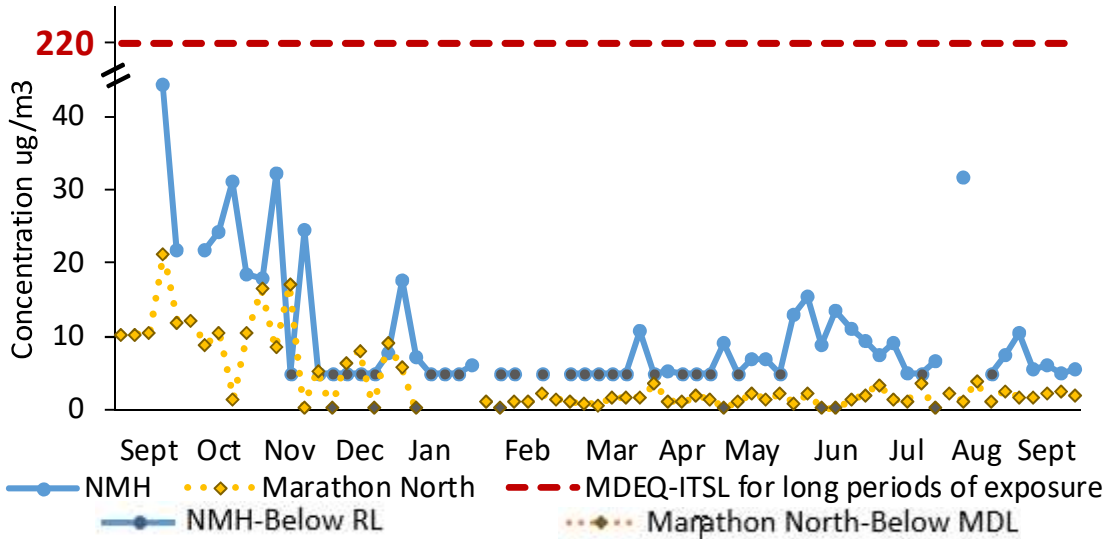


2-Methylnaphthalene

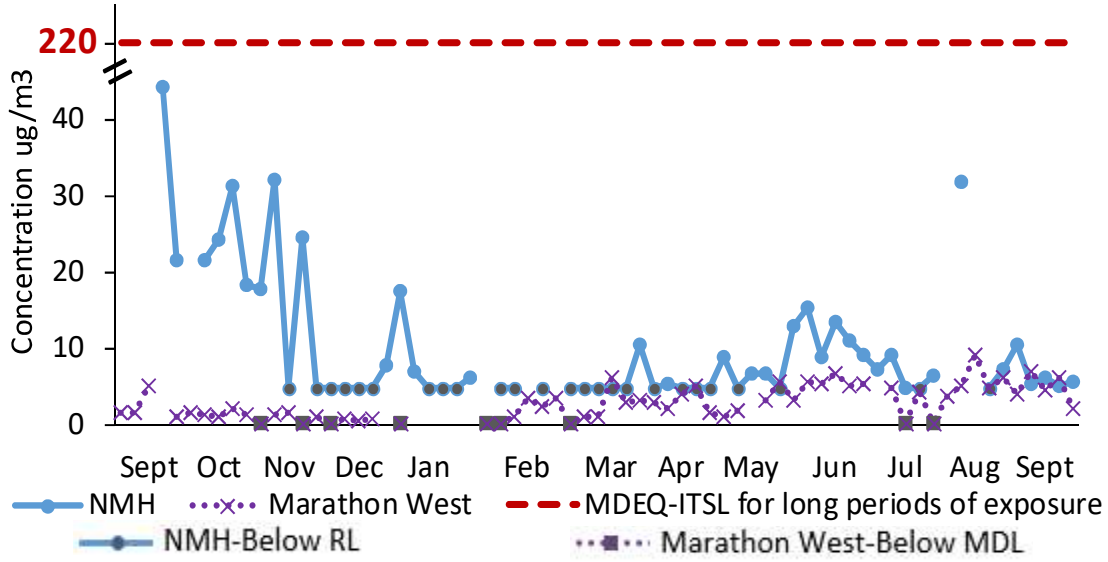


Air Toxics: Volatile Organic Compounds (VOCs)

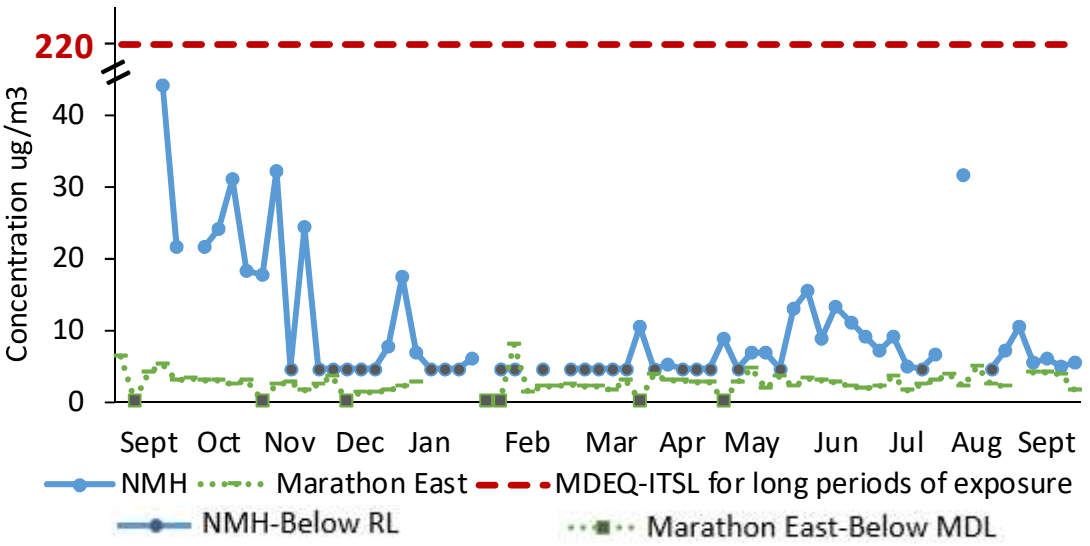
2-Propanol



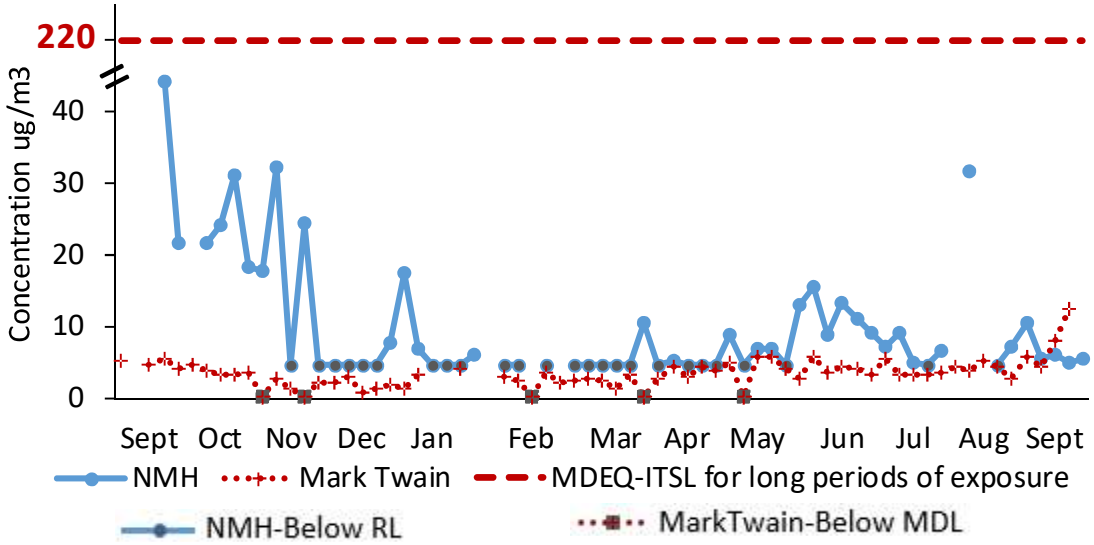
2-Propanol



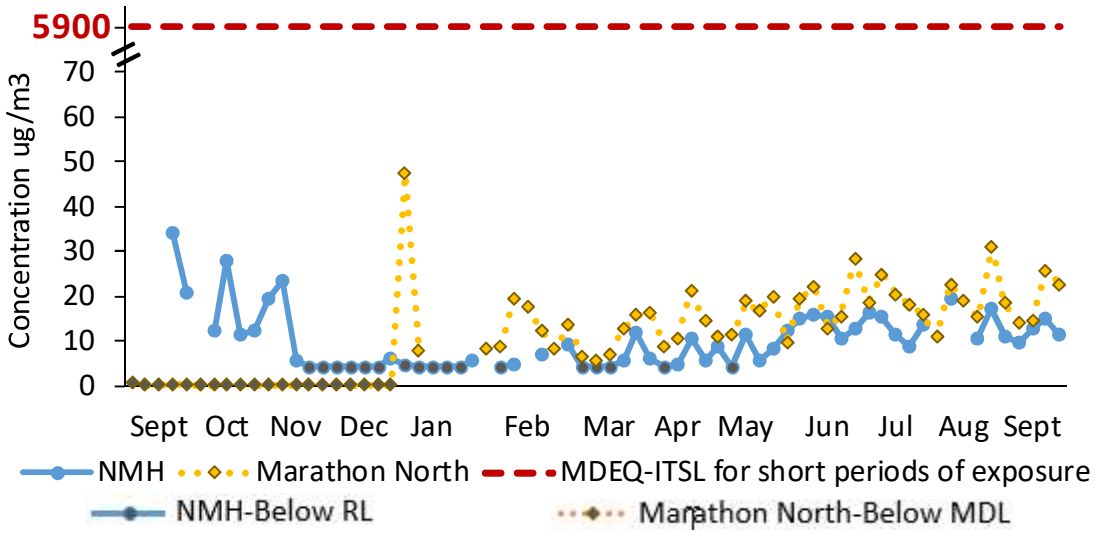
2-Propanol



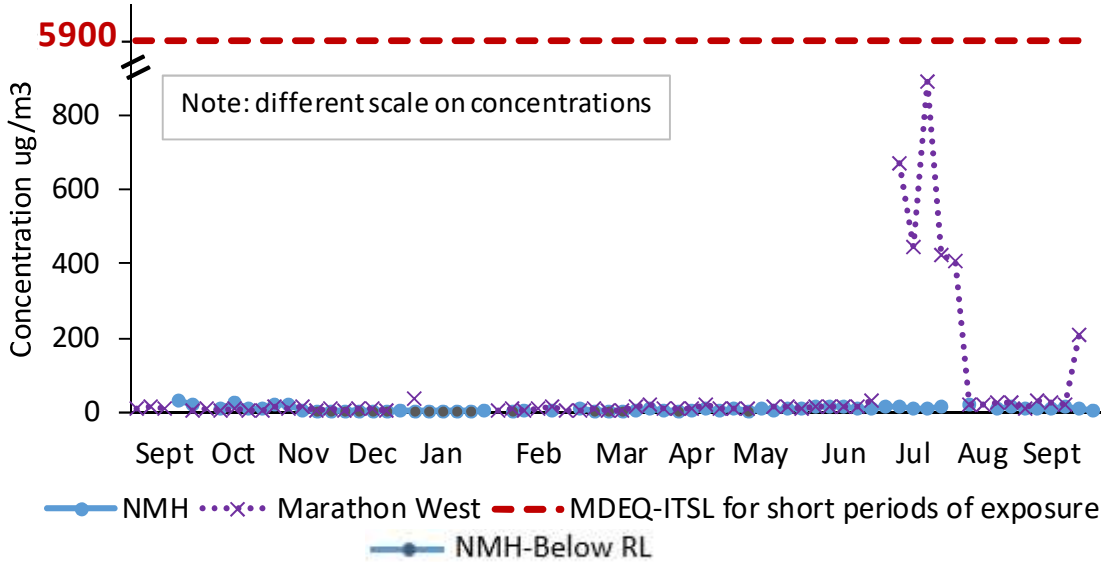
2-Propanol



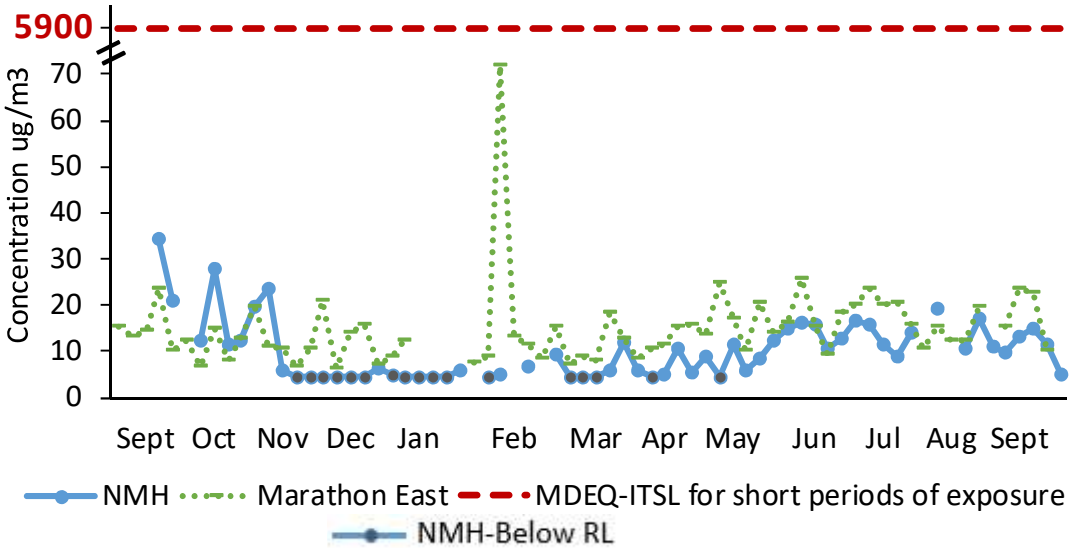
Acetone



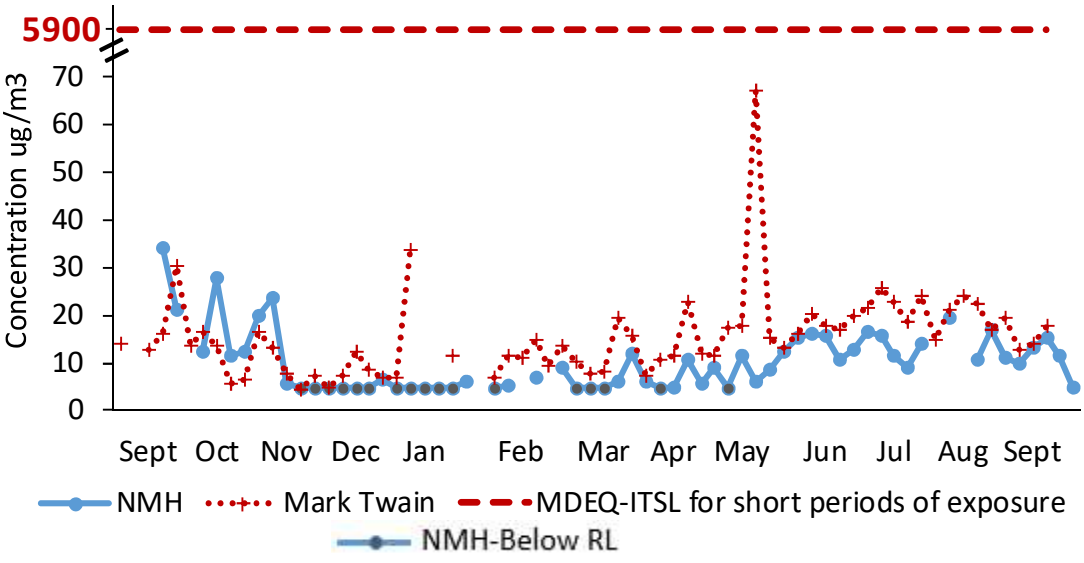
Acetone



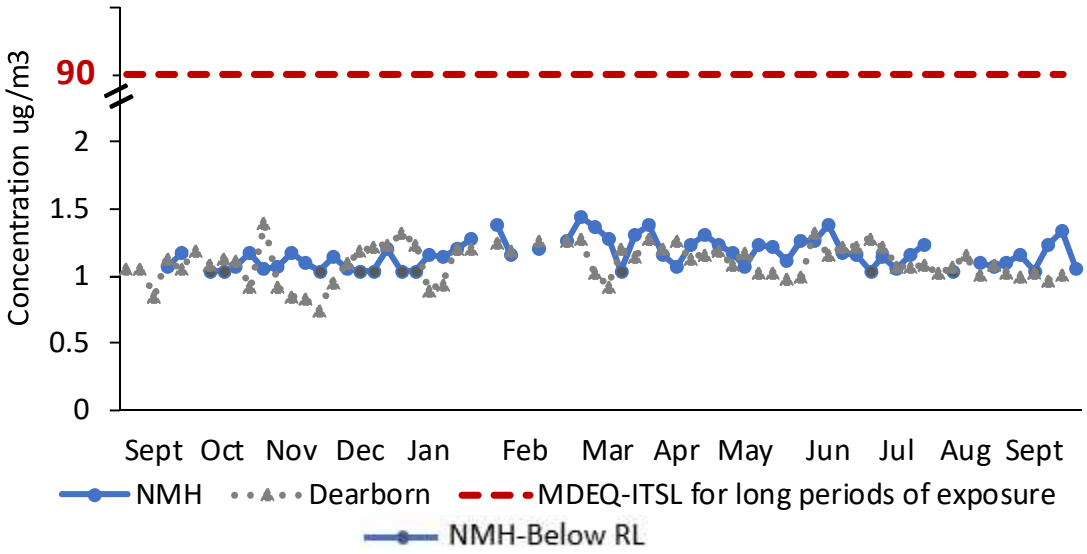
Acetone



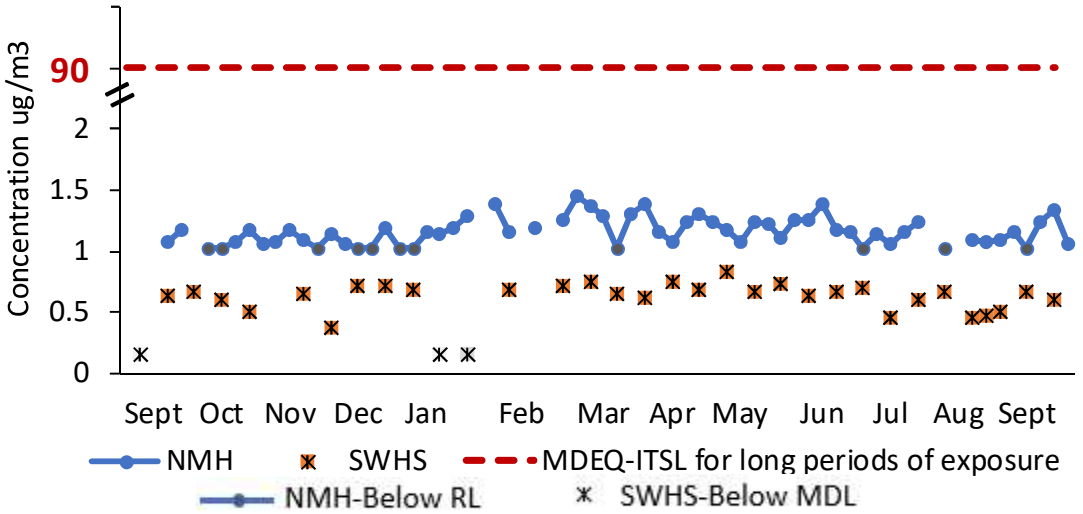
Acetone



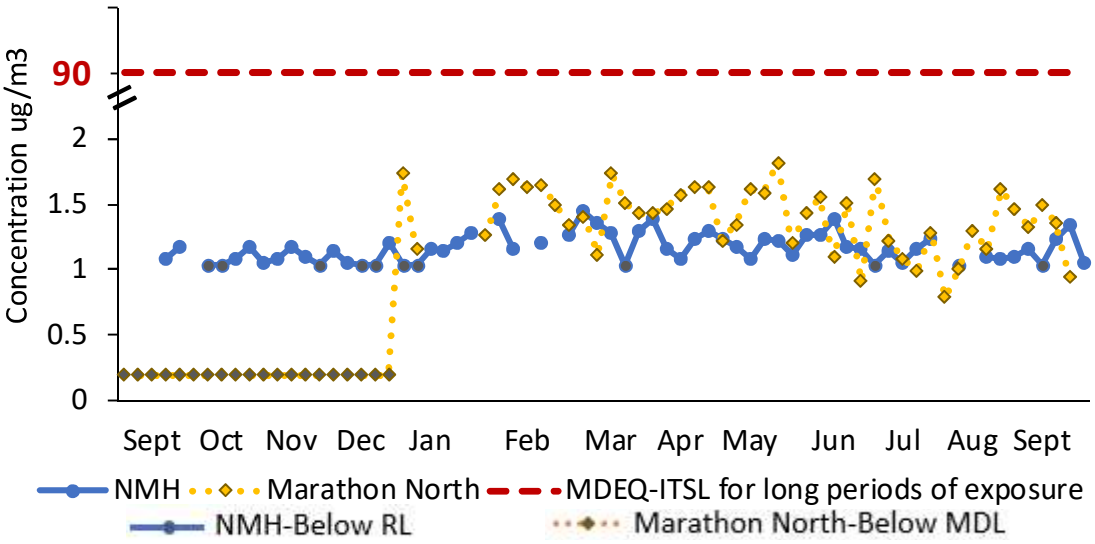
Chloromethane



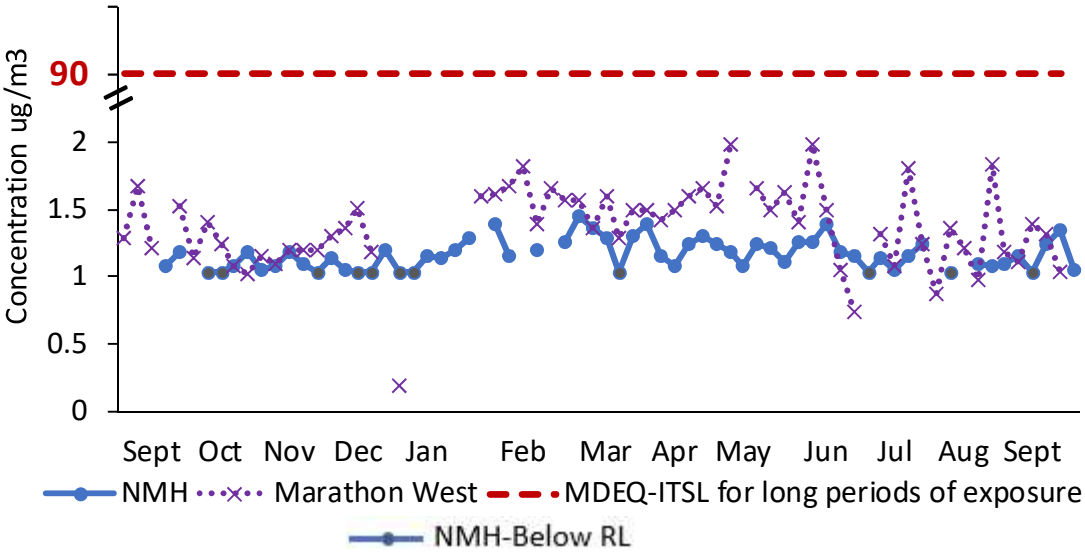
Chloromethane



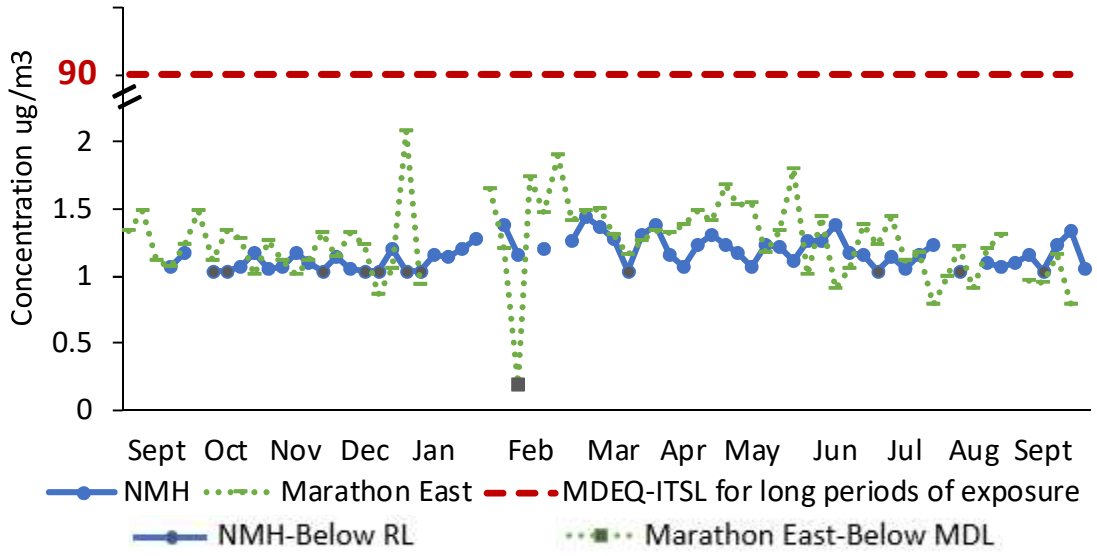
Chloromethane



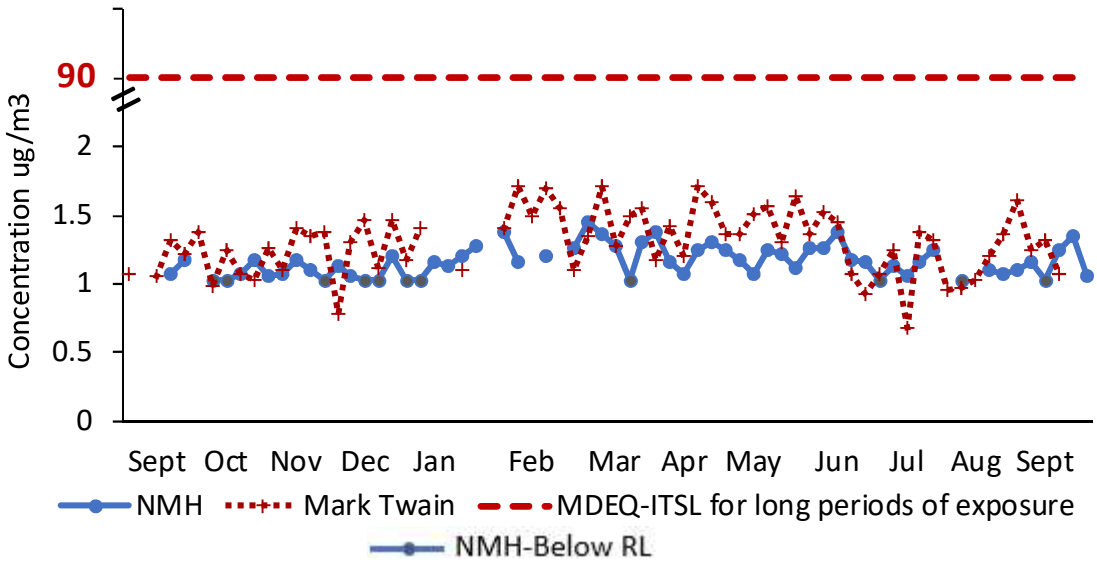
Chloromethane



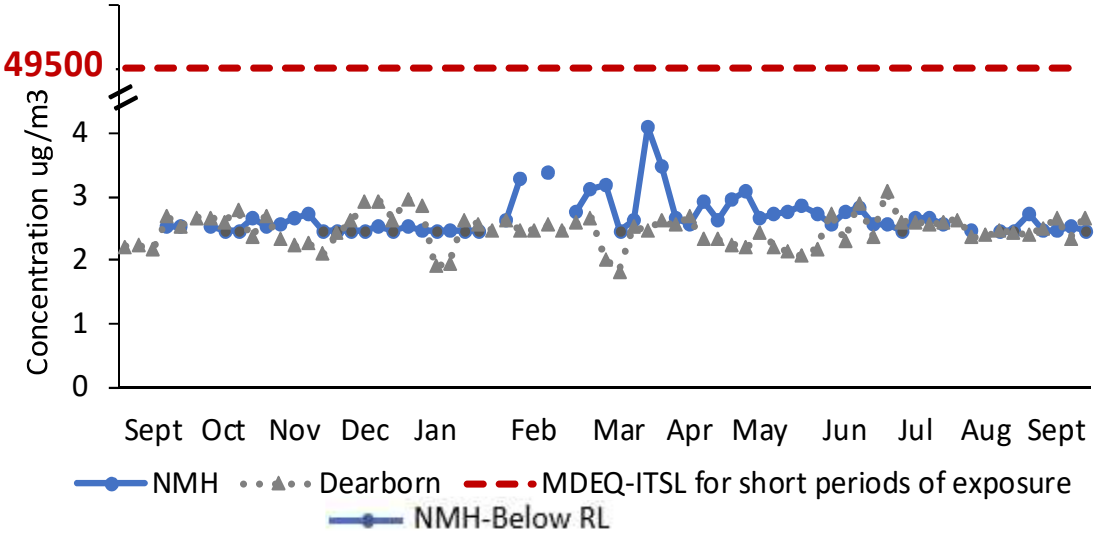
Chloromethane



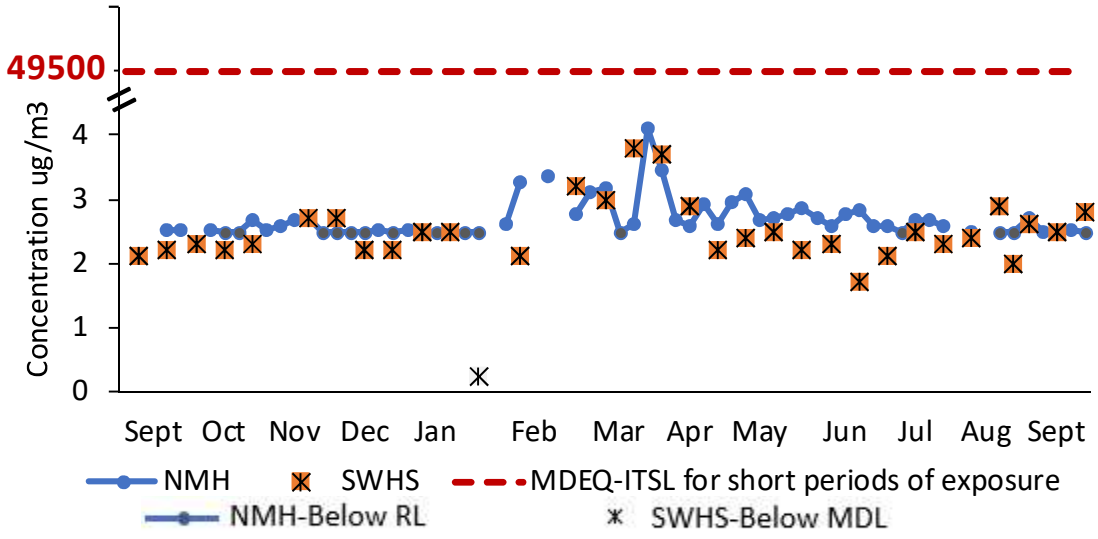
Chloromethane



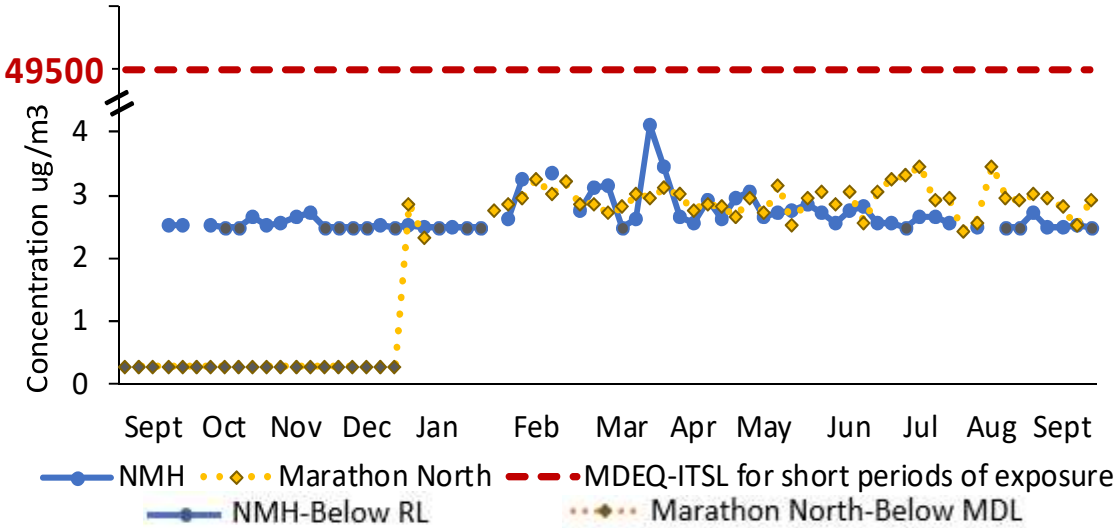
Dichlorodifluoromethane



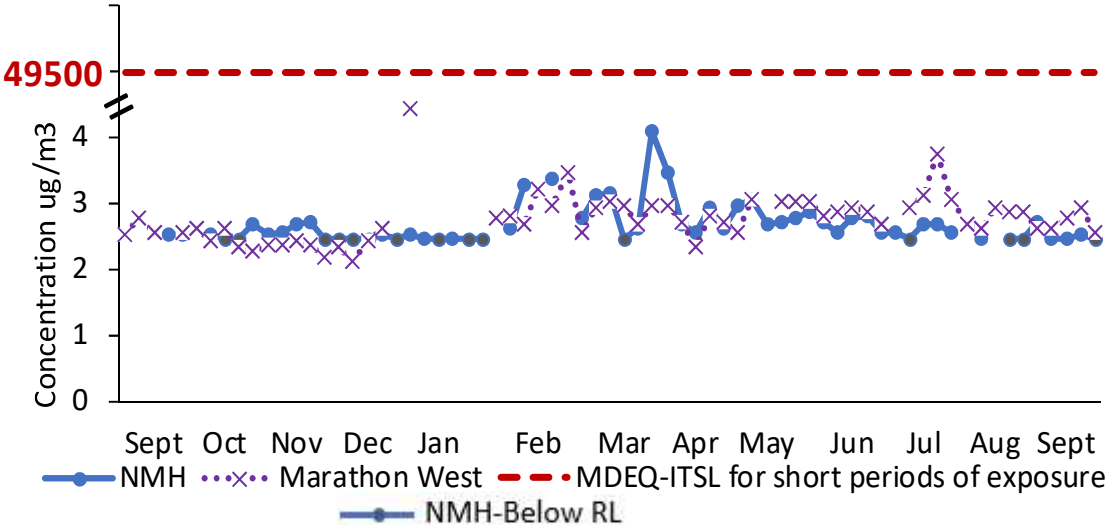
Dichlorodifluoromethane

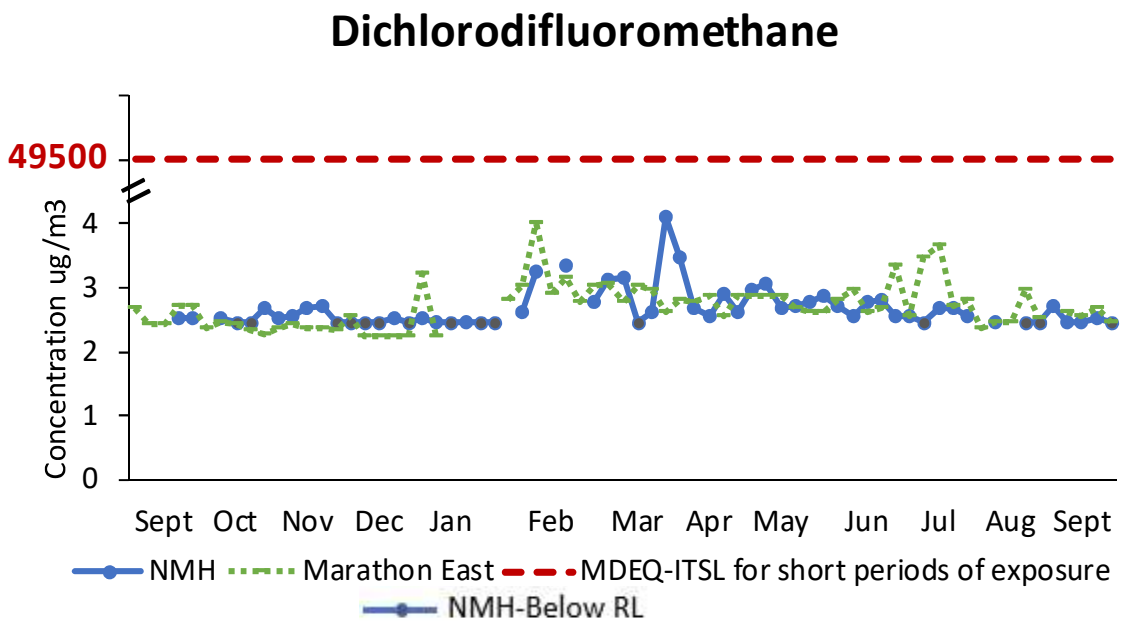


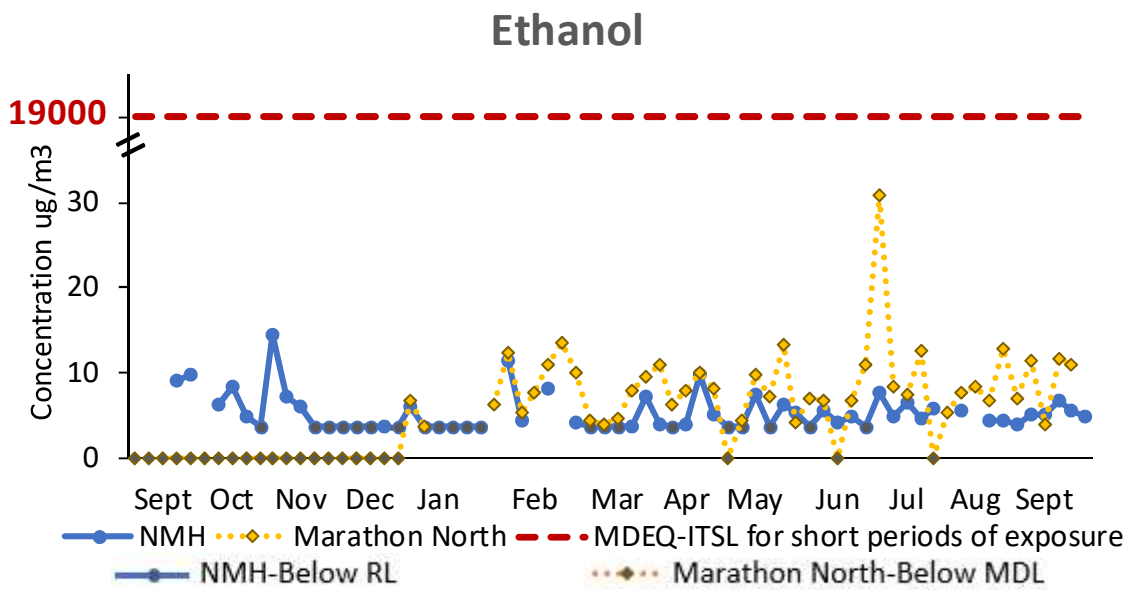
Dichlorodifluoromethane

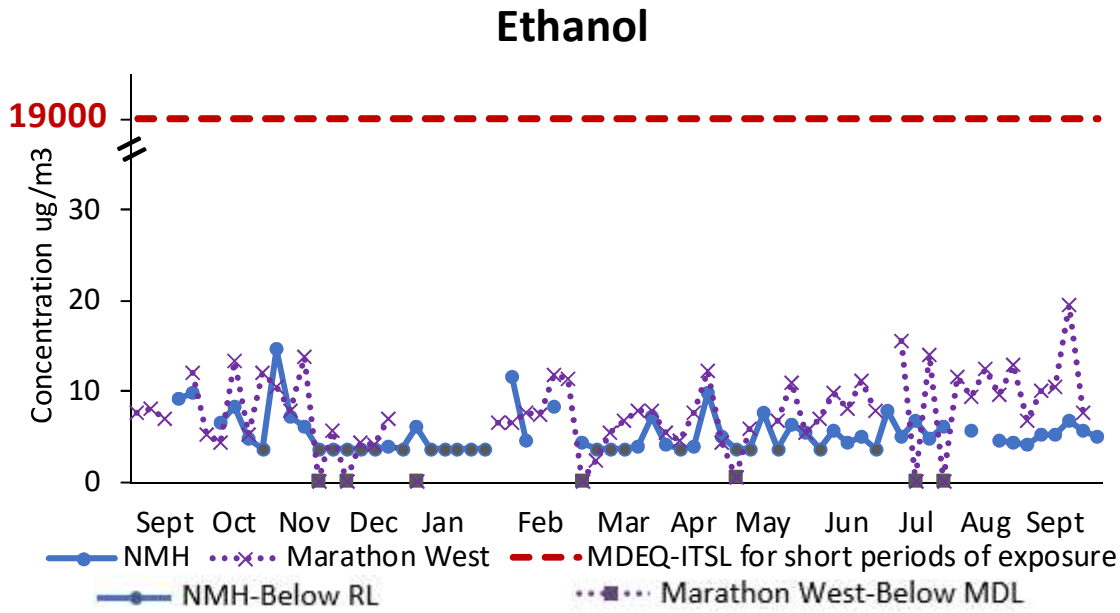


Dichlorodifluoromethane

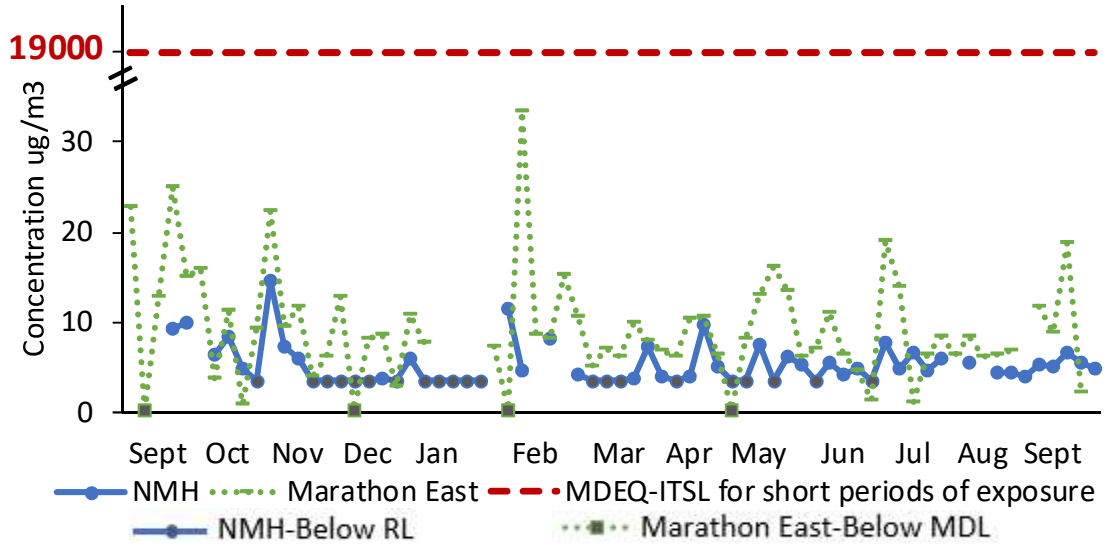



Dichlorodifluoromethane
49500
Concentration ug/m3
4
3
2
1
0
Sept
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sept
NMH
Marathon East
MDEQ-ITSL for short periods of exposure
NMH-Below RL

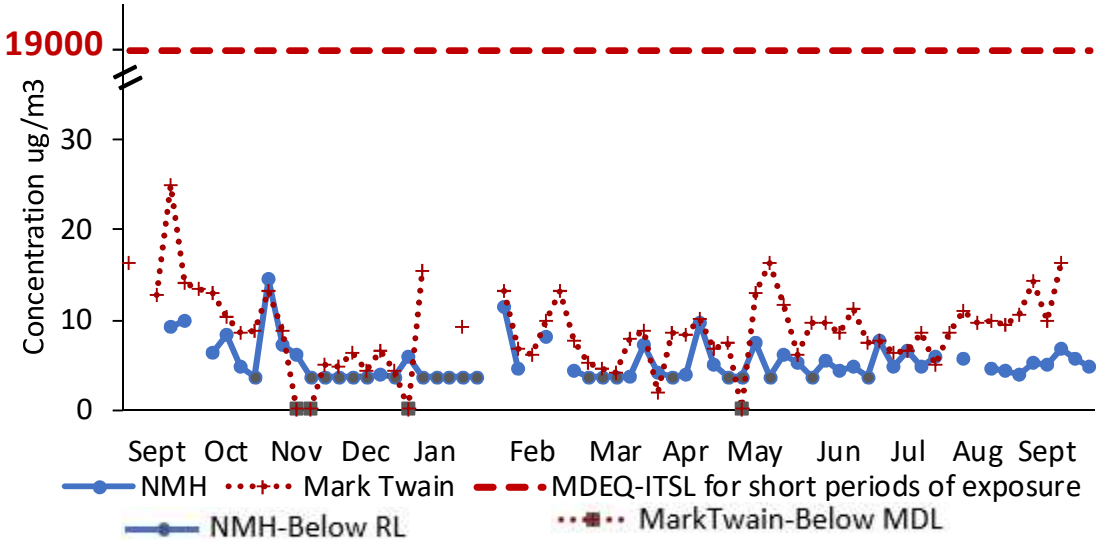

Ethanol
19000
Concentration ug/m3
30
20
10
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
Marathon North
MDEQ-ITSL for short periods of exposure
NMH-Below RL
Marathon North-Below MDL

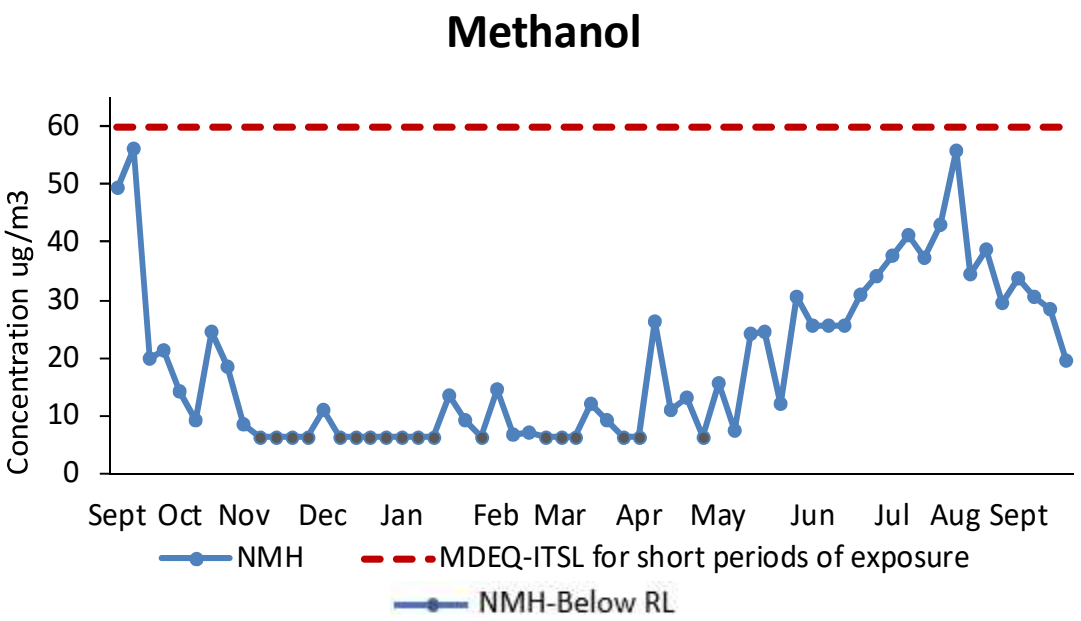

Ethanol
19000
Concentration ug/m3
30
20
10
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
Marathon West
MDEQ-ITSL for short periods of exposure
NMH-Below RL
Marathon West-Below MDL

Ethanol

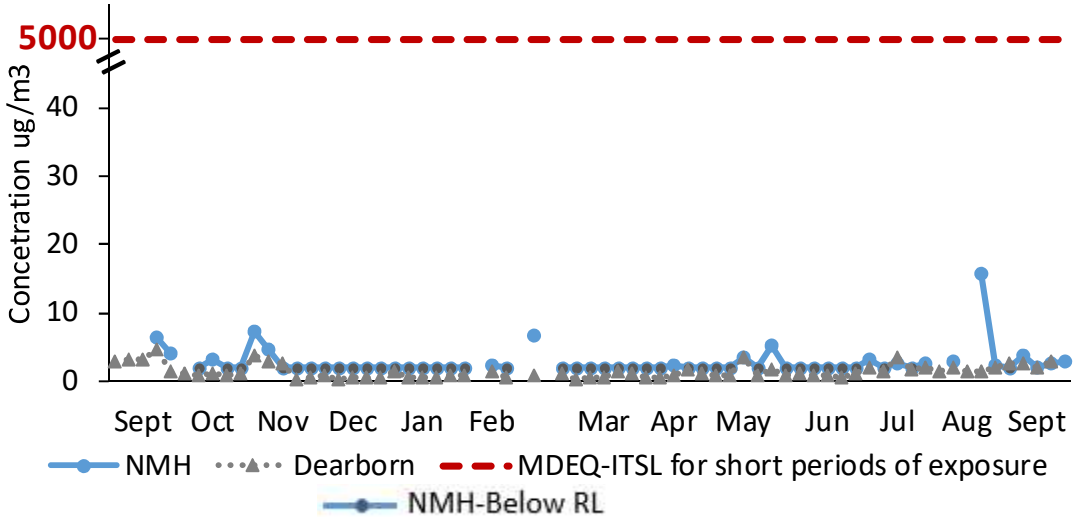


Ethanol

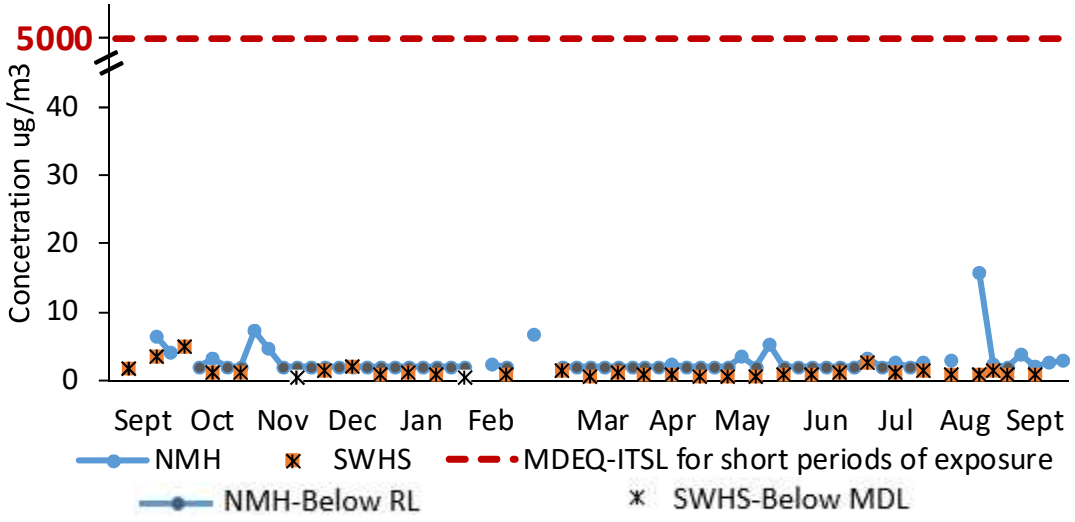



Methanol
Concentration ug/m3
60
50
40
30
20
10
0
Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sept
NMH
MDEQ-ITSL for short periods of exposure
NMH-Below RL

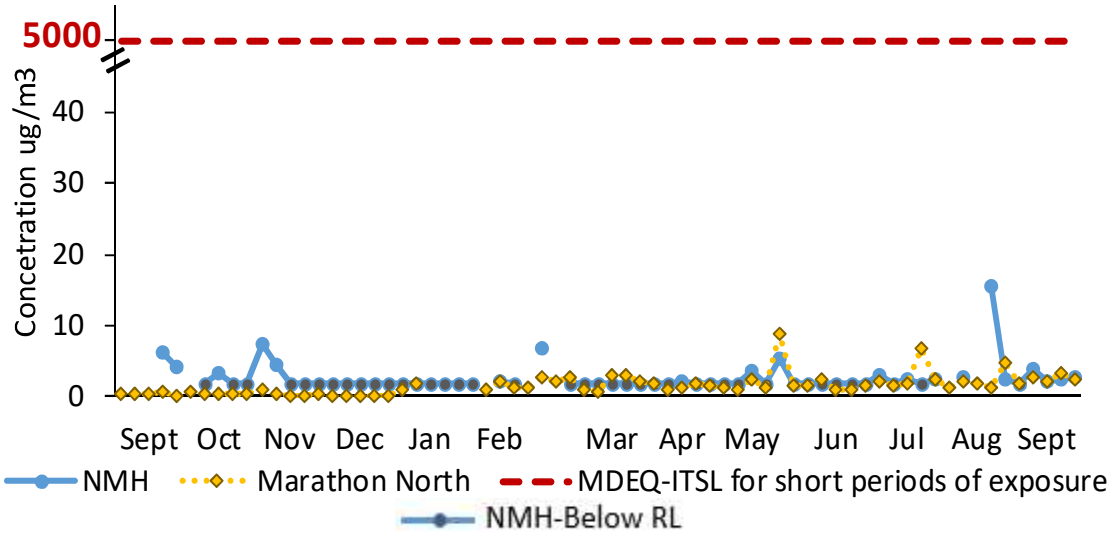
Toluene



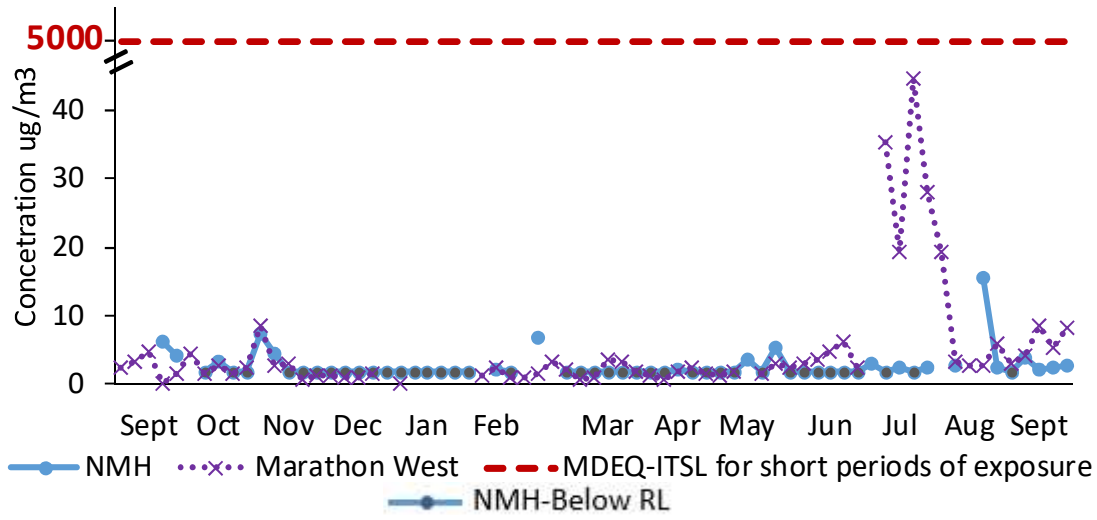
Toluene



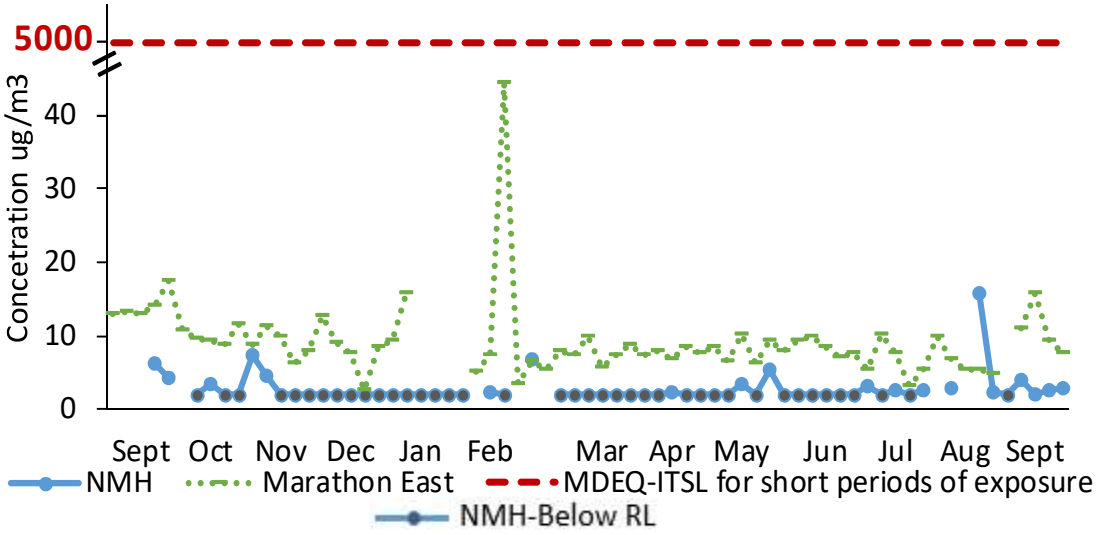
Toluene



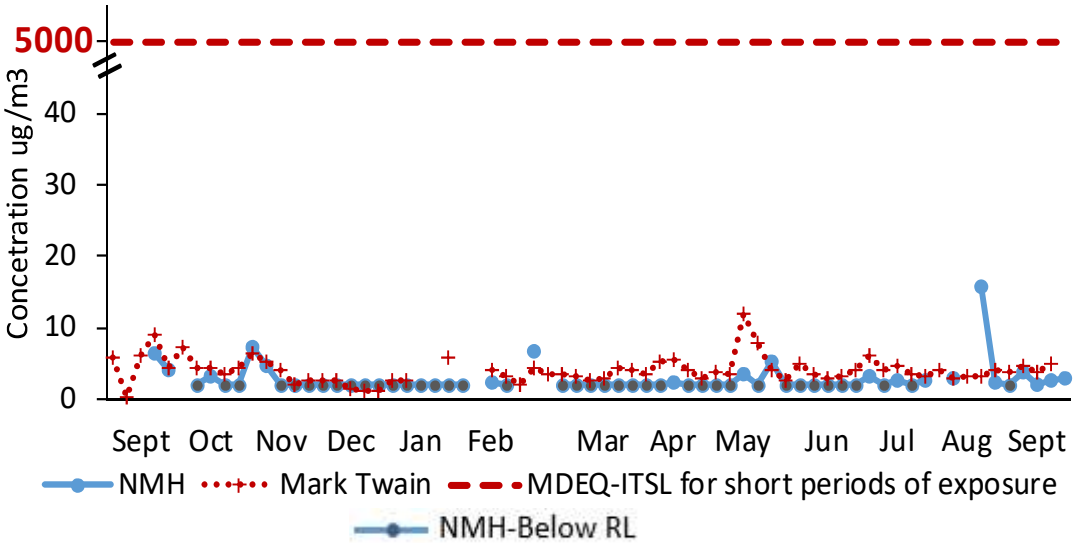
Toluene



Toluene



Toluene



Appendix C: Evaluation of Sulfuric Acid Results

Summary

Two of the 53 sulfuric acid samples exceeded short-term health-based limits, where sulfuric acid was present at concentrations that could cause respiratory irritation and were also potentially at levels that would cause lung function changes. This led to further investigation into the potential health risks associated with these levels and the potential source(s) of these levels.

Methods and Results

Air sampling began on September 30, 2016, for sulfuric acid. Sulfuric acid samples were collected as described in Appendix A. Samples were analyzed by TestAmerica Laboratories, Inc., and the reporting limit provided by the laboratory was approximately 2 micrograms (µg) per sample or 37 micrograms per cubic meter (µg/m^3). Samples that gave results above the reporting limit are summarized in Table 1 along with wind speed and direction information taken from the meteorological data from the MDEQ Fort Street air monitoring site.

Table 1. Sulfuric Acid Sampling Results

Sample Date	H_2SO_4 in (µg/m^3)	Wind speed (mph)/direction
9/30/2016	372	5/NE
11/8/2016	52	5/S-SW
11/26/2016	40	7/NW
4/7/2017	51	13/NW
4/25/2017	48	6/SE
5/19/2017	64	7/N
7/6/2017	40	5/SE, but variable
7/24/2017	677	10/N-NW
9/16/2017	57	5/S-SE

Background Levels of Sulfuric Acid

Sulfuric acid levels are not currently being monitored in the outdoor air by programs like the National Air Toxics Trends Stations. As a result, typical outdoor air levels of sulfuric acid are difficult to know. Around the 1980s, most sulfuric acid levels in the outdoor air in the United States were less than 5 µg/m^3 (ATSDR, 1998; Lioy and Waldman, 1989). These historical levels would be below the detection limit for an 8-hour sample collected with the method used in this study. Previous studies also show that higher levels occurred in the summer as compared to the winter, and higher levels occurred during the day as compared to the nighttime (ATSDR, 1998). One study estimated that peaks in sulfuric acid could have reached as high as 2,000 µg/m^3, with 1-hour averaging time during historical London air pollution episodes (Lioy and Waldman, 1989).

Short-term Health Limits of Sulfuric Acid:

There are a number of health limits for sulfuric acid from regulatory and health advisory agencies (Table 2). It should also be noted that sulfuric acid-related health limits from the Agency for Toxic Substances and Disease Registry (ATSDR) and the USEPA were considered, but not developed (ATSDR, 1998; USEPA, 1989). ATSDR, in particular, noted the complexity of factors that may influence health effects from sulfuric acid exposure. On the other hand, sulfuric acid has been well-studied, and all the short-term health limits listed below were derived with respect to health effects observed in controlled human studies. Furthermore, the AEGL-1 and MDEQ ITSL were derived with respect to controlled human studies that included the most sensitive known subpopulations, asthmatics.

Table 2. Health Limit for Sulfuric Acid

Health Limit (Agency Reference)	Health Limit (µg/m³), Averaging Time
AEGL-1 (USEPA, 2008)	200, 8-hr*
ITSL (MDEQ-AQD, 2015)**	120, 1-hr 1, annual
REL (NIOSH, 1978)	1000, 8-hr
TLV (ACGIH, 2004)	200, 8-hr***
PEL (OSHA, 2012)	1000, 8-hr

*AEGLs also have other averaging times (ATs). For sulfuric acid, all AEGL-1 values are 200 µg/m^3 regardless of the AT.
**These ITSLs were derived from CalEPA acute and chronic RELs.
***This benchmark is specifically applicable to thoracic particulate mass.

It is often most appropriate to use a health limit with the averaging time that matches the sample collection time. In this case, the averaging time would match an 8-hour sample collection time. Since sulfuric acid is expected to be a primary irritant where the health effects are dose-dependent and not time-dependent, health limits with either 1-hour or 8-hour averaging times are appropriate (USEPA, 2008). The MDEQ ITSL is based on a controlled study in asthmatics, where lung function changes were the critical effect and the no observable adverse effect level (NOAEL) was 450 µg/m^3 after 16 minutes of exposure. However, respiratory irritation has been shown to occur at 230 µg/m^3. So, the AEGL-1 is based on the more sensitive effect, but the MDEQ ITSL has been established at a level that is more health-protective. As a result, the MDEQ ITSL will be used in this evaluation because it is designed to be health protective for the public, including sensitive populations.

Health Risk Evaluation

As shown in Tables 1 and 2, there were two dates when sulfuric acid levels exceeded the short-term ITSL. Since respiratory irritation has been shown to occur at 230 μg/m^3, exposure to the levels measured on September 30 might cause a person to experience irritation symptoms like sore throat or coughing. However, even sensitive populations would probably not experience lung function changes. However, with exposure to the levels measured on July 24 (677 μg/m^3), an exposed person may have experienced both respiratory irritation and lung function changes, like bronchoconstriction.

With evaluating the health impacts from long periods of exposure, the 95% UCL is above the ITSL that protects against health effects from long periods of exposure. This ITSL is based on a controlled study in Cynomolgus monkeys, and lung changes were seen at 380 μg/m^3 after 78 weeks of exposure. Since there is no NOAEL, there is a lot of uncertainty about the level of sulfuric acid to which people may be exposed for a long period of time and not experience effects. Studies have shown that sulfuric acid can cause cancer in workplace settings (NTP, 2016). When enough information is available, these types of studies are used to calculate cancer risk levels. The cancer risk levels would be used to estimate the risk of the sulfuric acid levels that the public would breathe. However, there is a lack of information needed to determine a cancer risk level (MDEQ, 1996). And currently, no state or federal agency has calculated cancer risk levels for sulfuric acid. Furthermore, since the detection limit itself significantly contributes to the estimation of the level of sulfuric acid over a long period of time, there is a lot of uncertainty in the 95% UCL. As a result, there is not enough information from the current sampling results and the study used to derive the annual ITSL to reach conclusions about the public health significance of the long-term exposures.

Evaluation of Potential Sources

The results and the accompanying wind direction data were shared with the AQD district staff. The district staff were not able to identify an industrial source associated with elevated emissions of sulfuric acid. On the days when the two samples were collected that were above the health-based limits, the wind was out of the northern direction. However, there were other days when the wind direction was also out of the north, but the samples collected were non-detect for sulfuric acid. Collecting additional 8-hour samples for sulfuric acid are not practical for the identification of the source because the lag time between sampling and receiving the lab results is approximately 3 weeks. Instead, the AQD district staff is evaluating other techniques and strategies for identifying the source of sulfuric acid in the 48217 ZIP code.

Appendix D. Summary Statistics for New Mount Herman

This table describes the laboratory's ability to detect the pollutants. The average RL is the Reporting Limit, which is the value that the laboratory is confident in reporting. The MDL is the Method Detection Limit, which is the very lowest concentration the laboratory can detect and is based on repeating the analysis of known laboratory standards. Since the pollutant levels are not measured continuously, the true average level is not known. The mean is an estimate of the true annual average. The 95% UCL (upper confidence limit) is an estimate that is expected to be above the true annual average.

D.1 Criteria Pollutants:

Pollutants - 2017	Average	Maximum Value	Compares to (Standard)
Lead – Pb	0.004 µg/m^3	0.009 µg/m^3	0.004 µg/m^3 (3-month rolling: 0.15 µg/m^3)
$PM_{2.5}$	9.0 µg/m^3	1 hour: 122 µg/m^3 (July4th)	18 µg/m^3 (Daily 35) and 9.0 µg/m^3 (Annual 12)
SO_2	1.07 ppb	1 hour: 37.8 ppb	28 ppb (4th highest 1-hour value: 75 ppb)

µg/m^3: micrograms per cubic meter. ppb: parts per billion

D.2 Air Toxics:

Pollutants	Avg RL or MDL in µg/m^3	% Not Detected	Minimum Level Detected in µg/m^3	Maximum Level Detected in µg/m^3	95%UCL in µg/m^3	Mean in µg/m^3
1,1,1-Trichloroethane	2.7	100%	N/A	N/A	N/A	N/A
1,1,2,2-Tetrachloroethane	3.4	100%	N/A	N/A	N/A	N/A
1,1,2-Trichloroethane	2.7	100%	N/A	N/A	N/A	N/A
1,1-Dichloroethane	2.0	100%	N/A	N/A	N/A	N/A
1,1-Dichloroethene	2.0	100%	N/A	N/A	N/A	N/A
1,2,4-Trichlorobenzene	3.7	100%	N/A	N/A	N/A	N/A
1,2,4-Trimethylbenzene	3.8	100%	N/A	N/A	N/A	N/A
1,2-Dibromoethane	3.8	100%	N/A	N/A	N/A	N/A
1,2-Dichlorobenzene	3.0	100%	N/A	N/A	N/A	N/A
1,2-Dichloroethane	2.0	100%	N/A	N/A	N/A	N/A
1,2-Dichloropropane	2.3	100%	N/A	N/A	N/A	N/A
1,3,5-Trimethylbenzene	3.8	100%	N/A	N/A	N/A	N/A
1,3-Butadiene	1.1	100%	N/A	N/A	N/A	N/A
1,3-Dichlorobenzene	3.0	100%	N/A	N/A	N/A	N/A
1,4-Dichlorobenzene	3.0	100%	N/A	N/A	N/A	N/A
1,4-Dioxane	1.8	100%	N/A	N/A	N/A	N/A
2,2,4-Trimethylpentane	2.3	100%	N/A	N/A	N/A	N/A
2-Propanol	4.8	43%	4.917	44.250	13.56	7.918
3-Chloropropene	1.6	100%	N/A	N/A	N/A	N/A
Acetone	4.6	26%	4.823	34.210	10.870	8.981
Benzene	1.6	97%	2.141	5.112	N/A	N/A
Bromodichloromethane	3.4	100%	N/A	N/A	N/A	N/A
Bromoform	5.2	100%	N/A	N/A	N/A	N/A
Bromomethane	1.9	100%	N/A	N/A	N/A	N/A

Pollutants	Avg RL or MDL in µg/m³	% Not Detected	Minimum Level Detected in µg/m³	Maximum Level Detected in µg/m³	95%UCL in µg/m³	Mean in µg/m³
Carbon Disulfide	1.6	97%	2.46	2.709	N/A	N/A
Carbon Tetrachloride	3.1	100%	N/A	N/A	N/A	N/A
Chlorobenzene	2.3	100%	N/A	N/A	N/A	N/A
Chlorodifluoromethane	1.8	97%	1.874	121.000	N/A	N/A
Chloroethane	1.3	100%	N/A	N/A	N/A	N/A
Chloroform	2.4	100%	N/A	N/A	N/A	N/A
Chloromethane	1.0	18%	1.053	1.446	1.077	0.976
Chloromethyl Benzene	2.6	100%	N/A	N/A	N/A	N/A
Cis-1,2-Dichloroethene	2.0	100%	N/A	N/A	N/A	N/A
Cis-1,3-Dischloropropene	2.3	100%	N/A	N/A	N/A	N/A
Cyclohexane	1.7	100%	N/A	N/A	N/A	N/A
Dibromochloromethane	4.3	100%	N/A	N/A	N/A	N/A
Dichlorodifluoromethane	2.5	33%	2.522	4.105	2.619	1.868
Dichlorofluoromethane	2.1	100%	N/A	N/A	N/A	N/A
Dichlorotetrafluoroethane	3.5	100%	N/A	N/A	N/A	N/A
Ethyl Acetate	1.8	98%	1.838	1.838	N/A	N/A
Ethyl Alcohol	3.7	34%	3.788	14.570	4.966	4.093
Ethylbenzene	2.2	100%	N/A	N/A	N/A	N/A
Furan, Tetrahydro-	1.5	100%	N/A	N/A	N/A	N/A
Heptane	2.0	100%	N/A	N/A	N/A	N/A
Hexachloro-1,3-butadiene	5.3	100%	N/A	N/A	N/A	N/A
M&P-Xylene	4.3	98%	5.559	5.559	N/A	N/A
Methanol	6.2	30%	6.79	56.240	20.45	17.07
Methyl Butyl Ketone	2.0	100%	N/A	N/A	N/A	N/A
Methyl Ethyl Ketone	2.9	92%	2.95	5.015	N/A	N/A
Methyl Isobutyl Ketone	2.0	100%	N/A	N/A	N/A	N/A
Methylene Chloride	3.4	100%	N/A	N/A	N/A	N/A
Methyltertiarybutylether	1.8	100%	N/A	N/A	N/A	N/A

Pollutants	Avg RL or MDL in µg/m³	% Not Detected	Minimum Level Detected in µg/m³	Maximum Level Detected in µg/m³	95%UCL in µg/m³	Mean in µg/m³
N-Hexane	1.8	87%	1.798	3.878	N/A	N/A
O-Xylene	2.2	100%	N/A	N/A	N/A	N/A
P-Ethyltoluene	2.5	100%	N/A	N/A	N/A	N/A
Propylene	1.7	100%	N/A	N/A	N/A	N/A
Styrene	2.1	100%	N/A	N/A	N/A	N/A
Tetrachloroethene	3.4	100%	N/A	N/A	N/A	N/A
Toluene	1.9	67%	2.035	15.640	2.205	1.402
Trans-1,2-Dichloroethene	2.0	100%	N/A	N/A	N/A	N/A
Trans-1,3-Dichloropropene	2.3	100%	N/A	N/A	N/A	N/A
Trichloroethene	2.7	100%	N/A	N/A	N/A	N/A
Trichlorofluoromethane	2.8	100%	N/A	N/A	N/A	N/A
Trichlorotrifluoroethane	3.8	100%	N/A	N/A	N/A	N/A
Vinyl Acetate	3.5	100%	N/A	N/A	N/A	N/A
Vinyl Bromide	2.2	100%	N/A	N/A	N/A	N/A
Vinyl Chloride	1.3	100%	N/A	N/A	N/A	N/A
Hydrochloric acid	40	100%	N/A	N/A	N/A	N/A
Hydrogen cyanide	40	100%	N/A	N/A	N/A	N/A
Sulfuric acid	35	83%	40	677	119	57
Arsenic	0.0000084	0%	1.30E-04	0.005	0.00168	0.00119
Barium	0.0003348	0%	0.00553	0.047	0.0169	0.0153
Beryllium	0.0000056	0%	6.00E-06	0.000	0.000	0.000
Cadmium	0.0000084	0%	3.00E-05	0.001	0.000	0.000
Chromium	0.0001345	0%	0.00127	0.008	0.003	0.003
Cobalt	0.0000200	0%	7.00E-05	0.000	0.000	0.000
Iron	0.0030682	0%	0.124	1.128	0.495	0.446
Lead	0.0000000	0%	8.90E-04	0.009	0.004	0.004
Manganese	0.0000564	0%	0.0044	0.096	0.028	0.025
Molybdenum	0.0000100	0%	8.00E-05	0.006	0.001	0.001
Nickel	0.0000515	0%	7.80E-04	0.008	0.002	0.002
Vanadium	0.0000200	0%	1.90E-04	0.006	0.002	0.001
Zinc	0.0011050	0%	0.011	0.109	0.0505	0.0382

Pollutants	Avg RL or MDL in µg/m³	% Not Detected	Minimum Level Detected in µg/m³	Maximum Level Detected in µg/m³	95%UCL in µg/m³	Mean in µg/m³
1,2,4-Trichlorobenzene	0.03	100%	N/A	N/A	N/A	N/A
2,4,5-Trichlorophenol	0.03	100%	N/A	N/A	N/A	N/A
2,4,6-Trichlorophenol	0.17	100%	N/A	N/A	N/A	N/A
2,4-Dichlorophenol	0.03	100%	N/A	N/A	N/A	N/A
2,4-Dimethylphenol	0.03	100%	N/A	N/A	N/A	N/A
2,4-Dinitrophenol	0.17	100%	N/A	N/A	N/A	N/A
2,4-Dinitrotoluene	0.03	100%	N/A	N/A	N/A	N/A
2,6-Dinitrotoluene	0.03	100%	N/A	N/A	N/A	N/A
2-Chloronaphthalene	0.03	100%	N/A	N/A	N/A	N/A
2-Chlorophenol	0.03	100%	N/A	N/A	N/A	N/A
2-Methylnaphthalene	0.01	58%	0.035	0.074	0.028	0.022
2-Nitroaniline	0.03	100%	N/A	N/A	N/A	N/A
2-Nitrophenol	0.17	100%	N/A	N/A	N/A	N/A
3,3-Dichlorobenzidine	0.03	100%	N/A	N/A	N/A	N/A
3-Nitroaniline	0.03	100%	N/A	N/A	N/A	N/A
4-Bromophenyl phenyl ether	0.03	100%	N/A	N/A	N/A	N/A
4-Chloro-3-methylphenol	0.17	100%	N/A	N/A	N/A	N/A
4-Chloroaniline	0.03	100%	N/A	N/A	N/A	N/A
4-Chlorophenyl phenyl ether	0.03	100%	N/A	N/A	N/A	N/A
4-Nitroaniline	0.17	100%	N/A	N/A	N/A	N/A
4-Nitrophenol	0.17	100%	N/A	N/A	N/A	N/A
Acenaphthene	0.03	100%	N/A	N/A	N/A	N/A
Acenaphthylene	0.03	100%	N/A	N/A	N/A	N/A
Anthracene	0.03	100%	N/A	N/A	N/A	N/A
Benz(a)anthracene	0.03	100%	N/A	N/A	N/A	N/A
Benzo(a)pyrene	0.03	100%	N/A	N/A	N/A	N/A
Benzo(g,h,i)perylene	0.03	100%	N/A	N/A	N/A	N/A
Benzo(k)fluoranthene	0.03	100%	N/A	N/A	N/A	N/A
Benzo[b]fluoranthene	0.03	100%	N/A	N/A	N/A	N/A
Benzoic acid	0.17	99%	0.17	0.17	N/A	N/A
Benzyl alcohol	0.03	100%	N/A	N/A	N/A	N/A
Bis(2-chloroethoxy)methane	0.03	100%	N/A	N/A	N/A	N/A
Bis(2-chloroethyl) ether	0.03	100%	N/A	N/A	N/A	N/A
Bis(2-chloroisopropyl)ether	0.03	100%	N/A	N/A	N/A	N/A
Bis(2-ethylhexyl)phthalate	0.03	100%	N/A	N/A	N/A	N/A
Butyl benzyl phthalate	0.03	100%	N/A	N/A	N/A	N/A

Pollutants	Avg RL or MDL in µg/m^3	% Not Detected	Minimum Level Detected in µg/m^3	Maximum Level Detected in µg/m^3	95%UCL in µg/m^3	Mean in µg/m^3
Chrysene	0.03	100%	N/A	N/A	N/A	N/A
Dibenz(a,h)anthracene	0.03	100%	N/A	N/A	N/A	N/A
Dibenzofuran	0.03	100%	N/A	N/A	N/A	N/A
Diethyl phthalate	0.02	95%	0.044	0.058	N/A	N/A
Dimethyl phthalate	0.03	100%	N/A	N/A	N/A	N/A
Di-n-butyl phthalate	0.07	100%	N/A	N/A	N/A	N/A
Dinitro-o-cresol (4,6-dinitro-2-methyl phenol)	0.17	100%	N/A	N/A	N/A	N/A
Di-n-octyl phthalate	0.03	100%	N/A	N/A	N/A	N/A
Fluoranthene	0.03	100%	N/A	N/A	N/A	N/A
Fluorene	0.03	100%	N/A	N/A	N/A	N/A
Hexachloro-1,3-butadiene	0.03	100%	N/A	N/A	N/A	N/A
Hexachloro-1,3-cyclopentadiene	0.17	100%	N/A	N/A	N/A	N/A
Hexachlorobenzene	0.03	100%	N/A	N/A	N/A	N/A
Hexachloroethane	0.01	99%	0.039	0.039	N/A	N/A
Indeno(1,2,3-cd)pyrene	0.03	100%	N/A	N/A	N/A	N/A
Isophorone	0.03	100%	N/A	N/A	N/A	N/A
m-Cresol (3-methylphenol)	0.17	100%	N/A	N/A	N/A	N/A
m-Dichlorobenzene (1,3-dichloro benzene)	0.03	100%	N/A	N/A	N/A	N/A
Naphthalene	0.01	20%	0.034	0.146	0.072	0.062
Nitrobenzene	0.03	100%	N/A	N/A	N/A	N/A
N-Nitrosodimethylamine	0.03	100%	N/A	N/A	N/A	N/A
N-Nitrosodi-n-propylamine	0.03	100%	N/A	N/A	N/A	N/A
N-Nitrosodiphenylamine	0.03	100%	N/A	N/A	N/A	N/A
o-Cresol (2-methylphenol)	0.03	100%	N/A	N/A	N/A	N/A
o-Dichlorobenzene (1,2-dichlorobenzene)	0.03	100%	N/A	N/A	N/A	N/A
p-Cresol (4-methylphenol)	0.17	100%	N/A	N/A	N/A	N/A
p-Dichlorobenzene (1,4-dichlorobenzene)	0.03	100%	N/A	N/A	N/A	N/A
Pentachlorophenol	0.17	100%	N/A	N/A	N/A	N/A
Phenanthrene	0.03	100%	N/A	N/A	N/A	N/A
Phenol	0.03	100%	N/A	N/A	N/A	N/A
Pyrene	0.03	100%	N/A	N/A	N/A	N/A

Appendix E. Descriptions of Health Protective Limits for Air Toxics

The health protective limits for air toxics used in this study are the initial threshold screening levels (ITSLs) and initial risk screening levels (IRSLs). ITSLs and IRSLs are used in the AQD's permitting program. ITSLs and IRSLs are developed to protect against the most sensitive health effect (critical effect) that a pollutant might cause. They are also developed to reflect the best toxicological results available at the time. They are often developed from health limits from other state or federal environmental agencies.

References listed in the Health Limit Description Table
USEPA Integrated Risk Information System (EPA IRIS)
American Conference of Governmental Industrial Hygienists Threshold Limit Value (ACGIH TLV)
Agency for Toxic Substances and Disease Registry Minimal Risk Level (ATSDR MRL)
California Environmental Protection Agency Reference Exposure Level (CALEPA REL)
National Institute for Occupational Safety and Health Recommended Exposure Limits (NIOSH REL)
National Toxicology Program (NTP)
USEPA Health Effects Assessment Summary Tables (EPA HEAST)
Scientific Advisory Panel (SAP)
USEPA Provisional Peer-Reviewed Toxicity Values (EPA PPRTV)

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
ACIDS: Hydrogen Chloride (7647-01-0)	20 (Respiratory; EPA IRIS)			2100 (Respiratory; CalEPA REL)	
Hydrogen Cyanide (57-12-5)	0.8 (endocrine; EPA IRIS)			50 (Respiratory; ACGIH TLV ceiling)	
Sulfuric Acid (7664-93-9)	1 (respiratory; CalEPA REL)			120 (respiratory; CalEPA REL)	
METALS: Arsenic (7440-38-2)					0.0002 (lung; EPA IRIS)
Barium (7440-39-3)			5 (respiratory; ACGIH TLV)		
Beryllium (7440-41-7)		0.02 (respiratory; EPA IRIS)			0.0004 (lung; EPA IRIS)
Cadmium (7440-43-9)					0.0006 (lung; EPA IRIS)
Total Chromium (But Considered Trivalent (16065-83-1)			5 (respiratory; ACGIH TLV)		
Hexavalent Chromium (18540-29-9)	0.1 particulate (respiratory, EPA IRIS) 0.008 mist (nasal septum atrophy, EPA IRIS)				0.000083 (lung; EPA IRIS)
Cobalt (7440-48-4)			0.2 (respiratory; ACGIH TLV)		
Copper (7440-50-8)			2 (respiratory; ACGIH TLV)		

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Iron (Considered under PM_{10}) (7439-89-6)					
Lead (7439-92-1)					
Manganese (7439-96-5)	0.3 (neurological; ATSDR MRL)				
Molybdenum (7439-98-7)			30 (respiratory; ACGIH TLV)		
Nickel (7440-02-0)					0.0058 (respiratory; EPA IRIS)
Vanadium (using ITSL for vanadium pentoxide (1314-62-1)				0.5 (respiratory; NIOSH REL)	
Zinc (Considered under zinc stearate (557-05-1)			50 (respiratory; NIOSH REL)		
PAHs and VOCs:					
Naphthalene (91-20-3)	3 (respiratory; EPA IRIS)		520 (ocular; ACGIH TLV)		0.08 (nasal; NTP)
1,1,1-Trichloroethane (71-55-6)		6000 (neurological; EPA IRIS)			
1,1,2,2-Tetrachloroethane (79-34-5)					0.02 (liver; EPA IRIS)
1,1,2-Trichloroethane (79-00-5)					0.06 (liver; EPA IRIS)
1,1-Dichloroethane (75-34-3)	500 (renal; EPA HEAST)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
1,1-Dichloroethene (75-35-4)	200 (liver; EPA IRIS)				
1,2,4-Trichlorobenzene (120-82-1)	4 (renal; AQD)				
1,2,4-Trimethylbenzene (95-63-6)	185 (neurological; EPA IRIS)		1200 (respiratory; ACGIH TLV)		
1,2-Dibromoethane (106-93-4)	9 (nasal; EPA IRIS)				0.002 (nasal; EPA IRIS)
1,2-Dichlorobenzene (95-50-1)	300 (kidney; EPA IRIS)				
1,2-Dichloroethane (107-06-2)					0.04 (circulatory; EPA IRIS)
1,2-Dichloropropane (78-87-5)	4 (nasal; EPA IRIS)				0.2 (nasal; AQD)
1,3,5-Trimethylbenzene (108-67-8)	185 (neurological; EPA IRIS)		1200 (respiratory; ACGIH TLV)		
1,3-Butadiene (106-99-0)	33(ovary; TCEQ)				0.03 (leukemia; EPA IRIS)
1,3-Dichlorobenzene (541-73-1)	3 (thyroid; AQD)				
1,4-Dichlorobenzene (106-46-7)	800 (liver; EPA IRIS)				0.25 (liver; AQD)
1,4-Dioxane (123-91-1)	100 (nasal; EPA IRIS)			7200 (eyes, nose, and throat irritation; AQD)	0.2 (multi-organ; EPA IRIS)
2,2,4-Trimethylpentane (540-84-1)			3500 (neurological; NIOSH REL)		

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
2,4,5-Trichlorophenol (95-95-4)	350 (liver and urinary; EPA IRIS)				
2,4,6-Trichlorophenol (88-06-2)					0.3 (Leukemia; EPA IRIS)
2,4-Dichlorophenol (120-83-2)		11 (immune; EPA IRIS)			
2,4-Dimethylphenol (105-67-9)	70 (nervous; hematologic; EPA IRIS)				
2,4-Dinitrophenol (51-28-5)	7 (ocular; EPA IRIS)				
2,4-Dinitrotoluene (121-14-2)			2 (hematologic and nervous; ACGIH TLV)		0.009 (renal; AQD)
2-Chlorophenol (95-57-8)		18 (reproductive; EPA IRIS)			
2-Methylnaphthalene (91-57-6)	10 (respiratory; AQD LC50)				
2-Nitrophenol (88-75-5)		18 (Respiratory; AQD)			
2-Propanol (67-63-0)	220 (neurological; AQD SAP)				
3,3-Dichlorobenzidine (91-94-1)					0.002 (bladder; AQD)
3-Chloropropene (107-05-1)	1 (neurological; EPA IRIS)		31 (neurological; ACGIH TLV)		
4-Nitrophenol (100-02-7)	0.7 (ocular; AQD)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Acenaphthene (83-32-9)	210 (liver; EPA IRIS)				
Acenaphthylene (208-96-8)	35 (Mortality, liver and renal; AQD)				
Acetone (67-64-1)			5900 (irritation and neurological; NIOSH REL)		
Acetonitrile (75-05-8)	200 (mortality; EPA IRIS)				
Anthracene (120-12-7)	1000 (no effects seen; EPA IRIS)				
Acrylonitrile (107-13-1)	2 (respiratory; EPA IRIS)				0.01 (gastral; nervous; respiratory; EPA IRIS)
Benz(a)anthracene (56-55-3)					Based on benzo (a) pyrene IRSL
Benzene (71-43-2)	30 (immune; EPA IRIS)	30 (immune; ATSDR MRL)			0.1 (leukemia; EPA IRIS)
Benzo(a)pyrene (50-32-8)		0.002 (fetal; EPA IRIS)			0.001 (respiratory and gastral; EPA IRIS)
Benzo[b]fluoranthene (205-99-2)					Based on benzo (a) pyrene IRSL
Benzo(g,h,i)perylene (191-24-2)	13 (respiratory; AQD)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Benzo(k)fluoranthene (207-08-9)					Based on benzo (a) pyrene IRSL
Benzyl alcohol (100-51-6)	5000 (body weight; AQD)				
Bis (2-chloroisopropyl) ether (108-60-1)	140 (hematologic; EPA IRIS)				
Bis(2-chloroethyl) ether (111-44-4)					0.003 (liver; EPA IRIS)
Bis(2-ethylhexyl)phthalate (117-81-7)	70 (liver; EPA IRIS)				0.61 (liver; EPA IRIS)
Bromodichloromethane (75-27-4)					0.06 (urinary; EPA IRIS)
Bromoform (75-25-2)					0.9 (gastral; EPA IRIS)
Bromomethane (74-83-9)	5 (respiratory; EPA IRIS)				
Butyl benzyl phthalate (85-68-7)	700 (liver; EPA IRIS)				
Carbon Disulfide (75-15-0)	700 (neurological; EPA IRIS)				
Carbon Tetrachloride (56-23-5)	480 (liver; EPA IRIS)				0.17 (adrenal; EPA IRIS)
Chlorobenzene (108-90-7)	50 (kidney; EPA PPRTV)		440 (irritation and neurological; AQD)		
Chlorodifluoromethane (75-45-6)	50000 (kidney, adrenal, pituitary; EPA IRIS)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Chloroethane (75-00-3)		10000 (fetotoxicity; EPA IRIS)			
Chloroform (67-66-3)					0.4 (kidney; AQD)
Chloromethane (74-87-3)	90 (brain; EPA IRIS)				
Chloromethyl Benzene (27987-13-9)					
Chrysene (218-01-9)					Based on benzo (a) pyrene IRSL
Cis-1,2-Dichloroethene (156-59-2)	18 (kidney; EPA IRIS)				
Cis-1,3-Dichloropropene (542-75-6)	20 (nasal; EPA IRIS)				0.2 (lung; EPA IRIS)
Cyclohexane (110-82-7)		6000 (developmental; EPA IRIS)			
Dibromochloromethane (124-48-1)	70 (liver; EPA IRIS)				0.042 (liver; AQD)
Dichlorodifluoromethane (75-71-8)			49500 (liver; ACGIH TLV)		
Dichlorofluoromethane (75-43-4)					
Dichlorotetrafluoroethane (76-14-2)			69000 (respiratory; ACGIH TLV)		
Dibenzofuran (132-64-9)	40 (reduced organ weights and excess fat;EPA PPRTV)				
Dibenz(a,h)anthracene (53-70-3)					Based on benzo (a) pyrene IRSL

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Dimethyl phthalate (131-11-3)			50 (irritation; ACGIH TLV)		
Di-n-butyl phthalate (84-74-2)			50 (irritation; ACGIH TLV)		
Di-n-octyl phthalate (117-84-0)	470 (liver and thyroid; AQD)				
Dinitro-o-cresol (534-52-1)			2 (metabolic; ACGIH TLV)		
Ethyl Acetate (141-78-6)	3200 (liver; EPA IRIS)				
Ethyl Alcohol (64-17-5)				19000 (fetotoxicity; ACGIH TLV)	
Ethylbenzene (100-41-4)		1000 (developmental; EPA IRIS)			0.4 (kidney; AQD)
Fluoranthene (206-44-0)	140 (liver and urinary; EPA IRIS)				
Fluorene (86-73-7)	140 (hematologic; EPA IRIS)				
Tetrahydrofuran (109-99-9)	8000 (liver and neurological; AQD)				
Heptane (142-82-5)			3500 (NIOSH REL)		
Hexachloro-1,3-Butadiene (87-68-3)					0.05 (kidney; EPA IRIS)
Hexachloro-1,3-cyclopentadiene (77-47-4)	0.2 (respiratory; EPA IRIS)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Hexachlorobenzene (118-74-1)		0.35 (reproductive; ATSDR MRL)			0.0022 (liver; EPA IRIS)
Indeno(1,2,3-cd)pyrene (193-39-5)					Based on benzo (a) pyrene IRSL
Isophorone (78-59-1)				280 (irritation, nervous and malaise; ACGIH TLV)	3.7 (reproductive; EPA IRIS)
M-Cresol (108-39-4)			100 (nervous; NIOSH REL)		
M-Dichlorobenzene (541-73-1)	3 (thyroid; AQD)				
M/P-Xylene (108-38-3/106-42-3)	390 (impaired motor coordination; EPA IRIS)				
Methyl Butyl Ketone (591-78-6)	30 (neurological; EPA IRIS)				
Methyl Ethyl Ketone (78-93-3)		5000 (developmental; EPA IRIS)			
Methyl Isobutyl Ketone (108-10-1)			820 (neurological; ACGIH TLV)		2 (leukemia; AQD)
Methylene Chloride (75-09-2)	2000 (liver; EPA IRIS)			14000 (neurological; Cal EPA short-term REL)	60 (liver; EPA IRIS)
Methyl Tertiary-Butyl Ether (1634-04-4)	3000 (liver and kidney; EPA IRIS)				
N-Hexane (110-54-3)	700 (neurological; EPA IRIS)				

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
N-Nitrosodi-n-propylamine (621-64-7)					0.0005 (liver; AQD)
N-Nitrosodimethylamine (62-75-9)					0.00007 (liver; EPA IRIS)
Nitrobenzene (98-95-3)	9 (nervous and respiratory; EPA IRIS)				0.025 (endocrine, liver, urinary; EPA IRIS)
O-Cresol (95-48-7)			100 (nervous; NIOSH REL)		
O-Dichlorobenzene (95-50-1)	300 (no effects seen; EPA IRIS)				0.25 (liver; AQD)
O-Xylene (95-47-6)	390 (impaired motor coordination; EPA IRIS)				
P-Cresol (106-44-5)			100 (nervous; NIOSH REL)		
P-Dichlorobenzene (106-46-7)	800 (liver; EPA IRIS)				
P-Ethyltoluene (622-96-8)	350 (liver; AQD)				
Pentachlorophenol (87-86-5)	20 (liver; EPA IRIS)				0.009 (liver and endocrine; EPA IRIS)
Phenol (108-95-2)			190 (irritation, respiratory, and nervous; ACGIH TLV)		
Phenanthrene (85-01-8)	0.1 (default; AQD)				
Propylene (115-07-1)			8600 (respiratory; ACGIH TLV)		

Chemical Name (CAS#)	ITSL in µg/m³ based on averaging time				IRSL in µg/m³
	Annual (critical effect; reference)	24-hr (critical effect; reference)	8-hr (critical effect; reference)	1-hr (critical effect; reference)	(Type of cancer; reference)
Pyrene (129-00-0)	100 (urinary; EPA IRIS)				
Styrene (100-42-5)	1000 (neurological; EPA IRIS)				2 (leukemia; EPA)
Tetrachloroethene (127-18-4)	40 (neurological; EPA IRIS)	1400 (neurological; ATSDR MRL)			4 (liver; EPA IRIS)
Toluene (108-88-3)		5000 (neurological; EPA IRIS)			
Trans-1,2-Dichloroethene (540-59-0)		35 (neurological; EPA HEAST)			
Trans-1,3-Dichloropropene (542-75-6)	20 (nasal; EPA IRIS)				0.2 (lung; EPA IRIS)
Trichloroethene (79-01-6)		2 (immune and developmental; EPA IRIS)			0.2 (kidney; EPA IRIS)
Trichlorofluoromethane (75-69-4)				56200 (systemic; ACGIH TLV ceiling)	
Trichlorotrifluoromethane (76-13-1)		19140 (neurological; AQD)			
Vinyl Acetate (108-05-4)	200 (nasal; EPA IRIS)				
Vinyl Bromide (593-60-2)	30 (liver; EPA IRIS)				
Vinyl Chloride (75-01-4)	100 (liver; EPA IRIS)				0.11 (liver; EPA IRIS)
Methanol (67-56-1)		20000 (developmental; EPA IRIS)		28000 (neurological; Cal EPA)	

Appendix F. Other Air Monitoring Efforts in the 48217 ZIP code

USEPA Mobile Air Monitoring:

The MDEQ, Air Quality Division requested that the USEPA conduct a mobile monitoring investigation of air pollution in the neighborhoods near Marathon, and specifically, the former Jefferies School area. This monitoring was conducted in August 2017.

MDEQ Investigative Monitoring for VOCs

In August and September 2017, the MDEQ conducted VOC sampling at a residence in the northern part of the 48217 ZIP code. Samples were collected for 24 hours using the same sampling method and laboratory as the New Mount Hermon (NMH) site and Marathon. A total of 8 samples were collected. Four samples were collected on the USEPA published ambient air sampling schedule and the other four were collected on non-scheduled days. The goals of the north 48217 ZIP code study were to:

1. Evaluate whether any compounds were detected that are above health limits (AQD screening levels);
2. Compare results of north 48217 and the NMH site;
3. Compare the results to Marathon's monitors;
4. Compare the results to the MDEQ monitor on Waterman Street near the former Southwestern High School (SWHS); and
5. Compare results that were collected on regular sample days verses several Saturdays that were not scheduled sample days.

The results of the sampling at the northern and southern sites in the 48217 ZIP code did not identify any VOC compounds above the health limits. Except for ethanol, the MDEQ SWHS monitor site had higher concentrations of VOC compounds than both 48217 sites and the Marathon sites. Samples collected on weekends were not higher or substantially different from those collected on regularly scheduled sample days. Ethanol was detected at much higher concentrations at the northern 48217 site, but below the health limits of 19,000 micrograms per cubic meter ($\mu g/m^3$). The MDEQ SWHS samples are analyzed by a different laboratory that does not report ethanol in the data package. The table below documents the ethanol values in micrograms per cubic meter.

Summary of Ethanol Values:

Date	North 48217	New Mount Hermon (south 48217)	Marathon North site (Sanders St.)	Marathon West site (Schaffer-Dix)	Marathon East site (close to North 48217)	Marathon Mark Twain School site (close to NMH)
8/19/2017	193.0	malfunction				
8/23/2017	138.0	4.56 *(8/24/2017)*	6.9	9.7	6.5	10.2
8/29/2017	106.0	4.43	13.2	13.1	7.1	9.7
9/9/2017	729.0	5.24				
9/16/2017	760.0	5.16	4.0	10.6	8.9	10.1
9/23/2017	873.0	6.76				
9/28/2017	486.0	5.65	11.1	7.9	2.2	void
9/30/2017	122.0	4.96				

Marathon Air Monitoring Network:

Since 2012, Marathon has been conducting ambient air monitoring at four locations for various pollutants. Three are on the plant property and one is to the south at a school. One of the stations on Marathon's property, the Marathon-East site, is close to Fort and Pleasant Streets, which is near the Jefferies neighborhood. This data is submitted to the AQD each month and it is reported to the USEPA's Air Quality Database, which is available to the public.

USEPA Investigation Monitoring:

In 2011, some extensive air sampling was conducted near the former Jefferies School site. In response to the sewer gas issue, USEPA staff conducted some extensive indoor and outdoor air sampling for VOC sampling using the 24-hour 'summa canister method' (same as the MDEQ and Marathon) and some real-time measurement instruments. Along with indoor air, drain and sewer sampling, measurements were also conducted outside in the community. Monthly outdoor ambient air sampling was conducted from March 2011 through February 2012 in the areas of I-75 (near Pleasant), Liebold, Patricia, and Liddesdale Streets.

Monthly background samples were collected at Edsel & Patricia, Leonard & Deacon, Pleasant & Deacon, East Fort Street, and West Fort Street. The monthly ambient air VOC samples that were collected from March 2011 to February 2012 did not show elevated levels of benzene, one of the key VOC compounds. Mr. Brian Kelly of the USEPA Grosse Ile office was the primary contact and investigator.

Appendix G: References

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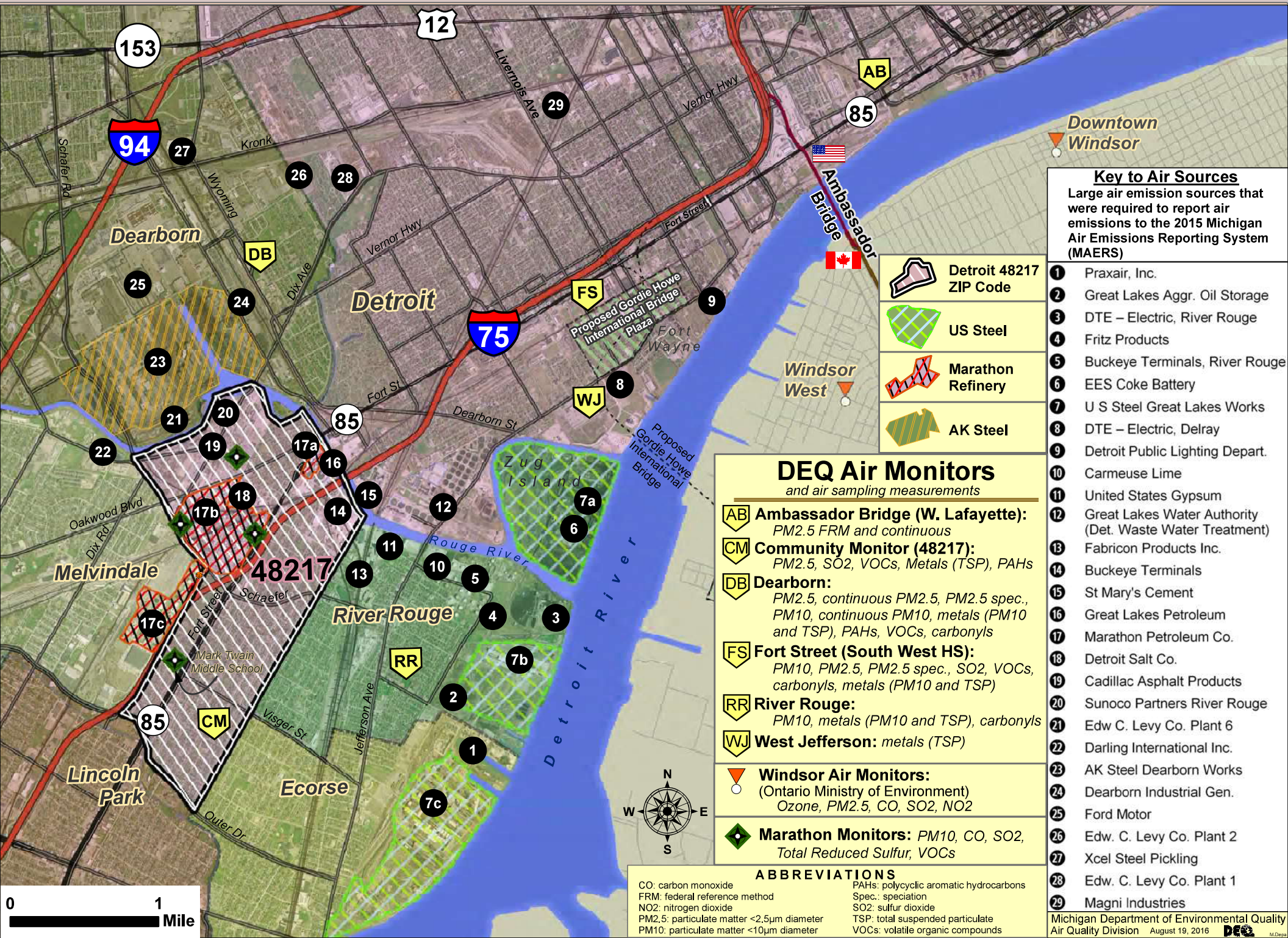
Appendix H: Map of Southwest Detroit with Emphasis on Emission Sources

Southwest Detroit Area — Air Emission Sources and Air Monitoring Locations

R-009271



Key to Air Sources

Large air emission sources that were required to report air emissions to the 2015 Michigan Air Emissions Reporting System (MAERS)

- Detroit 48217 ZIP Code
- US Steel
- Marathon Refinery
- AK Steel

1. Praxair, Inc.
2. Great Lakes Aggr. Oil Storage
3. DTE – Electric, River Rouge
4. Fritz Products
5. Buckeye Terminals, River Rouge
6. EES Coke Battery
7. U S Steel Great Lakes Works
8. DTE – Electric, Delray
9. Detroit Public Lighting Depart.
10. Carmeuse Lime
11. United States Gypsum
12. Great Lakes Water Authority (Det. Waste Water Treatment)
13. Fabricon Products Inc.
14. Buckeye Terminals
15. St Mary's Cement
16. Great Lakes Petroleum
17. Marathon Petroleum Co.
18. Detroit Salt Co.
19. Cadillac Asphalt Products
20. Sunoco Partners River Rouge
21. Edw C. Levy Co. Plant 6
22. Darling International Inc.
23. AK Steel Dearborn Works
24. Dearborn Industrial Gen.
25. Ford Motor
26. Edw. C. Levy Co. Plant 2
27. Xcel Steel Pickling
28. Edw. C. Levy Co. Plant 1
29. Magni Industries

DEQ Air Monitors

and air sampling measurements

- **AB Ambassador Bridge (W. Lafayette):** *PM2.5 FRM and continuous*
- **CM Community Monitor (48217):** *PM2.5, SO2, VOCs, Metals (TSP), PAHs*
- **DB Dearborn:** *PM2.5, continuous PM2.5, PM2.5 spec., PM10, continuous PM10, metals (PM10 and TSP), PAHs, VOCs, carbonyls*
- **FS Fort Street (South West HS):** *PM10, PM2.5, PM2.5 spec., SO2, VOCs, carbonyls, metals (PM10 and TSP)*
- **RR River Rouge:** *PM10, metals (PM10 and TSP), carbonyls*
- **WJ West Jefferson:** *metals (TSP)*

Windsor Air Monitors: (Ontario Ministry of Environment) *Ozone, PM2.5, CO, SO2, NO2*

Marathon Monitors: *PM10, CO, SO2, Total Reduced Sulfur, VOCs*

N W E S

ABBREVIATIONS

CO: carbon monoxide
FRM: federal reference method
NO2: nitrogen dioxide
PM2.5: particulate matter <2.5µm diameter
PM10: particulate matter <10µm diameter
PAHs: polycyclic aromatic hydrocarbons
Spec.: speciation
SO2: sulfur dioxide
TSP: total suspended particulate
VOCs: volatile organic compounds

Michigan Department of Environmental Quality
Air Quality Division August 19, 2016

City of Chicago
DOB New Applications for Ward 10

03/11/2020

Application Number : 100866729

Processed	Application Type	Display Address	Description of Work	Declared Valuation
03/11/2020	PERMIT - EASY PERMIT PROCESS	13045 S ESCANABA AVE CHICAGO IL 60633-	DETACHED FRAME GARAGE WITH SIDE DRIVE 24'X 24'	$28,170.00

Capacity		Applicant Contact Name	Applicant Contact Day Phone
APPL		THE GARAGE GUY INC	(773)583-8800
OTHER	EMERGENCY CONTACT	RANDY HARLEY	(773)583-8800
OTHER	OWNER OCCUPIED	THE GARAGE GUY INC	(773)583-8800
OTHER	OWNER OCCUPIED	WILLIAM CUADRADO	(773)491-3529

Application Number : 100866826

Processed	Application Type	Display Address	Description of Work	Declared Valuation
03/11/2020	PERMIT - NEW CONSTRUCTION	11554 S AVENUE O CHICAGO IL 60617-	*DIRECT DEVELOPER SERVICES * NEW CONSTRUCTION - PREFABRICATED METAL FRAME BUILDING BUILDING ON CONCRETE FOUNDATION FOR PROCESS EQUIPMENT; CLASS IV-A RECYCLING FACILITY.	$9,000,000.00

Capacity		Applicant Contact Name	Applicant Contact Day Phone
OWNER		HAL TOLIN	(773)382-0123

Application Number : 100866908

Processed	Application Type	Display Address	Description of Work	Declared Valuation
03/11/2020	PERMIT - ELECTRIC WIRING	2802 E 87TH ST CHICAGO IL 60617-	**ELECTRICAL ONLY PERMIT**400AMP SERVICE UPGRADE INCLUDES RISER, 3-GANG METER SOCKET, (3)100AMP PANELS AND GROUNDING. FOR MIXED-USE BUILDING.	$4,500.00

Capacity		Applicant Contact Name	Applicant Contact Day Phone
APPL		MICHAEL PETWAY	(773)354-9693
APPL		MICHAEL PETWAY	(773)354-9693

City of Chicago
DOB New Applications
for Ward 10
03/11/2020

Application Number : 100866910

Processed	Application Type	Display Address	Description of Work	Declared Valuation
03/11/2020	PERMIT - ELECTRIC WIRING	2802 E 87TH ST CHICAGO IL 60617-	**ELECTRICAL ONLY PERMIT****ELECTRICAL ONLY PERMIT**400AMP SERVICE UPGRADE INCLUDES RISER, 3-GANG METER SOCKET, (3)100AMP PANELS AND GROUNDING. FOR MIXED-USE BUILDING.	$4,500.00

Capacity	Applicant Contact Name	Applicant Contact Day Phone
APPL	MICHAEL PETWAY	(773)354-9693
APPL	MICHAEL PETWAY	(773)354-9693

Total number of applications for Ward 10 for 03/11/2020	4
Total value of construction for Ward 10 for 03/11/2020	$9,037,170.00

Total number of applications for Ward 10 for this period	***4***
Total value of construction for Ward 10 for this period	***$9,037,170.00***

CRAIN'S CHICAGO BUSINESS

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Why this industrial developer is making a big—and risky—bet on the city

NorthPoint Development is making a big, and some might say contrarian, bet on the city at a time when most industrial developers are stamping out huge warehouses in far-flung suburbs.

ALBY GALLUN

Scott Shigley

The former Republic Steel site on the city's Southeast Side.

NorthPoint Development is making a big, and some might say contrarian, bet on the city at a time when most industrial developers are stamping out huge warehouses in far-flung suburbs.

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NorthPoint Development's Tom George says transforming the property won't be easy: "The site is definitely a challenge."

Nearly two decades after workers punched out of their last shift at the Republic Steel factory on Chicago's Southeast Side, Tom George wants to remake the place so a new generation of workers can punch in.

George is overseeing a $164 million plan to turn the long-vacant site in Hegewisch into an industrial park that will employ as many as 660 people. With 2.3 million square feet of buildings spread over 196 acres, it would be the largest industrial development in Chicago since the creation of the neighboring 1.6 million-square-foot Ford supplier park more than 15 years ago.

It's a big, and some might say contrarian, bet on the city at a time when most industrial developers are stamping out huge warehouses in far-flung suburbs, where they can find plenty of land close to interstate highways, a key draw for tenants in trucking and logistics businesses. And in a postindustrial economy, it's companies that ship and store goods, not ones that make them, that eat up the vast majority of new industrial space today.

But the Republic Steel site is close to something else—a large labor pool—that may give George an edge as he courts tenants in a metro area with an unemployment rate hovering around 4 percent.

"The reality is that market forces are at a point where development of some of these sites, we believe, makes sense," says George, vice president at NorthPoint Development, the suburban Kansas City, Mo.-based firm backing the project. "I will admit that we're early . . . but we believe that

the market is there, that the search for employees and employable people is reaching an all-time high."

Mayor Rahm Emanuel is hoping he's right. The mayor's administration pushed for a $52 million tax-increment financing subsidy for the project, citing the jobs it would create. Including the 660 people expected to work for tenants there, the development will employ 650 construction workers, according to the city.

That's a lot by today's standards but a small fraction of Republic Steel's workforce back in the day. By one count, the factory's employment peaked at more than 6,300 in 1970, declining from there as domestic steelmakers struggled to keep up with overseas competitors. LTV, which took over Republic Steel in 1984, went bankrupt and closed the factory in 2001, ending nearly a century of steelmaking on the site.

The stark difference in past and projected employment underscores how foreign competition, automation and other efficiency gains have transformed the manufacturing sector over the past half-century. The trend has continued through the current economic expansion: Just 63,468 people worked in manufacturing in the city in 2018, down 3 percent from 2011, according to data from the Illinois Department of Employment Security.

Today, companies in transportation, distribution and logistics are driving demand for industrial space—and for workers. Employment in the transportation and warehousing sectors has eclipsed that for manufacturing in the city, rising to 67,970 in 2018, up 19 percent from 2011, according to IDES. The big growth in shipping and distribution—fueled in part by the rise of e-commerce—is a big reason industrial is arguably the hottest real estate sector in the Chicago area right now: The local industrial vacancy rate dropped to 6.34 percent at the end of 2018, its lowest level since 2001, according to Colliers International.

Though most of the action is out in the far suburbs along Interstates 88 and 55, industrial development has picked up near O'Hare International Airport and in the city. Many tenants, especially those in food and consumer products, want to be in "last-mile" locations close to big population centers, allowing them to limit delivery times. Northbrook-based Hilco Redevelopment Partners, for instance, plans a 1 million-square-foot warehouse in Little Village, just off I-55.

"Developers as a whole have been rewarded for having the guts to build in the city," says Colliers Executive Vice President Michael Senner.

LAND APLENTY

Aside from labor, the city offers another thing developers like: land. The deindustrialization of Chicago has left the city with more than 3,700 acres, or about 5.8 square miles, of vacant industrial property, according to the Cook County assessor. Three Chicago Loops would fit in that much

space, with plenty of land left over. The bulk of the vacant land, about 1,900 acres, sits in Hyde Park Township, a big area that includes much of the South Side, including the Republic Steel site and the massive South Works steel-mill site on the south lakefront.

George says NorthPoint has already fielded some inquiries from companies interested in moving to its project, called the Avenue O Industrial Park. He expects to lease the space to a mix of tenants in logistics, distribution and manufacturing. NorthPoint is getting ready to break ground on its first building, a 359,000-square-foot structure at Avenue O and 122nd Street. It is moving forward with construction on speculation, or spec, without lining up a tenant in advance.

The project could benefit from its proximity to Ford's big assembly plant, just around the corner, at Torrence Avenue and 130th Street. The Ford supplier park, which NorthPoint acquired in 2017, is full, with tenants including Tower International, which makes car frames, and Flex-N-Gate, which makes bumpers and other parts. Other auto-parts manufacturers may decide it's in their benefit to be close to the Ford plant as well.

Transforming the site into a 21st-century industrial park won't be easy. A few remnants of the old Republic Steel complex remain, including some neighboring industrial buildings along the Calumet River that aren't owned by NorthPoint. Nature has reclaimed some of the property, including a small herd of deer spotted on a recent site tour.

But much of the property is covered in slag, a nontoxic concrete-like byproduct of the steelmaking process. To prepare the site for construction, NorthPoint's contractors will need to drop huge weights from cranes—a process known as dynamic compaction—and haul in about 4 feet of soil to raise the buildings above the slag and the high water table. Much of the city's TIF subsidy will cover those site-prep costs, George says. "The site is definitely a challenge," he says.

Yet city officials hope the project will mark another in a series of steps to foster industrial development in Chicago. David Reifman, commissioner of the Chicago Department of Planning & Development, cites encouraging signs in nearby Pullman, where Method opened a soap factory several years ago and where Whole Foods recently moved into a large distribution center. And he touts a push to modernize and strengthen the city's system of industrial corridors.

"These kinds of victories are hard-fought, and I think they show continued vitality in the industrial sector," Reifman says.

Inline Play

By Rachel Morello-Frosch, Miriam Zuk, Michael Jerrett, Bhavna Shamasunder, and Amy D. Kyle

Understanding The Cumulative Impacts Of Inequalities In Environmental Health: Implications For Policy

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ABSTRACT **Racial or ethnic minority groups and low-income communities have poorer health outcomes than others. They are more frequently exposed to multiple environmental hazards and social stressors, including poverty, poor housing quality, and social inequality. Researchers are grappling with how best to characterize the cumulative effects of these hazards and stressors in order to help regulators and decision makers craft more-effective policies to address health and environmental disparities. In this article we synthesize the existing scientific evidence regarding the cumulative health implications of higher rates of exposure to environmental hazards, along with individual biological susceptibility and social vulnerability. We conclude that current environmental policy, which is focused narrowly on pollutants and their sources, should be broadened to take into account the cumulative impact of exposures and vulnerabilities encountered by people who live in neighborhoods consisting largely of racial or ethnic minorities or people of low socioeconomic status.**

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The persistence of health disparities and environmental inequalities in the United States has placed environmental health science and policy at a crossroads. Innovative scientific and regulatory approaches are needed to understand and address the cumulative, and potentially synergistic, effects of environmental and social stressors on the health of communities whose populations are mostly composed of racial or ethnic minorities or people of low socioeconomic status.

Advocates for such communities have long argued that their neighborhoods are beset by multiple environmental stressors, which could include air and water pollution and substandard housing. These community leaders also contend that existing regulations fail to protect residents adequately because the regulations are focused narrowly on pollutants and their sources.[1] Growing evidence shows that social stressors—including poverty, racial discrimination, crime, malnutrition, and substance abuse—also affect these communities.[2] Research is beginning to show how the cumulative effects of social and environmental stressors can work in combination to produce health disparities.[3]

With encouragement from scientists, policy makers, and environmental justice groups, regulatory agencies are beginning to consider the methodological challenges of addressing cumulative impacts in science and decision making.[4–6] These methodological challenges include how to evaluate and characterize the combined health effects of multiple environmental and social stressors on vulnerable populations, including the stressors' sources and the pathways of diseases. For example, the US Environmental Protection Agency has proposed a model for including psychological and social factors as integral components of cumulative risk assessment for predicting the potential health effects of pollu-

tion exposures in vulnerable populations.[7]

This article presents a synthesis of relevant research from the fields of social and environmental epidemiology, exposure assessment, and environmental justice. We believe that four key concepts underlie the emerging knowledge about the cumulative impacts of exposure to environmental hazards and social stressors.

First, health disparities between groups of different racial or ethnic makeup or socioeconomic status are significant and persistent, and exist for diseases that are linked to social and environmental factors. Second, inequalities in exposures to environmental hazards are also significant and persistent, and are linked to adverse health outcomes. Third, intrinsic biological and physiological factors—for example, age or genetic makeup—can modify the effects of environmental factors and contribute to differences in the frequency and severity of environmentally related disease. And fourth, extrinsic social vulnerability factors at the individual and community levels—such as race, sex, and socioeconomic status—may amplify the adverse effects of environmental hazards and can contribute to health disparities.

We highlight the evidence for these four concepts and conclude with a discussion of how this scientific foundation can help reshape regulatory science and decision making to reduce environmental health disparities and promote environmental justice among diverse communities.

Health Disparities

Research has documented systemic disparities in the incidence and severity of diseases between socioeconomic and racial or ethnic groups. A wide range of material, behavioral, psychosocial, environmental, and biological factors have been proposed to explain why social status is persistently linked to health.[2] Three health outcomes have been shown to be associated with both social and environmental stressors: adverse perinatal outcomes such as low birthweight and prematurity, cardiovascular disease, and self-rated health.

PERINATAL OUTCOMES African American infants are more likely to be delivered preterm and have low birthweight than white infants. These differences can result in higher risks of long-term health problems such as cognitive deficits, cardiovascular disease, and diabetes.[8] Socioeconomic and behavioral factors such as the mother's education, access to prenatal care, and substance use have been shown to contribute to poor perinatal outcomes—again, low birthweight and prematurity among them.[8] Research also indicates that prenatal stress resulting from maternal perceived discrimination, neighborhood deprivation, segregation, and income inequality are also linked to these poor perinatal outcomes, which suggests the importance of psychosocial pathways in the production of these racial or ethnic disparities.[9,10]

CARDIOVASCULAR DISEASE African Americans and people of low socioeconomic status have significantly higher rates of hypertension, heart disease, and stroke than whites and people of higher socioeconomic status.[11] Cardiovascular disease disparities have been linked to differences in biological risk factors such as diabetes, behavior such as physical inactivity, and the availability and use of primary and secondary preventive services.[12] Neighborhood environments have been linked to both the prevalence of heart disease and its risk factors.[13] Environmental pollutants, such as lead and ambient particulate matter—for example, extremely fine particles released into the air by vehicles and industrial plants that burn fossil fuels—have been linked to higher risk of cardiovascular disease.[14,15]

Emerging research has also linked the risk of developing cardiovascular disease in adulthood to early life events such as prenatal stress, which can disrupt development and cause heritable changes in gene expression. These so-called epigenetic changes can affect which genes are switched "on" or "off," which in turn can be associated with heightened disease risk.[16]

SELF-RATED HEALTH Self-rated health—a well-validated predictor of mortality, physical disability, chronic disease status, and health behavior[17]—is lower among racial and ethnic minorities and people of low socioeconomic status than others.[18] Researchers have found that racial disparities in self-rated health persist even after differences in socioeconomic status are controlled for.[19] The neighborhood people live in has been found to account for a large portion of the disparities between the way African Americans and whites rate their own health status.[20] This difference may be related to factors such as individual socioeconomic status, perceptions of neighborhood quality, health behavior, environmental quality, and psychosocial stress.[21]

Environmental Hazard Inequalities

Greater exposure to environmental hazards is one driver of health disparities found among communities of racial or ethnic minorities and those of low socioeconomic status. Research in this field has expanded from an initial focus on how close residents live to an environmental hazard, such as a highway or a major industrial facility, to encompass a broader investigation of

Poor communities suffer from a dearth of health-promoting resources.

the role that place plays in health. For example, a poor community populated by racial or ethnic minorities may also lack healthy food options,[22] high-quality green spaces, and recreational programs.[23] The lack of these positive factors can contribute to poor health.

PROXIMITY TO POLLUTING LAND USES AND TOXIC EMISSIONS Numerous studies have documented the disproportionate location of hazardous waste sites, industrial facilities, sewage treatment plants, and other locally undesirable and potentially polluting land uses in communities of racial or ethnic minorities and in socially disadvantaged neighborhoods.[24–26] Residents living near such facilities can be exposed to more pollutants than people who live in more affluent neighborhoods located farther from these sources of pollution.[27]

The residents of communities near industrial and hazardous waste sites experience an increased risk of adverse perinatal outcomes, respiratory and heart diseases, psychosocial stress, and mental health impacts.[28,29] Members of racial or ethnic minority groups and people of low socioeconomic status are also more likely than others to live near busy roads, where traffic-related air pollutants concentrate.[30] Research has linked a wide array of adverse health outcomes to residential proximity to traffic, including asthma,[31] low birthweight,[32] cardiovascular disease,[33] and premature mortality.[34]

EXPOSURES TO POLLUTANTS The poor and racial or ethnic minorities are disproportionately exposed to ambient air pollutants, which have been linked to respiratory and cardiovascular disease, adverse perinatal outcomes, diabetes, premature mortality, and other adverse effects.[35–38] Indoor environments also contribute to exposure disparities. Studies have found higher levels of indoor pollutants such as lead-based paint[39] and pollutants from industrial and transportation sources[40] in poor, African American, and Hispanic households than in other households.

Occupational exposures also constitute a source of environmental inequalities. For instance, Mexican American farm workers experience heightened exposure to organophosphate pesticides, which are associated with increased risk of cancer; preterm birth; and neurological, cardiovascular, and respiratory diseases.[41]

NEIGHBORHOOD ENVIRONMENTS Poor communities have an excess of health-damaging factors and a shortage of health-promoting amenities.[42] For example, residents of disadvantaged neighborhoods are exposed to more fast-food restaurants[43] and liquor stores than members of other communities. In particular, the presence of neighborhood liquor stores can influence health behavior and violence and can affect health both directly and indirectly.[44]

As noted above, poor communities also suffer from a dearth of health-promoting resources such as healthy food,[22] green spaces, and recreational programs,[23] whose lack can contribute to disparities in obesity rates and stress levels.[45,46] The confluence of these and other place-based factors contribute to the association between neighborhood socioeconomic status and adverse health outcomes.[20]

Intrinsic Factors: Biological Susceptibility

We use the term *susceptibility* to refer to intrinsic biological traits related to age, genetics, or preexisting health conditions that can create much variability in response to environmental stressors within a population.

AGE Children and the elderly experience heightened risk of pollution-related morbidity and mortality. The elderly are more susceptible to pollutant exposures because of their altered immune response and weakened respiratory and cardiovascular systems.[47] Children's susceptibility is associated with differences in rates of absorption, distribution, metabolism, and excretion of chemicals.[48] Exposure to stressors during childhood can greatly affect the development and functioning of organ systems well into adulthood.[49] Children have the potential for increased exposures to pollution because of their physical and behavioral activities, such as playing outside and frequent hand-to-mouth activity. Thus, their biological susceptibility combined with greater exposure to potentially toxic substances may put them at increased risk.

GENETICS AND GENE EXPRESSION Studies have found that certain genetic variants increase the effect of air pollution on respiratory symptoms, lung functioning, and asthma.[50] Where a child lives early in life, and the substances he or she is exposed to, can affect the development of disease in later life. These exposures may modify the patterns of gene expression—that is, turn genes "on" or "off"—which in turn triggers physiologic

changes and can potentially launch disease processes such as asthma or cancer.[16]

PREEXISTING HEALTH CONDITIONS Preexisting health conditions including diabetes, obesity, and cardiovascular disease can increase individual susceptibility to pollutant exposures. Studies have found that people with diabetes or a history of myocardial infarction are at heightened risk of cardiovascular morbidity and mortality associated with exposure to particulate matter.[51,52] In the United States, African Americans, Hispanics, and people of low socioeconomic status have higher rates of obesity, cardiovascular disease, and type 2 diabetes and are therefore more susceptible to environmental stressors.[11,53] Research is just beginning to link these disparities in preexisting conditions with neighborhood conditions.[45]

Extrinsic Factors: Social Vulnerability

We use the term *vulnerability* when describing how social constructs of race and class can amplify the effects of environmental exposures, with a focus on the pathway of psychosocial stress. We classify race as a social construct and not as a proxy for biological differences because research has consistently shown that race is a poor indicator for genetic variation in human populations and therefore should be understood as a social rather than biological category.[54]

Studies are uncovering the heightened vulnerability of people who belong to racial or ethnic minority groups or are of low socioeconomic status to environmental agents—a disparity that is not attributable to biological factors. Extrinsic factors that are socially related—such as race, ethnicity, socioeconomic status, and sex—can enhance the adverse effects of environmental exposures, such as short- and long-term exposures to air pollution.[55] Low neighborhood-level socioeconomic status may also amplify the risk of air pollution–related preterm births,[56] lower birthweight,[57] and adult mortality.[58]

Psychosocial pathways may link race and socioeconomic measures at the individual and area levels with the increased adverse impacts of environmental stressors. For example, studies indicate that exposure to violence and family stress increases the effects of traffic-related air pollution exposures on childhood asthma.[59,60] Low socioeconomic status and race or ethnicity have been linked to perceived stress as well as to biological markers of chronic stress.[61]

In addition to the direct effects of discrimination, social exclusion, and low socioeconomic status, the social and physical conditions of disadvantaged neighborhoods are also thought to contribute to psychosocial stress levels.[3] Researchers have proposed that the cumulative biological burden exacted by ongoing disruption of the body's stress-response system may explain the self-reinforcing effects or synergies observed among environmental and psychosocial stressors and may produce health disparities.[62,63]

Preexisting health conditions can increase individual susceptibility to pollutant exposures.

The cumulative physiological "wear and tear" resulting from chronic overactivity of the body's stress-response system may impair immune functioning and increase vulnerability to stressors[64] by increasing the absorption of toxicants into the body through increased respiration, perspiration, and consumption;[65] compromising the body's defense systems against toxicants; affecting the same physiological processes as environmental agents; and directly causing illness.[62]

Discussion

We have synthesized the scientific evidence underlying the cumulative impacts of environmental and social stressors and the multiple ways they can have a greater impact on communities of people who belong to racial or ethnic minority groups or are of low socioeconomic status. The four concepts of cumulative impacts that we outlined above have complex interrelationships and feedback loops (see the Appendix).[66]

Regulatory science and decision making must better integrate these four elements of cumulative impacts as a result of combined exposures, possible overlapping mechanisms and pathways for adverse health effects, and the potential for synergistic effects.[7] The National Research Council has also supported expanding scientific efforts to understand and address the multiple environmental and social stressors affecting community health.[67]

CUMULATIVE IMPACT ASSESSMENTS Regulatory agencies at the federal, state, and local levels are beginning to incorporate elements of cumulative impacts such as those described above into

The burden of proof is now placed on communities to demonstrate cumulative impacts.

assessment and planning procedures.[4,6] Nevertheless, the complexity of the task and the scarcity of scientific information and specific methodologies for assessing these cumulative effects have limited the scope of this work to date.[67]

One important challenge is how to characterize and mathematically model the interactions among environmental and social stressors, sources, pathways, and routes. Researchers are beginning to develop indices for aggregating environmental and social stressors. For example, Jason Su and colleagues developed an index to characterize social inequities in the cumulative effects of multiple air pollutants from both mobile and stationary sources at the regional level.[68] Still, the work to develop more sophisticated tools for assessing cumulative impacts and environmental disparities is in its infancy, and investigators are uncertain about the best way to cumulate and deal with interactions and overlapping components or pathways.

Fundamental to further work in this area is the need to better incorporate vulnerability into environmental health research, assessments, policies, and actions.[1] Current risk assessment practices address differential susceptibility for certain intrinsic biological factors (for example, age) by applying safety or default factors to protect biologically sensitive populations (such as children) in limited cases. However, the environmental risk assessment process does not apply such approaches to extrinsic factors—including neighborhood poverty, unemployment, lack of food security, and other psychosocial stressors—that can contribute to the heightened vulnerability of disadvantaged communities).[1,7,67] One potential reason for this omission is the persistent debate over pathways linking social vulnerability to environmental exposures. Researchers have established many dimensions of social vulnerability such as human and political capital, discrimination, and features of the built environment,[2] which should be taken into account in environmental health research and assessment practices.

Health impact assessment is an interdisciplinary approach to assessing the consequences of proposed policies, plans, and projects. This type of assessment features an explicit concern for socially excluded or vulnerable populations and uses a combination of quantitative, qualitative, and participatory techniques.[68–70] Health impact assessment may provide a promising path for incorporating cumulative impacts into assessments to guide decision making.

By considering together the baseline environmental conditions, health status, and vulnerabilities of the communities potentially affected by decisions, health impact assessments have the potential to address the complex causal pathways through which decisions can affect health.[71] Compared to risk assessment, which is mostly quantitative, health impact assessment is better able to deal with a scarcity of scientific information because it uses a diverse array of evidence for analysis—for example, epidemiological evidence along with qualitative observations of neighborhood social conditions and physical environments.

The inclusion of a broader array of evidence may result in more efficient and proactive measures than risk assessments, which rely heavily on toxicological evidence.[71,72] A key challenge, however, will be systematically integrating the health impact assessment process into environmental regulation and decision making.

POLICIES TO ADDRESS CUMULATIVE IMPACTS

The evidence that environmental and social stressors converge in disadvantaged communities and that residential context plays an important and independent role in health disparities indicates the need for targeted place-based and proactive approaches to policy making. One approach is to use cumulative impact screening to map, characterize, and target vulnerable communities for interventions that improve existing conditions and prevent future harm.[1]

The burden of proof is now placed on communities to demonstrate cumulative impacts, yet many disadvantaged neighborhoods may lack political clout or the capacity for civic engagement to push for regulatory action. The use of cumulative impact screening could remove this burden of proof from vulnerable communities and increase the likelihood that disadvantaged neighborhoods will receive focused regulatory attention.

Several agencies, such as the Environmental Protection Agency, are beginning to develop such tools to target enforcement and compliance activities nationally,[73] guide land use planning in California,[74] and inform regulatory programs at the California Air Resources Board.[75] As with health impact assessments, a critical issue will

be the linkage between assessments and the decision making authorities of the agencies.

Progressive approaches coming from local governments can provide some guidance for ways to systematically address cumulative impacts in vulnerable communities. The Environmental Justice Ordinance in Cincinnati, Ohio, for instance, requires new or expanding industrial facilities to demonstrate that they will not cause a "cumulative adverse impact" to the health and environment of the community in order to receive a permit.[76]

Similarly, Los Angeles is considering a "green zones" ordinance, which would use cumulative impact screening to guide municipal planning, the issuing of permits, and enforcement strategies to mitigate and reduce environmental hazards in disproportionately affected neighborhoods.[77,78] Such strategies could provide a more place-based, holistic, and proactive approach to environmental protection.

Conclusion

Communities of racial or ethnic minorities or people of low socioeconomic status are particularly vulnerable to environmental and social stressors. More holistic and transparent approaches to the regulatory science underlying decision making that affects such communities are needed. Screening methods can help regulators and policy makers more efficiently target efforts to remediate the cumulative effects of these exposures and environmental inequities, and to focus regulatory action at the neighborhood and regional levels. Because industrial and transportation development, as well as other land-use planning decisions, are often rooted within metropolitan regions and neighborhoods, regulatory interventions to mitigate the cumulative impact of environmental and social stressors on the health of disadvantaged communities will require multilevel, placed-based strategies.[79] ■

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ABOUT THE AUTHORS: RACHEL MORELLO-FROSCH, MIRIAM ZUK, MICHAEL JERRETT, BHAVNA SHAMASUNDER & AMY D. KYLE

Rachel Morello-Frosch is an associate professor at the University of California, Berkeley.

In this issue of *Health Affairs*, Rachel Morello-Frosch and coauthors make the case that regulators need to consider the cumulative effects of various environmental and social stressors on poorer communities or those populated by racial and ethnic minorities. It's not enough to look just at the impact of exposure to a particular chemical, for example. Studies have found that chronic social stress, such as being poor or being discriminated against racially, can make individuals and communities more vulnerable to environmental hazards.

Yet "policy makers have been slow to respond to the scientific evidence," Morello-Frosch says. She hopes that this article will encourage them to take a broader view of the causes of health concerns and look into the cumulative effect of various stressors.

Morello-Frosch is an associate professor at the University of California (UC), Berkeley, in both the Department of Environmental Science, Policy, and Management and the School of Public Health. She received both her doctoral degree in environmental health sciences and her master of public health degree in epidemiology and biostatistics from UC Berkeley. In 2010 she was awarded the American Public Health Association's Damu Smith environmental health achievement award.

Miriam Zuk is a graduate student in city and regional planning at UC Berkeley.

Miriam Zuk is a doctoral candidate in city and regional planning at the University of California, Berkeley.

Michael Jerrett is an associate professor in the Division of Environmental Health Sciences at the UC Berkeley School of Public Health. He received both his doctorate in geography and his master's degree in political science from the University of Toronto. In 2010 he was appointed to the National Academies Committee on Human and Environmental Exposure Science in the Twenty-First Century.

Bhavna Shamasunder is a graduate student in the Department of Environmental Science, Policy, and Management at UC Berkeley.

Bhavna Shamasunder expects to receive her doctoral degree from the Department of Environmental Science, Policy, and Management at UC Berkeley in May 2011.

Amy Kyle is an associate adjunct professor in environmental health sciences at the UC Berkeley School of Public Health. She received both her doctorate in environmental health sciences and her master of public health degree from UC Berkeley.

Assistance with General III document

Geertsma, Meleah <mgeertsma@nrdc.org>

Wed 3/11/2020 6:12 PM

To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Cc: Harley, Keith (kharley@kentlaw.iit.edu) <kharley@kentlaw.iit.edu>

1 attachments (151 KB)
Modeling Protocol Comments.pdf;

Hi Chris -
Reaching out to see if you might be able to help with a General III permit document question.

In reviewing the documents, we've come across several referencing a "modeling protocol" for the proposed new facility (see the attached email exchange). Typically as you know, modeling protocols are lengthy narrative documents explaining choices of inputs and modeling scenarios, with some data and tables as well. But I haven't been able to find any document matching such a description in the documents produced by IEPA in response to our several FOIA requests.

The only documents on the modeling that I've come across are this email and several pages of emissions tables. I'm assuming that there is some narrative, because Jeff Sprague refers explicitly in #2 to "the write-up."

Can you help determine if there is some modeling protocol that we haven't received to date? It's possible I've missed it in my review, so let me know if you're able to ID it in the docs produced to date.

Thanks so much,
Meleah

Sprague, Jeff

From: John Pinion <jpinion@rka-inc.com>
Sent: Monday, November 25, 2019 9:36 AM
To: Sprague, Jeff
Cc: Barria, German; Bernoteit, Bob; Layman, Robb
Subject: [External] RE: Modeling Protocol - General III, LLC
Attachments: 2019-11-21 GIII Modeling Protocol Revised Tables - Appendicies A & B.pdf

RK & Associates, Inc

Jeff,

Thank you for the prompt review of the modeling protcol. You will find our response (in blue text below) immediately following each of your

Please forward any comments or questions you have to my attention.

If you have any questions, please do not hesitate to contact me.

Regards,
John Pinion

RK & Associates, Inc.
2 South 631 Route 59, Suite B
Warrenville, Illinois 60555
Phone: 630-393-9000 x 208
Fax: 630-393-9111
Cell: 630-917-1455
E-mail: jpinion@rka-inc.com

From: Sprague, Jeff <Jeff.Sprague@Illinois.gov>
Sent: Wednesday, November 20, 2019 3:35 PM
To: John Pinion <jpinion@rka-inc.com>
Cc: Barria, German <German.Barria@Illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@Illinois.gov>; Layman, Robb <Robb.Layman@Illinois.gov>; Sprague, Jeff <Jeff.Sprague@Illinois.gov>
Subject: RE: Modeling Protocol - General III, LLC

John,
I've reviewed the electronic version of the modeling protocol, as well as the non-redacted hardcopy version, and have the following remarks for your consideration:

1.) The June-September, 2017 surface meteorological observations for the Midway Airport Station show considerable wind direction/wind speed data missing. If you choose to use the Midway site, I am recommending that you use the data for years 2012-2016. Furthermore, I am recommending that you use the coincident upper air sounding data for Davenport, Iowa in preparing the AERMOD-ready meteorological inputs. To facilitate your efforts, I have attached the surface characteristics files for Midway for your AERMET Stage 3 processing.

RKA will order the 2012 through 2016 met data from Midway Airport and will process the met data using the coincident upper air sounding data for Davenport, Iowa, and the surface roughness files you provided.

2.) The write-up was essentially silent on the issue of ambient air boundaries. It's important that documentation be provided (that is acceptable to IEPA) which demonstrates that the general public is effectively precluded from accessing General III LLC property where receptors have been excluded from the modeling.

There is security fencing on the north boundary and the northern part of the east boundary that leads to a guard shack with gates (occupied or closed when unoccupied). The southern boundary is a combination of fencing and berm, while the west boundary is the river. No Trespassing signs are posted around the boundary and no part of the boundary is adjacent to any public right away, which will limit casual access to the site by the general public.

3.) Building downwash parameters developed for structures other than those owned by General III LLC (i.e. for Reserve Marine Terminals, Regency Technologies, Napuck Salvage of Waupaca, and/or South Shore Recycling) should be based upon dimensional data obtained directly from the other facilities. This is especially true for building height measurements. Relying exclusively upon Google Earth for developing building dimension data can have significant shortcomings.

Drawings of the building with exact dimensions are not available. The coordinates of the building corners were determined using Google Earth. A site representative measured the height of the highest roof top on the two existing buildings south of the proposed GIII location. For the purposes of modeling, the highest roof top height measured for the north and south buildings will be assigned as the roof height for the entire building, which will provide conservative results from the downwash analysis.

4.) If maximum modeled impacts occur within that portion of the receptor grid where initial receptor spacing is greater than 100 meters, then a "sub-grid" of receptors with 100 meter spacing should be incorporated to delineate the "true" peak impact location.

Initial results show that the maximum off site impact occurs in the 100-meter portion of the receptor grid. If the final modeling runs identify impacts beyond the 100-meter receptor grid, a sub grid will be added to the area surrounding the point of maximum impact and the model will be re-run.

5.) Though Wisconsin's NR 445 Air Toxics Rule does not have annual non-carcinogenic ambient air standards for cobalt, cadmium, and nickel, there are "chronic" ATSDR Minimal Risk Levels for these substances, and the modeling analysis should address the maximum modeled concentrations against these levels. Additionally, there is a "chronic" ATSDR Minimal Risk Level for mercury that is tighter than the NR 445 standard, and should preferentially be considered.

The modeling results will consider the ATSDR Minimum Risk Levels for cobalt, cadmium, nickel, and mercury

6.) What are the emission units in Table A-1a and in subsequent tables? Do the values reflect a single hourly value, or do they reflect an aggregate value for all "active hours" (7 AM – 7 PM), "inactive hours" (7 PM – 7 AM), etc., specific to that table? For emissions from stockpiles that are assumed to be active for 12 hours per

day, are you distributing these emissions over 24 hours in developing your modeled emission rate, or are you applying an "active" hourly emission rate to all hours in a day?

The units of the metal emission rates in Tables A-1a, A-1b, B-4a and B-4b are in pounds/hour, based on the design hourly material handling rates.

Active and inactive stockpile emissions represent wind erosion emissions calculated using the spreadsheet available from the following Texas Commission on Environmental Quality (TCEQ) link:

https://www.tceq.texas.gov/assets/public/permitting/air/Guidance/NewSourceReview/emiss-calc-rock1.xlsx

Both the active and inactive stockpile emissions (wind erosion) are calculated as daily emission rates. The daily emission rates are divided by 24 hours per day to obtain hourly emission rates for modeling.

The emission rates for active periods represent normal operation of the site including emissions from all material handling emission points and wind erosion emissions from active stockpiles. The active stockpile emission rate is assigned to the stockpiles during periods when material is being added to, or removed from, a stockpile.

The emission rate for inactive periods represent emissions when material handling equipment is not operating, and emissions are limited to wind erosion emissions from inactive stockpiles. The inactive stockpile emission rate is assigned to the stockpiles during periods when no material is being added to, or removed from, a stockpile.

7.) Please provide a citation/reference for the use of 90% control of stockpile particulate emissions when the stockpile is in a partial enclosure of walls on three sides.

The TCEQ website (see link in the response to Item 6 above) identifies the following control efficiencies applicable to stockpiles. For three sided partial enclosures, the identified control efficiency ranges from 50 to 85% and the average value for this range 67.5% is applied for stockpiles with partial walls on three sides (partial enclosure).

Control Method	Control Eff. (%)	Control Factor (1 - ctrl eff)
None	0	1
Wet material	50	0.5
Water	70	0.3
Chemicals/foam	80	0.2
Partial Enclosure*	50-85	0.5-0.15
Full enclosure*	90	0.1
Enclosed by building*	90	0.1
Washed Sand/gravel	95	0.05
Washed Sand/gravel with water spray	98.5	0.015
Manufacturer Rating	0	0

The stockpile data provided in the initial protocol incorrectly assigned a control value of 0.1 for stockpiles with partial enclosures (partition walls on three sides). An updated set of Appendix A and Appendix B emission tables are attached to this response to identify the updated metal emission rates that incorporate the updated stockpile emission estimates that will be used in the modeling.

8.) Figure A-1 shows two separate volume sources for the "Pokers", yet only one volume source (V-4) representing "Poker Loadout" and "Poker Picker Chute to Stockpile" appears in Table A-2. Similarly, the "Poker North" and "Poker South" stockpile emissions are only represented by volume source V-4 in Table A-3. Will the model have two separate volume sources representing these emissions (for example, V-4a and V-4b), or are the emissions combined into just one volume source (V-4)?

Poker stockpile wind erosion emission are calculated for both the north and south Poker stockpiles. Total Poker stockpile emissions were assigned to a volume source V4 that spatially represents only the north Poker stockpile.

9.) Figures A-1 and B-1 show geometric shapes indicated by dashed and stippled red lines representing an area of emissions that will constitute volume sources. Most of these geometric shapes cannot by themselves represent the final shape and dimensions of volume sources, because volume sources are constrained to be the same length in the "x" and "y" directions. Please provide a table specifying the model inputs for each of the volume sources created and explanatory remarks regarding the release heights of the volume sources and the derivation of initial lateral and vertical dimensions.

The Volume Source outlines on Figures A-1 and B-1 identify the individual emission units that comprise the total volume source emission rate. The model input requires the x and y dimension to be the same and have been input accordingly.

The height of the individual emission units that comprise each volume source is reviewed, and the maximum height is selected as the height of the volume source. The length of the group of sources is selected as the length of the volume source. The volume source parameters to enter in the model were derived as follows:

- Release Height = Volume Source Height divided by 2.0
- Initial Lateral Dimensions = Volume Source Length divided by 4.3
- Initial Vertical Dimensions = Volume Source Height divided by 2.15

The following table provides a summary of the volume source dimensions used as model inputs.

Volume Source	Height of Emission Sources (ft)	Length of Source Group (ft)	Release Height (ft)	Initial Lateral Dimensions (ft) (σ_{y0})	Initial Vertical Dimensions (ft) (σ_{z0})
V1	4	10	2.00	2.3256	1.8605
V2	60	84	30.00	19.5349	27.9070
V3	4	6	2.00	1.3953	1.8605
V4	25	50	12.50	11.6279	11.6279
V5	25	20	12.50	4.6512	11.6279
V6	35	60	17.50	13.9535	16.2791
V7	30	20	15.00	4.6512	13.9535
V8	30	20	15.00	4.6512	13.9535
V9	25	25	12.50	5.8140	11.6279
V10	6	20	3.00	4.6512	2.7907
V11	35	120	17.50	27.9070	16.2791
V12	35	120	17.50	27.9070	16.2791
V13	6	20	3.00	4.6512	2.7907
VN1	40	100	20.00	23.2558	18.6047
VN2	40	100	20.00	23.2558	18.6047
VN3	25	100	12.50	23.2558	11.6279
VN4	25	100	12.50	23.2558	11.6279
VN5	25	100	12.50	23.2558	11.6279
VN6	25	40	12.50	9.3023	11.6279

0.70884288

0.5670804

If you should have any questions in regard to these comments, please feel free to contact me.

Best regards,

Jeff

Jeffrey Sprague
Modeling Unit, Manager
Air Quality Planning Section
Bureau of Air
Illinois Environmental Protection Agency

(217) 524-4692
Jeff.Sprague@Illinois.gov

From: John Pinion <jpinion@rka-inc.com>
Sent: Tuesday, November 19, 2019 9:35 AM
To: Sprague, Jeff <Jeff.Sprague@Illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@Illinois.gov>
Cc: 'Freeborn & Peters LLP; Zwick, Ann (azwick@freeborn.com)' <azwick@freeborn.com>; GII, LLC; Labkon, Adam (adamlabkon@general-iron.com) <AdamLabkon@General-Iron.com>; GII, LLC; Kallas, Jim (jimkallas@general-iron.com) <jimkallas@general-iron.com>
Subject: [WARNING: ATTACHMENT UNSCANNED][External] Modeling Protocol - General III, LLC

RK
& Associates, Inc.

Jeff,

Please find attached a copy of the modeling protocol for metal emission impacts from the proposed General III, LLC scrap metal recycling facility at 11600 South Burley Avenue in Chicago.

Please note that the attached copy has Figures A-1, A-2, B-1 and B-2, that depict the Ferrous Material Processing System and Non-Ferrous Material Processing Facilities, are redacted and marked as Trade Secret.

We will be submitting two hard copies of the protocol to your attention, one will be the attached redacted copy and the other will be an unredacted copy containing the above referenced figures marked as Trade Secret. A Justification for Trade Secret information will also be submitted with the hard copies.

The Trade Secret figures are essentially identical to the figures submitted to IEPA on November 14, 2019, with Justification for designation as Trade Secret. The only difference is that Figures A-1 and B-1 show the limits of the multiple volume sources used for modeling.

The tables, in Appendix A and B, that identify the individual emission sources included in each proposed volume sources are not claimed as Trade Secret.

If you have any questions, please do not hesitate to contact me.

Regards,
John Pinion

RK & Associates, Inc.
2 South 631 Route 59, Suite B
Warrenville, Illinois 60555
Phone: 630-393-9000 x 208
Fax: 630-393-9111
Cell: 630-917-1455
E-mail: jpinion@rka-inc.com

Print Cancel

To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Cc: EXT Harley, Keith <kharley@kentlaw.iit.edu>
Subject: [External] Re: Illinois EPA FOIA Response

Thanks Chris - the modeling documents omission makes sense given my recent query about the modeling protocol and IEPA's response. A call as you propose sounds good. My schedule is pretty haphazard these days, but I can likely do tomorrow (Thurs) early afternoon or 4-5, or Friday morning between about 9 and noon.

Best,
Meleah

From: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Sent: Wednesday, March 25, 2020 12:10 PM
To: Geertsma, Meleah <mgeertsma@nrdc.org>
Cc: EXT Harley, Keith <kharley@kentlaw.iit.edu>
Subject: RE: Illinois EPA FOIA Response

Hello Meleah –

There are definitely more documents and it is not boilerplate language. I think the answer may be that records never got files from the modeler although some of that information maybe in the previous permit files. This has been a bit difficult for me to bird dog since I have not seen the files myself and have been corresponding via email about the information. If you thought a quick call with me and the manager of the Records Unit would be helpful (I think it might) then I could arrange that. He is in the office (I am working from home) and we could go over the information to determine if it is indeed information you want.

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Wednesday, March 25, 2020 11:19 AM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Cc: EXT Harley, Keith <kharley@kentlaw.iit.edu>
Subject: [External] Fw: Illinois EPA FOIA Response

Hi Chris - touching base on our recent renewed FOIA request for documents related to 11600 S Burley. You had previously indicated that the agency did not have any new submissions from the applicant, I believe; I'm wondering whether the response I received below indicates that there may be paper file submissions of which you were not aware, or if this effort is more standard protocol to make sure nothing is being missed (but it's unlikely there are any responsive paper files).

Could you circle back around with the permitting and enforcement folks to see if you can get some clarity on this question? It would be helpful given the additional time delay in response, esp if IEPA continues to move forward with the permitting process.

Best,
Meleah

From: Johnson, AJ <Anwar.Johnson@illinois.gov>
Sent: Tuesday, March 24, 2020 2:12 PM
To: Geertsma, Meleah <mgeertsma@nrdc.org>
Cc: Dowson, Sharon <Sharon.Dowson@Illinois.gov>
Subject: FW: Illinois EPA FOIA Response

R 009294

RE: Update on metals recyclers?

Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Thu 4/2/2020 9:04 AM
To: Geertsma, Meleah <mgeertsma@nrdc.org>

Good morning Meleah –

I wholeheartedly agree and obviously I am frustrated as well. This is why I have parroted internally what Keith has been saying for a while, which is to get more information online. Unfortunately, in discussing this with the Records Unit and others it is not that simple to have everything scanned up front and on the web. For General Iron, various people are maintaining files and the Records Unit does not know who those people are unless someone tells them. Furthermore, I do not know either since I am not in the Bureau of Air actively working on the project. In my old role, I would have had a better idea who exactly was doing what on a project. As you can see, this whole process is very dependent on humans catching things thus the issues.

At any rate, yes, let's continue to work together and brainstorm on ways to improve the process.

Best,

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Wednesday, April 1, 2020 10:20 AM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Subject: [External] Re: Update on metals recyclers?

Hi Chris - circling round on this prior exchange to note that, in the course of reviewing materials from IEPA sent in response to our most request FOIA request, there are a number of items that appear to date between our Jan meeting with IEPA and early Feb when I circled around with you below. This is on top of the air quality modeling protocol that was mistakenly left out of early FOIA responses due to it appears lack of checking with the modeling folks.

This is not to critique your role, but to simply point out that there's a need for greater transparency, clarity and timeliness around permitting documents on the agency's side. Look forward to working with you to try to improve the situation!

Best,
Meleah

From: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Sent: Friday, February 7, 2020 5:02 PM
To: Geertsma, Meleah <mgeertsma@nrdc.org>
Subject: RE: Update on metals recyclers?

Hello Meleah –

I checked with legal and permits and they did not think anything new has been submitted since the last FOIA although we will probably receive its response to the VN very soon. I will be out on Monday and back in the office on Tuesday, although it seems you may be traveling by then.

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284

R 009295

(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Wednesday, February 5, 2020 9:23 AM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Subject: [External] Update on metals recyclers?

Hi Chris –
Circling around to see if you have any updates that you can share on the metals recyclers, both/either the permitting for General III and the permitting/investigation of the S Burley facilities. I also wanted to touch bases to see if you have any thoughts on the best way for us to keep current on records requests, re our discussion of FOIAs on the call with IEPA staff.

It would be great if we could connect before this upcoming Tues, as I then head into a stretch of work travel and vacation.

Thanks,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

NATURAL RESOURCES
DEFENSE COUNCIL
20 N. WACKER DRIVE, SUITE 1600
CHICAGO, IL 60606
T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

R 009296

RE: Question on General III documents

Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Tue 5/5/2020 2:56 PM

To: Geertsma, Meleah <mgeertsma@nrdc.org>
Cc: Sprague, Jeff <Jeff.Sprague@Illinois.gov>

Hello Meleah –

Jeff and I were able to access the spreadsheet via this link: https://www.tceq.texas.gov/assets/public/permitting/air/Guidance/NewSourceReview/emiss-calc-rock1.xlsx. When reviewing materials from General III, Jeff recalls following the link and accessing the spreadsheet online but not necessarily downloading it.

I hope this helps,

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Tuesday, May 5, 2020 1:24 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Cc: Sprague, Jeff <Jeff.Sprague@Illinois.gov>
Subject: [External] Question on General III documents

Hi Chris -
I'm wondering if you can help me find a document/file in the General III record. The attached set of emails references use of a TCEQ template for calculating stockpile emissions (see response to Jeff's question #6). Did the company provide the version of the spreadsheet that it used for these emissions estimates, and if so has it been provided to us either in the set of "repository documents" available online with the draft permit and/or in response to our FOIA request? My expert is asking for it (he seemed to think we don't have it yet and I'm not quite sure what the spreadsheet would look like myself, if different from the emission tables included in the application).

(Also note that the link provided by the applicant to TCEQ's template seems to be dead.)

Cc'ing Jeff in case he's familiar with this spreadsheet.

Thanks so much,
Meleah

MELEAH GEERTSMA

Senior Attorney, Environmental Justice

NATURAL RESOURCES

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CHICAGO, IL 60606

T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

R 009298

RE: General Iron aka GII LLC

Geertsma, Meleah <mgeertsma@nrdc.org>

Mon 2/10/2020 4:55 PM

To: Harley, Keith <kharley@kentlaw.iit.edu>; Pressnall, Chris <Chris.Pressnall@illinois.gov>
Cc: Nancy Loeb <n-loeb@northwestern.edu>; Layman, Robb <Robb.Layman@illinois.gov>; Frost, Brad <Brad.Frost@illinois.gov>; Mohr, Kent <Kent.Mohr@illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@illinois.gov>; Barria, German <German.Barria@illinois.gov>; Jones, Eric E. <Eric.E.Jones@illinois.gov>

All –

With our thanks again for engaging in a discussion around metals recyclers in environmental justice communities, I'm writing with additional follow-up on our commitment to provide information relevant to the various metals recycling permitting actions in Chicago.

First, we draw your attention to comments that our groups submitted to the Chicago Dept. of Public Health (CDPH) with regards to that agency's proposed new local regulations for large recycling facilities: https://www.chicago.gov/content/dam/city/depts/cdph/InspectionsandPermitting/Comment_NRDC_SETF_SSCBP_LVEJO_6-21-19.pdf.

The exhibits to the comments are available at this Dropbox link: https://www.dropbox.com/sh/0wh459ez9iv1lai/AABTdvjK5hxUFg1j5gG0BY6ha?dl=0

In particular, we would like to highlight the following sections:

1. The California study and comment text discussing its findings and other related sources of information on impacts, pages 2-6 (see page 2, Exhibit 2, for the full California study – the link in the footnote is now dead, but the pdf is available via the Dropbox link)
2. The discussion of air emissions in particular, including the Houston study (pages 3-4); grinding emissions and other small facilities emissions (page 15, fnt 43); and the Minneapolis Northern Metals example of dust from ASR processing (page 16, fnt 46). We also note that the actions taken against Northern Metals by the Minnesota Pollution Control Agency contain a number of cautions regarding metals recycling, and we encourage IEPA to familiarize itself with these actions, to the extent the staff has not yet reviewed.
3. The auto shredder residue (ASR) sections at pages 4 and 19-22.

We also are sending our supplemental comments to CDPH on torch cutting and ASR (comments and exhibits are available at this link): https://www.dropbox.com/sh/338rqxbccdxkmx2/AAD99r9AJXYt-xhFeTH_xULza?dl=0

Finally, we are sharing the link to CDPH's inspections database, where as we mentioned on our call IEPA can find descriptions of activities and conditions at the 11600 S Burley facilities, including chronic paving problems and evidence of metallic fines and ASR distributed over the site (there is a small search window at the upper left corner): https://data.cityofchicago.org/widgets/i9rk-duva

Again we thank you for your continued attention to this important issue; please do not hesitate to reach out to our attorney group if you have any questions or comments.

Best,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

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mgeertsma@NRDC.ORG
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From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Monday, January 27, 2020 10:46 AM
To: Pressnall, Chris <Chris.Pressnall@illinois.gov>

Cc: Nancy Loeb <n-loeb@northwestern.edu>; Geertsma, Meleah <mgeertsma@nrdc.org>; Layman, Robb <Robb.Layman@illinois.gov>; Frost, Brad <Brad.Frost@illinois.gov>; Mohr, Kent <Kent.Mohr@illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@illinois.gov>; Barria, German <German.Barria@illinois.gov>; Jones, Eric E. <Eric.E.Jones@illinois.gov>
Subject: General Iron aka GII LLC

Hi -

Thank you for participating in our conversation about the active and proposed facilities located at 11600 S. Burley in Chicago.

I'm writing to follow up on our commitment to provide information about the General Iron's operations at its existing location. As we discussed, these operations are one basis for community concerns about the transfer of this business and its operations to 11600 S. Burley. More specifically, our clients are concerned that this business and its operations could be a source of poorly controlled shredder emissions, fugitive particulate matter and releases of auto shredder residue. Moreover, in the context of permitting, our clients are concerned that actual and potential emissions from the shredder and other operations at 11600 S. Burley are not well characterized, and do not form the basis for making fundamental permitting choices.

Part of this concern is based on inspection and enforcement activity which is occuring at the existing General Iron facility. I'm attaching a packet which relates to this concern. The packet includes: 1. a Narrative Evaluation prepared by a Chicago Inspector on December 18, 2019; 2. a Narrative Evaluation prepared by a Chicago Inspector on December 23, 2019; and, 3. eight Chicago Notices of Violation issued based on observations that took place on 12/10/19, 12/16/19, 12/18/19 and 12/23/19. As you will see, City Inspectors consistently observed a failure to control and suppress dust to prevent off-site migration, auto fluff that "became scattered by the wind and migrated off-site", and releases of untreated shredder emissions that occurred despite the RTO and scrubber.

Again, thank you for meeting and for engaging the public health, environmental and environmental justice concerns we are expressing on behalf of our clients.

- Keith Harley, Attorney for Southeast Environmental Task Force

R 009300

Delete ···

RE: 1986 IDPH/IEPA study of cancers in Lake Calumet area

Label: NRDC 50-Year Permanently Delete (50 years) Expires: Wed 9/5/2068 2:28 PM

PC

Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Tue 9/18/2018 3:28 PM
To: Geertsma, Meleah
Cc: Espedido , Charlie

Hello Meleah –

It does not appear that we have an electronic copy of the study but our librarian indicated that we do have three paper copies (although one is going out on loan). If you cannot get the copy at UIC perhaps you could request one of IEPA's copies through interlibrary loan??? What is your timeframe?

Chris Pressnall
Environmental Justice Officer
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Monday, September 17, 2018 3:39 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Cc: Espedido , Charlie <cespedido@nrdc.org>
Subject: [External] 1986 IDPH/IEPA study of cancers in Lake Calumet area

Hi Chris –

I'm wondering if you might be able to help me track down a study; I think we may have found a copy at UIC's library, but am not sure just yet, and it would be great regardless if you have an e-copy that you can share.

While reading an older report on water contamination around Lake Calumet, I came across reference to a 1986 cancer study of the Southeast Side (note that the text describes this as an IDPH report, but then cites it as an IEPA publication):

IEPA. 1986. The Southeast Chicago Study: An Assessment of Environmental Pollution and Public Health Impacts, Springfield, March.

"The Illinois Department of Public Health published a study of cancer mortality in the Lake Calumet area (IEPA, 1986). This study concluded that there was excessive mortality for all cancers in the area compared with the national averages. The study found excessive instances of lung and prostate cancer in white males and excessive bladder cancer in white females of the area. This study, which examined only cancers which resulted in death and not all occurrences, speculated that the possible causes could be attributed to occupational and environmental exposure."

https://www.ideals.illinois.edu/bitstream/handle/2142/1927/RR-E50.PDF?sequence=1

Best,

Meleah

MELEAH GEERTSMA

Print Cancel

Re: 11600 S Burley

Geertsma, Meleah <mgeertsma@nrdc.org>
Wed 1/22/2020 4:52 PM

To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; EXT Harley, Keith <kharley@kentlaw.iit.edu>; Nancy Loeb <n-loeb@northwestern.edu>; Layman, Robb <Robb.Layman@Illinois.gov>; Frost, Brad <Brad.Frost@Illinois.gov>; Mohr, Kent <Kent.Mohr@Illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@Illinois.gov>; Barria, German <German.Barria@Illinois.gov>; Jones, Eric E. <Eric.E.Jones@Illinois.gov>

Thanks again for a very helpful call today - we appreciate all the time taken by multiple IEPA staff. As discussed, I'm sharing a link to CDPH's environmental inspections database, where you can find entries for the 11600 S Burley facilities (to search, click on the very small magnifying glass in the upper left corner):

https://data.cityofchicago.org/widgets/i9rk-duva

Best,
Meleah

From: Pressnall, Chris
Sent: Wednesday, January 22, 2020 2:15 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; EXT Harley, Keith <kharley@kentlaw.iit.edu>; Nancy Loeb <n-loeb@northwestern.edu>; Geertsma, Meleah <mgeertsma@nrdc.org>; Layman, Robb <Robb.Layman@Illinois.gov>; Frost, Brad <Brad.Frost@Illinois.gov>; Mohr, Kent <Kent.Mohr@Illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@Illinois.gov>; Barria, German <German.Barria@Illinois.gov>; Jones, Eric E. <Eric.E.Jones@Illinois.gov>
Subject: 11600 S Burley
When: Wednesday, January 22, 2020 3:00 PM-4:00 PM.
Where: Telephone

-- Do not delete or change any of the following text. --

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Exhibit 218

Fugitive Particulate Operating Program
General III, LLC –
11600 S Burley Avenue - Chicago, Illinois
June 25, 2020

R17421-7.2

Prepared for:
General III, LLC
1909 North Clifton Avenue
Chicago, Illinois 60614
Attn: Mr. Jim Kallas

Prepared by:
John G. Pinion
Principal Engineer
RK & Associates, Inc.

RK & Associates Inc
2 South 631 Route 59
Suite B
Warrenville, Illinois 60555
Phone: 630-393-9000
Fax: 630-393-9111

TABLE OF CONTENTS

TABLES

FIGURES

RK
& Associates, Inc.

1.0 INTRODUCTION

This Fugitive Particulate Operating Program (Program) has been prepared for the General III, LLC (GIII) scrap metal recycling facility as a condition of Illinois Environmental Protection Agency (IEPA) Construction Permit No. 19090021.

GIII is a recycling facility (Facility) located in an existing established industrial district. GIII is configured to process 1,000,000 tons per year of shreddable recyclables in various forms to produce uniform grades of ferrous and non-ferrous metals. Proposed scrap handling and processing activities include raw material receiving, sorting, shredding, metal separation, recovery of ferrous and non-ferrous metals, and shipment of finished products to customers.

The objective of this Program is to identify, monitor, and treat (as may be necessary) sources of Visible Emissions (defined in Section 1.3). GIII is implementing this Program to meet applicable regulatory standards.

1.1 Facility Location and Contact Information

Business Name:	General III, LLC
Source Location:	11600 South Burley – Chicago, Illinois 60617 Hyde Park Township, Cook County Illinois
Latitude/Longitude	41.685201° N / -87.545847" W – Approximate Location of Front Gate
Office/Mailing Address:	1909 N. Clifton Avenue – Chicago, Illinois 60614
Authorized Representative Responsible for this Program:	Mr. Jim Kallas – Environmental Manager 847-508-9170 – jimkallas@general-iron.com
IEPA Site ID No.:	031600SFX
SIC Code:	5093 – Scrap and Waste Materials
NAICS Code:	423930 – Recyclable Material Merchant Wholesalers

1.2 Regulatory Requirements

1.2.1 General Limitation for Fugitive Particulate Matter – 35 IAC 212.301

GIII is subject to the general limitation for fugitive particulate matter identified in 35 IAC 212.301, which requires that:

No person shall cause or allow the emission of fugitive particulate matter from any process, including any material handling or storage activity, that is visible by an observer looking generally toward the zenith at a point beyond the property line of the source.

1.2.2 Requirement to Prepare and Implement a Fugitive Particulate Operating Program

Pursuant to 35 IAC 212.302, a Fugitive Particulate Operating Program is required for any facility with operations belonging to specified groups of Standard Industrial Classification (SIC) Codes **and** that are located within a specified area. GIII is located in Cook County, which is a specified area under 35 IAC 212.302; however, GIII's SIC Code (5093 Scrap and Waste Materials) is **not** among the specified SIC codes. Therefore, GIII is not subject to a requirement to have a Fugitive Particulate Operating Program.

Although not required by regulations, this Fugitive Particulate Operating Program establishes the best management practices that will be used to minimize potential Visible Emissions and ensure compliance with 35 IAC 212.301.

1.3 Definition of Visible Emissions

For the purposes of this Program, "Visible Emissions" means the existence of visible fugitive particulate matter emissions that threaten to cross the Industrial Campus Boundary.

Visible Emissions do not include steam (water vapor), engine combustion exhaust, and particulate matter emitted from permitted exhaust stacks with or without a pollution control device because each permitted exhaust point has a separate opacity limit and particulate mass emission limit included in the facility construction/operation permit.

1.4 Industrial Campus Boundaries

For the purposes of this Program, the "property line" as referenced in 35 IAC 212.301, is the boundary of the existing Industrial Campus located at 11600 South Burley Avenue in Chicago, Illinois identified in Figure 2-2 (Industrial Campus Boundary).

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& Associates, Inc.

2.0 FACILITY SITE MAP

The location of GIII is shown on Figures 2-1 and 2-2. GIII operates on approximately 25 acres within the Industrial Campus. Four other affiliated material recycling businesses are located within the Industrial Campus. Combined emissions from these other businesses qualify for, and are currently registered under, IEPA's Registration of Smaller Source (ROSS) Program.

The GIII scrap metal recycling facility is shown on Figure 2-3. The Facility Site Map indicates the locations of the Facility boundaries, buildings, location of material handling and processing areas, shredder enclosure, shredder emission control system, stockpiles, truck scales and facility vehicle entrance.

When initially constructed the Facility surface area will be comprised of 62% concrete and asphalt pavement and 8% stormwater retention pond. The remaining area includes ancillary support buildings, green space and unpaved surface consisting compacted asphalt gravel, asphalt grindings or similar materials.

RK & Associates, Inc.

Facility Site Map

RK
& Associates, Inc.

3.0 FACILITY OPERATIONS AND APPLICATION OF BEST MANAGEMENT PRACTICES FOR MITIGATION OF VISIBLE EMISSIONS

Raw materials are delivered to the facility from a variety of sources including retail, commercial/industrial accounts via trucks or contract haulers and peddlers via peddler vehicles. Peddlers and semi-trucks entering the facility first pass through a truck scale.

Semi- trucks are then directed to a material staging area near the raw material stockpiles. Designated Facility personnel inspect all loads for unauthorized materials in accordance with Facility procedures. In this regard, the facility is subject to a Feed Stock Management Plan requirement in the facility construction permit. After unloading, the semi-trucks and peddler vehicles exit the Facility after passing over the appropriate truck scale.

The shredding process produces ferrous metal and Automobile Shredder Residue (ASR) which contains non-metallic material, non-ferrous metal and a limited amount of ferrous metal. Ferrous metal is processed to remove non-metallic material through a series of material handling steps in the Ferrous Metal Processing system to produce clean ferrous metal.

The ASR is directed to a stockpile for temporary storage prior to processing. ASR is transferred a short distance from the ASR stockpile to the Non-Ferrous Metal Processing system using a rubber-tired loader. ASR is processed by a variety of advanced material handling and separation equipment in the Non-Ferrous Metal Processing system to recover various sizes and grades of non-ferrous metals. Non-metallic material removed by the Non-Ferrous Metal Processing system is directed to a stockpile prior to being loaded into semi-trucks for off-site disposal at an appropriately licensed landfill.

Wherever the information in this Section 3 references application of water for mitigation of Visible Emissions, the following limitations are applicable:

- Application of water will be limited following precipitation events exceeding 0.1 inches.
- Application of water cannot be performed when temperatures are near or below freezing because water application will create unsafe conditions. During these time periods, the facility will lower the posted speed limit to 5 mph.

Table 3-1 summarizes facility operations with the potential to generate Visible Emissions and the Best Management Practices (BMPs) that will be utilized to achieve compliance with 35 IAC 212.301. For the purposes of this Program, compliance with 35 IAC 212.301 is determined at the Industrial Campus Boundary. Detailed descriptions of the BMPs are presented in Section 4.0.

Table 3-1 – Summary of Facility Operations and Best Management Practices for Mitigation of Visible Emissions

Operation	Best Management Practices					
	Inspections/ Observations	Water Atomizing Dust Bosses	Sweeping/ Watering of Paved Areas	Watering of Unpaved Areas	Additional BMPs	As Described In Section
Raw Material Unloading/Handling	X	X	X		Feed Stock Management Plan	3.1
Material Transfer Points	X	X			Conveyor covers on selected conveyors	3.2
Intermediate and Product Stockpiles	X	X	X		Partial enclosures (side walls) on selected stockpiles	3.3
Fluff Storage and Loadout	X	X	X		Fluff storage bin with steel walls on three sides and equipped with a cover.	3.4
Material Loadout	X		X		Water spray	3.5
Traffic Areas – Paved Areas	X	X	X		Water Truck, Sweeper, and vehicle speed limit of 10 mph	3.6
Traffic Areas – Unpaved Areas	X	X		X	Water Truck, Sweeper, and vehicle speed limit of 10 mph	3.7
Employee Parking	X		X	X	Speed bumps and speed limit signs to limit speed to 10 mph.	3.8
Vehicle Tarping					Trailers of outbound Fluff will be tarped.	3.9
Barge Loading	X				Specially designed chute extending downward from end of conveyor. When using mobile equipment drop distances will be reduced and water will be applied to material prior to loading.	3.10
Rail Car Loading	X				Minimize drop distance. Water material prior to loading.	3.11
Industrial Campus Boundary	X				Identify the source(s) of Visible Emissions and take corrective actions as described herein.	3.12

3.1 Raw Material Unloading/Handling

Raw scrap in bulk trucks (semi-trailers) is dumped on the ground near the shredder infeed conveyor where cranes equipped with magnets or grapples sort through the material and place it on a raw material stockpile or onto the shredder infeed conveyor of the shredder. These or other cranes equipped with magnets or grapples then transfer the material from the stockpiles to the shredder infeed conveyor.

The space available for stockpiling raw material is limited, and therefore, the material is typically processed within several days of its receipt. The raw material stockpiles will not be used for long term storage.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of each raw material unloading and handling area for the presence of Visible Emissions three times per day and record the results on a Visible Emissions Observation and Control (VEOC) form. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. Dust Boss water atomizers will be positioned to mist the raw material handling area and will be utilized to mitigate Visible Emissions.

ii. Areas adjacent to raw material handling operations will be included in the watering and sweeping of paved areas described in Section 3.8.

3.2 Material Transfer Points

Material will be primarily transported through the Ferrous and Non-Ferrous Material Processing Systems on a series of belt conveyors. A material transfer point is the point at which material from an upstream conveyor is transferred to a downstream conveyor, the point at which an upstream conveyor feeds a piece of processing equipment, or the point at which a piece of processing equipment discharges material onto a takeaway conveyor. Visible Emissions from a transfer point may occur when the material being transferred has a high concentration of fine material and low moisture content.

Figure 3-1 identifies conveyors in the Ferrous Material Processing System that are equipped with covers, which are limited to the ASR takeaway conveyors and the Fluff take away conveyors.

Figure 3-2 identifies conveyors in the Non-Ferrous Material Processing System that are equipped with covers, which include all outside conveyors except those that convey clean metallic products that do not contain material that is subject to becoming Visible Emissions.

A. **Inspections/Observations:**

i. Trained personnel will conduct visual observations of specific areas that include material transfer points for the presence of Visible Emissions three times per day and record the results on a VEOC form. When Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. **Visible Emissions Mitigation Measures:**

i. Water will be applied to facility areas with the highest potential for Visible Emissions.

3.3 Intermediate and Product Stockpiles

The space available for stockpiling intermediates and products is limited and, therefore, these materials are typically processed or shipped off site regularly. These stockpiles will not be used for long term storage of materials.

A. **Inspections/Observations:**

i. Trained personnel will conduct visual observations of material stockpiles for the presence of Visible Emissions once per day at each stockpile with the results recorded on a VEOC form. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. **Visible Emissions Mitigation Measures:**

i. Dust Boss water atomizers will be positioned to mist stockpiles when Visible Emissions are observed.

i. With the exception of the Raw Material stockpiles, the two Ferrous Metal Stockpiles, and the ASR stockpile, all stockpiles identified in facility emission estimates will have solid partitions on three sides.

ii. Areas adjacent to stockpiles will be included in the watering and sweeping of paved areas described in Section 3.8.

3.4 Fluff Storage and Loadout

"Fluff" is the term used to refer to the waste product from the Non-Ferrous Material Processing System.

The Fluff Storage Bin has been designed to mitigate Visible Emissions from the bin. The Fluff Storage Bin is enclosed on three sides by steel walls and on the top with a fixed cover.

One side of the bin is required to be open to allow access for a rubber-tired end loader for material loadout to trucks. The open side of the bin faces west, away from residential areas located east of the facility. A Dust Boss is also located near the west side of the bin to mitigate Visible Emissions.

A rubber-tired end loader is used to transfer fluff from the Fluff Storage Bin to trailers. After the trailers are filled, they are tarped before they leave the facility.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of the Fluff Storage Bin for the presence of Visible Emissions three times per day and record the results on a VEOC form. At least one of these observations will be made during Fluff loadout. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. A Dust Boss water atomizer, located near the bin, will be used to mist the west side of the bin to mitigate fugitive dust and the material loadout area if Visible Emissions are observed.

ii. Areas adjacent to the Fluff Storage Bin will be included in the watering and sweeping of paved areas described in Section 3.8.

3.5 Truck Loadout

Product loadout occurs when stockpiled material is transferred to trucks using a rubber-tired loader, or material handler.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of each loadout area that is active at the time the observations are performed. Each active material loadout area is observed for the presence of Visible Emissions three times per day and results are recorded on a VEOC form. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. Water will be applied to material and adjacent loadout areas when Visible Emissions are observed.

ii. Areas adjacent to material loadout activity will be included in the watering and sweeping of paved areas described in Section 3.8.

3.6 Paved Areas

The paved areas with the highest potential for Visible Emissions are the traffic routes used by vehicles delivering raw material or transporting materials from the site.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of paved vehicle traffic routes for the presence of Visible Emissions and record the results on a VEOC form. The most frequently traveled routes will be observed three times per day and less traveled routes and non-traffic paved areas will be observed once per day. Observation locations will be identified prior to facility startup.

B. Visible Emissions Mitigation Measures:

i. Speed limit signs, limiting vehicle speed to 10 mph, will be posted on vehicle travel routes.

ii. Water will be applied to the most frequently used paved areas at least once per day, subject to the weather conditions identified above. Water will be applied to less frequently traveled routes at a frequency required to mitigate Visible Emissions, subject to weather conditions identified herein. Additional applications may be made in response to Employee Observations.

Operation of the water truck will be documented in a water truck log that will identify the area(s) where water is applied, the approximate amount of water applied, the time of application, the name of the person operating the water truck, and the reason for application (i.e., routine daily application or in response to an Employee Observation). If water is not be applied, the reason will be noted on the VEOC form.

iii. Sweeping of the most frequently traveled routes will occur at least once per day when the facility is operating subject to the weather conditions identified above. Sweeping of less frequently traveled routes will occur at a frequency required to mitigate Visible Emissions, subject to weather conditions identified herein.

Operation of the sweeper will be documented in a sweeper log that will identify the area(s) swept, the date/time sweeping was performed, the name of the person operating the sweeper, and the reason for sweeping (i.e., routine daily sweeping or in response to an Employee Observation). If sweeping is not performed, the reason will be noted on the VEOC form.

iv. Rumble Strips will be installed at the entrance to the outgoing scale to remove loose material from exterior of vehicle trailers and vehicle tires.

The Rumble Strip area will be routinely inspected, and accumulated material removed on a regular basis to ensure effective operation.

3.7 Unpaved Areas

Limited areas within the Facility that are not paved with concrete or asphalt are covered with compacted asphalt grindings or similar material. Visible Emissions from unpaved areas are associated with vehicle use.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of unpaved areas for the presence of Visible Emissions and record the results on a VEOC form. The most frequently used areas will be observed three times per day and less frequently used areas will be observed once per day. Observation locations will be identified prior to facility startup.

B. Visible Emissions Mitigation Measures:

i. Speed limit signs, limiting vehicle speed to 10 mph will be posted on vehicle travel routes.

ii. Water will be applied to the most frequently used unpaved areas at least once per day subject to the weather conditions identified above. Water will be applied to the less frequently used areas at a frequency required to mitigate Visible Emissions, subject to weather conditions identified herein. Additional applications may be made in response to Employee Observations.

Operation of the water truck will be documented in a water truck log that will identify the area(s) where water is applied, the approximate amount of water applied, the time of application, the name of the person operating the water truck, and the reason for application (i.e., routine daily application or in response to an Employee Observation). If water is not be applied, the reason will be noted on the VEOC form.

iii. If Visible Emissions are observed from unpaved areas during weather conditions that prohibit water application, alternative control measures will be evaluated. Evaluation and potential application of alternative mitigation measures will be based on operating experience and routine observations. Alternative mitigations measures may include but are not limited to minimizing activity in unpaved areas, application of surfactant prior to winter conditions, or placement of additional asphalt grindings or similar material.

3.8 Employee Parking Area

There is administrative parking adjacent to the administration building inside of the Facility. The administrative parking area will be maintained as described in Section 3.8.

There is also an employee parking lot located east of the railroad tracks that parallels the east Industrial Campus Boundary and just north of vacated 116th Street, which is a nonpublic street west of Avenue O used by the Facility under an existing easement agreement.

Because employee vehicles will not routinely enter the facility, material track-in to the parking area will be negligible.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of the employee parking lot for the presence of Visible Emissions and record the results on a VEOC form. The parking area will be observed once per day when employees are entering or leaving the area. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. The employee parking area will be equipped with speed bumps and speed limit signs will be posted to limit vehicle speeds to 10 mph.

ii. When Visible Emissions are observed, water will be applied to those areas.

Operation of the water truck will be documented in a water truck log that will identify the area(s) where water is applied, the approximate amount of water applied, the time of application, the name of the person operating the water truck, and the reason for application (i.e., routine daily application or in response to an Employee Observation).

iii. Sweeping of the paved areas of the employee parking lot will be performed once per month subject to the weather conditions identified above.

Operation of the sweeper will be documented in a sweeper log that will identify the area(s) swept, the date/time sweeping was performed, the name of the person operating the sweeper, and the reason for sweeping (i.e., routine daily sweeping or in response to an Employee Observation).

3.9 Vehicle Tarping

Tarps are utilized on outgoing Fluff trailers because this material has the potential to become airborne during transport. Fluff trailers are tarped before leaving the Facility.

Based on operating experience, Fluff is the only material, incoming or outgoing, that has the potential to become airborne during transportation. It is not practical to tarp trailers of inbound scrap metal, outbound trailers of shredded metal or other products because these materials do not generate airborne material during transport and, if covered, tarps would be cut or torn by pieces of scrap and further damaged during transport. The Illinois Department of Transportation (IDOT) governs the transport of material on roadways.

Outbound rail cars and barges filled with shredded steel and other products are also not tarped because these materials do not generate airborne material during transport. Outbound trucks, rail cars and barges are all constructed with solid floors and side walls but have open tops to facilitate loading and unloading.

A. Inspections/Observations:

i. Outbound rail cars and trucks leaving the site, including Fluff trailers, are visually inspected by scale operators.

These inspections are part of the normal responsibilities of the scale operators and are not recorded or otherwise documented.

B. Visible Emissions Mitigation Measures:

i. Fluff trailers are tarped before leaving the Facility.

3.10 Barge Loading

Barges will be loaded by a conveyor equipped with a specially designed chute. Barges could also be loaded by mobile equipment, in which case, water will be applied to the material to mitigate potential for Visible Emissions.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of Barge Loading for the presence of Visible Emissions at least once during the loading of each barge and record the results on a VEOC form. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. When loading barges with a conveyor, the conveyor will be equipped with a specially designed chute extending downward or a water spray to mitigate Visible Emissions.

ii When loading barges with mobile equipment, drop distances will be minimized and water will be applied to the material to mitigate Visible Emissions.

iii. Areas adjacent to Barge Loading will be included in the watering and/or sweeping of paved and/or unpaved areas described in Sections 3.8 and 3.9.

3.11 Rail Car Loading

Rail cars are loaded by material handlers that include end loaders, grapples, and magnets. Grapple and magnet operators are trained to limit the drop distance of material into the rail cars to minimize the potential for Visible Emissions.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations of Rail Car Loading for the presence of Visible Emissions at least once each day during the loading of rail cars and record the results on a VEOC form. If Visible Emissions are identified, observers will notify the Facility Manager who will be responsible for deployment of Visible Emissions mitigation measures.

B. Visible Emissions Mitigation Measures:

i. Material drop distances will be minimized by grapple and magnet operators to minimize the potential for Visible Emissions.

ii. When loading rail cars with mobile equipment, drop distances will be minimized and water will be applied to the material to mitigate Visible Emissions.

iii. Areas adjacent to Rail Car Loading will be included in the watering and/or sweeping of paved and/or unpaved areas described in Sections 3.8 and 3.9.

3.12 Industrial Campus Boundary Line Observations for Visible Emissions

Observations will be performed at the North, South, East, and West Industrial Campus boundaries.

A. Inspections/Observations:

i. Trained personnel will conduct visual observations at least once per day of the North, South, East and West boundaries of the Industrial Campus for the presence of Visible Emissions and record the results on a VEOC form.

B. Visible Emissions Mitigation Measures

i. If Visible Emissions are noted crossing the Industrial Campus boundary, facility personnel will investigate potential sources of the observed Visible Emissions and take corrective action to mitigate the observed Visible Emissions.

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& Associates, Inc.

4.0 RECORDKEEPING

Records will be maintained as required by this Program and the permit.

4.1 Meteorological Data

An onsite meteorological data station (met station) will be installed and operated to record hourly temperature, wind speed, wind direction, barometric pressure, relative humidity, and precipitation amounts. The met station will be centrally located at a minimum height pursuant to applicable USEPA protocols and guidance. Met data will be downloaded and stored electronically at the Facility.

Meteorological data will be recorded and maintained electronically on site. Data will include hourly temperature, wind speed, wind direction, barometric pressure, relative humidity, and precipitation amounts.

4.2 Visible Emissions Observation and Control Form

A Visible Emissions Observation and Control (VEOC) Form will be used to record the results of Visible Emissions observations described in Section 3 and the corresponding mitigation measures applied.

The VEOC form will include the following information:

- Date/Time
- Name of Observer
- Area(s) Observed
  - Time of Observation
  - Visible Emissions Observed – Yes/No
    - Approximate migration distance from source (ft)
  - Mitigation Measures Applied – Yes/No
    - If Yes, identify Mitigation Measures Implemented

4.3 Water Truck Log

The water truck will make routine rounds in the areas identified in Figure 4-2. A log of water truck use will be generated by the operator to record water applications to paved and unpaved areas. This log will include:

- Date/Time
- Reason No Watering Was Performed (if applicable)
- Name of Water Truck Operator
- Reason for Water Application
  - Scheduled, or

  - Corrective Action in response to a Visible Emissions Observation
- Area(s) of Water Application
  - Time of Application
  - Approximate Amount of Water Applied (gallons)

4.4 Sweeper Log

A log of sweeper operation will be generated by the operator to record sweeping events. This log will include:

- Date/Time
- Reason No Sweeping Was Performed (if applicable)
- Name of Sweeper Operator
- Reason for Sweeping
  - Scheduled, or
  - Corrective Action in response to a Visible Emissions Observation
- Area(s) Swept
  - Time of Sweeping

4.5 Dust Boss Water Application

A water meter will be used to document the daily volume of water applied by the Dust Boss system. Figure 4-1 identifies the anticipated location of Dust Bosses.

4.6 Visible Emissions Mitigation Equipment Replacement and Maintenance

Records of replacement or maintenance performed on Visible Emissions mitigation equipment will be performed in accordance with manufacturers recommendations and records will be maintained by the Facility personnel. This information will identify:

- Maintenance performed on the water truck
- Maintenance performed on the sweeper
- Maintenance of Dust Bosses
- Replacement of Dust Bosses or other equipment

4.7 Monthly Inspections of Visible Emissions Mitigation Equipment

Facility personnel will perform monthly visual inspections of the following Visible Emissions mitigation equipment to ensure it is in good operating condition and functioning as intended.

Monthly visual inspections of the following equipment will be performed to ensure these are in good condition.

- Shredder Enclosure
- Ferrous Material Processing System Conveyor Covers
- Non-Ferrous Material Processing System Conveyor Covers
- Fluff Storage Bin
- Barge Loading Chute
- Water application systems

Results of these inspections will be recorded on a form that will include the following information:

- Equipment Being Inspected
- Date/Time of Inspection
- Person Conducting Inspection
- Check List of Equipment Features and Condition (acceptable / unacceptable)
    - Description of unacceptable conditions
- Date of corrective action (if required).
    - Description of Correction Action (if required)

The above referenced checklists will be developed after construction is complete.

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5.0 VOLUNTARY QUARTERLY REPORTING

Although not required, the following information will be reported to the IEPA on a quarterly basis. Quarterly reports will be submitted by the first day of the second month following the end of each calendar quarter.

January through March	Submitted May 1st
April through June	Submitted by August 1st
July through September	Submitted by November 1st
October through December	Submitted by February 1st

Each quarterly report will include the following information:

- Industrial Campus boundary line observation records
- Water Truck Log
- Sweeper Log
- Dust Boss system water application (gal/day)
- Summary of equipment replacement and maintenance of Visible Emissions mitigation equipment.

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6.0 PROGRAM AMENDMENT

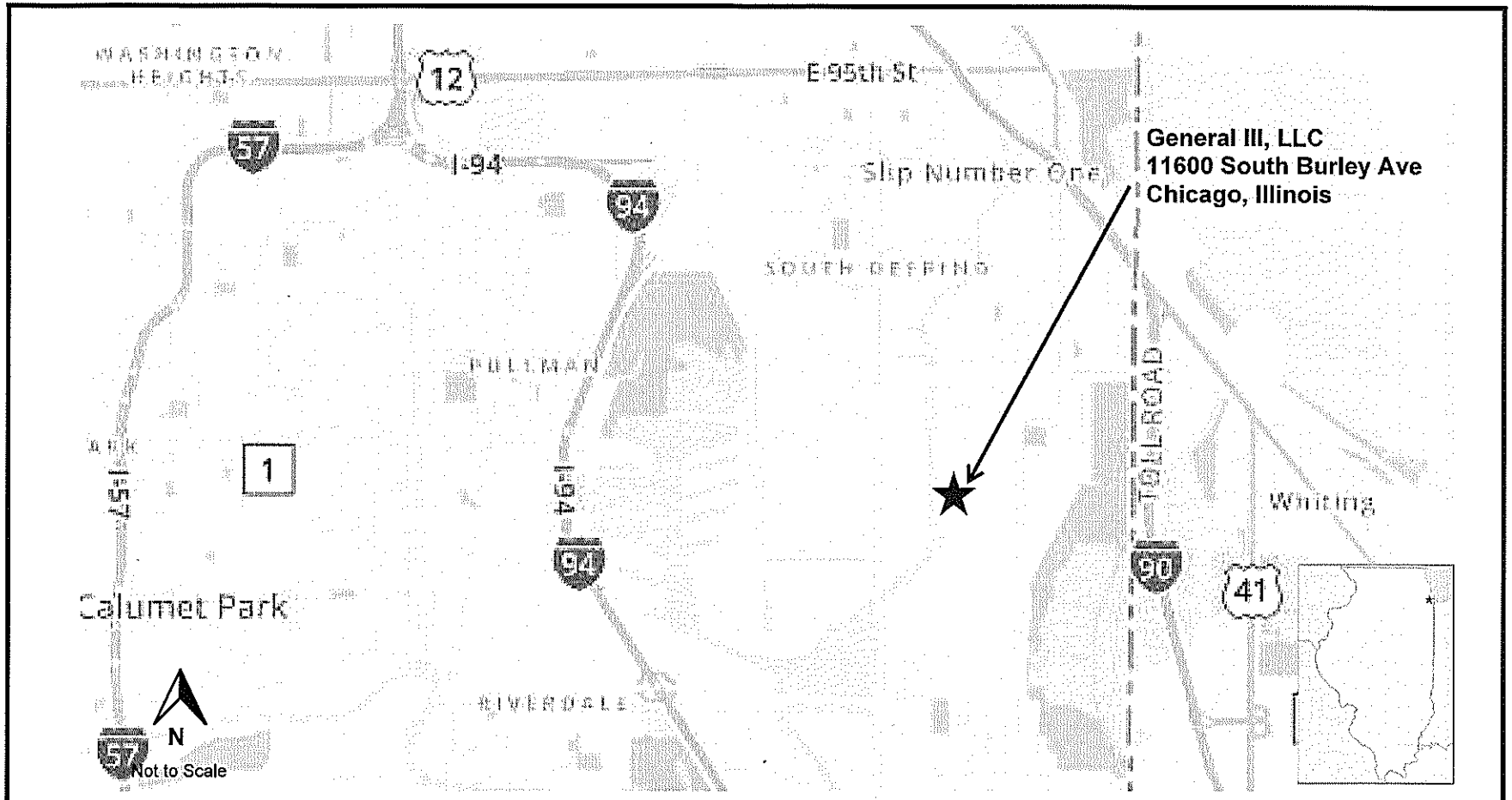
This Fugitive Particulate Operating Program shall be amended from time to time so that the operating program is current. Program amendments will be submitted to the Illinois EPA within thirty (30) days of such amendment. Any future revision to this Program made by GIII is automatically incorporated by reference as an enforceable condition of the Facility construction/operation permit, unless it is expressly disapproved, in writing, by the Illinois EPA. In the event that the Illinois EPA notifies GIII of a deficiency with any revision to the Program, GIII will revise and re-submit the Fugitive Particulate Operating Program within thirty (30) days of receipt of notification to address the deficiency.

RK
& Associates, Inc.

Fugitive Particulate Operating Program

General III, LLC
11600 South Burley
Chicago, Illinois 60614

FIGURES



RK & Associates, Inc. 2S631 ROUTE 59, SUITE B WARRENVILLE, IL 60555 630-393-9000/630-393-9111	Fugitive Particulate Operating Program		Facility Location Map General III, LLC 11600 South Burley, Chicago, Illinois		2-1
	DRAWN BY:	APPROVED BY: JGP	PROJECT NUMBER R19439-7.1C	DATE DRAWN 11-01-2019	REVISED DATE

RK & Associates, Inc.

General III, LLC
Fugitive Particulate Operating Program

RK & Associates, Inc. 2S631 ROUTE 59, SUITE B WARRENVILLE, IL 60555 630-393-9000/630-393-9111	Fugitive Particulate Operating Program	**Facility Layout Map** **General III, LLC** **11600 South Burley, Chicago, IL**			2-2
	DRAWN BY:	APPROVED BY: JGP	PROJECT NUMBER: R19439-7.10	DATE DRAWN: 11-01-2019	REVISED DATE

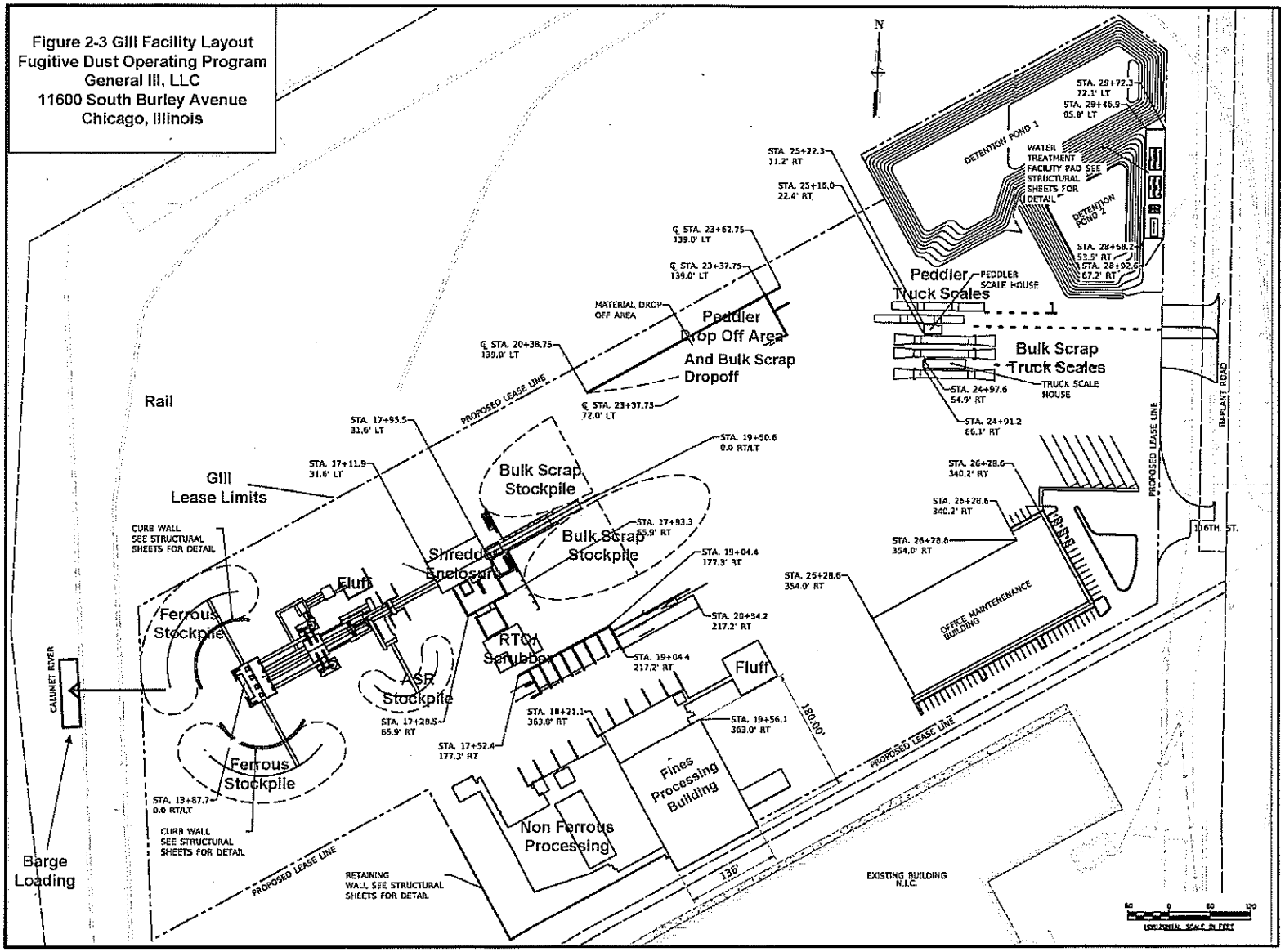
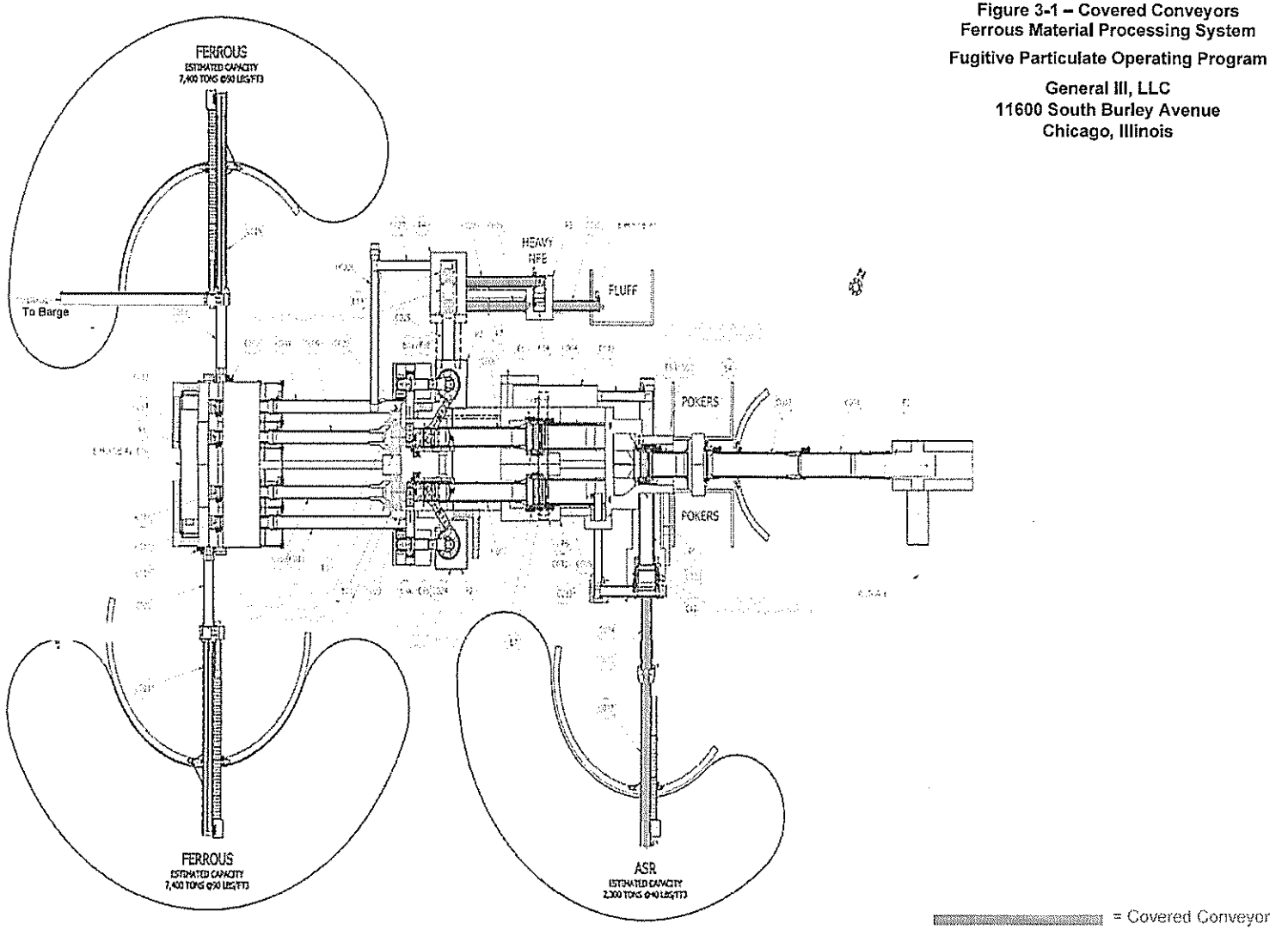


Figure 2-3 GIII Facility Layout
Fugitive Dust Operating Program
General III, LLC
11600 South Burley Avenue
Chicago, Illinois
N
Rail
GIII
Lease Limits
Barge
Loading
CALUMET RIVER
Ferrous
Stockpile
Fluff
Shredder
Enclosure
Bulk Scrap
Stockpile
Bulk Scrap
Stockpile
RTO/
Scrubber
ASR
Stockpile
Ferrous
Stockpile
Fluff
Fines
Processing
Building
Non Ferrous
Processing
Peddler
Drop Off Area
And Bulk Scrap
Dropoff
MATERIAL DROP
OFF AREA
Peddler
Truck Scales
PEDDLER
SCALE HOUSE
Bulk Scrap
Truck Scales
TRUCK SCALE
HOUSE
DETENTION POND 1
DETENTION
POND 2
WATER
TREATMENT
FACILITY PAD SEE
STRUCTURAL
SHEETS FOR
DETAIL
OFFICE MAINTENANCE
BUILDING
EXISTING BUILDING
N.I.C.
PROPOSED LEASE LINE
CURB WALL
SEE STRUCTURAL
SHEETS FOR DETAIL
RETAINING
WALL SEE STRUCTURAL
SHEETS FOR DETAIL
136'
190.00'
116TH ST.
IN-PLANT ROAD

Figure 3-1 – Covered Conveyors
Ferrous Material Processing System
Fugitive Particulate Operating Program
General Ill, LLC
11600 South Burley Avenue
Chicago, Illinois



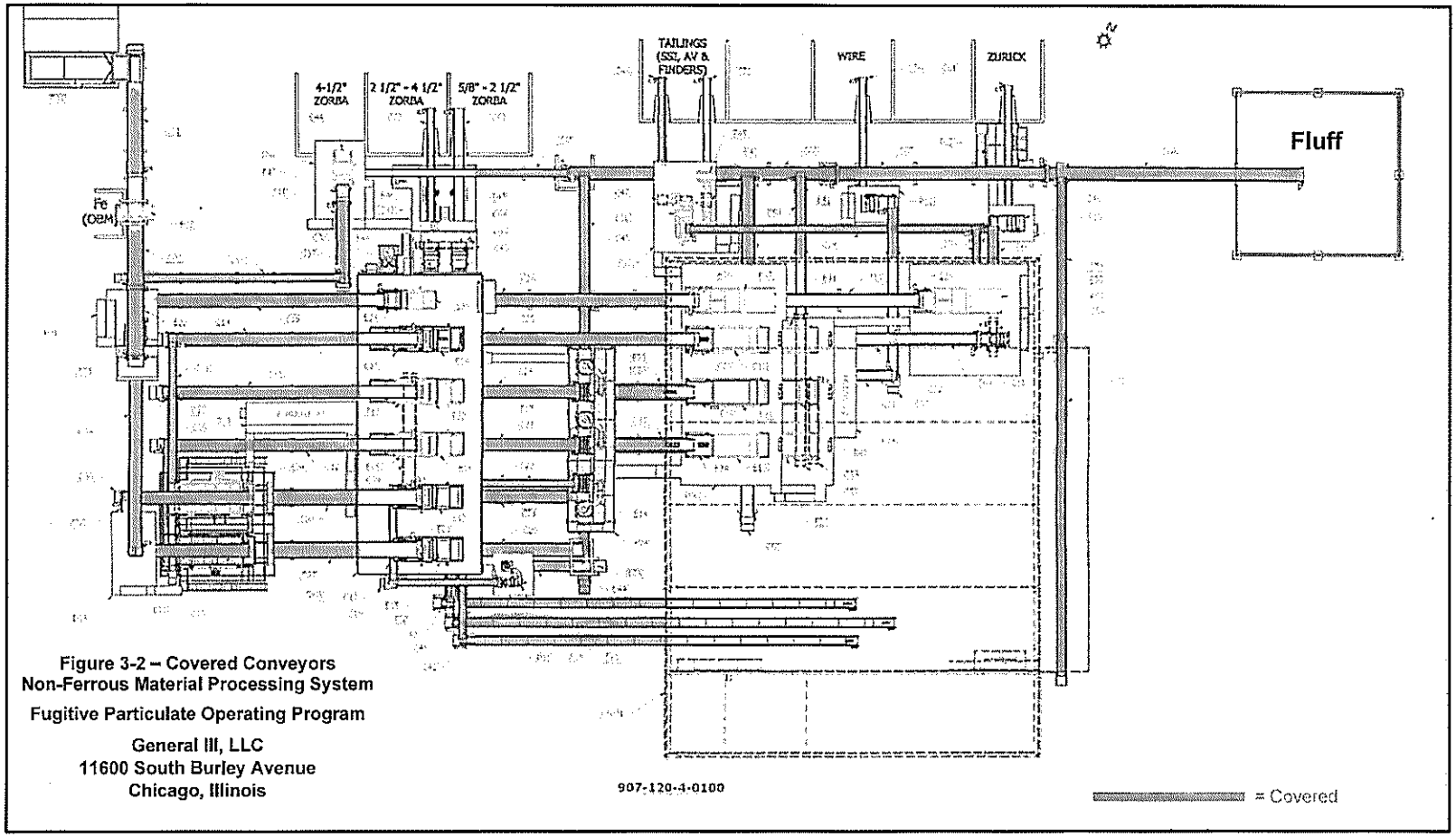
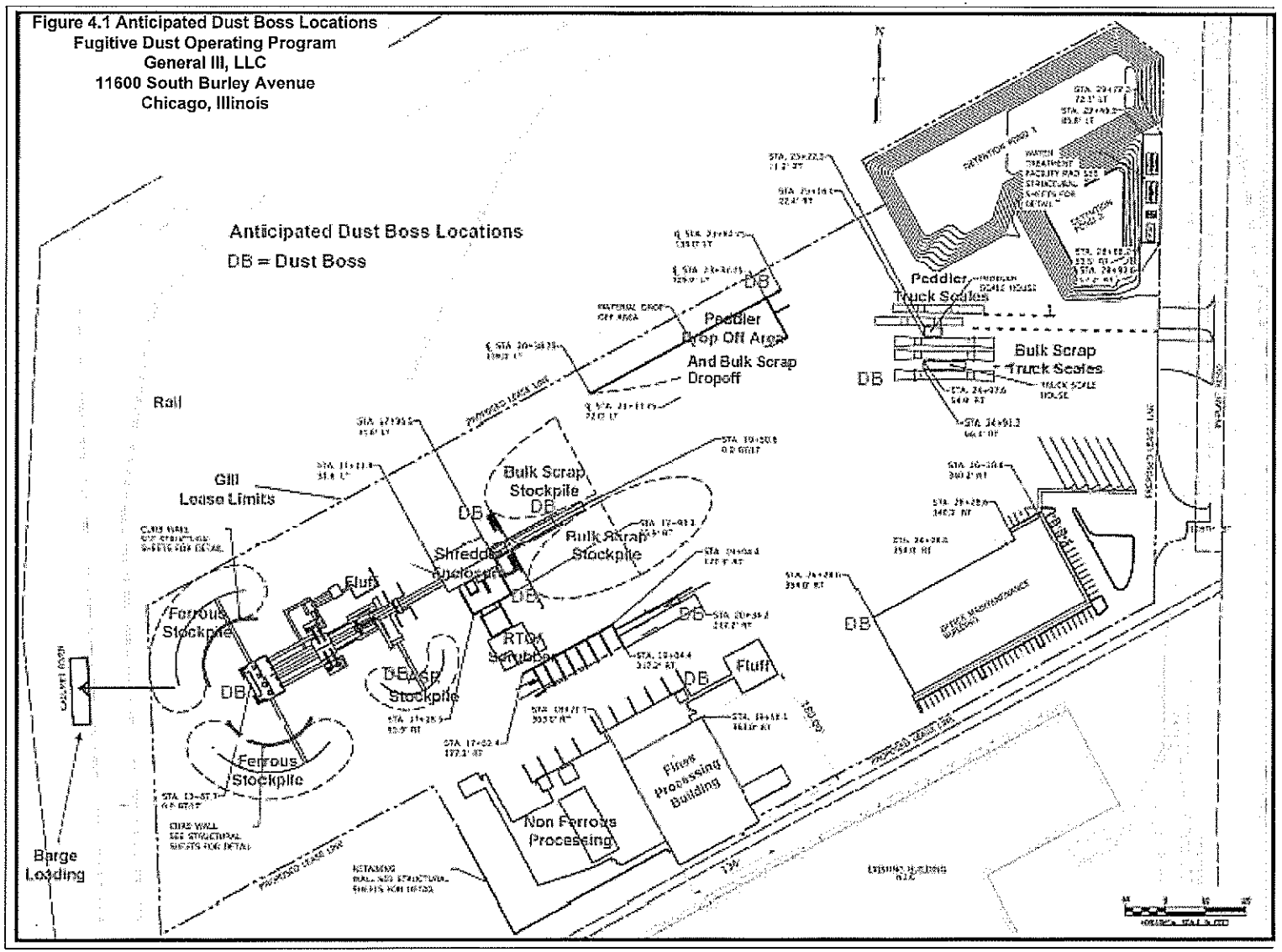


Figure 3-2 – Covered Conveyors
Non-Ferrous Material Processing System
Fugitive Particulate Operating Program
General III, LLC
11600 South Burley Avenue
Chicago, Illinois

Figure 4.1 Anticipated Dust Boss Locations
Fugitive Dust Operating Program
General III, LLC
11600 South Burley Avenue
Chicago, Illinois



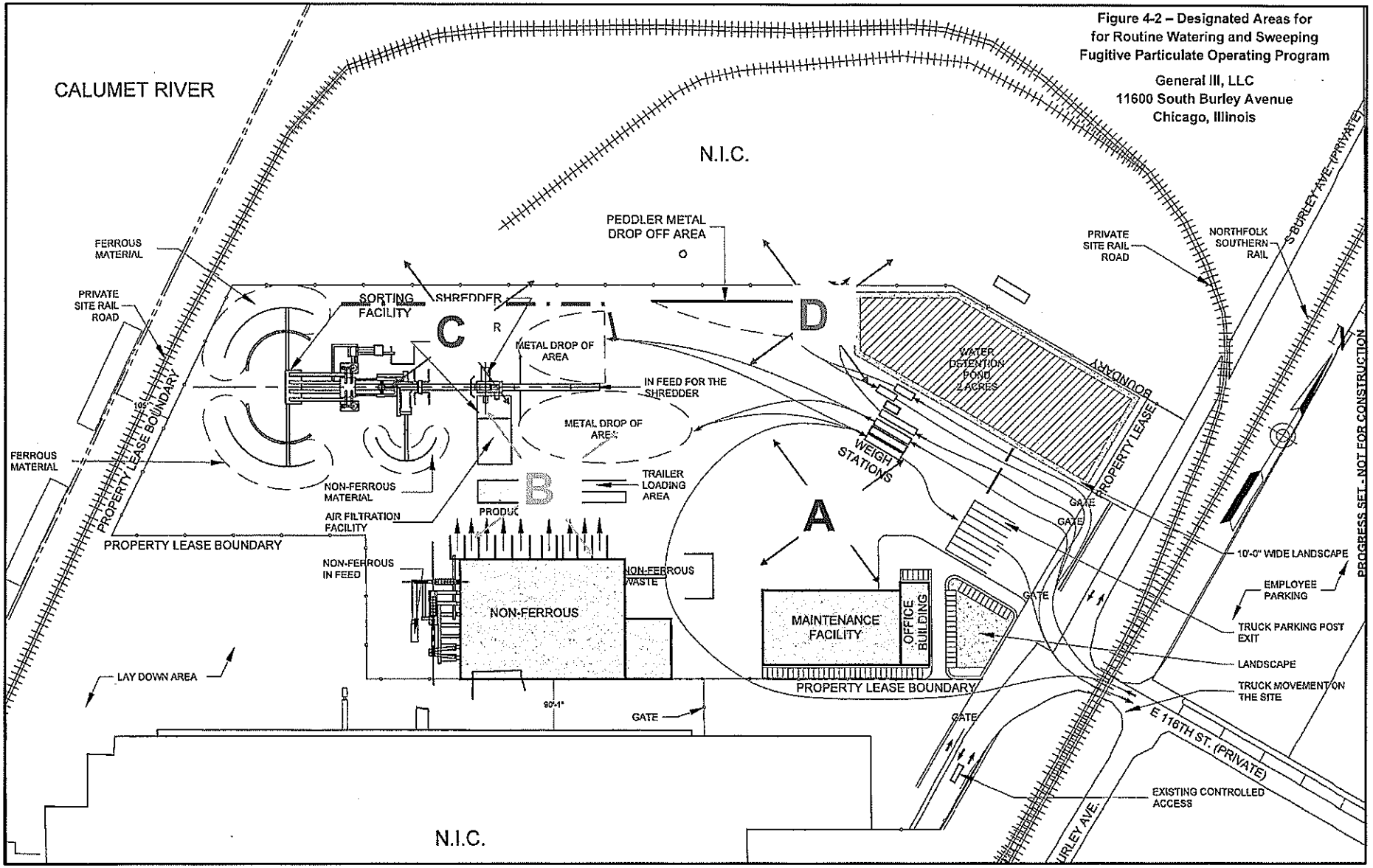


Figure 4-2 – Designated Areas for
for Routine Watering and Sweeping
Fugitive Particulate Operating Program
General III, LLC
11600 South Burley Avenue
Chicago, Illinois
CALUMET RIVER
N.I.C.
PEDDLER METAL
DROP OFF AREA
FERROUS
MATERIAL
PRIVATE
SITE RAIL
ROAD
SORTING
FACILITY
SHREDDER
C
R
D
METAL DROP OF
AREA
IN FEED FOR THE
SHREDDER
METAL DROP OF
AREA
WATER
DETENTION
POND
4 ACRES
PRIVATE
SITE RAIL
ROAD
NORTHFOLK
SOUTHERN
RAIL
S BURLEY AVE (PRIVATE)
PROPERTY LEASE
BOUNDARY
FERROUS
MATERIAL
NON-FERROUS
MATERIAL
B
TRAILER
LOADING
AREA
WEIGH
STATIONS
AIR FILTRATION
FACILITY
A
GATE
GATE
PROPERTY LEASE BOUNDARY
NON-FERROUS
IN FEED
NON-FERROUS
WASTE
NON-FERROUS
MAINTENANCE
FACILITY
OFFICE
BUILDING
GATE
10'-0" WIDE LANDSCAPE
EMPLOYEE
PARKING
TRUCK PARKING POST
EXIT
LANDSCAPE
TRUCK MOVEMENT ON
THE SITE
LAY DOWN AREA
90'-1"
GATE
PROPERTY LEASE BOUNDARY
GATE
E 116TH ST. (PRIVATE)
EXISTING CONTROLLED
ACCESS
BURLEY AVE.
N.I.C.
PROGRESS SET - NOT FOR CONSTRUCTION

R 009338

Exhibit 219

From: Guy, Jeff
To: EPA.PublicHearingCom
Bcc: Adelina Avalos; Alfredo Romo; Amy Genender; Amy Genender Feltheimer; Ana Sanchez; Andres Villegas; Andrew Del Giudice; Andy Daglas ; Angel Avalos ; Angelica Delacruz; ANN M. ZWICK; Annamarie Garza; Aracely Galvan; Arlene Ramos; Betty Jo Joy; Brian Cavanaugh; Brian gabriel; Carlos Cerda; Carolina Diaz Martinez ; Caroll Ordas; Carolyn A. Marsh; Ceasar Rodriguez ; Chalres Stark; Christopher O"Hara; Corina Pedraza ; Cristina Rodriguez; Cynthia Strickland; Damien M. Spaulding ; Damon Watson; Danielle Austin-Cano; Deeana Mendoza; Diana Barthelemy; Eddie Luna; Edwin Gonzalez; Elena Calvillo; Elihu K Blanks; Emma Cullnan ; Enriqueta Pacheco; Erik Ramirez; Erik Wallenius; Gail Molinaro; Gigi Buis; Gina Ramirez; Haley McKeever; Herminia Vanna; ibamfxd@gmail.com; James and Angie Rodriguez; James Kinney; Jennifer Walling; Jessica Chavarria; Joann Podkul-Murphy; Jocelyn Rangel; Joel Cortes; John Ashenden ; John Stajcic; John Tabares; Jordan Diab; Jose Rodriguez; Joseph and Bertha Aguilar; Juan Rojas; Judith Andrade; Julio Ponce; Keith Harley; Kiana Courtney ; Kimerly Boreczky; L. Rachel McKinzie; Lara Compton; Linda Young; lresteviz@gmail.com; Luis M. Alvarez; Margaret Cortes; Maria Borja; Maria Valerio; Mark Hagan; Mark Mitrovich; Mark Velez; Mary Esquivel; Matt Kraemer; Mautice Elion; Maxwell Evans; Meleah Geertsma; Merrick O'Connell; Michael Caldie; Miles Vance; Ms. Robateau; Nancy Loeb; Nancy Pacheco; Nelly Martinez; Nicholas Valdez ; Nick Radakovich ; Nicolette Cooke; Olga Bautista; Pam Navarro; Pastor Matt Zemanick ; Peggy Salazar; Rachel Roti; Rafael Razo; Ricardo DeLeon; Richard L. Martinez, Jr.; Rita Malfeo-Klein; Robert Adolfson ; Rocio Ochoa ; Rose Joshua; Sandra Leon ; Silvia Vaca; Terry Evans; Terry Herlihy ; Theodora Cunningham; Thomas Ward; Tom; Tom Meyer; Tony Paz ; Viviana Arellano; Wayne Garritano; Yolie Rangel
Subject: Construction Permit No. 19090021/Cook County
Date: Thursday, June 25, 2020 5:03:00 PM
Attachments: image001.png
General Iron Responsiveness Summary.pdf

Hello,

On June 25, 2020, the Illinois EPA issued Construction Permit No. 19090021 to General III, LLC to construct and operate a scrap metal recycling plant to be located at 11600 South Burley Avenue in Chicago, Illinois.

The permit and responsiveness summary are both available on the Illinois EPA website at https://www2.Illinois.gov/epa/public-notices/boa-notices/Pages/archive.aspx. To access the documents for this proceeding, please click the above link and enter "General III LLC" in the "Facility Name" box and press "Search". The responsiveness summary is attached to this email.

The Illinois EPA held a virtual public hearing in this matter on May 14, 2020. The background information for this permitting action, the comments made during the hearing and submitted during the comment period, and the Illinois EPA responses are provided in the attached responsiveness summary.

Thank you for your interest in this permit decision.

Jeffrey J. Guy
Illinois EPA
Office of Community Relations
(217) 785-8724
Jeff.Guy@illinois.gov

From:	Guy, Jeff
To:	EPA.PublicHearingCom
Bcc:	cagarcia19@yahoo.com; Charles Stark; Daniel Villarreal; David Ogulei; garcia.emile@gmail.com; Hal Tolin; John Pinion; Josh Ellis; Margaret Galka; Mark A. Weintraub; migcit2@yahoo.com; mmendoza13@yahoo.com; Neighbors for Environmental Justice; Renée L. Grigorian; Robin Lam; Samira Hanessian; Susan Sadlowski Garza; Ted Stalnos; Zac Halden
Subject:	Construction Permit No. 19090021/Cook County - Chicago/General III, LLC
Date:	Thursday, June 25, 2020 5:06:00 PM
Attachments:	General Iron Responsiveness Summary.pdf image001.png

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Thank you for your interest in this permit decision.

Jeffrey J. Guy
Illinois EPA
Office of Community Relations
(217) 785-8724
Jeff.Guy@illinois.gov

Exhibit 219

Responsiveness Summary
June 25, 2020
Construction Permit General III, LLC
Source ID No.: 031600AGJ
Application No.: 19090021

Table of Contents

INTRODUCTION

This document is a Responsiveness Summary prepared by the Illinois EPA in conjunction with the issuance of a construction permit to General III, LLC (General III) for a scrap metal recycling facility to be located at 11600 South Burley Avenue in Chicago, IL. This document provides a written response to significant, permit-related comments raised at public hearing and during the related written public comment period.

RECENT EVENTS

The Director and staff of the Illinois EPA share a sincere appreciation and sympathy for the hardships that many residents of Illinois and particularly Chicago's Southeast Side have endured in recent months due to the COVID-19 pandemic. The pandemic dramatically altered daily life for almost everyone in our Nation and in many other countries around the globe. The public health impact of the virus has been felt most severely by several vulnerable segments of our society including the elderly and patients living in long-term healthcare facilities, individuals with certain respiratory or cardiovascular co-morbidities or weakened immune systems, and, as we have learned more recently, communities of color have contracted and died from the disease in disproportionate numbers. The related social and economic impacts caused by the virus, which have ranged from the closures of our schools, governmental offices and religious activities, the shut-down of non-essential businesses, and the fears and isolationism that accompanies social distancing, to the loss of friends and loved ones who succumbed to the contagion, are nothing short of profound. Regrettably, these and other effects of the pandemic are still being felt, even as medical science and public health officials continue to fight and monitor the disease, and our collective efforts turn to restoring some semblance of normalcy to our lives.

The recent protests posed a separate set of physical and emotional difficulties for many residents in Chicago and surrounding communities. National events that ignited the protests are slowly giving way to a renewed sense of commitment to end systemic racism. For the many thousands of peaceful protesters marching in the region, these events have given voice to their frustrations with our institutions, past and present, and sounded a call for not just institutional reforms but for a change in how we interact with each other as human beings. For others, the shadow of violence in the wake of some protests provoked anxieties about the safety of their communities, as suggested by comments received during the public comment period urging a delay in the current proceeding.

The confluence of these events during the current permitting process was unfortunate. However, while various regulatory activities at different levels of government were canceled or delayed, essential activities conducted by state agencies continued without significant interruption as part of Governor J.B. Pritzker's Disaster Proclamations and Executive Orders responding to the COVID-19 crisis. This essential work included activities overseen by the Illinois EPA in the area of environmental permitting.

The Illinois EPA administers its permit programs pursuant to the requirements of the Illinois Environmental Protection Act and implementing regulations, including a decision deadline under which the Illinois EPA must act on a given permit application. These requirements are at the heart of why the current action cannot be delayed. Moreover, permit applications remained pending with the Illinois EPA from before the start of the pandemic, and some applicants, including General III, continued to work with Illinois EPA Permits staff throughout the Spring in anticipation of securing the necessary permits. As more people return to work and businesses reopen, and as broader sectors of our economy become more functional again, applicants are inquiring about their projects and submitting new applications. These signs point to the need for us to continue the administration of permit programs.

Due to the COVID-19 pandemic and subsequent Proclamations and Executive Orders by Governor Pritzker limiting large public gatherings, the Illinois EPA as with all other agencies and governmental bodies in the State, was not able to provide an "in-person" hearing in this matter. In lieu of a traditional hearing venue, the Illinois EPA opted to provide a "virtual" hearing, where participants called in by phone or joined by computer to make comments or listen to the proceedings. A virtual hearing comports with all requirements of 35 IAC Part 166, Subpart A, while also minimizing the threat of COVID-19 exposure to the public. These steps sought to balance the interests of public safety with the need to implement existing programs consistent with legal requirements.[1]

PUBLIC OUTREACH

Pursuant to an IEPA environmental justice notification for the new construction permit, advocacy groups submitted a request for hearing on the project. Recognizing the significant public interest in the facility, IEPA issued a notice of public comment period beginning on March 30, 2020 and two virtual public hearing sessions on May 14, 2020. The purpose of this action was to allow for public participation in the permitting process for a draft construction permit developed by the Illinois EPA's Bureau of Air.

The public outreach associated with the application for construction permit was not required by statute or regulation but, rather, was discretionary on the part of the Illinois EPA's Director. A hearing officer was designated, the notice was issued, and the comment period and the informational permit hearing were all conducted, in accordance with applicable regulations found at 35 Ill. Adm. Code Parts 166 and 252. The notice of the comment period and virtual hearing was posted to the agency website, as well as forwarded to numerous elected officials and persons known to be interested in the matter, including representatives from various environmental advocacy groups. Contemporaneous with the notice, the draft permit and related documents from the administrative record were also posted to the Illinois EPA's website.

Instructions detailing how to participate in the informational hearing, either through oral comments or simply listening in to the proceedings, were also posted. The notice and instructions for hearing participation included numerous references to agency contacts (either the Hearing Officer or the Office of Community Relations) for any questions or concerns (e.g., requests for interpretation, informational or special needs, assistance with WebEx).

The public hearing was held on May 14, 2020. As originally scheduled, the Illinois EPA held two sessions: the first session was held at 1:30 pm and featured seven speakers and approximately 117 participants, and the second session was held at 6:00 pm and featured 14 speakers and approximately 86 participants. All told, over 200 people participated in the public hearing, far exceeding the level of participation shown in recent informational permit hearings concerning projects in EJ areas. A Webex recording of the hearing sessions was later posted to the agency website.
https://www2.illinois.gov/epa/public-notices/boa-notices/Pages/default.aspx

[1] **Even now, public gatherings of uncertain size are still prohibited. A gathering of more than 200 people as participated in the public hearing is not envisioned until the state has reached Level 5 of the Governor's plan. This would only result in the issuance of a permit by default or a permit denial, the latter of which is not supported by the administrative record.**

It can be noted that the Hearing Officer and Office of Community Relations assisted participants in advance of the hearing and several speakers during the two sessions. They also worked assiduously with all commenters who contacted the Illinois EPA to assure timely receipt of comments, including several commenters who sought help with more voluminous comments to avoid the necessity of printing and mailing.

The public comment period ran for 77 days, thus affording the public nearly two and half months to consider the planned permitting action. Approximately 329 people submitted written statements, submissions and exhibits during the comment period, again exceeding the level of past participation in previous projects impacting EJ areas. Oral and written comments generally expressed opposition to the project and the accompanying participation process, with many people urging the Illinois EPA to suspend or deny the application for construction permit. While acknowledging the voiced opposition to the process, the level of participation supports the Illinois EPA's position that the right of the public to voice their concerns about the project was assured.

SPECIAL MENTION

Before the company can begin operations at the Burley Avenue location, it must also receive permits from the City of Chicago, including one pursuant to the City's new rules for large recycling facilities. The new rules, effective June 5, 2020, implement the City's Recycling Facility ordinance and include additional requirements that General Iron meet in order to begin operating at the southeast side location. The City's rules provide minimum standards for what is required in a permit application, including information to demonstrate that the facility will be designed and operated in a manner that prevents public nuisance and protects the public health, safety, and the environment. The rules also contain location, operational, and design standards applicable to large recycling facilities such as General III, including vehicle and traffic requirements, noise monitoring, air quality standards, and air emission monitoring.

DECISION

On June 25, 2020, the Illinois EPA issued a construction permit for General III, LLC. This final permit determination was rendered after consideration of all comments and in accordance with the Illinois Environmental Protection Act.

Significant changes have been made to the draft permit in response to public input and are noted in Attachment A to this Responsiveness Summary.

BACKGROUND

On September 25, 2019, General III, LLC applied for a permit to construct a scrap metal recycling facility to be located at 11600 South Burley Avenue in Chicago, Illinois.

This application for permit arises based on an agreement between the City of Chicago, General Iron Industries, and RMG Investment Group that the existing scrap metal recycling operations of General II, LLC, at 1909 North Clifton Avenue in Chicago, Illinois cease and relocate, matters for which the Illinois EPA had no involvement and for which it has no legal role.

Rather, the Illinois EPA is the state permitting authority charged with permitting Illinois sources consistent with applicable state and federal laws and regulations. General III is required to obtain an air pollution control construction permit from the Illinois EPA Bureau of Air prior to beginning construction because it is a new emission source. For additional background information, please refer to the Project

Summary, which is available on the Illinois EPA Public Notice webpage:
https://www2.Illinois.gov/epa/public-notices/boa-notices/Pages/archive.aspx.

As the scrap metal recycling facility is relocating to a site that the Agency would deem to be within an environmental justice area, the Agency sent an EJ notification on October 1, 2019, consistent with its environmental justice public participation policy. This letter was mailed to 48 persons, including numerous groups and elected officials representing the local community. This environmental justice letter elicited a response sent to Director Kim on October 30, 2019, from Keith Harley, on behalf of Southeast Environmental Task Force, the Chicago South East Side Coalition to Ban Petcoke and the Natural Resources Defense Council, requesting an Environmental Justice Analysis, a hearing and a subsequent written public comment period for the proposed facility. Acknowledging the request for hearing, and in recognizing the public interest in the proposed project, the Agency determined that it was appropriate to hold a public hearing on the permitting transaction.

AVAILABILITY OF DOCUMENTS AND ILLINOIS EPA CONTACT

Copies of the construction permit that has been issued, as well as this Responsiveness Summary, are available for viewing by the public at the Illinois EPA's Headquarters at 1021 North Grand Avenue East in Springfield.

Copies are also available electronically at:
https://www2.illinois.gov/epa/public-notices/boa-notices/Pages/archive.aspx

Printed copies of these documents are also available free of charge by contacting
Brad Frost
Office of Community Relations.
217-782-7027
brad.frost@illinois.gov

QUESTIONS AND COMMENTS WITH RESPONSES BY THE ILLINOIS EPA

Comments are shown in conventional text and responses are shown in boldface. Comments and responses are arranged by subject matter, paraphrasing and grouping similar comments and questions. Numerous comments in this document are depicted in a condensed or paraphrased from, rather than recited in full. In other instances, comments are retained in original form because of their complexity or level of specificity.

All significant comments relating to the draft construction permit or that otherwise fall within the Illinois EPA's scope of permit authority are being addressed in this Responsiveness Summary. This framework necessarily does not answer some of the comments raised at the public meeting or during the comment period but this is appropriate due to the inability to address matters outside of the Illinois EPA's regulatory expertise.

Public Participation

1. The Illinois EPA should take public comment on the proposed issuance of the permit into consideration.

The Illinois EPA held extensive public outreach on its permitting transaction. The outreach included a 77-day written public comment period and a two-session public hearing wherein individuals could make oral comments that were entered into the hearing record. The Agency has reviewed those comments and this document responds to significant comments that are pertinent to the Agency's decision, process and review.

2. The affected community is largely Hispanic yet there was no information in Spanish including the notice.

The Agency frequently interacts with bilingual residents throughout the State on a number of issues. When a need or desire for services is evidenced or expressed, the Agency does everything in its power to provide those services to the best of its ability. The Agency has not been lax in providing translation services where local representatives or persons expressed simply a desire for such services, even while the use of those services at Agency meetings has not been robust; this includes recent outreach for permitting, rulemaking and cleanup programs. The Agency has also been responsive to local groups and representatives that have come forward with suggestions for changes and enhancements to the translation services that it provides. Additionally, the Agency has made strides in providing routine Spanish language services including by the hiring of a bilingual employee in its Office of Community Relations to help with such needs.

The Agency has conducted extensive outreach on the SE side of Chicago going back decades, with established contacts and regular communications with advocacy groups, elected officials and individuals on the SE side of Chicago including the East Side neighborhood, including holding and attending meetings and hearings on numerous projects and subjects. In past Agency meetings and hearings on the SE side of Chicago, neither need or desire for translation services have been requested or evidenced, nor has the Agency received comment previously that these services were not provided at hearings and meetings on the SE side of Chicago. Translation services are a large expense, and while the Agency is happy to provide those services when there is a need or an expressed desire, the Agency policy to this point has been to allow for the request of translation.

In the case of General III, a statement allowing for the request for translation, specifically including American Sign Language services, was included in the public notice. The Agency was in regular communication with local groups and their representatives and did not receive a request for translation either prior to issuance of the notice or subsequently to the notice but prior to the hearing. A simple request, by phone, letter, e-mail or other communication, would have produced from the Agency such notice and translation. No request was forthcoming until comments made at the public hearing and post-hearing and beyond a general complaint, the complainants did not identify individuals that needed the service. The good faith efforts of the Agency are adduced by the fact that although no request was received, the Agency was prepared to provide services during the hearing and had a translator available. No commenters used the services of the translator.

It should be here noted that in keeping with current Agency practice that since a request was received during this transaction, although at too late a point in the process to provide services during this transaction, for future transactions in this area, the Agency will provide translation of notices and other documents and work with community groups to determine the need for translation services at meetings and hearings.

3. This permitting process did not allow for meaningful public participation as the hearing was not

being translated into Spanish—the language of a significant proportion of the affected community—and the notice to ask for Spanish translation was not in Spanish. It seems highly unlikely that people would be able to ask for translation service if the notice is in a language that they do not understand. Thus, interested and affected persons likely missed out on any information shared in the public hearing.

As mentioned in other responses, the Agency had numerous communications with representatives of groups representing neighboring residents. Neither in conversations nor submittals by these groups, although other specific perceived deficiencies were outlined, was a request for translation enumerated.

It should be here noted that in keeping with current Agency practice that since a request was received during this transaction, although at too late a point in the process to provide services during this transaction, for future transactions in this area, the Agency will provide translation of notices and other documents and work with community groups to determine the need for translation services at meetings and hearings.

4. Very few local residents knew about the hearing or how to participate.

   There are also issues with advertising for an online [hearing].

   SETF cannot provide training to remedy this problem because its office is closed and its leadership, members and local residents are required to be distant from one another. As a small non-profit, SETF is experiencing almost insurmountable complications to continue functioning, let alone to mount a major campaign to facilitate public participation in an unfamiliar venue.

The Illinois EPA in performing notification of a hearing must meet certain statutory requirements of 35 IAC 166 Subpart A. In addition to those requirements, the Agency seeks to inform persons and groups that it may be aware have an interest in the project. In no instance does the Agency have complete information on the residents that may be interested in participating in its outreach proceedings and relies to a certain extent on groups and elected officials that are interested in environmental issues in the locality. One such group is the Southeast Environmental Task Force (SETF) who has been a longstanding and reliable partner in helping the Agency provide community outreach to interested residents on the South East side of Chicago.

However, while the Agency appreciates that groups are willing to partner in assistance, in particular SETF, this does not abrogate the Agency's responsibility for community relations. The Agency was thoughtful in establishing the procedures for its first virtual hearing. The Agency established the hearing in such a manner that the only need to participate was a telephone.

5. The Illinois EPA needs to work with elected officials at the city and state level to get information to the community members who will be impacted by this facility.

The Agency has contacts with officials in the City and specifically on the South East side. Notice of the hearing was sent to many elected officials, including Chicago's Mayor and Clerk, the County Board Chair, Clerk and State's Attorney, Chicago City Council's Environmental Protection and Energy Committee, federal Senators and Representatives, the state Senator and Representative, the local Alderman, the Attorney General, and the Cook County Board Environment Committee. Additionally,

various local and state agencies were notified as well as numerous non-profit and local interest groups.

6. A virtual public hearing during a pandemic is not acceptable; it did not provide a meaningful opportunity for public participation.

With respect to holding a public hearing/comment period during a pandemic, state government is still functioning and has responsibilities regardless. Also, the statutory and regulatory provisions associated with the evaluation of permitting requests, such as acting in a timely manner (permit application), are still in place. Illinois EPA is obligated to act in a certain period of time in regard to state construction permits. The initial 90 days set forth in Section 39a of Act was waived by the applicant late last year and two times since. The current decision deadline is June 25, 2020 and the applicant has made clear it will not waive this decision beyond this date. The permit will be issued by default if the Illinois EPA fails to act on the permit by this date. General III would have a legal defense or protection from having to obtain a construction permit; under this scenario, important conditions of the draft permit (e.g. testing, reporting, monitoring, record keeping) would not be put in put in place. Therefore, Illinois EPA makes all manner of attempt to avoid issuing permits by default.

Although this process is a departure from the past with respect to hearing venues, the procedural rules for Agency hearings at 35 IAC 166 accommodate for this type of hearing – the purpose of which is to enable the Agency to receive comments from the public regarding a draft permitting action.

7. The permitting process utilized for the Draft Permit hindered meaningful public participation. Outside of a pandemic, limiting public hearing to an online forum is a deterrent to public participation for those who do not have the broadband width to participate. It impedes the spirit of an actual public hearing—people cannot see any visual aids that would otherwise be present, and both they and the decisionmakers do not see the numbers of people in support of or opposed to a position. Neither body language nor emotion are conveyed as well over the phone or computer. A public hearing also does not usually have people register ahead of time to speak as was the case here, thereby limiting the voices of those who did not receive notice in time.

The online format of the hearing was established in a thoughtful manner to as closely resemble an "in-person" hearing as possible. As noted in other responses, the purpose of a hearing is to accept oral comments accurately into the hearing record for review by the Agency staff as part of a permit review. The Agency at any hearing tries to maximize the amount of time for public comment. The Agency typically minimizes its presentations at a hearing and rarely if ever utilizes visual aids as these tend to make Agency presentations lengthier with detriment to the amount of time available for public comment. In this instance the Agency did provide some visual aids that it believed to be helpful because of the new nature of the "virtual" format without taking extra time away from the amount of time to comment. It is also typical to have commenters register to speak prior to the hearing so that the Agency hearing officer may gauge how much time to allow for each speaker without impeding the opportunity to make comment for those who register later. Further, the hearing officer allowed all commenters that had contacted him prior to the beginning of the hearing a slot to provide comments regardless of whether they had met the deadline established in the notice. As noted in other responses, the Agency's decision-making is not based on opposition or support for a project but instead on the legal and technical merits of the proposal outlined in the application.

8. Illinois EPA has persisted with holding the public hearing and written comment period during the

local, state and national COVID-19 pandemic, coupled with demonstrations around racial injustice that have rocked Chicago and the nation. During this time, it is absurd to expect the residents of this overburdened community – residents who are struggling to protect themselves and their families from disease, layoffs, racial injustice and literally bullets in their streets – to be able meaningfully to participate in a permit process. This non-inclusive process has a clear impact on an environmental justice community and requires Illinois EPA to step back from issuing a permit until true community participation is made possible.

During the pandemic, people didn't have the health, means, or resources to participate, particularly in low income/minority community, already disadvantaged.

This reflects the racism that causes southeast Chicago to be a sacrifice zone.

This process lacked regard for the community and was racist.

While the pandemic has certainly caused changes to the usual or customary proceedings of numerous public bodies, the operation of public business must continue, particularly in light of the uncertainty in the length of time needed to have in place real remedies to COVID-19. Protection of the environment is important enough public business that the legislature has passed numerous laws over the last 50 years directing Agencies to be established, actions to be taken on regulation, and public monies to be expended in this pursuit.

While a public process is not a statutory requirement of the review of projects such as General III, the Agency believes it important to solicit public input on its decisions, particularly in areas it designates as environmental justice, and make such improvements to a permit as may come about as review of public comments allow. The Agency also believed it important to hold a public hearing and the associated process and comment period for this project and to seek the additional time necessary to achieve that end. Changes and improvements have been made to the permit mainly because of its location and the comments received. Due to the proposed location of the facility the Agency took additional considerations in regard to the impact on the community and provided additional outreach.

While the hearing was of necessity different than the usual hearing, the Agency made several enhancements and was thoughtful about the process such that it was inclusive for the public. Any hearing at any time will not allow all members of the public to participate. By the Agency historical standards, the hearing for General III was well attended with significant participation and written comments exceeding all but a few of the actions for which the Agency has held comment periods. In example of this, two recent, pre-pandemic, highly controversial permit hearings in the Chicagoland area, concerning the CAAPP permits for BWAY and Midwest Generation's Waukegan coal-fired power plant, drew attendance of approximately 40 and 35 respectively. Both were "in-person" hearings for controversial sources located in environmental justice areas.

It should also be noted that written comments submitted during the comment period carry the same weight as oral comments made at the hearing, as evidenced by this responsiveness summary.

9. In a pandemic, people are even further limited in their ability to participate—people can have broadband connection limitations, and moreover, people—especially on the East Side—are facing

the health implications of a pandemic and are rightfully more consumed with surviving this global emergency. The public should not be limited in their ability to meaningfully participate.

As noted in other answers, the Agency's intent within the strictures imposed by the pandemic and the requirements of Illinois law is to provide robust and effective outreach. As also noted, the process resulted in a public hearing and lengthy written comment period. Based on the number of comments received, participation in the hearing, and the resulting enhancements made to the permit as a result of the outreach process, the Agency believes that meaningful participation through its community outreach process has been effective in this case.

10. The hearing was inaccessible to community residents many of which are poor and lack technology.

    [I have] received many text messages/phone calls from community members that cannot login or participate or do not have the resources or capability.

    Neither SETF's members nor other local residents have participated in this type of hearing. Many do not have the technology and/or technical capability to participate.

The only technology needed to participate in the hearing was a telephone. Consideration was also give to the fact that people connecting by telephone may be using a cell phone and potentially limited cell phone minutes, thus the Agency established procedures allowing for commenters to have a relatively defined time when they would be called on for comment and allowed for commenters to request a more specific time if they had a need for such. The meeting was also recorded so that those who couldn't otherwise listen to a particular session or to the hearing as a whole could peruse the hearing at their convenience.

Additionally, contact information for the Agency was included in the notice and the Agency responded to all requests for assistance sent to it before and even during the hearing. These included e-mails directly to the Office of Community Relations and chats through the WebEx system. Further, between the two sessions, the Agency proactively contacted persons that had signed up to speak at the first session but that did not come on the line and at the commenters choice either scheduled them to speak at the 2nd session or gave them information on how to submit written comments; Similarly, the one person who did not come on the line to make comment at the second session was contacted after the hearing to inform on how to submit written comments.

For those that did not choose to comment but instead wanted to listen to the hearing, in addition to the live event, a recording was posted such that anyone of the public could listen to the proceedings at a later time.

11. The hearing process was difficult, and people struggled to connect and failed to connect.

The Agency is unaware of any specific persons and was not contacted before, during or after by any persons that were not able to connect and thus missed the opportunity to make oral comments. Additionally, for those who only desired to listen to the hearing, the Agency posted a recording of the hearing. The point of the public comment period and hearing is to afford the public and opportunity to comment. That opportunity to comment in writing or orally existed beginning March 30, 2020 and ending June 15, 2020.

12. People with impairments could not participate.

A statement allowing for the request for translation, specifically including American Sign Language services, was included in the public notice. The Public Notice provided guidance on contacting the Agency for an accommodation in this regard and no requests were made.

13. There should be another hearing so comments from Spanish speaking people are not limited to writing.

While this comment was made at the hearing, as noted in other responses, the Agency had a translator available at the hearing to translate for any person that would have needed such service to make their comment. All commenters that signed up to make oral comments were accommodated in the process.

14. Was there both translation of Agency statements and the opportunity for commenters to be translated?

Without a request for translation, the Agency did not have a good understanding of what services would be needed or who would need those services and thus how best to provide those services in the virtual hearing format. The Agency had a Spanish language translator available at the hearing if a commenter had come onto the line with a need to speak Spanish to make their comment. Without a request, this may have resulted in a slower or different process than the process that would have been established if a request was received timely before the hearing. No commenters requested or availed themselves of the translation services.

15. The process should provide for more public interaction and different ways to engage.

Since no specifics are provided, the Agency is unclear on the process changes desired. The Agency works with representatives and groups to provide appropriate and effective outreach; however, a hearing is a more structured and defined process both statutorily and in practice. While Agency hearings tend to be more interactive, and therefore the Agency feels, more informative than some similar agencies, notably federal counterparts, the purpose is still primarily to accept public comments into the record through recording or transcription. The Agency's Office of Community Relations is available to work with communities and groups to provide other forms of outreach and tools for public interaction. An OCR contact is listed in this document if further discussions along these lines is desirable.

16. More communication between the Illinois EPA and community is requested.

The Agency also desires to build substantive and lasting connections with communities in the State. This serves to help the Agency better understand the local environmental conditions as experienced by the local community and helps inform Agency decisions. To this end, the Agency has an established Office of Community Relations, whose purpose is to establish and participate in mutual dialogue with communities in the State relative to the authorities of the Agency. The Office of Community Relations has been in existence since the early days of the Agency. Similarly, and more recently, the Agency has established an Office of Environmental Justice. One among other duties is to specifically provide additional services of a similar nature to communities that meet the Agency definition of Environmental Justice.

17. Illinois EPA's website is not user-friendly and time consuming when searching for documents.

While the Agency houses numerous programs and services on its website, the Agency has prioritized certain programs on the front page, including public notices. The webpage provides a direct "Quicklink" easily visible for users of the website. Nonetheless, if difficulty is experienced in finding information on the website, the Agency's Office of Community Relations is always available to provide additional assistance. Most of the contacts on the Agency Contacts page go directly to the Office of Community Relations and the notice itself included contact information for two employees of the Office.

18. Will a hearing transcript be available?

The relevant hearing regulations require a transcript or recording of the hearing to be made available. A recording of the hearing was made and link to the recording posted to the Agency website on May 26, 2020. Interested persons can find the link at https://www2.illinois.gov/epa/public-notices/boa-notices/Pages/archive.aspx

19. How does the Illinois EPA weigh our comments? For example, if 100% of our comments are fully opposed to this permit, will the Illinois EPA not grant the permit?

As mentioned in the hearing officer's opening statement in the General III permitting matter, the Illinois EPA bases its decisions on the governing law and regulations. There is no way for the Illinois EPA to account for general opposition comments in the permit review. However, the Illinois EPA reviews and considers all comments received. And certain comments such as suggestions on enhancements to the permit may be reflected as part of permit decisions.

20. A petition was received with over 5500 signatures opposing General III.

    A petition was received with over 1500 signatures supporting General III.

The Agency must act on substantive issues within its express statutory and regulatory authority, not public opposition or favor for projects. That a project is located in one place or another, or is moving from one place to another, is properly the realm of zoning and land-use decision-making. To this end, the City of Chicago made clear decisions, where those decisions properly rest at the local level. A note here is made that the City must make additional decisions in approval of this project pursuant to its new rules for large recycling facilities.

21. Most of the participants who testified asserted that Illinois EPA's decision was fundamentally unfair and defeated the purpose for a public hearing.

The express intent of a public hearing and the associated process is the solicitation of public comments so that the Agency, within its authority, may contemplate and act on these comments in its permitting transaction. A virtual hearing achieved this end and comports both with the regulations and the practice of numerous other public bodies under similar circumstance. While there may be aspects differing between a "virtual" and "in-person" hearing, the underlying intent of a hearing was served, and even secondary considerations not provided for in regulation or guidance such as answering of questions and explication of the Agency permit were achieved.

22. Polluters request one-year construction permit or a 5-year, 10 year, or lifetime permit, so it is prudent to have more public hearings, more public notice, and more public input so that the community is fully aware of what is coming into their neighborhood.

The Agency has established an Environmental Justice notification process to do just this in areas that meet the Agency definition for environmental justice, such as the SE side of Chicago which includes the East Side neighborhood. As discussed above, this process resulted in the request for hearing and numerous communications with representatives of local groups interested in the proposed facility. Information on the Agency Environmental Justice program and how to sign-up for EJ notifications may be found at https://www2.illinois.gov/epa/topics/environmental-justice/Pages/default.aspx

23. [Due to] COVID-19 and local civil unrest it was not feasible for these aligned organizations to coordinate fully on a single set of comments [and thus] meaningfully participate.

The Agency does not require groups or individuals to coordinate their submissions. The Agency reviews all comments received and from all sources. As noted in other responses, the Agency has received an extraordinary number of comments in this matter. As always, the Agency appreciates the engagement by the public in its process and recognizes the considerable sacrifice in time and energy that the public makes in reviewing documents and commenting on permit transactions. The comments are valuable to the Agency's review and have helped the Agency to provide an enhanced permit that has significant conditions and requirements for the protection of the environment.

24. The agency lawyer did not appropriately respond to a hearing question regarding the consideration of violations by General Iron at its existing facility in the review of the permit application for the new facility.

The Illinois EPA conducts informational permit hearings, such as was done in this instance, to hear concerns from the public with the draft permit and/or proposed project.[2] While questions are sometimes asked of the panel, these questions commonly only elicit brief answers from the panel members. This is by design, as it allows for maximum participation by those in the hearing audience who wish to speak and assure that the hearing can be completed within the allotted time. General questions are usually answered by the hearing panel with a general answer, and a drawn-out answer by a panel member can risk taking away time otherwise best given to members of the public for their presentations. More detailed responses are provided to those hearing questions that are significant or complex, together with similar questions or comments submitted during the comment period, in the Responsiveness Summary.

In this instance, the response to the question raised at hearing was appropriately responsive to the question posed to the panel and was not prejudicial error. A speaker in the first session of the hearing asked two questions at the conclusion of his remarks, including how the Illinois EPA had considered the violations at the existing General II facility in the review of the project. The panel member, answered the question in roughly three parts. First, the panel member stated that the Illinois EPA did not consider alleged violations in its review of the permit application. Second, the

[2] **This general point was evident in the Hearing Officer's opening remarks**.

panel member briefly provided the reasoning for his answer.[3] Lastly, the panel member acknowledged exceptions to the rule that he had briefly described, stating that "there are limited exceptions to that but, by and large, that is the rule that we are controlled by."[4]

25. In the same incident as above, the Agency lawyer did not refer to the three parts of the statute that governed the legal issue, conflating them in a confusing and misleading fashion and did not adequately explain the caselaw authorities and existing law.

As discussed elsewhere, only two of the three cited parts to Section 39(a) are relevant to the consideration of adjudicated noncompliance or a past compliance history. The third part of the statute cited by the comment is a general authority by which the Illinois EPA is guided in developing conditions for a permit, allowing for the inclusion of terms that are "necessary to accomplish the purposes of this Act, and as are not inconsistent with the [Board] regulations…"[5] As mentioned, while this legal authority served as the basis for the inclusion of many of the construction permit's terms, including new conditions added in response to comments, there was no error committed by not mentioning it in relation to matters of prior enforcement history. Written comments and the Illinois EPA's more detailed response to comments are for matters such as this.

Environmental Justice

26. The most important reason to deny this permit is because it epitomizes institutional environmental racism. Racist outcomes do not require racist intent. We do know the intent behind the permit request, nor of the reviewers, and we are not claiming to. But based on the following three components, we are confident of the outcome.

The Illinois EPA strongly rejects any insinuation that racism played any role in the review of this permit application. The Agency's review was performed strictly according to relevant legal and technical requirements.

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[3] "And the reason for that is that our review is pretty much constrained to what is outlined within a permit application and is pretty much just addressing whether or not there are operational or design capabilities that are set out in a project that… whether those will meet applicable requirements. We cannot review or consider violations at another facility as in the case of GIII here having a previous operation at the Clifton Avenue address. The reason for that boils down to caselaw that Illinois courts have developed in the past in interpreting the Environmental Protection Act. That caselaw has directed the Agency to assure that we confine our review to just matters of the application and not to compliance and enforcement considerations."

[4] *See,* Hearing Recording beginning at 36.26. A related written comment regarding the panel member's response to the same question is baseless. The comment states: "[A hearing speaker], a resident living near General Iron, testified about the negative health consequences and a history of violations, prompting an Illinois EPA attorney to immediately intervene to discount this testimony." SETF comments, dated June 15, 2020. The panel member was "prompted" only by a general question asked by the speaker, at the conclusion of his remarks, concerning any review of violations in the permit review. The response by the panel member did not discount any testimony of the speaker.

[5] *See,* 415 ILCS 5/39(a). This authority bears no relation or significance to the consideration of alleged violations, which are addressed by the more specific criteria identified in the two preceding sentences of Section 39(a).

27. Why was there no EJ analysis as requested?

In order to analyze the environmental justice impacts of the proposed relocation of the source, the Illinois EPA first looked to the demographics and then reviewed discretionary modelling conducted by the permit application. In order to evaluate demographic information, the Illinois EPA utilized the Agency's Geographic Information System (GIS) mapping tool EJ Start. EJ Start identified the area as an "area of EJ concern" pursuant to the Illinois EPA's EJ Public Participation Policy (https://www2.illinois.gov/epa/topics/environmental-justice/Documents/public-participation-policy.pdf). As such, the Illinois EPA sent an environmental justice notification letter early in the application process and which ultimately led to requests for a public hearing, which was not statutorily required, but was granted given significant public outreach. The Illinois EPA therefore conducted enhanced public outreach in accordance with existing policies. In addition, recognizing the concern for the proposed location of the source being located in an area of EJ concern, the Illinois EPA requested and obtained modelling from the permit applicant in order to determine whether there would be significant impacts for emissions from the shredding operation.

28. The public hearing was not consistent with the Agency's EJ policy.

Much of the Agency's Environmental Justice Policy is concerned with enhanced public outreach, which as discussed herein, the Illinois EPA conducted via an environmental justice notification letter and subsequent discretionary public hearing.

On September 25, 2019, the Agency received an application from General III, LLC to construct a new scrap metal recycling facility at 11600 South Burley Avenue in Chicago. The Agency is subject by law to a maximum 90-day review time for an application of this nature unless the applicant waives such restriction. Additionally, for an application of this nature, public notice is not required by law or regulation. As such, to provide an opportunity for the public to become aware and have an opportunity to request information and provided feedback, the Illinois EPA has established an EJ notification process for facilities that will be located in a designated EJ area. It is important in cases such as this where a 90 day decision deadline is in place that the Agency send the EJ notification letter in a timely manner so that the public has as much notification and time as possible to request and review documents and ask questions of the Agency. In keeping with this practice, on October 1, 2019, the Agency issued an Environmental Justice notification letter. This letter was mailed to 48 persons, including numerous groups and elected officials representing the local community. This environmental justice notification letter elicited a response sent to Director Kim on October 30, 2019, from Keith Harley, on behalf of Southeast Environmental Task Force, the Chicago South East Side Coalition to Ban Petcoke and the Natural Resources Defense Council, groups that the Illinois EPA routinely works and has conversations with about projects on the South East side of Chicago; groups that as evidenced by past interactions represent a broad swath of residents in SE Chicago including the East Side neighborhood. The letter expressly requested an Environmental Justice Analysis, a hearing and a subsequent written public comment period for the proposed facility. Acknowledging the request and in recognizing the public interest in the proposed project, the Agency determined that it was appropriate to hold a public hearing on the permitting transaction. The Agency had numerous communications with these groups or their representatives. Additionally, Agency staff had conversations with these same parties to discuss issues and answer questions about the other facilities that are currently on the site and that will be a single source with GIII once the facility has relocated.

As an additional point, the Agency places great importance on its Environmental Justice program and ensuring that minority and low- income persons in Illinois are able to have information about and input into Agency decisions consistent with sound EJ principles. The seriousness of our consideration of the input received leads the Agency frequently, as in the case of the GIII application and permit, to make demands of facilities over and above legal requirements in the submittal and review of application materials and conditions of the permit. Demands made of the applicant are described in other responses in this document and changes to the draft permit may be found in Appendix A of this document.

29. The public hearing was inadequate: (a). it was only in English;
the Illinois EPA Spanish interpreter did not interpret anything said by Agency officials or English speaking participants so the hearing discriminated against Spanish speaking residents in this community;
(c) there is no way for Spanish speaking residents to listen to the recorded hearing unless they found their own interpreter; and
According to the Illinois EPA's EJ Policy, "The EJ Officer will determine when public notices should be bi- or multi-lingual, where these notices should be published, and when translators should attend hearings. The EJ Officer will also review and approve the proposed response to EJ comments raised at hearing or in written comments, and coordinate this response among the Bureaus, Division of Legal Counsel and the Office of Community Relations.

The Illinois EPA Office of Environmental Justice coordinates with the Office of Community Relations in accordance with the Illinois EPA's Environmental Justice Policy on translation issues, with the EJ Office goal to establish guidelines and Community Relations to implement those within the Agency outreach. As mentioned elsewhere, the public notice requested that anyone needing translation services contact the Illinois EPA and no one did. Notwithstanding, the Illinois EPA had a Spanish speaking employee on hand at all times during the hearing. As discussed elsewhere, the Illinois EPA seeks to work with local communities and representatives to determine appropriate outreach. The Illinois EPA acknowledges the comment and though the Agency believed that it had been having sufficient conversations in the days and months leading up to the notice and hearing, the Agency hopes to work closely with groups in the future to ensure that these types of issues are more fully addressed.

30. Agency did not translate its own comments during hearing (e.g. how to submit written comments)

Although the Illinois EPA hearing notice mentioned the process to request interpretation, the Illinois EPA should not place the burden of requesting interpretation on an Environmental Justice community, a low-income minority community. Instead, the Illinois EPA should proactively research the basic demographic and linguistic isolation statistics of every Environmental Justice community (available on the US Census website) before every public hearing (whether in-person or virtual) to ensure full public participation in the permitting process.

The Illinois EPA recognizes this concern and, in the future, hopes to work closely with community members and groups to evaluate the need for translation services in addition to the steps mentioned in the comment. As mentioned elsewhere, while the Agency must operate within its statutory constraints, including time constraints, the Agency prides itself on being responsive to communities

and their needs or desires as relate to the outreach the Agency performs and did not believe that its outreach was lacking as it related to the need or desire for translation. The Illinois EPA has in the past and will continue to evaluate issues concerning translation and appreciates the input of local community groups as expressed in these comments and dialogues that the Agency enjoys in its regular outreach.

31. In addition to the problematic public participation process, Illinois EPA's broader permitting action will result in significant, disproportionate impacts on communities of color and other protected classes, in violation of federal and state civil rights laws

There is no information in the record to suggest that issuance of the construction permit will result in significant, disproportionate impacts. The Illinois EPA reviewed modelling conducted by the permit applicant, which did not demonstrate any significant adverse impacts. Furthermore, the Illinois EPA has an air monitor at nearby Washington High School, which will provide information concerning emissions impacts of the shredding operation.

32. The Agency should especially pay attention to the history of this facility because General Iron is moving to an area of environmental justice concern. The Illinois legislature has recognized that the principle of environmental justice requires that no segment of the population, regardless of race, national origin, age, or income, should bear disproportionately high or adverse effects of environmental pollution. 415 Ill. Comp. Stat. Ann. 155/5. Moving this facility to the East Side community does just that.

415 Ill. Comp. Stat. Ann. 155/5 references the Findings in the Illinois Environmental Justice Act. The Act goes on to provide for the formation of the Illinois Environmental Justice Commission to address these Findings. An Illinois EPA representative is designated by the EJ Act to serve as a Commissioner on the Commission and the Agency is further directed to provide administrative support to the Commission. The EJ Act does not place additional authority with the Agency to address permitting, zoning, or otherwise provide regulatory direction to the Agency.

33. The Draft Permit fails to consider the cumulative impacts on the East Side community to which the facility is moving. When there are potential environmental impacts in an area of environmental justice concern, the Agency is supposed to look at the information provided as well as other available information to assess whether there are potentially significant adverse environmental impacts.

As described above, the Illinois EPA looked at the modelled emissions impacts and has an air quality monitor on Washington High School, both of which provide information concerning potential environmental impacts. While the Illinois EPA can and does evaluate environmental impacts from sources during a permit transaction, there is not currently any Illinois or federal law or regulation addressing cumulative impacts in the context of a permitting transaction. Without a legal mandate, the Illinois EPA is limited as to what it do can regarding cumulative impacts (e.g., more stringent permit conditions).

34. [I] oppose yet another heavy industrial facility notorious polluter relocating from the well-off, predominantly white Lincoln Park community, to this environmental justice community. The Mayor's Office behind closed doors facilitated an agreement whereby General Iron would leave the higher income and largely white Northside Lincoln Park neighborhood by 2020 and relocated to the

Southeast Side environmental justice community. Mayor Lightfoot's election in 2019 did not change the overall trajectory.

As noted in this comment, the Agency does not have authority or review over land-use and zoning decisions. For decisions within the boundary of the City, this authority resides with the City.

35. This is not the just and equitable process or outcome that Illinois EPA purports to uphold.

The Agency followed its Environmental Justice Public Participation Policy, a policy that has well served the Agency and the commenters on numerous occasions including the present instance. Notwithstanding, the Illinois EPA has acknowledged and demonstrated in practice that the policy is a living document, one that has and will be revised based on real world experience and input from environmental justice communities. While the commenters may not like the decision at the end of the review process, the Illinois EPA strives to ensure that the public outreach process is as robust as possible. The steps taken in this case, pursuant to the Agency's EJ Public Participation Policy, provided for meaningful input from the public.

The Agency issued an environmental justice notification letter which solicited a hearing request. The Agency held a hearing including written comment period. Additionally, the Agency worked with various local groups to answer questions related to the application. While the hearing was of necessity different than the usual hearing, the Agency made several enhancements and was thoughtful about the process such that it was inclusive for the public.

Information Sharing

36. How may I get access to the readings taken from the air monitoring station at G.W. High School?

The monitoring information is readily available to the public through requests to the Agency under the Freedom of Information Act. For ease, requests of this nature may be submitted to Brad Frost of the Office of Community Relations, who will then forward them to the Agency Records Unit for response. To directly request the documents, the FOIA request form may be found at https://external.epa.illinois.gov/FOIA

37. What is the best way to maintain a direct line of communication with the Illinois EPA if emissions are seen from this facility?

Directions on how to submit complaints and observations are found on the Agency's pollution complaint page, https://www2.illinois.gov/epa/pollution-complaint/Pages/default.aspx There you will find an online form for ease of submittal that includes all of the information that the Agency requests.

All complaints are investigated by the Illinois EPA. Notably, for complaints relating to sources located within the City of Chicago, the Illinois EPA often seeks the assistance of the City of Chicago Department of Public Health. Of course, any violations of City ordinances would be addressed by the City and violations of the Environmental Protection Act would be addressed by the Illinois EPA.

38. Can members of the general public request information directly from the source?

The public is certainly free to communicate with a source regarding requests, questions, comments or concerns. Often, sources welcome the exchange and find it mutually beneficial. For example, some sources afford tours so that the public may see what it is they do. However, the source is not under a statutory obligation to directly provide to the public reports relative to its operations that are regulated by the Agency. Notwithstanding, the information required to be reported to the Agency under the permit is available under the Freedom of Information Act; and, as noted elsewhere herein, the reporting obligations have been expanded under the issued permit.

39. The permit should require notification to the public, in addition to Illinois EPA, of any emissions violations.

The permit contains numerous reporting obligations incumbent upon General III. Notably, a key reporting requirement relates to deviations from the terms of the permit. Information reported to the Illinois EPA by General III is available to the public under the Freedom of Information process. FOIA requests may be made by request to the Agency; the online FOIA request form may be found at https://external.epa.illinois.gov/FOIA For assistance in this regard, please contact the Office of Community Relations contact listed in the introductory section of this responsiveness summary.

40. Page 23 of the draft construction permit says "the owner or operator of a subject VOM source shall collect and record all of the following information each day and maintain the information at the source for a period of three years." The Illinois EPA should require the company to post all monitoring data weekly on a publicly available website, given the company's record of past violations.

The permit contains numerous recordkeeping obligations incumbent upon General III. The records that are to be maintained are voluminous. Reporting all of this information to the Illinois EPA or posting same to a website would not be practical. Rather, key information in ensuring compliance with applicable terms is reported to the Illinois EPA. This information is available to the public.

Cumulative Risk

41. I would hope that the Illinois EPA will consider the cumulative burden on the Southeast Side community when evaluating this new facility.

While not statutorily or regulatorily required to perform any cumulative impact analysis, General III performed air dispersion modeling to address its impacts on ambient air quality. The modeling looked at metallic hazardous air pollutants, with special attention to lead and manganese. The modeling demonstrated that the air impact will not exceed any established standards. A robust inventory of other local sources was included in the modeling inventory and any other potential sources are accounted for through use of the monitoring station at Washington High School for background monitoring values.

42. EPA should consider all emissions (total amount) not just from this location, but other nearby emission sources.

The Illinois EPA has endeavored to address the contributions from other sources in the region to the two hazardous air pollutant metals believed to be of significance – lead (Pb) and manganese (Mn). Not only was there a robust inventory of other sources included in the modeling inventory, but a background monitored concentration was added to the modeled impacts to account for potentially unknown, unpermitted, natural and/or distant sources.

43. The EPA to not just consider the emissions from this one location, but instead add these emissions to the total amount that the neighbors of Eastside and the students of GWHS will be exposed to. If we think of the environment surrounding this facility and the school as a bathtub, the proposed emissions are only adding to a bathtub that is already full of emissions from other sources nearby and there is little to nothing being done to empty the tub. I have already cited the Air Dispersion Modeling Protocol document. In that same section, RK & Associates are asking the EPA to allow them to not count emissions collected at the Washington High School air monitoring station on days when the wind is not blowing from the southwest.

The Illinois EPA has endeavored to address the contributions from other sources in the region to the two hazardous air pollutant metals believed to be of significance – lead (Pb) and manganese (Mn). Not only was there a robust inventory of other sources included in the modeling inventory, but a background monitored concentration was added to the modeled impacts to account for potentially unknown, unpermitted, natural and/or distant sources. The Illinois EPA directed the permit applicant's consultant to use conservative background values obtained from the analysis of total suspended particulate samples from the Washington High School monitor. For lead, this represented the highest three-month rolling average concentration for years 2016-2018. For manganese, the background values represented the maximum 24-hour average and annual average concentrations during those same years. The monitored values did not selectively eliminate emissions collected from any wind direction, including "when the wind is not blowing from the southwest." The Illinois EPA is well aware of air pollutant levels in the Lake Calumet region of Cook County and the need for maintaining health-protective levels.

44. Another failure of the EPA was its failure to consider the George Washington High School air monitoring data when drafting the permit. This data shows that the Southeast Side neighborhood already deals with the state's highest levels of toxic heavy metals, chromium and cadmium, as well as sulfates."

The Illinois EPA required the company to perform ambient air modelling and submit such to the Agency as part of its application, an atypical request for a facility of this size. This modeling used data from the Washington monitor as its background ambient data.

45. The applicant has failed to describe and Illinois EPA has failed to consider cumulative impacts of permitting a new source of heavy metals in an already overburdened EJ community, which has among the highest monitored levels of airborne metals in entire state.

While not statutorily or regulatorily required to perform any modeling in the application, the Agency required General III to perform air dispersion modeling demonstrating that the air impact will not exceed any established standards for the HAP metals. lead and manganese. Notwithstanding that the monitor at Washington High School registers metals as a fraction of the captured PM emissions, the levels do not exceed any health-based ambient air standards for metals.

46. GIII did not consider the impact of the existing operations at the site.

GIII performed air dispersion modeling for metallic HAPs in support of the air construction permit application and demonstrated that the air impact will not exceed any established standards. The Illinois EPA later evaluated the increase in metallic HAPs from the four SCPM facilities in conjunction with the GIII HAP emissions but did not find any increases of potential concern. Metal HAP emissions from the SCPM Entities' ROSS affected sources are less than 0.1 tons annually.

47. The cumulative effects of this pollution are already causing negative health consequences to residents, including asthma and other respiratory illnesses.

The community already has health problems like asthma. The cumulative effects of existing pollution are already causing negative health consequences to residents, including asthma and other respiratory illnesses.

Concern with health issues (e.g. students with asthma, chronic lung problems) in area with citation of data from Respiratory Health Association

The Agency recognizes that low-income and minority communities may struggle with health issues at rates disproportionate to the general population. While certain state and federal environmental regulations are based on health data, e.g National Ambient Air Quality Standards, the Agency's statutory authority rests with the regulation of sources of air pollution. The statutory authority to work toward healthy outcomes for the State's population rests with the federal, state and local Health Departments as health outcomes are resultant from numerous and complex factors of which ambient air quality may be one, but except in rare instances, only as a secondary or aggravating factor to other more systemic issues. The past fifty years of environmental regulation have resulted in large reductions in point source emissions and large improvements to ambient air quality throughout the state.

48. The site is located within the Calumet Industrial Corridor and the greater Calumet region, where multiple industries contribute to poor air quality. Compared to citywide averages and most other industrial corridors in Chicago, there are higher rates of chronic obstructive pulmonary disease and heart disease within this corridor, signaling existing negative health impacts. Residents of the Southeast Side should not be asked to bear yet another health burden.

While the Agency recognizes that the SE side is home to the Calumet Industrial Corridor these designations and the resultant zoning are City of Chicago land use planning decisions. As regards the Illinois EPA's authorities, the area is in attainment for all health-based National Ambient Air Quality Standards with the exception of ozone, a non-attainment area that generally covers six counties and two partial counties in the Chicago metropolitan area.

49. What is the Illinois EPA doing to address environmental health disparities and inequities? How can Illinois EPA continue to allow heavy polluters negatively impact the health of residents on the southeast side?

Within its statutory authority, the Agency provides certain enhancements to its permitting. In this instance, these included requiring ambient air modeling in the application; permit enhancements

including increased recordkeeping; a plan to mitigate fugitive emissions; and an Environmental Justice outreach process by which the public was notified of the application receipt triggering a request for a public hearing. The resulting public comments had an impact on the final content of the issued permit.

50. The neighborhood (East Side) adjacent to the proposed General Iron facility is an Environmental Justice community. According to the US Environmental Protection Agency's EJSCREEN tool, the area within 1 mile of this proposed facility falls in the 93rd percentile for particulate matter (PM2.5)

The whole of the East Side neighborhood is defined an environmental justice area by the Illinois EPA's EJ mapping tool. As such, and described in more detail elsewhere in this document, there were certain enhancements made to the Agency process and ultimately to the permit based on this designation.

51. Concern that this is a residential area with school and parks in vicinity of the proposed location.

The Agency has no role in zoning, neither in the siting of facilities, nor in the emplacement of public or educational facilities, nor in the determination of appropriate barriers, distance or otherwise, between residential and commercial or industrial parcels. More specifically, local land use is the exclusive determination of local units of government, in this instance, the City of Chicago.

52. Potential and likely effects—direct, indirect and cumulative—of the proposed action should be taken into consideration.

Historically, the evolution of environmental regulation is such that the underlying statutes and rules are developed to address and minimize the likely potential emissions and effects from a particular industry and for larger sources to account for the impact of a facility on ambient air quality. Although this facility will not be a major source; nonetheless, the Agency had the company perform certain analysis to evaluate the impact of likely pollutants on ambient air quality.

53. Requests that any new facility be evaluated for its capacity to provide a net reduction in the air pollution burden on the community.

This suggestion is a requirement for new major sources of air pollution in non-attainment areas under the state rules for Major Stationary Source Construction and Modification (35 IAC 203). In this case, the Chicago metropolitan area is non-attainment for ozone. Chicago and indeed the whole of the state has demonstrated attainment for all other NAAQS pollutants. As a non-attainment area for ozone, oxides of nitrogen and volatile organic material are regulated as precursor chemicals. New major sources or major modifications to existing sources of NOx or VOM pollution must obtain reductions over and above the potential amount of new pollution. General III does not meet the definition of a major new source or major modification for either NOx or VOM and thus this requirement does not apply to this permitting transaction.

54. The EPA has already designated the Southeast Side neighborhood as an area that is "environmentally overburdened." (See, https://www.epa.gov/il/environmental-issues-southeast-chicago). The EPA's website boasts that it has "empowered" this community and suggests that it is attempting to "ensure the area's continued progress." Granting the proposed permit makes a mockery of the EPA's environmental justice designation and discredits the EPA's own promise to help this community.

The commenter is pointing to a United States Environmental Protection Agency webpage and verbiage. Nonetheless, the Illinois EPA does not dispute that most if not all of the SE side of Chicago has an environmental justice designation, indeed, it is the Illinois EPA's mapping that designates the area as such; USEPA's EJSCREEN tool does not give such designation. With such designation, the Illinois EPA enhances its review and outreach on projects. As mentioned elsewhere, this does not remove Illinois EPA's responsibility to take action on applications in a timely manner or to make determinations in compliance with state and federal law and rules.

55. The Illinois EPA should deny General Iron a permit based on the on the levels of pollution the new facility is expected to emit, taking into consideration the EPA's own recognition that the Southeast Side neighborhood is already overburdened with environmental hazards.

The USEPA includes this language on its website, and defines overburdened in its EJ 2020 Glossary, https://www.epa.gov/environmentaljustice/ej-2020-glossary Notwithstanding there are no statutory or regulatory authorities assigned to this definition but rather it guides policy. Similarly, there is not a state-level definition of "overburdened communities" either in statute or SIP and no clear state-level activities that should occur for such community except as provided for in the Illinois EPA's Environmental Justice Policy and EJ Public Participation Policy.

The Illinois EPA does define the area as environmental justice[6], and had no statutory bases for denial, but included enhancements to its outreach and permitting process which resulted in a more robust permit.

56. It is time for the Illinois EPA to protect the health of our community for future generations.

The environmental laws as currently written, specifically the Clean Air Act, include mechanisms to reduce air pollution over time including requirements for development of state plans to improve and maintain ambient air quality and reduce emissions from stationary sources, among other emission reductions. This has achieved for the State and nation significant and important reductions in pollutants since the inception of the Clean Air Act in 1970, including improved air quality for ozone, sulfur dioxide, and particulate matter, including lead and other heavy metal emissions. These mechanisms in the Act still apply and continue to drive environmental progress on air quality. That said, the Act does not prohibit new stationary sources; it instead provides for regulation of stationary sources, including a requirement for permitting to provide a legally enforceable document that sets out the relevant and applicable environmental regulations, compliance, recordkeeping and reporting requirements that must be met.

57. It is critical that we don't add another massive polluter on the Southeast side.

While the facility is an addition to several operations currently at the site, it is not a major source of emissions as defined by the Clean Air Act. The source will have emissions that are below major

[6] It should be noted that the Illinois EPA does not define "communities" or municipalities definitionally as environmental justice. The Illinois EPA uses census block groups for demographic analysis, defines each block group and includes a buffer to ensure largely unpopulated industrial or commercial areas do not inadvertently fall out of the definitional area, see Illinois EPA's Environmental Justice Public Participation Policy and EJ Mapping Tool, http://www.epa.illinois.gov/topics/environmental-justice/index

source levels. And in fact, the existing sources at the site, which all currently are ROSS sources will be required to obtain FESOP permits as a single source with these additional operations.

58. The Southeast Side faces among the highest cumulative environmental burdens in the City of Chicago and the state, given these impacts and numerous other environmental threats in combination with sociodemographic factors that make the community more susceptible to environmental impacts. As a matter of environmental justice, the community overall should not be subjected to the additional pollution from the proposed facility.

While it is not within the statutory or regulatory authority of the Agency to determine zoning or deny permits that otherwise would comply with the applicable environmental laws and rules, the Agency has had the company submit additional information, including modeling to assess the impact on local ambient air quality, and added enhancements to the permit because of the recognition that the facility is proposed for an area that meets the Agency definition of environmental justice.

59. The record claims that there is a buffer between the facility and residences, but several residences are within a half-mile radius of the proposed site. There are also a high school and a park about a half-mile away, along with an elementary school and another park within a mile of the proposed site.

It is not within the statutory or regulatory authority of the Agency to determine zoning including the establishment of appropriate setbacks or buffers between residential and commercial or industrial areas. Indeed, the Act does not consider setbacks or buffers as acceptable for sources of air pollution. Instead, the Act determines the property boundary as the only acceptable division between neighboring parcels and provides that visible emissions may not cross the property boundary except under certain limited conditions.

60. There are at least 10 permitted facilities in the area that will continue to negatively impact the health of the residents.

The Illinois EPA is aware of the sources in the area as companies must obtain and keep current either permits or registrations for sources of air emissions. Indeed, this is one of the substantive requirements of the Act to ensure that the Agency has an accurate inventory of sources such that when further reductions are needed to meet State Implementation Plan goals, an inventory is on hand to assess how best to reduce emissions to achieve state and federal air quality goals.

Zoning

61. Why is this plant not acceptable in Lincoln Park, but is acceptable down here?

Zoning and local land use decisions are not the purview of the State. This authority rests with local decision makers, in this instance the City of Chicago and Chicago City Council.

62. Why is it that these companies are coming to the southeast and southwest sides?

Again, the Agency has no role in zoning or siting of facilities. More specifically, where a facility may locate is the exclusive determination of local units of government. In this instance, the determination that General III may locate at Burley Avenue was the decision of the City of Chicago.

63. Why did this company pick this area?

The Illinois EPA does not play a role in determining where a facility may locate. An agreement between the City of Chicago, General Iron Industries, and RMG Investment Group was reached such that the existing scrap metal recycling operations of General II, LLC, at 1909 North Clifton Avenue in Chicago, Illinois cease and relocate, matters for which the Illinois EPA had no involvement and for which it has no legal role.

64. This permit involves racially unjust siting. GIII is proposing to relocate a harmful industrial use from a wealthier, whiter part of the city to one that has more black and brown residents. Again, racist outcomes do not require racist intent. The outcome of this relocation is to remove a health hazard from an affluent white neighborhood and place it in a lower-income Latinx neighborhood. Institutional racism, intentionally or not, produces outcomes that chronically favor or disfavor racial groups. That is exactly what a permit for this would do. This is most assuredly a racist outcome.

    There is environmental racism embedded in this relocation and it represents poor land-use planning.

The Illinois EPA has no role in locating or relocating sources nor in land use planning.

65. The City of Chicago has embarked upon a process of Industrial Corridor Modernization, reviewing and potentially modifying existing land uses within its industrial corridors. Some corridors, such as along the North Branch of the Chicago River, are complete, while others, such as the Calumet River, are not. At best, it is premature to relocate an industrial facility of this magnitude given that this planning process has not yet occurred. At worst, relocating this project would have an outsized influence on any future planning efforts, incentivizing other businesses to similarly move to the Southeast Side. This plant should not be relocated until a planning process is allowed to occur.

As the commenter notes, it is the City of Chicago who has embarked upon this process of industrial corridor modernization. And it is the City of Chicago that is making determinations as to where particular sources may locate. Indeed, the City still has determinations and permits that must be obtained by the company prior to relocation and certainly before construction and or operation of the scrap metal recycling operations at the Burley site.

Such activity is not within the statutory purview of the Illinois EPA. The issuance of the construction permit to General III is independent of and does not bear on the relocation. Indeed, while the permit would authorize the source to construct at the Burley Avenue location, it does not require the source to relocate there.

66. This permit involves racially unjust siting. GIII is proposing to relocate a harmful industrial use from a wealthier, whiter part of the city to one that has more black and brown residents. Again, racist outcomes do not require racist intent. The outcome of this relocation is to remove a health hazard from an affluent white neighborhood and place it in a lower-income Latinx neighborhood. Institutional racism, intentionally or not, produces outcomes that chronically favor or disfavor racial

groups. That is exactly what a permit for this would do. This is most assuredly a racist outcome.

Once again, the Illinois EPA does not make zoning or siting decisions. An agreement between the City of Chicago, General Iron Industries, and RMG Investment Group was reached such that the existing scrap metal recycling operations of General II, LLC, at 1909 North Clifton Avenue in Chicago, Illinois cease and relocate, matters for which the Illinois EPA had no involvement and for which it has no legal role.

Permitting

67. The application was not complete. General Iron's current facility experienced an explosion that caused significant damage to the facility and equipment in use there. The permit application represents that this equipment will be relocated to and used at the 11600 S. Burley Avenue site. The transfer of any equipment that can cause this kind of catastrophic failure requires that the permit application be revised to address risks related the proposed use of any equipment, its control efficiency, and the applicant's ability to operate the equipment safely and effectively. Further, existing emission estimates and air quality models do not account for emissions during periods of catastrophic failure and also must be revised. And, additional permit terms and conditions are clearly necessary to prevent future accidents and to ensure the integrity of the equipment and the applicant's operating systems.

The application contained the necessary information for the Illinois EPA to issue the construction permit. As a rule, permit forms seek information to assist an agency's evaluation of an application, however, the Illinois EPA is not without jurisdiction to base its permit decision on matters outside of the permit forms (e.g. its own institutional knowledge or judgement). In this instance, the application contained enough information to demonstrate that the source would not cause a violation of the Act.

The existing site did experience an incident at the Hammermill Shredder system on May 18th that damaged the control for the shredder system including the RTO. By letter dated May 20th, the Illinois EPA communicated its expectation that GII, LLC, retain a third-party consultant to perform a comprehensive investigation and evaluation of the incident and submit a report of same to Illinois EPA for its review. That evaluation would include a root cause analysis of the incident and of any necessary replacement of or repairs to the control train. Such investigation and evaluation was undertaken and is ongoing. Based on recent communications between Illinois EPA's staff and General III, as well as counsel for same, it appears that the RTO is reparable and that measures can be put in place to ensure that a further incident of this type can be avoided including a safety bypass valve. The Illinois EPA will continue to monitor that situation along with the USEPA and the City including reviewing the reports of the evaluation.

The construction permit is issued to the scrap metal recycling facility on the basis that it can comply with applicable requirements most notably Pollution Control Board Part 218, Subpart TT, which requires an overall reduction in uncontrolled VOM emissions of 81%. With the proposed RTO and enclosure, the requisite demonstration has been made. This demonstration will be verified via post construction emissions testing of the control and enclosure. The permit is for an RTO, not necessarily the RTO from the existing site. In the event, it is determined that the existing RTO cannot be utilized, a like RTO could be constructed. Regardless, the issued permit requires the source to install, operate

and maintain a continuous monitoring device for the inlet gas stream to the control train for the Hammermill Shredder System for the flammability of this gas stream as a percentage of the LEL of this stream. The LEL monitor would ensure that prior to reaching the LEL and potentially causing an explosion, the scrap metal feed to the shredder would be cut and the gaseous emissions stream would bypass the control train. Bypass events cannot be predicted but would be expected to be limited in number and duration. The estimated emissions impact is expected to fit within the established permit limits. Records and reports of such events are required under the issued permit.

68. Is the permit decision being rushed? What is the Illinois EPA's timeframe?

The permit is not being rushed, as the timeframe for permit decisions is governed by the Environmental Protection Act. The relevant provisions of Section 39(a) of the Act provide that if there is no action by the Illinois EPA within 90 days of receipt of the permit application, the applicant may deem the permit issued by operation of law. *See, 415 ILCS 5/39(a).* A permit that issued by operation of law is simply a type of enforcement shield, protecting a permittee from the allegation that source is constructing or operating without a permit. A permit issued by operation of law does not provide for substantive requirements that would ordinarily appear in a permit, such as numerous testing, monitoring, recordkeeping and reporting requirements detailed in the permit. Consequently, the Illinois EPA strives to avoid permit issuance by default.

General III's permit application was received by Illinois EPA on September 25, 2019, and multiple extensions of the statutory decision deadline were obtained to allow sufficient time to review the application, prepare a draft permit, and allow for public input. In fact, the time taken by the Illinois EPA to review the application and allow for public outreach was three times longer than the standard statutory time allowed for this type of permit application.

69. The permit should be denied. It is within the Illinois EPA's discretion.

Under the Environmental Protection Act, the Illinois EPA is required to issue a permit to an applicant upon proof that the proposed facility or equipment will not cause a violation of the Act or promulgated regulations. *See*, *415 ILCS 5/39(a).* This standard is a mandatory one, expressed in the language of the provision as a "duty" that is imposed upon the Illinois EPA. While agency deliberation of certain aspects of the permit may be grounded in the exercise of discretion, the broader legal standard governing permit issuance or denial limits the discretion of the Illinois EPA. The Illinois EPA finds that the legal standard noted above has been met. Nothing in the record, including the public comments on the draft construction permit, adduces otherwise.

70. Will you consider extending this process and making an adjustment to your decisional timeline, to allow equitable and robust participation for the community?

The decisional deadline associated with this construction permitting action is statutorily established – 90 days from receipt of application. That decision has already been waived more than once to accommodate for modeling and public participation, among other. The applicant has indicated an unwillingness to provide a further waiver. To avoid a default decision on the matter, the Agency must take action by June 25, 2020.

71. Please create a moratorium on permitting during a pandemic.

The Illinois EPA is a creature of statute. It does not possess the authority to create a moratorium on permitting.

72. The Illinois EPA cannot ignore public comment and approve the construction permit.

The Illinois EPA reviewed all comments provided at the public hearing and submitted during the public comment period. The Illinois EPA is generally responding to all comments that are significant and, as frequently happens, has made various changes to the permit in response to the comments, as discussed later in this document.

73. No company should be permitted to operate if that company poses a risk of serious health issues to the public.

Permits for the construction or operation of emissions units or control equipment may be acquired under the Environmental Protection Act upon a showing that there is no violation of the Act or applicable regulations. 415 ILCS 5/39(a). Except for some requirements that are developed on a health-based standard (e.g. National Ambient Air Quality Standards), this legal standard for permit issuance may not appear to directly account for risks posed to human health from an activity or exposure to a particular pollutant. This does not mean that the permitting process ignores these risks, only that they are accounted for, indirectly, through an evaluation of the rules and regulations that a stationary source must meet when constructing and operating new emissions units or control devices. The Act contains several enforcement provisions that are available to restrain violations, such as injunctions that can be sought by prosecutorial authorities under Sections 42(e) and 43, and by any persons adversely affected in fact under Section 45. Other statutory or common law remedies exist that complement the enforcement remedies under the Act.

74. Is it fair to say public comments would not prevent the permit's issuance, unless a commenter can somehow prove General Iron would violate said regulations?

Again, permits for the construction or operation of emissions units or control equipment may be acquired under the Environmental Protection Act upon a showing that there is no violation of the Act or applicable regulations. 415 ILCS 5/39(a).

75. How does the permit process work for existing equipment?

To remove emission units or air pollution control equipment from a property, a permit is not required. To relocate or "construct" that same piece of equipment at a new property a permit is required. In this case, General III has indicated that the RTO is being relocated. Thus, a construction permit for that RTO is necessary. However, it must be noted that there is no requirement to relocate any of the equipment from the existing location to the new location. Rather, the requirement is to obtain a permit for the operations that will be conducted at a given site and to demonstrate that the source can operate in compliance with applicable requirements.

76. It was misleading for the hearing panel to state that the Illinois EPA has no choice but to issue a permit to a source if the source will be in compliance with the regulations.

Under the Environmental Protection Act, the Illinois EPA is required to issue an air permit to an applicant upon proof that the proposed facility or equipment will not cause a violation of the

Environmental Protection Act or the Pollution Control Board's Subtitle B regulations. This standard is expressed as a statutory duty, not an exercise of discretion, and it focuses on whether the proposed facility or equipment will possess the design and operational capabilities to comply with environmental requirements.

Public comments frequently question why compliance problems occurring at another facility operated by the applicant (as relevant here), or at the same facility in the case of a new or renewed operating permit, are not factored into the permit review process. In general, and for the reasons described elsewhere, the Illinois EPA's review of an application does not look to past practices at the source (or the same source at another location) but, rather, on the ability of an applicant to comply prospectively with the applicable requirements that govern the emissions source that is being constructed or operated. In the case of air construction permits, this review reflects the required standard of issuance and the application content requirements mentioned above, which focus on prospective compliance and not aspects of enforcement.

77. How did the Illinois EPA consider violations from General II's existing facility in the review of the construction permit application for a new facility on the East Side.

As stated at the public hearing, the Illinois EPA did not consider alleged violations at the existing facility in its review of the construction permit application for the new facility. As a general rule, the Illinois EPA does not consider the enforcement-related history of an applicant as part of the permit review process. This is because the structure of the Environmental Protection Act, as revealed in its provisions, divides permitting and enforcement functions into separate programs, though there are limited exceptions that will be discussed later. The Act provides for a state-wide program that is aided by private remedies, namely, the enforcement provisions found at Titles VIII and XII, to hold polluters responsible for the harm that they cause.[7]

Civil enforcement can be brought through a filing of a complaint in a circuit court or with the Board against any person that violates the Act, Board regulations or a permit. Legal actions can be initiated by state prosecutorial officials or by any person through a citizen's suit. Such cases can involve extensive discovery proceedings, pre-trial procedures, and eventually either a settlement or a trial (or evidentiary hearing) to determine liability and requested relief (civil penalties, injunction, cease and desist, etc.) sought in the complaint. A complainant bears the burden of proof in a civil enforcement action.

Permitting programs are codified at Title X of the Act and in the Board's implementing regulations, including 35 Ill. Adm. Code Part 201 governing state air construction permits. These requirements assure that the permit review is conducted as a record proceeding, which is part of an intricate administrative continuum between the Illinois EPA and the Pollution Control Board. Under Section 39(a) and Part 201, the Illinois EPA reviews an application for air construction permit according to a formal standard of issuance and permit content requirements, as discussed above, and other rules of procedures.

If an applicant appeals an agency decision to deny or issue the permit, the Board acts as an overseer to determine whether the permit decision, based exclusively on the record prepared by the Illinois EPA, is supported by the relevant standard of administrative review. The burden of proof in a permit

[7] **415 ILCS 5/2(b).**

appeal is on the applicant and because the review is based only on the record assembled by the Illinois EPA, discovery proceedings are usually limited. Other procedures not addressed by the Act or implementing regulations may also be relevant to the Illinois EPA's permitting role. This includes procedural due process implications outlined by appellate court rulings beginning nearly forty years ago. A seminal case is *Martell v. Mauzy,*[8] which laid the groundwork for later recognition that the programs are separate. The federal district court decision held that the Illinois EPA's denial of an operating permit based on "putative" (or alleged) violations[9] required a pre-denial hearing by the Illinois EPA, as opposed to the usual post-decision appeal procedures before the Board, because it deprived the applicant of recognized liberty interests protected by procedural due process.

Other cases followed, establishing the basic principles that have frequently been cited by the Illinois EPA at informational permit hearings and in responsiveness documents for many years. The Illinois Third District Appellate Court affirmed the Pollution Control Board's decision that a special waste stream permit was improperly denied on the grounds of alleged violations cited from a parallel pre-enforcement action.[10] In citing to the Board's opinion that the Act's procedures for permitting and enforcement are "separate and distinct," the appellate court affirmed the Board and upheld the latter's inference that the permit denial process was "improperly" used in lieu of enforcement.[11] [12]

As mentioned, there are limited exceptions to the general rule described above. Notably, two exceptions originate from statutory amendments by the Illinois General Assembly to the Act in 2003 in P.A. 93-575 (93rd General Assembly). The amendments introducing these exceptions to Section 39(a) of the Act did not eclipse the existing framework of the Act or its implementing regulations, as much of that construct was left untouched. The legislature also did not overrule existing caselaw and, as such, the changes simply memorialized existing caselaw and other provisions of the Act that existed at the time.

The first exception created by the amendments to Section 39(a) allows for agency discretion in considering "prior adjudications of noncompliance" with the Act for environmental releases by an

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[8] **511 F. Supp. 729 (N.D. Ill. 1981).**

[9] **The purported authority for the permit denial was Section 39(e), later re-codified at 39(i). The grounds for the denial of the operating permit rested with a history of alleged violations involving refuse disposal facilities, including a past enforcement action involving USEPA, two past and one pending state enforcement actions, a pending *quo warranto* action and agency inspection reports.**

[10] ***See, EPA v. PCB,* 252 Ill. App. 3d 828 (3rd Dist. App. Ct. 1993).**

[11] ***Id.* at 830. The ruling also illustrates the difference between evaluating a source's compliance status (viewed through an enforcement lens) and determining whether a permit application meets the Act's requirements for permit issuance (viewed through the Act's standard for permit review). This is shown by the court citing to application materials showing that the applicant's analyses of compounds used in its special waste streams were below regulatory limits, thus negating the grounds cited for permit denial.**

[12] ***See also, ESG Watts, Inc., v. PCB,* 286 Ill. App.3d 325, 334-335 (3rd Dist. App. Ct. 1997)(agency consideration of alleged violations was not proper permit denial was supported for other reasons); *The Grigoleit Co. v. EPA*, PCB No. 89-184 (November 29, 1990)(if IEPA has waste concerns, the proper mechanism to address those concerns is an enforcement action rather than a denial of a permit).**

applicant. The Illinois EPA only uses this authority rarely, in large part, because judicial (or quasi-judicial) rulings based 'on the merits' of an environmental enforcement case are uncommon. The bar set by these criteria is high, as it is perhaps meant to protect against a potential deprivation of the same interests claimed by the applicant in *Martell v. Mauzy.* Based on institutional knowledge, the Illinois EPA has used analogous, but more specific authority found in Section 39(i) in a handful of prior occasions.[13]

The other exception introduced in the 2003 amendments allows for agency discretion in imposing reasonable conditions relating to a "past compliance history" with the Act as is necessary to correct, detect, or prevent "noncompliance." *See,* 415 ILCS 5/39(a). The Illinois EPA does not routinely employ this authority, as it is also prudently viewed to hold a high bar by requiring demonstrated, not merely alleged, noncompliance. However, the Illinois EPA will sometimes incorporate relevant requirements from a final adjudication into a construction or operating permit, often doing so at the request of a respondent who has been directed to undertake a permitting change as a result of a settlement.

78. The Illinois EPA should deny the permit application for a construction permit because of adjudicated violations relating to the General Iron (or General II) facility.

A permit denial of General III's application for a construction permit based on the application before the Illinois EPA is not justified or authorized by the provisions of the Environmental Protection Act. Section 39(a) provides that the Illinois EPA may consider a permit applicant's prior adjudications of noncompliance with the Environmental Protection Act if the noncompliance involved a release of some contaminant to the environment. The Illinois EPA did not consider the entirety of General Iron's past compliance history cited in the comments to this proceeding because nearly all of it fails to satisfy the legal criteria set forth in the provision.

For purposes of this exception to the rule, an adjudication is generally regarded as a judgment by a court (or quasi-judicial body), relating to the Latin term "*judicare*," which means "to judge."[14] The concept of an adjudication consists of a formal determination 'on the merits' of the legal controversy.[15] The federal district court's ruling in *Martell v. Mauzy* is informative in this regard, as

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[13] **Sheridan-Joliet Land Development, LLC, denial letter dated August 14, 2018 (denying a renewal of clean construction and demolition debris development/operating permit due to a PCB enforcement adjudication); City of Morris and Community Landfill Company, denial letter dated May 11, 2001 (denying a request for significant modification to a development permit as a result of a criminal felony conviction); and *ESG Watts Inc. v. PCB,* 286 Ill. App.3rd 325 (3rd Dist. App. Ct. 1997)(denying renewal applications for a landfill's waste-streams based on a circuit court finding of liability and administrative citations).**

[14] ***See, Merriam-Webster On-line Dictionary*** **(www.merriam-webster.com) ("transitive verb: to make an official decision about who is right in (a dispute)"); Wikipedia (https://en.m.wikipedia.org) ("the legal process by which an arbiter or judge reviews evidence and argumentation, including legal reasoning set forth by opposing parties or litigants, to come to a decision which determines rights and obligations between the parties involved").**

[15] **Some might assert that the term should also include any type of court decree, including a settlement agreement resolving a case short of actual litigation, but such a notion misses the mark. A consent decree approving a settlement does not entail a judicial determination "on the merits."**

the "risk of erroneous deprivation" of the applicant's protected liberty interests was, at least in part, because the alleged violations had not been adjudicated.[16]

In many instances cited in comments, the claimed adjudications stem from administrative citations issued by the City of Chicago. It is not plainly evident that the resolution of those citations constituted a formal adjudication of noncompliance under the Act. The administrative citations issued by the City do not address infractions that arise from the Environmental Protection Act but, rather, are ordinance violations. A municipality's ordinances are entirely separate from the General Assembly's legislative enactments and, in this instance, nothing in the Act signals that the legislature meant for the Illinois EPA's purview to act upon ordinance violations. In this regard, it is not relevant that the facts relating to the citations correspond to matters that might be alleged under the Act, as Section 39(a) speaks to only the State's sovereignty.

79. The Illinois EPA should deny approval of the construction permit application for General III due to both admitted and adjudicated violations historically caused by Reserve Management Group/South Chicago Property Management ("RMG/SCPM") operating at the site of the planned construction of the General III facility.

For clarification of the record, and based on institutional knowledge, there are four manufacturing facilities that conduct metal recycling operations at the existing South Burley Avenue site where the planned construction of the General III facility will occur. The entities consist of Reserve FTL (d/b/a Reserve Marine Terminals), Napuck Salvage of Waupaca, LLC, South Shore Recycling, LLC, and RSR Partners, LLC (d/b/a Regency Technologies) and are collectively known as South Chicago Property Management, Ltd. ("SCPM"). SCPM is a corporate affiliate of two holding companies, RMG Investment Group, LLC, and RMG Investment Group II, LLC, who are doing business as Reserve Management Group ("RMG").

As previously discussed, the administrative citations issued by the City concerning the SCPM-related facilities are not adjudications involving the Environmental Protection Act but, rather, violations of City ordinances. There is also no indication in the record of this proceeding that violations by SCPM, who currently oversees the operations of the four manufacturing facilities at the existing site, would constitute a formal adjudication, or even noncompliance with the Act, relative to GIII's permit application.

Although the permit application indicates that the General III will be a single source together with the SCPM-related facilities, and the construction permit includes a permit condition to that effect, a source designation only addresses the respective roles and responsibilities of facilities recognized as a single source in the context of permit classification, though it can, on rare occasion, affect rule applicability too. However, a source designation used in classifying permitted sources under the Clean Air Act Permit Program ("CAAPP") and the FESOP should not be confused with shared or joint liability amongst related entities under applicable laws. As discussed elsewhere, how General III and the SCPM-related facilities opt to permit their single FESOP source, whether as single or multiple FESOP permits, will be addressed in the operating phase of the project.

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[16] **511 F. Supp at 741 (i.e. applicant lacked an "evidentiary hearing of any kind" regarding state settlement order and pre-enforcement orders considered by the Illinois EPA in its denial).**

80. RMG/SCPM has admitted to noncompliance with the Environmental Protection Act in a letter sent to the Illinois EPA in November 2019, such that there is a basis for a past adjudication with the Act for permit denial. The noncompliance relates to the failure of the manufacturing facilities to historically obtain the proper operating permits and the admission(s) addressed in the letter are not paper violations but involve unpermitted releases of pollutants to the environment.

As mentioned in a prior response, the Illinois EPA does not view SCPM to be the same legal entity as the permit applicant involved in this proceeding.[17]

Additionally, the Illinois EPA does not view a voluntary self-disclosure letter submitted under the enforcement provisions of Section 42(i) as evidence of a formal adjudication for purposes of Section 39(a), such that it could be considered in a permit review. Although a pre-enforcement letter could contain admissions, they would not be adjudicative in nature.

81. The noncompliance by the SCPM-related facilities occurred over many years and the discovery of such violations was inevitable given that they are mentioned in the General III permit application. It was grossly unfair and contrary to the Act [for the Illinois EPA] to offer the companies enforcement protections with respect to the noncompliance.

For reasons mentioned above, the Illinois EPA did not consider the pre-enforcement investigation of the SCPM-related facilities, including the self-disclosure letter, as evidence of noncompliance by General III in this permit proceeding.[18]

82. The structure of the Environmental Protection Act should compel the Illinois EPA to recognize the past violations being addressed by the City of Chicago, who acts as a local environmental agency and maintains a close relationship with the Illinois EPA, as adjudications of noncompliance with the Act. Such recognition will promote the goal of encouraging the coordination of environmental protection by local governments.

The Illinois EPA recognizes the strong working relationship with the City of Chicago in the investigation of emissions sources in the region, as well as the significance and value that the relationship provides to the residents and the State of Illinois. However, the reach of Section 39(a), including the Illinois EPA's consideration of a possible permit denial based on adjudicated noncompliance with the Act, depends upon the applicability of facts to the law. In this case, even the most liberal construction of the Act's relevant provisions cannot reconcile the issuance of a permit denial with the absence of a formal adjudication of noncompliance with the Environmental Protection Act. Recognizing and promoting the involvement of local governments in environmental protection efforts is important but not germane to the analysis of this permit application.

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[17] **Because the Illinois EPA declines to consider the SCPM self-disclosure letter to be within the scope of review of the General III application, the notion that the nature of the unpermitted operations should constitute a release of contaminants to the atmosphere for purposes of Section 39(a) is moot.**

[18] **To assist the public's understanding concerning a matter of possible interest, the Illinois EPA notes that any relief (i.e., enforcement protections) in a civil penalty assessment provided by the State of Illinois in response to a voluntary self-disclosure letter does not arise unless or until a formal enforcement action is commenced and resolved through either a negotiated settlement or adjudication.**

83. Nowhere does the Act expressly state that the Illinois EPA cannot consider adjudications of local air ordinances as a basis for denying a permit under Section 39(a).

The Illinois EPA is a creature of state law, which means that its legal authority derives from the laws enacted by the General Assembly and approved by the Governor. Such authority takes the form of expressed powers, as found within the enactment's provisions, or implied powers, to the extent necessary to execute the expressed powers. The absence of specific authority in the law (e.g., "nowhere in the Act does it say") does not create a source of authority for an administrative agency, it simply confirms that no such authority exists. Put another way, the Illinois EPA's powers are defined in relation to the Act, and do not include the vast universe of authorities that are not otherwise specifically prohibited.

In this instance, if the Act does not expressly provide for the consideration of enforcement-related matters that stem from local air ordinances, or are not implied from those expressed powers contained in the Act, the Illinois EPA plainly lacks the authority to consider such things in its permitting capacity. The Act neither expressly provides for, nor otherwise implies, that violations of local air ordinances are within the purview of the Illinois EPA's permit review under Section 39(a).

84. Thirty-three unresolved administrative citations involving General Iron are currently pending with the City of Chicago, delayed in their resolution and rescheduled for hearings due to the COVID-19 pandemic. Because the citations involve repeated and substantive violations that relate to matters addressed by this permitting action, the Illinois EPA should postpone the permit decision to allow for the resolution of the citations so that they may be considered in the permit's review.

The Illinois EPA acknowledges the administrative delays associated with governmental affairs during the COVID-19 pandemic and understands the desire expressed by the comment to account for all relevant information that could support a basis for a permit denial. However, the Illinois EPA is unable to extend the decision deadline and, in any event, could not evaluate the citations even if resolved in favor of the City. This is because the Illinois EPA lacks an ability to unilaterally postpone or extend the current decision deadline and, as mentioned elsewhere, the administrative citations process represents the sovereign power of the City to enforce violations its municipal ordinances, not noncompliance with the Environmental Protection Act.

85. Evidence of noncompliance by the SPCM-related facilities from multiple sources, including prior admissions from a pre-enforcement process overseen by the Illinois EPA, liability findings by the City of Chicago and past City inspection reports, should be considered by the Illinois EPA in imposing more stringent conditions in any issued permit.

As discussed elsewhere, SCPM is not the permit applicant in this proceeding. The fact that the SCPM-related facilities will be treated as a single source for purposes of future FESOP permitting does not now, and will not prospectively, affect issues relating to the liability. As also discussed, the cited allegations from the comments do not relate to noncompliance with the Act.

Separately, the Illinois EPA does not construe Section 39(a) of the Act as authorizing permit conditions based only on allegations of noncompliance with the Environmental Protection Act, as suggested by

the comment. The text of this part of Section 39(a) provision speaks plainly to "noncompliance"[19] and does so without qualifying its meaning as either alleged or adjudicated. In comparison to other provisions of the Act, when the legislature means "alleged violations" it employs the modifier expressly, as in the case of the Act's pre-enforcement process where it is quite sensible. 415 ILCS 5/31(2018).[20] In other contexts, the General Assembly seems to find reliance on mere allegations as antithetical to the Act's history and purpose. For example, the Board is not able to consider past enforcement history of a respondent in its determination of civil penalties unless the noncompliance is adjudicated.[21] It is also incongruous to suggest that the Illinois EPA can permissibly craft permitting conditions from mere allegations under the Section 39(a) when any revocation of a permit by the Board requires a formal enforcement action.[22]

In the recent past, the Illinois EPA asserted that the "noncompliance" language of the statute's text is best thought synonymous with "adjudications," in part, for reasons to avoid constitutional problems.[23] However, the Illinois EPA will allow for the consideration of admitted or uncontested matters in this analysis, to the extent that such proof support a showing of noncompliance. Note that court-approved settlement agreements containing admissions of liability or a clause allowing the Illinois EPA's use of the agreement for purposes of an adjudication under Section 39(a) would signal a court's affirmation of such a finding.

86. Evidence of noncompliance by the General Iron facility from multiple sources, including liability findings by the City of Chicago, pending citations before the City and past City inspection reports, and USEPA enforcement actions against General Iron should be considered by the Illinois EPA in imposing more stringent conditions in any issued permit.

The previous response answers several of the reasons why evidence of many of the alleged violations cited by comments cannot be considered by the Illinois EPA in this proceeding. One issue remaining is the effect of USEPA's consent agreements and administrative settlements on the Illinois EPA's ability to impose permit conditions under Section 39(a).

Based on the comment and its supporting attachments, prior USEPA investigations and resulting lawsuits involving the former owner of the facility, General Iron, occurred on at least three occasions in the last two decades, culminating in lawsuits resolved by way of a consent decree in 2006 and two

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[19] The language used in the relevant text, as introduced to the Act as an amendment in 2003, essentially refers to "noncompliance" twice: the first time indirectly, as "past compliance history" would seem synonymous with noncompliance, and the second time directly.

[20] There are also instances where the term is unqualified but there is no need for a modifier, as the context is one in which the liability for actual noncompliance is being, or already has been, determined. *See,*

[21] 415 ILCS 5/42(h)(5). *See also,* 415 ILCS 5/42(b)(4-5)(2018)(assessing an additional penalty amount for certain administrative citation matters is restricted to a "second or subsequent adjudication violation" of the relevant provision).

[22] 415 ILCS 5/33(b).

[23] See, Illinois EPA Responsiveness Summary for Sterigenics U.S., LLC, Willowbrook I, pages 68-70, dated September 20, 2019.

administrative settlement agreements in 2012 and 2019. The earlier consent decree from 2006 does not purport to be a fully executed order, as it is not signed by the parties or the presiding judge, and it is not clear whether it is still in effect, as it contains a termination clause that may likely have been executed by now. The decree also only addressed federal matters[24] and therefore does not fall within the scope of the Section 39(a).

The administrative order from 2012 cites a single day of violation by the facility with the Board's fugitive emissions standard[25] and the regulatory equivalent of Section 9(a) of the Act. The 2019 administrative order cites to four inspection dates alleging that the facility failed to control VOM emissions below the applicability thresholds of the Board's Part 218 regulations.[26] The order also alleges that the facility operated as a major source without a requisite Title V operating permit, citing to the Illinois Clean Air Act Operating Permit Program.[27] Both orders required corrective action by the facility, including obtaining the necessary permits from the Illinois EPA.

The two administrative orders are within the scope of the Illinois EPA's authority under Section 39(a) for the consideration of permit conditions, as they reflected noncompliance with the Act through the State's Implementation Plan. The Illinois EPA reads the administrative orders as a fair acknowledgement by General Iron of its agreement with the terms of the orders, including statements asserting the company's failure to meet emission control requirements from the Board's Subtitle B regulations (i.e., fugitive emissions standard and Part 218, Subpart TT.

However, the Illinois EPA will not exercise discretion to apply the administrative orders to impose new conditions in the construction permit, as circumstances do not warrant them. It would also require significant record support, should General III appeal the imposed permit conditions, to support a showing of the *necessity* for conditions to correct or prevent the noncompliance addressed by the administrative orders.[28] It is noted that comment(s) do not allude to specific conditions that are necessary to address noncompliance covered by the orders.

87. Evidence of noncompliance by another facility, Chicago Rail and Port, should be considered for the GII facility because of fugitive dust violations addressed by USEPA in a Notice of Violation letter.

The record of this proceeding does not indicate that the referenced facility currently has any relationship to General III or the SCPM-related facilities such that it should be considered in this permit proceeding.

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[24] **The complaint alleged that the respondent knowingly disposed of appliances containing substances used as a refrigerant pursuant to 40 C.F.R. §82.154(a) and 82.156(f).**

[25] **35 Ill. Adm. Code 212.301.**

[26] **35 Ill. Adm. Code 218.980(a)(1) and (b)(1).**

[27] **415 ILCS 5/39.5(2)(c)(1).**

[28] **At this stage of development, the facility has already installed the controls and performed the necessary emissions testing that were an outgrowth of the allegations, and the related permitting requirements addressed only the existing facility, not a new one at a different location.**

88. The Illinois EPA should ask Governor Pritzker to postpone the statutory deadline or declare the permit application incomplete.

The Illinois EPA is not inclined to seek a postponement of the current decision deadline through use of an executive order or otherwise, as the permit application contains all the requisite information to be deemed complete. To be accurate, the current deadline of June 25th governing the Illinois EPA's review of the construction permit application reflects the applicant's waiver of the decision deadline, not the original timeframe set forth in Section 39(a) of the Act.

89. Another source of authority under Section 39(a), which references the use of conditions "necessary to accomplish the purposes of the Act, and as not inconsistent with" Board regulations," is relevant to this proceeding. It provides broad authority for the imposition of conditions that go beyond the regulations if the two criteria reflected in the text are met.

The Illinois EPA agrees that this authority is relevant to this proceeding and, indeed, it is by far the most common source of authority used in the development of a construction permit for emission sources or equipment required by Section 39(a). Generally speaking, the language reflects a kind of catch-all authority and for many permits issued by the Bureau of Air, the authority is usually cited generically, and usually only once, for a wide range of conditions that are not expressly identified elsewhere in the Act or implementing regulations.

But this authority does not extend beyond its plain wording, as this comment contemplates. In fact, the Illinois EPA's role as a permit authority is tempered as much by the role that the Pollution Control Board shares under the Act as by Section 39(a). The Illinois EPA cannot misappropriate the role of the Board as the State agency charged with setting environmental control standards. The Board may even be guided by this concept when the statute's text comes into focus in permitting appeals, as more often than not, the Board sets a noteworthy bar in judging the "necessity" of operating conditions.[29]

90. The plain language of the [catch-all] authority of Section 39(a) contrasts with a misleading statement by one of the members of the hearing panel, who said that the Illinois EPA had no choice but to issue a construction permit to a source if the source will be in regulatory compliance.

This comparison tries to combine different concepts, leading to an incorrect conclusion. The reference to Section 39(a) relates to the scope of authority in setting permit conditions and the statement regarding permit issuance based on regulatory compliance is a restatement of the standard of permit issuance. Incidentally, because the restatement is a fairly accurate representation, there is nothing misleading about it.

91. The Illinois EPA is in error when it contends that it may only deny a permit a permit under Section 39(a) if there is an adjudicated liability finding by a circuit court or the Board (citing to a previous responsiveness summary discussion and footnote accompanying the Sterigenics permit proceeding).

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[29] ***See, IEPA v. Jersey Sanitation Corp.,* 784 NE2d 867, 875-875 (4th Dist. Ct. App. 2003)(holding that petitioner was required to show that its [closure/post-closure] plan, which agency found lacking, "would not result in any violation of the Act and the modifications, therefore, were arbitrary and unnecessary").**

The discussion referenced in the cited responsiveness summary responded to a question regarding whether the Illinois EPA could deny a permit on grounds of past violations. The answers outlined in that earlier discussion are generally in accord with responses in this document, including the Illinois EPA's contention that the Act requires an adjudication if a past history of violations is the basis for a permit denial under Section 39(a).[30] The comment is mistaken in the belief that the document cites to a proposition that no other basis for permit denial exists under Section 39(a) than for of an adjudicated liability, as there are numerous other grounds that can form the basis for a permit denial.

92. The Illinois EPA is hypocritical when it claims that permitting is separate from enforcement, especially given the lack of enforcement activities conducted by the Illinois EPA in the last 15 years. The Illinois EPA cannot fail to meet its enforcement and permitting responsibilities and then rely on those failures to justify agency inaction, as it causes a vicious cycle and evidence of a failed agency.

The Illinois EPA appreciates the candor of this and related comments, but its enforcement programs are not at issue here. Certainly, the Illinois EPA is not above criticism in the performance of its responsibilities, and residents of the local community and throughout the State are free to express their displeasure with the Illinois EPA's implementation of its many roles.

The point at issue is about how an organization, a state agency whose authorities are defined by statute, perceives its roles, and performs its responsibilities, under existing laws and regulations. As mentioned, the Illinois EPA's permitting and enforcement programs typically operate independently of one another as a matter of course, as they have for many years. There is no doubt that the caselaw authorities cited in this document, and the principles that informed them, have been an organizing principle in bringing about this separation.

93. Illinois EPA must include permit conditions that provide the community with data about the facility's emissions.

The permit as revised has enhanced recordkeeping and reporting requirements. Notably, records and reports of the results of emissions testing are required under the revised permit. Also, quarterly reports are required under the final permit. These reports would include data about the facility's emissions. All reports required under the permit will be available to the public.

94. I am concerned for what a permit application review is constrained to.

Illinois EPA is generally constrained to what is contained in a permit application, such as whether applicable requirements will be met. The Illinois EPA cannot review/consider violations at another facility, as in this case, due to Illinois case law and interpretation of the permit Environmental Protection Act. As a result, Illinois EPA review is confined to matters of the application and not to compliance or enforcement considerations, with some limited exceptions.

95. The draft permit should require General Iron to keep records of emissions control testing and emissions for a longer period of time and should be made available to the public upon request.

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[30] **In retrospect, footnote 6 could have observed that a liability adjudication might also originate with a federal district court (or body acting in a quasi-judicial capacity) provided that the Act or implementing regulations in Illinois is the basis for the noncompliance addressed in the controversy.**

Generally, the records that are required under the permit have a retention period of five years. This is the customary retention period for FESOP and CAAPP sources. Unlike the records of the State, the records of a facility are not available to the public upon request. However, the records are available to the State upon request, which records would then be available to the public under the Freedom of Information Act.

96. Both Condition 19 and Condition 21 require that records be kept for "at least" a period of time, these two conditions contain inconsistent lower bounds – three years and five years.

Condition 19 merely recites the recordkeeping required by specific rule. Condition 21 addresses recordkeeping that goes beyond that rule. The timeframe for record retention in Condition 21 is consistent with that required of FESOP and CAAPP sources. That there are two discreet record retention periods is not an issue. To reconcile the two would serve to undermine the greater retention requirement.

97. Descriptions of the Ferrous and Non-Ferrous Material Separation Systems on page 1 of the draft permit are inconsistent with the emission limits for these Systems contained on pages 14-16. Illinois EPA must correct all descriptions and ensure that all emissions estimates, modeling based on those estimates, and proposed limits and monitoring, recordkeeping and reporting requirements encompass all proposed emission sources/units associated with their respective Systems.

The Illinois EPA acknowledges the inconsistency and has revised the permit to accurately list emission units. In short, the magnetic separators, box separators, and the stacking conveyors are not in addition to, but are the 70 conveyor transfer points.

98. We note that there appears to be a grammatical error in Cond. 10(b) – it may be that the provision omits an "and" between "unpaved areas" and "shall be treated."

This comment has been addressed.

Single Source

99. As part of its permit review and contrary to its well-established permitting standards, the Illinois EPA failed to address the SCPM-related manufacturing facilities that will be co-located with General III at the new facility.

The Illinois EPA addressed the single source permitting issue relating to this proceeding in accordance with applicable law and consistent with past practices. The permit application acknowledged that the General III facility will comprise a single source for purposes of permitting under the Act with the existing SCPM-related entities located at the site. In view of the relevant single source criteria that is reflected in Section 39.5 of the Act, together with the acknowledgement from the application, the Illinois EPA did not question treating the various facilities as a single permitted source. This is reflected in the draft and final permit at Condition 1e.

100. Despite apparently concluding that the General III and SCPM-facilities are a single stationary source, the Illinois EPA is conducting separate permitting activities of the two, which improperly segments all of the pollutant-emitting activities at the source. The current application provides an incomplete picture of the source and a single application is needed that combines the comprehensive emission-requirements into a single construction permit for the source.

As this permit proceeding involves an application for construction permit, the Illinois EPA is addressing matters relating to the development of the project, including the design and operating capabilities of General III's emissions units and control equipment that will be authorized by the permit. The application does not address activities relating to the SCPM-related activities due to the fact that those sources do not require a construction permit, independently or in conjunction with the project. At present, the SCPM facilities are operating pursuant to an existing Registration of Smaller Source ("ROSS") registered under SCPM's name. Condition 1e of the draft construction permit recognizes that General III is a single source with SCPM. Beyond this recognition, it is not necessary for the draft permit to contain any other requirements relative to the issue.

The Illinois EPA is aware that General III must submit a Federally Enforceable State Operating Permit ("FESOP") application on CAAPP forms in order to avoid major source status under the CAAPP. Based on institutional knowledge, the Illinois EPA is also aware that SCPM will be submitting a FESOP application at the same time. This indicates that the sources anticipate obtaining separate FESOP permits, notwithstanding that the facilities are sharing the same FESOP source status.

This approach is consistent with applicable law and past practices, which is illustrated in a USEPA petition response involving U.S. Steel Corporation issued December 3, 2012 (Petition No. V-2011-2). In denying a petition point addressing similar concerns expressed by the comment, USEPA observed that Title V permit authorities may issue "multiple title V permits to a single Title V source" provided that the compliance obligations for each facility are clear and that all applicable requirements are contained in a Title V permit. *Id.* at page 26. In its decision, USEPA declined to require the Illinois EPA's processing of U.S. Steel's Title V permit to be consolidated with a separate supporting facility, Gateway Energy & Coke Company. Both facilities were treated as a single source. The discretion in the permit authority likely relates to a recognized need to provide flexibility in reporting and other permit obligations in the context of a single source classification, given that different responsible officials or personnel will be overseeing the responsibilities of the respective facilities.

101. General Iron's operating permit application has not been acted on by the Illinois EPA in years. Deferring a single source determination to the operating permit phase of permitting for the source is inadequate.

The Illinois EPA is not deferring any single source determination, as the decision to treat the General III and SCPM-related facilities as a single FESOP source is being memorialized in the construction permit. The processing of the operating permits for the sources will be addressed in the future, in parallel fashion to the extent practicable.

102. The applicant has failed to describe, and the Illinois EPA has failed to consider the proposed new source along with the other sources already located at South Burley as a single source for air permitting purposes.

As elsewhere discussed, the existing SCPM Entities will be a single source with General III and will be

required to obtain a Federally Enforceable State Operating Permit. The other entities will be addressed, along with General III, during that operating permit application process.

103. "The Draft Permit fails to consider all of the RMG facilities in the Potential to Emit or air quality modeling of the proposed GIII."

The SCPM Entities continue to qualify for eligibility under the Registration of Smaller Sources (ROSS) program. Sources are eligible for the ROSS program if combined actual emissions of PM, CO, NOx, VOM and SO2 from non-exempt sources are less than 5.0 tons per year, or less than 10 tons over the two most recent years and total hazardous air pollutant (HAP) emissions are less than 0.50 tons per year. The ROSS program is mandatory meaning that if a source meets the eligibility criteria, it must be registered in the program. Absent changes in operation or new information, the SCPM entities must remain in the ROSS program until General III triggers the requirement to seek an operating permit.

Ambient air impacts from these operations are accounted for in the background monitoring values at the Illinois EPA's monitoring station at Washington High School, which evidences attainment of the NAAQS for PM.

Periodic Monitoring/ Practical Enforceability

104. The Draft Permit is unenforceable. Numerous permit limits, in particular on fugitive sources, are vague, require only weak or nonexistent testing or monitoring, and/or require insufficient recordkeeping, with virtually no mandated reporting.

As is explained elsewhere, this construction permit for this minor source does not require the content associated with permitting of major sources of emissions and specifically that associated with Clean Air Act Permit Program permitting. There is no requirement for periodic monitoring such as testing, monitoring, recordkeeping and reporting in this minor source construction permit. Notwithstanding, in response to comment, the Agency has clarified and enhanced many requirements within the permit.

105. The permit lacks specificity and is not enforceable.

Further specificity is not needed to make the permit enforceable. The applicable regulations and requirements that would apply to the facility are clear. Further, the construction permit requires General III to conduct emission testing, monitoring, and recordkeeping to show compliance with new emission limits and control requirements. The permit also requires GIII to prepare and implement plans for Operation and Maintenance and Feedstock Management as well as a Fugitive Emissions Operating Program.

106. The permit lacks monitoring and recordkeeping/reporting requirements to ensure compliance with and enable enforcement of the limits on the hours of operation. With respect to the shredder, noise monitoring can and should be used to track shredder operations on a continuous basis for purposes of determining compliance with the limit on hours of operations.

The permit as revised now includes a recordkeeping requirement relative to hours of operation per day, month and year for each process area. The draft permit already required deviation reporting from the hours of operation requirement. Illinois has no noise program, and regardless is not inclined to use noise to know whether a source is operating. Hours of operation is a very common consideration in determining and limiting the emissions of a source. Never has noise been the means by which compliance with the hours of operation was assured or determined.

107. Concern with Agency undercounting emissions from metal recyclers; these facilities have been miscategorized as minor emitters of pollution.

It is true that there is limited data on the emissions from scrap metal recyclers and that their emissions impact has not been readily understood. Given its national presence and role, USEPA took the lead on the matter in Illinois seeking emissions testing of select sources. Through that testing it was determined that the scrap metal recycling operation on Clybourn was a major source of VOC emissions. The USEPA entered an administrative order mandating the installation and destruction efficiency testing of an RTO. Under this construction permit, the Illinois EPA is also requiring emissions testing. That testing and the data resulting therefrom will prove instructive relative to the emissions from such operations.

108. The Draft Permit is utterly lacking in any control requirements and monitoring, recordkeeping and reporting requirements sufficient to ensure compliance with these limits by various "fugitive" sources on an ongoing, continuous basis.

The draft permit was not completely devoid of control, recordkeeping and reporting requirements. Fugitive control requirements included enclosure, sweeping and watering, and reporting was required for deviations. However, in response to comment additional the Fugitive Emissions Operating Program has been enhanced as has the recordkeeping and reporting.

109. Illinois Environmental Protection Agency should impose new permit conditions to control emissions and address General Iron's long history of non-compliance.

It is not clear what additional control requirements the commenter seeks to have imposed. The scrap metal operation is only subject to regulatory requirements for visible and particulate matter emissions and for emission of volatile organic material. The sole control requirement to which the source is subject applies to the Hammermill Shredder System and necessitates the reduction of uncontrolled VOM emissions by at least 81%. The Illinois EPA cannot unilaterally create and impose additional control requirements by way of this permit.

110. I am concerned for boilerplate restatements in the permit.

The use of boiler plate restatements of regulatory requirements is a practice of the Agency for efficiency in certain types of permitting as well as to minimize errant restatements of regulatory requirements. This approach creates no legal or technical issues, rather it serves to identify applicable rules and related provisions such as test methods.

111. Condition 10, merely contains vague, general control obligations for storage piles, roadways, vehicle loading and unloading, and other transfer points that simply list available control measures in the alternative and state that control shall be done "in accordance with" a required operating program,

for which Condition 10 lays out minimum requirements, along with incorporation by reference of a December 2019 fugitive particulate operating program and a provision for updating the operating program and incorporating it into the permit.

This approach presents no legal or technical issues. However, in response to comment, requirements addressing fugitive visible emissions have been clarified and enhanced in the permit and fugitive particulate operating program.

112. Condition 13 sets forth a restatement of Section 201.282 that confusingly includes a directive that sources "shall" conduct testing, followed by a permissive clause that Illinois EPA "may" require an owner or operator to conduct testing and a clause that Illinois EPA "shall have the right" to conduct tests at Illinois EPA's request; 13(a) only includes a vague commitment by Illinois EPA to require the facility to test its pollution control equipment when Illinois EPA deems it is a "reasonable time[]" to do so.

The condition does not include a directive that sources shall conduct testing followed by two clauses. Rather, the condition indicates that the source shall be subject to Agency requests for source testing as well as Agency conducted testing. Also, condition 13 is a mere recitation of the regulatorily established obligations for a source to test. Any testing specifically called for in the permit is set forth elsewhere in the permit.

113. Condition 14 sets forth references to the methods for conducting monitoring and testing of various emissions sources set out in Sections 212.107 to 212.110, including methods for visible emissions and opacity;

The condition simply makes clear the appropriate reference methods for testing.

114. Cond. 16(g) includes a statement that satisfactory completion of the initial test is a prerequisite to issuance of an operating permit, which in theory could set an outer boundary on delays. However, given Illinois EPA's practice of sitting on permit applications for extended periods of time we have concerns that testing may be delayed indefinitely.

Initial testing required under the permit is to be conducted within a defined window of time. Subsequent testing addressed in the permit is also to be conducted at a defined point. As drafted, the permit does not provide for delays in testing. As to permitting, the Illinois EPA has never had a practice of sitting on permits. However, there was a period, when for myriad reasons including limited resources, the Illinois EPA fell behind in permitting and a backlog was created. In recent years that backlog has largely been eliminated in the CAAPP and it has been significantly reduced in the FESOP program.

115. Condition 25 sets forth a requirement to submit a report to Illinois EPA "[i]f there is an exceedance of or deviation from the requirements of this permit as determined by the records required by this permit or otherwise."

This condition is one of the most if not the most important permit condition. This condition requires the reporting of any deviation from any requirement in the permit as determined not just by the records required under the permit but by any credible evidence.

116. Section 9(a) on page 8 does not indicate how often the facility should be required to do visual inspections or otherwise inspect or evaluate its pollution controls.

In response to comment, the Illinois EPA is requiring the expansion of the Maintenance Plan required at condition 11(h) in the draft permit to include all maintenance activities required under this issued permit. This plan will address practices and frequency, among other.

117. I have concern for the operating program and maintenance plan. The permit should specify what, at a minimum, must be in those plans to ensure protection of public health.

As is stated on the face of the permit, the terms of the operating program are incorporated into the permit, with the program itself as an attachment. The practices detailed in the program are intended to minimize visible fugitive particulate matter emissions and ensure compliance with the Board's Part 212 regulations. In response to comment the operating program has been enhanced. The maintenance plan, which has been expanded to additional equipment, is now required to be submitted 90 days prior to startup of the covered equipment. The plan will address maintenance activities and frequencies among other.

118. The hazardous air emissions permitted in section 12(b) should be reduced to 0 tons per year. Alternatively, Illinois EPA and General Iron should demonstrate to the public why this cannot be done and demonstrate that the pollution controls selected are those that will reduce hazardous air emissions to the lowest possible amount, i.e. that they are the best available control technologies.

Among its other responsibilities, the Illinois EPA is the permitting authority in Illinois. In that role, pursuant to and consistent with statutory and regulatory requirements, it is the Illinois EPA's duty to ensure sources are appropriately permitted. During the permit review process, the Illinois EPA determines whether a source has demonstrated that it can comply with the Environmental Protection Act and applicable regulations thereunder. The purpose of any issued permit is to memorialize the statutes, regulations and related terms such as recordkeeping and reporting applicable to the permittee and with which the source must comply as it is constructed and operated. In this instance, there is no basis for the imposition of an emission limit of 0 on the hazardous air pollutants.

119. "Emissions limitations in the Draft Permit are based on underestimated emissions of air pollutants, Likewise, the permit is based on artificially high control assumptions and greatly underestimated emissions for a range of fugitive sources including paved roads, vehicle loading/unloading, and piles)."

As has been stated elsewhere, where technically feasible, testing to validate the nature and quantity of emissions and the efficiency of controls has been required in the draft permit and further enhanced in the final permit.

120. The Draft Permit improperly assesses emissions from torch cutting and fails entirely to propose controls for torch cutting.

General III does not perform torch cutting, thus this activity is not addressed in the permit.

121. Conditions are lacking in the permit for emission controls that will achieve compliance with permit limits, and other conditions of the draft permit are unenforceable as being too vague, have no objective sufficiency or have no measures, including monitoring, record-keeping and reporting, by which to ensure compliance with particulate matter source and fugitive emissions.

The comment presumes the Illinois EPA can impose emissions standards and any related means of ensuring that a source will meet the requisite standards through this proceeding. However, the Illinois EPA does not wield a broad, or plenary, authority in its permitting role under the Act. The Act vests rulemaking authority for environmental control standards in the Board, not the Illinois EPA.[31] Analogous to the rule that permitting is no substitute for enforcement, it can be said that the Illinois EPA's permitting function is no substitute for the Board's rulemaking function.

From a legal perspective, it must also be observed that the state construction permit process for minor or synthetic air emission sources does not possess the rigors of major source programs. There is not a clear path to achieving controls and ancillary measures ordinarily reserved for New Source Review permitting. Periodic monitoring, a notion that springs from the Title V program, is similarly out of reach. USEPA has previously approved the relevant parts of the Illinois SIP as it relates the existing legal framework for state construction permits issued pursuant to Section 39(a) of the Act and the Board's Part 201 regulations. Region V staff also routinely reviews draft and final FESOP permits issued under this same regulatory framework, as they did in the case of the draft permit.

In general, a permit issued by the Illinois EPA is merely a vessel containing the relevant requirements that apply to the stationary source. The permitting role required of the Illinois EPA for a state construction permit (and operating permits that do not comprise major sources) is to mirror the basic control standards imposed upon a stationary source by the Act and Board regulations, and to provide basic measures for assuring compliance with the regulations and/or the permit. This approach is supported by the Part 201 regulations in the monitoring and testing provisions (Subpart J) and the records and reports provisions (Subpart K).

As mentioned elsewhere, the final construction permit includes additional monitoring that will be obtained through the development and operation of plans, and additional emissions testing, records and reporting requirements.

122. Many of the requirements of the fugitive particulate operating program ("FPOP") are practically unenforceable because they are overly vague and lack sufficient monitoring, recordkeeping and reporting details, or general sufficiency, to ensure continuous compliance with 35 Ill. Adm. Code Part 212.

The permit contains appropriate conditions for a state construction permit for the proposed emission source and control equipment. The more substantive rules for fugitive emissions (or dust) is commonly addressed by the Board's Subpart K regulations found at Section 212.301 and Sections 212.302-212.310 and 212.312). The former is a narrative standard that prohibits fugitive particulate emissions from any process that is visible beyond the property's boundaries when looking towards the zenith. The latter is the fugitive particular matter operating program requirements, which is designed to identity and implement best management practices to control fugitive dust activities at a site. General III is subject to the narrative visible emissions standard but not the operating program,

[31] **415 ILCS 5/5(b).**

as the facility's Standard Industrial Classification (SIC) code does not include the two-digit major groups specified in Section 212.302.

In the absence of applicability of the Board's Subpart K regulations, the Illinois EPA could have attempted to impose broad, cut-from-whole-cloth permit conditions, possibly even compelling many of the dictates regarding controls and timing requested by some comments. But given the possibility of an appeal, the Illinois EPA opted to pursue an alternative path for obtaining comprehensive measures for fugitive dust control. Successfully negotiated in other permits under similar circumstances, the FPOP is essentially a product of General III's willingness to commit to voluntary measures for controlling fugitive dust from the site. These voluntary measures, in turn, are incorporated into the construction permit and made enforceable through the most recent version of the plan submitted by General III on June 25, 2020.

123. The draft permit fails to ensure that the 30% opacity limit will be met for the facility's fugitive emissions sources, thus excluding them from a requirement that applies to process units and fugitive sources alike.

In response to comments, the draft permit will be amended to clarify that fugitive sources at the facility are subject to the opacity requirements of 35 Ill. Adm. Code 212.123. In addition, opacity observations are being included in the final permit to assure that the fugitive sources demonstrate an ability to comply with the emissions standard.

124. The draft permit allows for an improper automatic approval of a future revision to the FPOP and, in doing so, disallows the right to public review and comment prior to its approval.

Condition 10(i) of the draft permit provides that in the event a future revision to the FPOP is made during the permit term, the revision is automatically incorporated into the permit subject to the right of the Illinois EPA to approve the revision. The comment is therefore not correct in stating that the revision is automatic. However, the comment does correctly note that in the event that a future revision is incorporated to the permit, it will occur without undergoing public review, as there will be no permitting transaction contemporaneous with the change to the FPOP. In view of the FPOP's relative importance for source compliance with the permit's fugitive emission standards, and the protective requirement that the revisions must be consistent with Condition 10e and 10f, the Illinois EPA believes it is appropriate for FPOP revisions to go into the permit sooner rather than later. In this regard, the benefits obtained from fugitive dust controls through in-term revisions to the FPOP out-weighs the right of public review.

125. The draft permit allows for an improper post-issuance submission of the Contingency Plan required by 35 Ill. Adm. Code Part 212, Subpart U, thus disallowing the right to public review and comment of the document.

The submission of the Contingency Plan is tied to the submittal requirements set forth in Subpart U in Part 212. More specifically, sources subject to the rule after July 1, 1994, must submit contingency measure plans to the Illinois EPA for review and approval within 90 days following of the date that the source becomes subject to the rules. Condition 9b simply mirrors the regulatory requirement governing submission of the plan.

126. The permit allows several conditions of the permit to improperly defer the selection of multiple control options to the source and relegates the specificity of the permit's obligations to the FPOP.

For the reasons described above, the Illinois EPA exercised its discretion to address fugitive particulate emissions from the site through the avenue of a FPOP that the permittee has agreed to implement, and which will be enforceable through the incorporation by reference of the permit.

127. The emissions testing and monitoring under the draft permit is virtually nonexistent and contains conflicting requirements with respect to the Illinois EPA's testing authorities.

Emissions testing from the draft permit obligates the applicant to undertake an initial test with 60 days of the date that raw materials are first processed through the shredder, with an emissions protocol for the emissions testing submitted to the Illinois EPA within 90 days of issuance of the construction permit. *See,* Condition 16. Additional emissions testing and monitoring requirements have been added in response to public comment, as detailed elsewhere in this document. This includes capture efficiency testing as part of the testing evaluation of the RTO, testing of select pollutants from the fines processing system, testing of select pollutants from the Shredder system and opacity observations.

Contrary to the comment, there is no contradictions in the conditions relating to the testing authorities, as found in Condition 13. These requirements merely restate the testing requirements set forth in Part 201, Subpart J.

128. The permit does not contain any references to Section 9(a) of the Act and 35 Ill. Adm. Code 201.141, which are an on-going compliance requirement and was addressed by the Illinois EPA through its evaluation of air quality impacts in its air quality modeling.

The comment misapprehends the nature of the Section 9(a) prohibition and the similar standard found at 35 Ill. Adm. Code 201.141 in the Board's Part 201 regulations. The prohibitions contained in both requirements are narrative standards designed for implementing the Act's broad enforcement remedies.[32] Prohibitions are enforceable but only on a relative basis, as when evidence is adduced to show that conduct does not comport with the standard. The relativity of prohibitions make them meaningful in the enforcement realm, where they provide a broad outline with which to allege elements of a violation, as in the case of a polluter who is alleged to have caused air pollution or a violation of the Board's standards. But they are less relevant in permitting, where emission standards or limitations must be quantitatively certain.

Generally speaking, the use of statutory or regulatory prohibitions urged by comments are not included to air construction or operating permits. In addition, it is not clear how the cited prohibitions would have been factored into the air quality modeling of the project, in contrast perhaps to noncompliant sources. Efforts to gauge the impacts of general prohibitions would be futile.

129. The FPOP states that certain emission sources located within the Shredder system are potential sources of fugitive emissions.

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[32] **Similar statutory prohibitions are found in close proximity to Section 9(a) that include the prohibition against constructing or operating any equipment or facility without a permit and the open burning of refuse. *See,* 415 ILCS 5/9(b) and (c).**

In response to comments, the draft permit will be amended to clarify that the three conveyors associated with the Shredder system and referenced in the FPOP are not potential sources of fugitive sources.

130. The FPOP contains repeated usage of "as needed" in describing when controls will be applied and is in need for elaboration of objectivity. Similarly, the FSOP fails to specify which sources or areas are subject to the different controls.

In response to comments, some changes to the FPOP will be made to enhance the specificity of its provisions. However, neither the FPOP or draft permit is the appropriate venue for dictating the time, place and manner of fugitive dusts controls, as that venue is more appropriately addressed by the Board in its rulemaking role. In the absence of a type of operating program that applies to a source under Subpart K, which similarly does not dictate the requirements suggested by the comments, the Illinois EPA's broader approach to employing the use of the FPOP is not unreasonable and reflects considered judgment.

Stack Testing

131. What is emissions testing or stack testing and why is it not performed before the permit is issued and before the controls are used at the source to confirm that the controls will work and should be permitted?

Stack testing is a tool used to determine a source's compliance status with applicable control efficiencies. General III is subject to a control efficiency. Compliance with this efficiency will be determined by an initial stack test, and thereafter periodic stack testing.

Stack testing appropriately and necessarily is to be conducted after construction or installation of emission units and air pollution control equipment. Testing before construction is not an option as the units would not yet exist nor be in operation at a location. The purpose of the testing is to assess the efficiency of the control systems when in use at the source. As such, the testing necessarily must occur after issuance of the construction permit and when in use at the source.

132. Why are the details of the emissions testing to be performed not set forth in the permit?

Certain details of the testing will be set forth in an emissions test protocol. This protocol shall be prepared by an independent third-party consultant and submitted by General III and, after review and approval by the Illinois EPA, will serve as the guide for testing. However, the requirement for testing, the frequency of that testing and the methods to be used for testing are all set forth in the issued permit.

133. With respect to testing, are there standards of how frequent testing results would be available. Testing every week is requested.

For the scrap metal recycling operations addressed by this permit, there are no standards addressing the frequency of testing beyond the initial testing required by rule or permit. That lack of standards in

not unique to this sort of operation Given this is a construction permitting action for what will be a minor source of emissions falling within the Federally Enforceable State Operating Permit program, periodic monitoring in the form of testing (beyond the initial testing) is neither necessary nor the norm. The draft construction permit did require initial testing to demonstrate compliance with applicable rules and emissions and permitted emissions limits. And, in response to comments, the Illinois EPA has expanded emissions testing. For example, the RTO is now subject to periodic testing as frequently as annually under certain circumstances.

134. The draft construction permit lists emission limits based on stack tests conducted in May/June 2018 and November 2019 at General Iron II, LLC (ID#031600BTB), located at 1909 N Clifton Ave, Chicago. These emission limits are improper as they rely on tests conducted at the company's current location and not at the proposed location. The Illinois EPA should require stack tests during the 1-year construction phase at the proposed facility location (11600 South Burley Avenue, Chicago).

The limited reliance on the earlier testing of the RTO is not improper. Indeed, that earlier testing evidences the destruction efficiency of the RTO that may be constructed at the Burley site. In the absence of such testing information, the Illinois EPA would be forced to rely upon information from the manufacturer, information from similar units in similar operations, estimations, institutional knowledge and reasoned engineering judgement. As a practical matter, testing necessarily occurs after the construction of an emission unit and or air pollution control equipment. It simply cannot occur prior. Thus, in making construction permitting decisions, unit or control-specific test data is often not available. As to post construction, the draft permit required initial emissions testing and the final issued permit has expanded the requisite testing. With this site-specific testing, compliance with applicable regulatory requirements and emissions limits under the permit can be assessed for the General III operations at the Burley site.

135. The permit should contain measures that require General Iron III LLC to more frequently check and publicly report the current destruction efficiencies of the RTO and other pollution control technology.

As previously noted, the source will be conducting initial and periodic testing of the RTO and balance of the control train. The information from the testing will be available to the public.

136. With respect to pollution mitigations, what is being done at the new facility compared to current facility to give residents peace of mind?

Notably, the Hammermill Shredder System is new and there will be improved capture at the enclosure. And, in contrast to the existing site, there will be Method 204 capture testing of the enclosure that will definitively establish the extent of the capture. There will also be a Feedstock Management Plan and an Operations and Maintenance Plan, as well as an enhanced Fugitive Emissions Operating Program. There will be differential pressure monitoring of the roll media filter. And there will also be limits on hours of operation for purposes of limiting emissions.

137. Condition 6-2(c)(iii). If the control devices are not run with the same parameters during testing as they are for normal operations, then the test would not address normal operation and therefore could not verify compliance.

The cited condition does not exist in the draft permit, however the comment seems to relate to testing conditions. Emissions testing is to be performed under conditions that are representative of

how the source normally operates. How a source operates during successful testing establishes parameters on future operations until the next test event.

138. The Draft Permit is based on artificially high control assumptions and underestimated emissions from the Hammermill Shredder. There is substantial evidence of uncontrolled emissions from the shredder in its current location, including with the hood/RTO set-up. These shortcomings are exacerbated by weak testing and monitoring requirements that omit continuous monitoring, FLIR and other options.

    The application describes the shredder as being located within a "partial enclosure with… a vented metal roof," outfitted with a "capture hood" for routing shredder emissions to the RTO and scrubber.

The Hammermill Shredder will be located in a partial enclosure with acoustic roof and wall panels. The majority of one side of the enclosure, adjacent to the shredder, is a solid wall extending to ground level. The remainder of that wall and the other three walls consist of acoustic panels that extend to approximately 18 feet from ground level. Rubber belts extend downward covering a portion of the lower 18 feet. There will be an open area at the bottom to allow access to the interior of the enclosure for equipment maintenance. Shredder emissions are captured by a hood located over the top of the shredder and are routed to the shredder emission control system. The capture of the enclosure will be determined by testing. Short of testing, there is no definitive way to establish the actual capture efficiency and thus to quantify any uncontrolled emissions. Destruction efficiency testing will also be performed. After testing, compliance with Subpart TT of the Pollution Control Boards' regulations and with emission limits will be confirmed. The destruction efficiency set forth in the application is technically reasonable and has been demonstrated previously with the RTO at the Clifton location. The capture efficiency presented in the application was 95%. It is reasonable that with the proposed air flow and the improved enclosure the capture could achieve 100%. The permit as drafted aggressively addresses both destruction efficiency and capture.

139. The capture efficiency of the rubber-lined conceptual enclosure (in combination with wet suppression for PM) is unlikely to exceed 50% as an engineering judgement. It could be even lower given the high degree of wear of this type of enclosure over time, which makes the effectiveness over the long-term even more questionable, and the potential for irregular use of wet suppression (see below with respect to General Iron's and RMG's track record with wet suppression). 81% control.

As noted above, the capture efficiency set forth in the application is not unreasonable as a technical matter. Regardless, the capture efficiency will be established by way of initial emissions testing. Thereafter periodic testing will ensure the level of capture at the time of testing and at which the source can demonstrate compliance with Subpart TT and emissions limitations set forth in the permit. In keeping with its historical practice, the Agency did not factor in any degradation of emission units or controls. Rather, periodic emissions testing is the primary means by which the Illinois EPA ensures the continuing integrity of emission units and air pollution control equipment.

140. To the extent that such shredders require a cleaner, more specific feedstock on the front end, Illinois EPA should require enforceable feedstock sorting and cleaning.

The Illinois EPA has revised the construction permit to require a Feedstock Management Plan. This plan will address the materials that the facility receives, cleans, sorts and processes. This plan is to be submitted for Illinois EPA review and approval 90 days prior to General III receiving any materials at the Burley site.

141. The hood structure at the current General Iron location has been reported as allowing emissions to escape before the control devices. CDPH inspectors have observed "untreated emissions" and sometimes smoke escaping the top and sides of the shredder. Indeed, CDPH inspectors have noted that the emission controls do not appear to be working, and that the shredder has a hood but is not fully enclosed, causing emissions to escape the shredder before the treatment process and rendering the RTO and scrubber ineffective for those escaped emissions. As one inspector stated in January 2020, "being able to observe emissions escaping the shredder leads me to believe that the equipment capturing the emissions is insufficient."

The Illinois EPA is aware of the observations of the City of Chicago Department of Public Health. Indeed, these observations have been the subject of discussions with USEPA as well as the City. Learning of the observations by the City and knowing that the USEPA had brought and technically resolved an administrative action against General Iron for noncompliance with Subpart TT, requiring that the RTO be installed and subjected to emissions testing, had witnessed the testing, and had reviewed and approved the test report, the Illinois EPA reached out to the USEPA inquiring of any requirement for full enclosure or 100% capture, any concern for the destruction efficiency of the RTO, and any concern for noncompliance with Subpart TT, indicating that any concerns would most appropriately be addressed by the USEPA given the earlier order. Also, the Illinois EPA not only discussed the matter with the City but accompanied City inspectors to the facility where the Illinois EPA and City observed the Hammermill Shredder, enclosure and control system, and discussed the nature and function of same.

The Illinois EPA is not aware of information that suggests that the RTO is not achieving the destruction efficiency of 98% demonstrated during the most recent testing. Thus, there is no basis to conclude that "the controls are not working or are ineffective." The Illinois EPA is likewise not aware of any information that suggests that the capture efficiency is not what is was on the day of the most recent testing. The hooding is not a full enclosure, nor does it need to be as a regulatory matter nor pursuant to the federal administrative order. As it is not fully enclosed it should be understood that some quantity of emissions will be uncontrolled as they will not reach the RTO, whereas the emissions that do reach the RTO will be reduced by 98%. (And one must ensure that the steam that is often present at the enclosure is not confused for emissions.) This does not evidence that the "enclosure or capture is insufficient." Rather, the enclosure is a partial enclosure, and it achieves whatever capture such partial enclosure can achieve. The capture and control together shall provide for an overall control of 81% as is required under Subpart TT.

However, any issues with the Hammermill Shredder System at the Clifton site are not being formally considered as part of this permit proceeding. Rather, what is being considered is the application that delineates a new Hammermill Shredder and an enhanced enclosure with control train and contains a demonstration of compliance with applicable regulatory requirements.

142. Illinois EPA must require GIII to employ a fully enclosed shredder design with no openings.

The shredder is subject to Subpart TT, which requires 81% overall control of emissions. Subpart TT does not establish a floor for capture nor a floor for control. It does not require 100% capture nor full enclosure nor does it require 100% control nor specify the control equipment to be utilized. As such, the Illinois EPA has no basis to require General III nor any other source subject to Subpart TT to install a total enclosure.

143. If the applicant and Illinois EPA determine such a fully enclosed design is infeasible, they must fully explain this determination on the record and provide further measures to continuously and stringently control the emissions that will escape the shredder, the enclosure, and the hood capture setup as proposed. Additional VOM measures may be needed in order to meet Subpart TT's 81% control requirement (additional feedstock cleaning measures are one additional front end VOM control that may significantly reduce VOM from the shredder and so that should be considered). Such measures must be accompanied by robust recordkeeping and mandated reporting obligations.

As explained elsewhere, full enclosure is not in the first instance a matter of feasibility. Rather, it is a matter of statutory and regulatory authority and applicability. The Illinois is obligated to permit units that emit that are not otherwise exempt and air pollution control equipment. In doing so it is obligated to apply applicable regulatory provisions. It may add conditions to permits to further the purposes of the Act, but not without limitation. In a situation such as this, where there is an applicable regulation that quite clearly establishes the regulatory requirement, the Illinois EPA is not at liberty to utilize its permitting process to create a different more onerous requirement. That would be a matter for rulemaking.

The permit makes clear the applicability of Subpart TT. The permit establishes an initial test to demonstrate compliance with Subpart TT. The permit as enhanced also provides for testing thereafter to ensure ongoing compliance between test events. Based on the application, compliance with TT has been demonstrated. The Agency has required a Feedstock Management Plan in the final permit.

144. Monitoring of uncontrolled emissions must be included and consist of ground-based continuous VOM monitoring, such as AERARAE monitors and ground-based continuous PM monitoring as well as FLIR monitoring. The Draft Permit should require at least monthly, and preferably real-time, reporting of this monitoring data to be made public on Illinois EPA's website, The Draft Permit should require upfront provision of "stack" testing protocols for the Hammermill Shredder, and mandatory repeat testing on a quarterly, with requirements to do regular feedstock characterization testing and conduct emissions testing with significant changes in the feedstock. Such mandatory repeat testing is also needed given the likely deterioration of the hood over time.

The initial VOC emissions testing will assess the nature of the enclosure and definitively determine its capture efficiency. The revised permit now calls for subsequent emissions testing. The frequency of testing is either annually or every 5 years depending on the nature of the enclosure. It is not more frequent as these test events will be time involved; there will be protocol submittals and reviews, testing, and test result submittals and reviews. These activities associated with testing cannot reasonably be completed within any one quarter. The suggestion for testing quarterly is impractical as it would have the effect of the source and the Agency being in a never-ending testing mode – never establishing the compliance status from one test before the chain of activities commenced for the next test. And, periodic monitoring will be established based on testing. The monitoring will not consist of ambient monitoring nor will is consist of FLIR monitoring as neither can determine the quantity of emissions escaping from a unit at the facility nor the facility as a whole. The testing will be pursuant to protocol submitted before conduct of the testing as has been the long-standing practice of the state and federal government. As always, the testing will be representative and will establish the operating parameters for the tested units until the next test event. And, the feedstock concern is now addressed via a Feed Stock Management Plan and will also be addressed as part of any emissions testing protocol.

145. The November 2019 stack test conducted at the existing facility, and upon which the permit's emission limits are based, was performed with 50 percent ELVs in the feed. However, the permit does not include permit conditions that take into account this operating condition at the time of the stack test. EPA's experience with hammermill metal shredders indicates that, in general, the higher the proportion of ELVs in the feed the higher the VOM and organic hazardous air pollutant (HAP) emissions from the shredder. EPA has also observed that draining of fluids from ELVs before they are fed to the shredder will generally reduce actual VOM and organic HAP emissions from hammermill shredders. EPA requests that ILLINOIS EPA consider incorporating into the permit terms and conditions that address the maximum percentage of ELVs allowed in the feed, and whether or not fluids are drained from ELVs before they are fed to the shredder, consistent with the operating conditions at the time of the relevant stack test. Alternatively, Illinois EPA may clarify in the permit record how such permit provisions are unnecessary for this facility.

As addressed elsewhere herein, the Illinois EPA is requiring capture and control efficiency testing. The conditions under which testing will occur will form the basis for conditions relating to later operations. The Illinois EPA is inclined to limit conditions in this construction permit based on prior test events. Rather, it will create conditions based on test events at the new location that are reflective of the conditions during those test events including feed. The test events will seek to ensure the destruction efficiency under representative worst case conditions, which may or may not be the 50% ELV feed. As to the fluid draining, the Illinois EPA has required the development and implementation of a Feed Stock Management Plan, which plan is to be submitted to and approved by the Illinois EPA well before the testing. Fluid draining would be addressed in this Plan. Prior to testing, an emissions testing protocol is to be submitted to the Illinois EPA for approval. This protocol will address the particulars of the testing including test methods and procedures and feed among other.

146. Condition 5d requires the Permittee to operate emission capture and control equipment which achieves an overall reduction in uncontrolled VOM emissions of at least 81 percent from each emission unit. Based on the emission estimates included in the permit record, it appears Illinois EPA assumed the hood capture efficiency to be 100 percent. EPA requests Illinois EPA to supplement the permit record to provide support for the 100 percent hood capture efficiency used for calculating emissions and setting emission limits. If Illinois EPA's analysis shows that the proposed facility would not continuously achieve 100 percent capture in practice, please consider adjusting the emission factor in Condition 12b(i) to account for potential uncaptured VOM emissions. In this regard, it may be necessary to incorporate into the permit additional provisions for estimating the capture efficiency that would be used to calculate actual emissions. EPA is available to assist Illinois EPA with developing appropriate procedures for this purpose, which may include the use of EPA Test Methods 204 through 204F, computational fluid dynamics modeling, or visible emissions observations, as appropriate.

The Illinois EPA did assume a hood capture efficiency of 100 percent. This is not unreasonable based on the application which set forth a capture efficiency of 95%, high air flow, and an enhanced enclosure relative to the existing site (where the assumed capture seemingly approximated 83%). In addition to destruction efficiency testing, the permit calls for capture testing. After compliance with regulatory provisions and permitted emissions, limits can be evaluated.

147. We note as discussed with respect to conveyors within the shredder enclosure, that sources that can in fact be enclosed are not properly considered sources of fugitive emissions and their emissions count towards major source thresholds for facilities like GIII.

Correct, the Hammermill Shredder System in the entirety is a process emission unit. No part of the system including the conveyors is considered a fugitive emission source. All emissions from the Hammermill Shredder System count toward major source thresholds.

Fugitive Particulate Operating Program

148. Fugitive Particulate Operating Program fails to acknowledge applicable legal requirements.

The Fugitive Emissions Operating Program identifies 35 IAC 212.301 as the rule for which the program is designed to ensure compliance. This rule prohibits visible fugitive emissions beyond the property line.

149. The FPOP characterizes itself as a "voluntary" program because the source is not otherwise covered by the express requirement to prepare such a plan contained in Section 212.302.

Notwithstanding that the source is not subject to the regulatory requirement to develop and implement a FPOP, the permit requires such a program and the measures set forth within. Identified as a Fugitive Emissions Operating Program, neither the Program nor the measures set forth in the Program are voluntary.

150. FPOP is otherwise unenforceable as a practical matter.

The Fugitive Emissions Operating Program addresses the operations and best management practices that will serve to minimize fugitive emissions. It also sets forth record keeping and reporting. The program is not required to satisfy the letter of practical enforceability given that this is a state construction permit transaction for a minor source of emissions who is not even subject to the regulatory requirement for such program.

151. The applicant can include specificity on the operations that are expected to generate more fugitive emissions, and specificity on the controls to be deployed to these areas and specifics on how they will be deployed, control can be built into the front-end design.

The Ferrous Separation System, Non-Ferrous Separation System, and the Miscellaneous Fugitive sources are the categorical operations that generate fugitive emissions. The June 25th version of the Fugitive Emissions Operating Program more clearly delineates the best management practices to be utilized in these areas.

152. There is little to no discussion of controls to be used for truck, rail or barge unloading or even confirmation that rail and/or barge loading occurs on the GIII property.

The Fugitive Emissions Operating Program has been revised to clarify that General III will conduct loading of rail and barge. Additionally, the location of these activities and the measures that will be used to address fugitive emissions from truck, barge and rail loading have been clarified.

153. As noted above loading of at least trucks and rail cars should occur in enclosures.

There is no regulatory requirement applicable to the source that requires an enclosure for truck or rail car loading. However, measures to minimize fugitive emissions from these activities are addressed in the Fugitive Emissions Operating Program. For example, tarping, sweeping and watering address visible emissions from truck travel. For rail car loading, watering and minimization of drop distances are employed.

154. Illinois EPA must impose objective, stringent measures to control fugitive dust from piles, transfer points, and roadways.

Again, the scrap recycling facility is not subject to the regulatory requirement for a fugitive emissions operating program. However, to ensure compliance with 35 IAC 212.301 which prohibits visible emissions from crossing the property line, the Illinois EPA has required the development of a Fugitive Emissions Operating Program. This program addresses the best management practices for piles, transfer points and roadways.

155. Illinois EPA should require evaluation and deployment of full enclosure for conveyors, vehicle loading/unloading, piles and other transfer points associated with all three Systems.

There is no regulatory requirement applicable to the source that requires full enclosures for conveyors, vehicle loading and unloading, piles or other transfer points. Notwithstanding, the Fugitive Emissions Operating Program addresses the measure that will be taken to minimize fugitive emissions from these areas.

156. Must specify where specifically the Dust Bosses will be deployed and under what operating and weather conditions Illinois EPA should require that Dust Bosses “shall” be used at all times during active working of piles and vehicle loading, as opposed to allowing for use of this equipment “as needed” or only after the fact if visible emissions are identified.

The Fugitive Emissions Operating Program contains diagrams indicating where the Dust Bosses will be located. The Program as revised in response to comments is more robust in terms of specific commitments.

157. Illinois EPA also should require use of dry fogging systems at low temperatures when regular wetting procedures cannot be deployed effectively.

The Illinois EPA could see minimal distinction between the use of the Dust Bosses and the dry fogging system. Further, there is no legal basis for such technical requirement.

158. Chicago’s Department of Public Health June 2020 large recycling facility regulations require substantial control of ASR, Section4.4.2. That ASR can reasonably be stored in a full enclosure also renders emissions from ASR piles point source emissions, not fugitive emissions.

As addressed in the fugitive plan incorporated by reference into this permit, that subset of ASR that is fluff will be stored in a 3-walled, covered enclosure. It is not a full enclosure as the source needs to access the pile with material moving equipment such as end loaders. There are no applicable state or federal regulations that specifically call for enclosure much less a full enclosure of ASR. However, in looking at the ordinance as a point of reference, and while the Illinois is not in the habit of interpreting City ordinances, it notes that in the cited provision the enclosure requirement applies to post processed ASR, which is seemingly the fluff. Further, the ordinance does not expressly call for a full enclosure. Moreover, there is nothing that suggests that the ASR can reasonably be stored in a full enclosure. It is true that the ASR piles are point sources.

159. Illinois EPA must impose conditions to prevent auto fluff from migrating offsite.

Auto fluff is a subset of ASR. The conveyor to the fluff storage is covered. The fluff will be stored in a 3-walled, covered enclosure. Also, trucks hauling the fluff from the site will be tarped. This and other mitigative measures such as visual observations, watering and sweeping will ensure that the fluff does not migrate offsite.

160. Regular (at least monthly) testing of ASR should be required to characterize the content of the material, which may vary significantly with feedstock.

Illinois EPA is requiring a Feedstock Management Plan to address material screening and sorting and related issues.

161. The Illinois EPA should require regular moisture content testing for ASR.

The ASR comes off the shredder sufficiently wet (having been wetted by the spray system on the shredder) so as to make moisture content testing unnecessary.

162. The application mischaracterizes Section 212.123 as follows: "Section 212.123(a) prohibits the emission of smoke or other particulate matter from any process source to exceed 30% opacity." The FPOP repeats this misstatement of Section 212.123 by recognizing only the applicability of the prohibition on visible emissions beyond the fence line contained in Section 212.301 to fugitive sources. Nor does the FPOP include any mention of opacity limits as applicable to fugitive sources, let alone actual monitoring of opacity using Method 22 at each source of fugitive emissions to ensure compliance with this applicable provision. Indeed, the word "opacity" is only used three times in the operating program, in each case to explain that certain point sources that do have opacity limits are not in fact fugitive sources.[89] This omission/mischaracterization creates a conflict with the Draft Permit, which as discussed above appears to recognize the applicability of 212.123 to fugitive emission units.

The revised permit makes clear the applicability of 35 IAC 212.123 to all emission units encompassed within the Hammermill Shredder System, Ferrous Separation System, Non-Ferrous Separation System, Fines Building, and Miscellaneous Fugitive Emissions. The Fugitive Emissions Operating Program is the means of ensuring compliance with 35 IAC 212.301. Separate compliance assurance measures are included in the permit for 35 IAC 212.123.

163. The FPOP creates a conflict with the Draft Permit with respect to the applicable legal requirements.

The final permit has attempted to address any confusion or conflict.

The practically enforceable constraints on fugitive emissions are those found in the Pollution Control Board's Part 212 regulations. The measures in the FPOP are intended to assure compliance with the applicable provisions of the Part 212 regulations. There is no obligation for periodic monitoring in this construction permit much less periodic monitoring to assure compliance with a prohibition against air pollution.

164. The FPOP mysteriously claims that the three conveyors located within the shredder enclosure and uncaptured emissions from the shredder itself constitute "potential sources of fugitive emissions," in contrast to shredder emissions within the enclosure that in fact end up captured by the hood setup.

The FPOP has been revised to exclude the shredding operation. Indeed, as the permit makes clear, the shredding operation in the entirety is not a fugitive source. Rather it is a point source with emissions capture and control, with the extent of capture and control to be established by way of destruction efficiency and capture testing.

165. The FPOP fails to objectively describe the specific conditions under which the limited visible emissions testing will occur. See e.g., FPOP at p8, stating that visual observations will be conducted "three times per day," without specifying when, under what operating and weather/atmospheric conditions, and for what duration such observations will occur.

The revised Fugitive Emissions Operating Program now specifies that visible emissions observations will be taken from one to three times daily at raw material unloading/handling, material transfer points, intermediate and product stockpiles, fluff storage and loadout, material loadout, traffic areas, employee parking, barge, rail and truck loading, and the plant boundary. The precise time of the readings is not mandated, however, records of the date, time, location, observation and any response are to be kept.

166. The fugitive particulate operating program also contains a puzzling provision that describes additional visible emissions identification by "other employees" who are "trained to identify Visible Emissions," but whose observations will NOT be recorded in the same format as the visible emissions monitoring by "designated trained personnel."

This provision has been deleted within the latest revision to the program.

167. How will pollution from the roads be addressed?

Roads within property will be addressed by way of visible observation, sweeping and watering. The fugitive plan also includes vehicle speed limitations. Lastly, the permit limits the hours of operation of General III including truck operations.

Ambient Air Monitoring

168. What will the ambient monitoring tell us?

It will tell us the amount of a particular pollutant in the ambient air. While it is sometimes possible, under certain conditions, to determine the approximate direction from which pollution is originating, it will not directly identify the contributing source or sources of the pollutant.

169. More ambient monitoring stations are needed.

The Illinois EPA has designed its ambient air monitoring network to provide timely air pollution data to the public, to meet federal requirements, to support compliance with ambient air quality standards and emissions strategy development, and support air pollution research studies. This network satisfies or exceeds all relevant criteria. Regardless, the expansion of the network would not occur in the context of a permitting action.

170. Continuous ambient air monitoring is necessary to ensure that facilities are not causing or contributing to levels of PM and/or air toxics that exceed the NAAQS or other health-based thresholds, in particular with respect to fugitive emissions.

Again, ambient monitoring will only tell us the amount of a particular pollutant in the ambient air. It will not directly identify the contributing source or sources of the pollutant. Further, the existing monitoring network is sufficient to address the emissions from General III. Lastly, the existing monitoring data evidences compliance with the NAAQS for PM.

171. Illinois EPA must require fence line continuous monitoring of PM and metals to ensure compliance with the prohibition of air pollution.

The existing monitors in the vicinity, including those at Washington High School, evidence compliance with the NAAQS for PM. In the context of this construction permit for a minor source, there is no statutory or regulatory requirement for and the Illinois EPA is not inclined to attempt to stretch its authority to insert a requirement for the installation of fence line monitors.

172. The Illinois EPA should require fence line particulate monitoring surrounding the perimeter of the facility to ensure compliance with Illinois fugitive dust regulations. A combination of fence line monitoring and video surveillance can help ensure the facility is following Illinois pollution regulations and would represent a step forward in Illinois EPA requiring state-of-the-art technology to protect the health and wellbeing of Illinois residents.

As noted, the Illinois EPA is not inclined to require fence line PM monitoring at the perimeter of General III, nor video surveillance. The existing monitors in the vicinity, including those at Washington High School, evidence compliance with the NAAQS for PM.

173. Recent resident observations have frequently contended that General Iron facility in Lincoln Park frequently operates beyond their permitted hours of operation. If the Illinois EPA is to issue this permit, the Illinois EPA should require the installation of a 24/7 surveillance camera to ensure hours of operations restrictions are being followed.

Hours of operation is a common constraint found in a permit, the purpose of which is generally to limit emissions. The typical practice for ensuring compliance with such requirement is the inclusion of recordkeeping and reporting requirements. There is no legal or technical basis for surveillance

monitoring to ensure compliance with this limitation on hours of operation. It is believed that the hours of operation referred by the commenter relates to the relocation agreement with the City.

174. The federal monitors are not near the current site of General Iron. The data gathered around the existing General Iron location shows concentrations of air quality that are unhealthy (or "show unhealthy levels of fine particulates"). See Exhibit A, Maps of Air Quality Monitoring Data Around General Iron Facility.

These concentrations are from personal, small sensors. These monitors measure very short timeframe concentrations – down to the second in some cases. While these sensors can provide useful indicator information, they are not federally approved for comparison to any NAAQS and are not subject to the same rigorous standards of quality control and quality assurance as Illinois EPA monitors. Additionally, the reported concentrations, often listed as "brief" or for only a few seconds, have no direct comparison to PM2.5 standards. The current standards for PM2.5 are measured on an annual basis and a 24-hour basis. For the small sensor concentrations to be compared to an Air Quality Index value, a 24-hour concentration needs to be established. Exceedances of the 24-hour standard are rare. The Illinois EPA monitoring data at monitors nearest to the current site do not show unhealthy levels of fine particulates and, in fact, that area, along with the entire State of Illinois, is in attainment with the PM2.5 National Ambient Air Quality Standard.

175. Given that much of the pollution control equipment will be moving to the South Burley Avenue location, which is in a frontline community, the Agency should first consider the monitoring data from the existing facility. David, relate that the monitoring data on Clifton and monitoring data for Burley say the same thing.

As noted above, the monitoring data from the monitors nearest to the existing facility demonstrate that the area is in attainment of the particulate matter standards, as is the case for the new location and the entire State of Illinois. One benefit of the new location is that the prevailing winds will typically carry emissions toward nearby Illinois EPA monitors, which will provide good information about the nearby ambient air.

176. In General II, LLC's initial submission of repository documents, the introduction states: "There are no Illinois EPA or USEPA regulations limiting emissions of specific metals or requiring an ambient impact analysis." Can this truly be the case and if so, has it always been the case?

Yes, it is true that there are no regulations limiting specific metals that apply to this scrap metal recycling facility. Rather, the scrap metal recycling facility it is subject to the Pollution Control Board's rules applicable to visible and particulate matter emissions and to volatile organic material emissions. Further, it is true that there is no requirement for an ambient impact analysis for a facility of this type and size. And this has always been the case.

177. Have any of the applicable standards currently being applied to this proposed permit changed over the course of the last 3 ½ years and if so, in what way.

It is not clear whether the commenter is referring to the standards that govern the permitting process or the source itself. Regardless, the answer is the same – no, there have not been any changes in the last 3 ½ years. The requirements applicable to construction permitting and the public process are long

established. Likewise, the Pollution Control Board's air pollution control regulatory requirements that are applicable to this source are long established.

178. In October 2019, ELPC air quality monitoring data showed concentrations of poor air quality close to existing General Iron facility, which creates doubts about the adequacy of the pollution controls to protect the community. Of great concern are the intersections at Clifton and Kingsbury, and the intersection at Kingsbury and Wisconsin which have had PM 2.5 readings greater than 35 ug/m^3. See Attachment A.

As noted above, while these sensors can provide useful indicator information, they are not federally approved for comparison to any NAAQS and are not subject to the same rigorous standards of quality control and quality assurance as Illinois EPA monitors. Additionally, the reported concentrations, often listed as "brief" or for only a few seconds, have no direct comparison to PM2.5 standards. The current standards for PM2.5 are measured on an annual basis and a 24-hour basis. For the small sensor concentrations to be compared to an Air Quality Index value, a 24-hour concentration needs to be established. Exceedances of the 24-hour standard are rare. The Illinois EPA monitoring data at monitors nearest to the current site do not show unhealthy levels of fine particulates and, in fact, that area, along with the entire State of Illinois, is in attainment with the PM2.5 National Ambient Air Quality Standard. Based on a review of the application, the source has demonstrated that it can comply with the Pollution Control Board's regulations for organic material and visible emissions.

Modeling

179. Why was the modeling performed?

The Illinois EPA requested air quality modeling of hazardous air pollutant (HAP) metal emissions from General III in support of the construction permit application.

180. Who performed the modeling?

A third-party consultant for General III performed the modeling which was then audited by the Illinois EPA.

181. What does the modeling conclude?

Predicted modeled concentrations were compared against the National Ambient Air Quality Standard for lead, and for other metals against the Agency for Toxic Substances and Disease Registry (ATSDR) risk levels and Wisconsin Department of Natural Resources (WDNR) air toxics rule. Predicted concentrations were well below the identified limits. For carcinogenic substances, the inhalation risk was calculated using USEPA or California Air Resource Board unit risk factors. Estimated risk levels for all carcinogenic substances were less than 1 in 1,000,000.

182. The prevailing wind direction of the proposed new site (from SW to NE) means that majority of emissions will be blown toward G.W. High School and G.W. Elementary School and students will be exposed to PM and other emissions, such as manganese.

It is true that prevailing wind direction in the Chicago area is generally from the southwest. In such a situation, the prevailing winds would typically carry emissions toward the George Washington schools and thus the monitors that are located there. There are three types of monitors at George Washington High School – PM10, PM2.5, and lead/metals/TSP. The Illinois EPA would consider the Washington High School monitors to be very well situated to measure the air that may be impacted by emissions from this source. And, the monitors are measuring attainment with the National Ambient Air Quality Standard for PM10, which is designed to be protective of human health and the environment.

183. "The Draft Permit is based on deficient air quality modeling. The modeling assumes exceptionally high and artificial levels of control from the Hammermill Shredder; omits the co-located, unpermitted sources already operating at Burley as well as other known nearby sources of fugitive air toxics; fails to justify employing Wisconsin's air toxics rules versus other available state approaches; and omits PM10 modeling altogether."

Since the proposed General III PM10 emission rates would not exceed regulatory thresholds triggering the requirement for modeling, the applicant was not required to do so. Rather, the modeling was performed at the request of the Illinois EPA. The Illinois EPA was aware that Wisconsin had promulgated a rulemaking that had resulted in a relatively comprehensive set of toxic air contaminant air quality standards. Many of them comparable to or identical with values issued or used by other entities that may be regarded as more appropriate for off-site health risk evaluation. Capture and control of emissions is discussed elsewhere herein. Importantly, the actual capture and control will be definitively determined through emissions testing required under the issued construction permit. As to the other operations at the Burley site, they will be addressed along with General III during the operating permit phase of review.

184. The Illinois EPA cannot issue permit as the modeling demonstrates General III will violate the prohibition on air pollution.

The Lake Calumet region of Cook County (and the entire State of Illinois) are in attainment with the primary and secondary PM10 NAAQS. Since the proposed General III PM10 emission rates would not exceed regulatory thresholds triggering the requirement for modeling, the applicant was not required to do so. Equally relevant, however, is the Agency's firm expectation that Genera III's proposed PM10 emission rates would not "cause air pollution" as a result of the facility's contribution to existing ambient loadings in the Lake Calumet region. There was not an "omission" of PM10 modeling, there was simply a targeted focus on metallic HAPs. Manganese concentrations were modeled that represent 24-hour average and annual average concentrations. The 24-hour average concentrations are considered short-term average impact predictions. Though California has an 8-hour average Reference Exposure Level for manganese, the Agency is unaware of any federal agency or any other states issuing or using an 8-hour exposure level. The modeling analysis reflects conservative assumptions about facility operations and emissions-generating activities. These are believed to be consistent with the language of the draft permit and therefore lend support to the permit decision.

185. Emissions estimates in the air quality modeling are unsupported and otherwise inappropriate. The proposed hammermill shredder will not be completely enclosed. Therefore, any assumption that 100% of the particulate matter generated will be captured and controlled is not correct. Unless and until the shredder fugitive emissions are quantified and included in the metals and particulate matter modeling, the application materials before the agency cannot be relied upon for permit issuance.

The Agency stands by the permit and modeling. Notwithstanding, the actual capture and control will be addressed through emissions testing as set forth in the permit. With the results of that testing, additional modeling will be performed.

186. The conveyor emission factors are of concern. The applicant provided detailed particulate matter emission calculations regarding the ferrous material processing emissions, that largely rely upon AP-42, Section 11.19.2 Crushed Stone Processing and Pulverized Mineral Processing. The emission factor tables in AP-42, Section 11.19.2 provide two factors (controlled and uncontrolled) with controlled factors applicable to operations utilizing wet suppression. The controlled factors reflect an approximate 95% reduction in emissions due to wet suppression. The applicant assumes that a natural moisture content above 1.5% allows the use of the controlled factors without wet suppression equipment in operation. There is nothing magical about a 1.5% moisture content that immediately affords 95% reduction in fugitive dust emission generating potential equivalent to wet suppression. Depending on the material involved, significant fugitive dust emission generating potential can exist at moisture contents significantly in excess of 1.5%. Unless and until the conveyor emission calculations are corrected and the revised estimates included in the metals and particulate matter modeling, the application materials before the agency cannot be relied upon for permit issuance.

It is acknowledged that there are shortcomings in attempting to apply some AP-42 emission factors and associated emission suppression assumptions to scrap metal processing operations. Despite that, the Agency believes that the applicant adopted a reasonable approach in developing the conveyor emission estimates. And again, the modeling was not statutorily or regulatorily required to be performed as part of the application nor review process for this construction permit.

187. The non-ferrous material processing system includes a fines processing system controlled by four dust collectors. Three of the dust collectors vent indoors with the fourth venting to atmosphere. The applicant estimates particulate matter emissions from the fourth dust collector (DC-01) utilizing the potential airflow and an assumed exit loading of 0.005 grains per cubic foot (gr/cf). A more appropriate grain loading to estimate particulate matter emissions from DC-01 is in the range of 0.04 gr/cf. The applicant's proposed factor is simply not tenable given the type of collection systems in use at these types of operations nationwide. The applicant's proposed 0.005 gr/cf factor represents the pinnacle of particulate control from a state of the art, brand new baghouse equipped with polyester filter bags and reverse jet pulse cleaning. Absent substantial justification and documentation, the usual and customary factor of 0.04 gr/cf should be used. Unless and until the DC-01 emission calculations are corrected and the revised estimates included in the metals and particulate matter modeling, the application materials before the agency cannot be relied upon for permit issuance.

Regulatorily, the factor would need to be at least 0.03 gr/cf for PM10, thus the suggested factor could not be utilized. The permit requires testing of the DC-01 dust collector, to demonstrate compliance with the expected grain loading performance of this control device.

188. The modeling approach relative to roadways is not appropriate. A more robust and appropriate approach given general engineering knowledge/experience, the history of failed paving at General Iron and the RMGSCPM facilities and the vagueness of pavement-related requirements in the Draft Permit and FPOP is to use a simplified fugitive dust estimate, taken from AP-42 Section 13.2.3 Heavy Construction Operations. The recommended emission factor is 1.2 tons/acre/month. Annual

emissions can be therefore estimated using estimates of potentially erodible acreage. To allow for a portion of the area which might be paved (assumed to be 20%), we suggest that this emission factor be applied to the rest (i.e., 80%) of the total GII acreage at the rate of 1.2 tons/acre/month. Unless and until the vehicle traffic emission calculations are provided for review and comment, the application materials before the agency cannot be relied upon for permit issuance.

Ideally, estimates of re-entrained roadway particulate emissions should be based upon site-specific (road segment-specific) characteristics and established (generally accepted) emission factors. Speculation regarding pavement degradation as the basis for applying an alternative emission factor that is based only upon a single set of field studies (AP-42, p.13.2.3-1), rather that the applicant's use of an emission factor that "is based on a regression analysis of 83 tests" (AP-42, Section 3.2.1), should be considered suspect and potentially without merit. The commenter's proposed emission factor choice would potentially grossly overstate paved roadway fugitive emissions, certainly for a newly constructed operation. If the City of Chicago requires that all roadways at the GIII facility be paved, then the modeling analysis becomes more conservative, since it includes unpaved roadway emission estimates, which are typically higher.

189. Modeling Inputs/Assumptions Used by the Applicant and Illinois EPA are Unsupported and Otherwise Inappropriate particularly as to meteorological datasets. Two National Weather Service meteorological datasets were used. Surface data was taken from the Midway Airport in conjunction with coincident air sounding data from Davenport, Iowa for the years 2012 through 2016. In general, use of one year of onsite meteorological data is the preferred approach in U.S. EPA modeling guidance. Use of five years of "off-site" meteorological datasets may be used unless (1) specific terrain, coastal proximity, or other unique geographical issues make such data unsuitable and/or (2) "on-site" meteorological datasets are available. In this case, given the proximity of the site to Lake Michigan and the Calumet River and the availability of surface data from three meteorological stations in close proximity to the site (KCBX, S.H. Bell, and Watco Terminal), use of the surface data from the Midway Airport cannot be supported. Unless and until the modeling is revised to include the surface data from the local meteorological stations, the application materials before the agency cannot be relied upon for permit issuance.

The Agency acknowledges that the use of "on-site" meteorological data is preferred in regulatory modeling applications. Unfortunately, the commenter's three recommended "meteorological stations near the site" do not actually represent "on-site" locations for the proposed General III facility. Furthermore, it hasn't been demonstrated that those datasets are sufficiently robust for a refined modeling application. The Midway International Airport surface observations were chosen because of the proximity of this National Weather Service site to the GIII site and because the data is representative of the complex circulation patterns and other meteorological factors that influence the GIII site.

190. With the exception of the regenerative thermal oxidizer (RTO) and DC-01, all of the proposed emission generating activities are treated as a volume source. Volume source representation for air dispersion modeling purposes is a complex combination of location, release height, initial lateral dimensions, and initial vertical dimensions. However, because the applicant redacted the process flow diagrams from the original modeling submittal with a claim of Trade Secret, this reviewer cannot vet the volume source representations. And while the applicant does provide some information about the location of the haul roads, the depiction is spartan. Unless and until all volume source

representations can be fully vetted, the application materials before the agency cannot be relied upon for permit issuance.

The applicant did indeed redact the diagrams showing the volume source groupings of emission sources from the original modeling submittal. However, these diagrams, though pictorially useful, did not actually show the precise location and dimensions of the volume sources modeled. That information is found in the model input files and the supporting documentation.

191. Unless and until all particulate matter emissions from the co-located operations are included in the modeling, the application materials before the agency cannot be relied upon for permit issuance.

Since analyzing for total PM, PM10, and/or PM2.5 was outside the scope of the modeling analysis for General III (which focused exclusively on metallic HAPs), any extension of that modeling analysis would not have included evaluating particulate matter (PM, PM10, PM2.5) for the four SCPM facilities. The Illinois EPA did evaluate the increase in metallic HAPs from the four SCPM facilities in conjunction with the General III HAP emissions but did not find any increases of potential concern.

192. Based on the applicant's own emissions estimates and modeling, the proposed General III will result in exceedances of the PM10 NAAQS and unacceptable short-term manganese impacts. Impacts of manganese exceed the 8-hour Reference Exposure Level of 0.17 micrograms per cubic meter (ug/m3) established by the California Office of Environmental Health Hazard Assessment OEHHA. Unless and until impacts (including regional sources such as the significant known sources of fugitive manganese along the Calumet River that are not reflected in Illinois EPA's inventory can be shown to reside below 0.17 ug/m3, the application materials before the agency cannot be relied upon for permit issuance. This is especially true given the history of manganese issues in this environmental justice community.

The manganese modeling conducted by the applicant and reviewed by the Agency simulated 24-hour and annual averaging periods. A Wisconsin air quality standard and an ATSDR Minimal Risk Level (MRL), respectively, represented the human health standards against which the 24-hour and annual modeling results were compared. Modeling was not conducted for an 8-hour averaging period. The California Environmental Protection Agency Office of Environmental Health Hazard Assessment (OEHHA) 8-hour inhalation Reference Exposure Level of 0.17 ug/m3 can be viewed as a guideline level rather than as a bright line standard. As indicated in OEHHA's Air Toxics Hot Spots Program Technical Support Document for the Derivation of Noncancer Reference Levels, "a reference exposure level (REL) is an airborne level of a chemical that is not anticipated to present a significant risk of an adverse non-cancer health effect."

193. PM air quality modeling was not conducted, without explanation, despite the prohibition on air pollution, which encompasses causing or tending to cause air pollution in violation of the National Ambient Air Quality Standards. Based on the applicant's own emission calculations and modeling approach, impacts of particulate matter less than 10 microns in aerodynamic diameter (PM10) (added to background) exceed the 24-hour National Ambient Air Quality Standard (NAAQS) of 150 ug/m3. Unless and until PM10 impacts (including background) can be shown to reside below 150 ug/mg (24-hour average), the application materials before the agency cannot be relied upon for permit issuance.

As indicated previously, an expansion of the modeling analysis to address total PM10 was considered unnecessary by the Agency in a minor source construction permit transaction particularly when the Lake Calumet region of Cook County (and the entire State of Illinois) are in attainment with the primary and secondary PM10 NAAQS.

194. The applicant proposes to control emissions from the hammermill shredder with a control train including a regenerative thermal oxidizer (RTO). The presence of the RTO indicates high levels of volatile organic compounds (VOC), organic hazardous air pollutants (HAP), and other air toxics. Unless and until all reasonably identified HAP and air toxics are identified, quantified, and modeled, the application materials before the agency cannot be relied upon for permit issuance.

Organic hazardous air pollutants were not modeled because Table 3-1C of the permit application and Table 3-1C in the Updated Emissions Estimate document (January 27, 2020) indicated that the quantity of emissions would be quite small. The presence of an RTO does not at all automatically suggest that organic HAPs will be present, as many facilities use RTOs to control non-HAP VOCs. Further, there was no requirement to do modeling in the first instance.

195. We support Illinois EPA's investigation into the air toxics impacts of this facility on air quality and health, however, the following short list identifies high-level issues identified in the health analysis:
    - Failure to assess PM10
    - Failure to fully justify use of the Wisconsin approach for air toxics, versus other available approaches for assessing air toxics in states such as Michigan, Minnesota, Ohio, California, and Texas
    - Failure to assess the combined impacts of multiple metals and other hazardous air pollutants ("HAPs") from the proposed GIII, and in the context of the overburdened Southeast Side
    - Failure to take into account non-cancer impacts of HAPs
    - Failure to assess the impacts of VOCs along with metallic HAPs
    - Failure to account for the toxicity of hexavalent chromium
    - Failure to evaluate available short-term health thresholds for certain HAPs, such as the 8-hour manganese threshold of 0.17 ug/m3
    - Failure to accurately account for fugitive emissions from nearby facilities, given shortcomings in the state's emissions inventory for such sources
    - Failure to take into account the mobile source-related emissions from the trucks, trains and barges that will accompany the proposed GIII and related sources
    - Failure to evaluate other proposed and/or in-construction nearby sources of air pollution, such as a proposed new SCPM recycling facility immediately to the East of GIII200 and large warehousing facilities by developer NorthPoint
    - Failure to take into account the multiple pollutant exposures via air, water and soil; historic and existing health burdens; and sociodemographic characteristics of the impacted population, as pertain to the overall cumulative vulnerability to impacts from air pollution that would be emitted from the proposed GIII Illinois EPA must address at least these shortcomings in a revised assessment of whether the proposed GIII will run afoul of the prohibition on air pollution.

The Illinois EPA was aware that Wisconsin had promulgated a rulemaking that had resulted in a relatively comprehensive set of toxic air contaminant air quality standards. Though many of the standards are apparently based on Threshold Limit Values established by the American Conference of Governmental Industrial Hygienists (ACGIH), and may be thought of by some as insufficiently protective of the general public and the environment, they are clearly comparable to or identical with

values issued or used by other entities that may be regarded as more appropriate for off-site health risk evaluation. The Illinois EPA had no obligation to perform the modeling much less to fully research what other state regulatory agencies are using, and how those standards were developed. The Illinois EPA does prefer using ATSDR Minimal Risk Levels, however, many of these may not be available for specific toxic air contaminants and specific averaging periods. The other "high-level issues" identified by the commenter above are either simply beyond the scope of the analysis, were known but considered insignificant, have already been addressed, and/or are excessively difficult to quantify or incorporate into the Agency's analysis.

196. The modeling seems to include approximate rather than precise locations for emissions sources. Do these sources need to remain at these locations? If so, what guarantees they will be so located.

There are no specific guarantees or express requirements that these sources will be precisely located at their identified locations; however, any significant deviation from the proposed locations could give rise to concern or even a violation of the issued construction permit. This is a matter that would be addressed in the compliance or enforcement process as would other deviations at this or any other source.

197. In the modeling GIII did not consider the impact of all sources of pollutants and assumed control levels that it cannot meet**.**

General III modeling accounted for emissions from the Hammermill Shredder system, conveyors, separators, storage piles and roadway traffic. Manufacturer-guaranteed control efficiencies are used to estimate emissions from point sources, which is standard practice particularly prior to or in the absence of facility specific emissions testing which is not possible during the construction permitting phase.

Published USEPA emission factors for material handling operations at metal shredding facilities do not exist. Therefore, surrogate emission factors from crushed stone processing were utilized. These surrogate emission factors may overstate particulate matter emissions because the material processed through a hammermill has a high moisture content, thereby reducing the potential for particulate matter emissions from the ferrous material processing operations.

198. GIII did not consider the cumulative impact in the community and the impact of the existing operations at the site.

While not statutorily or regulatorily required to perform any cumulative impact analysis, General III performed air dispersion modeling demonstrating that the air impact will not exceed any established standards for lead or manganese. Modeling of the existing SCPM entities was not performed. However, ambient impacts from these operations are accounted for in the background monitoring values at the monitoring station at Washington High School. The monitors have identified no NAAQS concerns.

199. I am concerned that diesel trucks were not included in the pollution assessment and that truck traffic will increase additionally because of the seven warehouses that are coming to the area.

The construction permit application includes emissions from roadways within site boundaries. There is no requirement to address off-site emissions from mobile sources. The warehouses that may be

added in the area are not relevant to this permitting action.

Inspections/Oversight/Compliance/Enforcement/Penalties

200. An additional concern is the lack of Illinois EPA inspections of and enforcement actions against pollution law violations at General Iron.

Inspections and compliance and enforcement actions are important statutory functions. However, any concerns in that regard are not germane to this permitting decision. Notwithstanding, federal air program guidance addresses the frequency of inspection. For a minor source of emissions such as this scrap metal recycling facility, that inspection frequency would be every five years. In addition, the source is the subject of periodic report reviews. Additionally, as discussed elsewhere, the Illinois EPA utilizes its partnership with the local unit of government, requesting assistance from them regarding complaint response. And, in a further measure to most effectively utilize the available resources, the Illinois EPA coordinates its efforts with the USEPA.

201. There has been issues at the existing site, what will you do about issues at the new site.

As a general matter, permits address applicable requirements and the means to assure compliance with such requirements, rather than the actions or consequences that would ensue from issues encountered in attempts to implement or comply with an issued permit. This is, in part, because one cannot anticipate all issues that might later develop, much less how those might be appropriately addressed in the permitting context. Further, some issues that may develop may not be permitting considerations but compliance or enforcement considerations. However, the Illinois EPA will be overseeing GIII operations in a myriad of ways and will appropriately address any identified issues.

202. Illinois EPA's statutory mandates not only include permitting but monitoring and enforcement of compliance of permits. By issuing this construction permit while refusing to acknowledge a well-documented negative track record of this company, the Illinois EPA is burdening the city and passing its mandate to a city government as opposed to taking responsibility for monitoring the permits issued by the agency.

The Illinois EPA is aware of its statutory mandates and takes them seriously. In making this permitting decision, the Illinois EPA is not ignoring its mandates but rather following them. Specifically, it is making this permitting decision as directed by statute. By no means does the issuance of this permit pass any state mandates to the City. Further, the City is not responsible for ensuring compliance with Illinois EPA issued permits nor state or federal regulations. Rather, the City is responsible for ensuring compliance with its ordinances and regulations.

203. Illlinois EPA has chosen not to conduct inspections or commence enforcement proceedings against General Iron or RMG, at most they have conducted limited investigations that have failed to remedy the ongoing problems.

The inspection, compliance and enforcement history at the existing scrap metal operations on Clifton is not relevant to this permitting action. Notwithstanding, the Illinois EPA did not make a choice to

not inspect the Clifton operations. It has been to the Clifton site twice in the last six months. In addition, the Illinois EPA utilized its local partner to respond to complaints relative to the source. Also, it coordinated with the USEPA in its efforts. Additionally, records received from the source were reviewed.

204. Staffer Eric Jones recommended that a voluntary self-disclosure be submitted.

Mr. Jones is an employee of the Bureau of Air Permit Section. In response to a phone call from the source informing the Agency of noncompliance, he simply conveyed that the information needed to be disclosed to the Compliance Section, and that disclosure indeed occurred. That disclosure formed the basis for a VN that is pending resolution. Irrespective of his message, a source can follow the state or federal self-disclosure provisions. Whether the disclosure satisfies the criteria of these provisions is a separate consideration.

205. Illinois EPA has dramatically downsized its staff in recent years, causing reductions in inspection and enforcement. Inspections of air-polluting facilities have declined 80 percent since 2003. Enforcement cases referred to the Attorney General have also declined. The community, City and USEPA have been left to police pollution on the Southeast Side, addressing pet coke, manganese and identifying multiple facilities operating without state permits, due to Illinois EPA's absence in its role of primary environmental regulator and enforcer.

There have not been any staffing cuts in recent years, rather staff losses through retirements or attrition that are the subject of very aggressive hiring efforts. Since the time Gov. Pritzker took office, the IEPA has made a renewed emphasis on both hiring and enforcement. In fact, in the first year of Gov. Pritzker's administration the IEPA issued the most violation notices since 2011 and issued the most referrals to the Attorney General's Office since 2015.

206. Illinois EPA has a delegation agreement with the City of Chicago, Department of Public Health essentially deputizing them as an enforcement partner carrying out the Act and to assist with the state Agency's enforcement actions, conduct inspections, note violations of state law, respond to citizen complaints, and keep records of inspections and violations.

The Illinois EPA has an agreement with the City; however, it is an IGA or Intergovernmental Agreement, not a delegation agreement. As such, the City is not delegated any of the authorities under the Environmental Protection Act and is not "deputized" in any regard. It does not carry out the Act nor does it have the authority to do so. The agreement does seek inspection services by the City, most notably in response to citizen complaints. In investigating these complaints under the IGA, the City is accessing the facilities via its own rights of access. In identifying any potential violations of state law or regulation, the City reports such information to the Agency. Any actions by the City relate to violation of local ordinance or regulation.

207. Chicago's Department of Public Health enforcement activities are a critical part of the state-local partnership, and recognition of this important role warrants treating the violations of local ordinances and rules in this case as constituting "non-compliance" with the Illinois Environmental Protection Act. Chicago's Department of Public Health actions as the primary air regulator and enforcer in Chicago, including under an express delegation agreement with the Illinois EPA.

The inspections under the IGA and particularly the complaint response are an important aspect of the state-local partnership. However, inspections by the local unit of government are not inspections by the State. Such inspections may serve to inform the Illinois EPA and may serve to address or resolve a citizen complaint. But, the City is not delegated inspection authority. It is not delegated compliance or enforcement authority. It is not delegated the authority to implement state regulations. Thus, observations of the City and any tickets issued for ordinance violations do not translate to a violation of the Environmental Protection Act. And while it plays a significant role in environmental protection, the City is not the primary regulator and enforcer of the Environmental Protection Act.

208. When these provisions are not met, General Iron III LLC must face severe enforcement penalties, these penalties should be acknowledged within the permit.

The Illinois Environmental Protection Act provides for the imposition of civil penalties for violation of the Act. It is not necessary to recite the provisions of the Act in this regard in a permit.

Explosion

209. That explosion renders the current permit application incomplete.

The explosion does not render the application incomplete. The application sets forth information that demonstrates that the source can comply with the applicable provisions of the Act and regulations thereunder.

210. I am concerned for the recent explosion at current facility and ask that the construction permit be delayed until a complete investigation can be done. The failed equipment is not reliable to control emissions at new facility.

Proximate to the explosion the Illinois EPA sent a letter that among other things sought both a report of any damage to the RTO and root cause of the explosion. The letter has been acknowledged and there exists a commitment to provide the reports when final. In the meantime, in the context of the pending application, General III has represented that it remains committed to the use of an RTO at the new site and believes that the use of the existing RTO remains a viable option. It further represents that measures have been identified to prevent explosions in the RTO. Those measures including the installation, operation, and maintenance of a continuous monitoring device for the inlet gas stream to the control train to the Hammermill Shredder System for the flammability of this gas stream as a percentage of the lower explosive limit of this stream, have been added to the issued permit.

211. “The transfer of any equipment that can cause this kind of catastrophic failure requires that the permit application be revised to address risks related the proposed use of any equipment, its control efficiency, and the applicant's ability to operate the equipment safely and effectively. Further, existing emission estimates and air quality models do not account for emissions during periods of catastrophic failure and also must be revised. And, additional permit terms and conditions are clearly necessary to prevent future accidents and to ensure the integrity of the equipment and the applicant’s operating systems.”

The incident at the RTO was not a failure of the control device, nor does is render the device unreliable at reducing the organic emissions from the shredder. The destruction efficiency of the RTO will be tested at the new location. As noted above measures have been added to the permit to guard against future incidents of this type. Emissions from events of this type will be included in the calculation of total VOM emissions from the shredder. However, an event of this type is likely of limited duration and impact. Information provided by General III estimates an impact of approximately 3 pounds of VOM per event. The Operations and Maintenance Plan and the Feedstock Management Plan will also serve to improve operations.

212. Illinois EPA must impose additional permit conditions to prevent explosions.

The draft permit has been revised to include a Lower Explosive Level monitor and set point. It has also been revised to include a bypass safety vent to ensure the release of VOM-rich materials that would otherwise threaten an explosion. This bypass safety vent will be equipped with a device that ensures and monitors its use. The emissions from the vent will be included in the determinations of compliance with Subpart TT and the permit emission limits.

213. Measures that ensure that General Iron III LLC will employ a sufficient amount of qualified operators that are highly trained in operating applicable pollution control technologies such as the Regenerative Thermal Oxidizer (RTO). As demonstrated by the recent explosion at General Iron's current location in the Lincoln Park neighborhood, General Iron III LLC does not currently have the capability to operate these technologies safely.

The Illinois EPA does not have the authority to dictate who a regulated or permitted entity employs nor their credentials with limited exception. An RTO is a well-established and common means of controlling volatile organic compounds and hazardous air pollutants. There are no operator or training requirements for an RTO under the Environmental Protection Act or the Clean Air Act.

214. The record for the Draft Permit also fails to take into consideration a recent explosion at the Clifton Ave. site. On May 18, 2020, General Iron was shut down due to two explosions there. Subsequently, Chicago Department of Public Health issued two citations totaling up to $6000 to General Iron for violation of Illinois state pollution standards. See Chicago Dept of Public Health, "Statement from CDPH on Citations to General Iron on Explosions at the Facility," Public Health (May 21, 2020), available at https://www.chicago.gov/city/en/depts/cdph/provdrs/healthy_communities/news/2020/may/statement-from-cdph-on-citations-to-general-iron-on-explosions-a.html. The City's investigation is still ongoing. Given that much of the equipment is supposed to be transferred to the South Burley Ave site on the East Side, the Agency should (or "at a minimum") reassess the permit to determine if the pollution control equipment and other operating equipment at the Clifton Avenue site still meets the parameters of the Draft Permit without resulting in noncompliance.

The City, the Illinois EPA and the USEPA are all aware of, involved with, and in communication on the explosion. The Illinois EPA has added provisions in the permit to minimize the risk of explosions in the RTO at the Burley site.

215. The permit should be denied because the EPA did not consider the George Washington air monitoring data or consider the likelihood and effect of failures of the Hammermill Shredder System.

The Illinois EPA did consider the data. There are three types of monitors at George Washington High School – PM10, PM2.5, and lead/metals/TSP. These monitors are very well situated to measure the air that may be impacted by emissions from this source. And, the monitors are measuring attainment with the National Ambient Air Quality Standard for PM10, which is designed to be protective of human health and the environment.

216. They require a lot of maintenance to ensure the controls are effective.

It is unclear what controls are being referenced. Regardless, the permit addresses maintenance of equipment with the requirement for an Operations and Maintenance Plan.

217. This permit must have provisions in place that require General Iron III to regularly prove that it operates the pollution control technologies to the highest standard.

The permit includes periodic monitoring including testing to ensure compliance with applicable regulatory requirements and the terms of the permit.

Miscellaneous

218. Can a third-party auditor be in charge of reporting and report to community?

General III, as owner or operator of the scrap metal facility bears responsibility for the obligations under the Environmental Protection Act and regulations thereunder. It is General III that is required to comply with the requirements to obtain a permit and to comply with the terms of the permit. As with all permits, the construction permit issued to General III includes record keeping and reporting requirements. Records and reports are subject to review by the Illinois EPA, among other. Reports and other information within the possession of the Illinois EPA constitute state records and are generally available to the public. Access to the information occurs by way of requests under the Freedom of Information Act. Failure to maintain the requisite records or to submit the requisite reports subjects a source to compliance and enforcement actions as provided for under the Environmental Protection Act. In this instance, there is no basis for the inclusion of a condition requiring the retention and use of a third-party auditor by General Iron. Notwithstanding, the permit has been revised to require that the testing required under this permit will be performed by independent-third party contractors. Also, the protocols and plans required under this permit will be prepared by third-party contractors.

219. How do we know that you can't be influenced by this economic powerhouse?

The Illinois EPA is a creature of statute and its responsibilities and authorities are dictated by same. Employees of the Illinois EPA are individually subject to ethical constraints. The permitting program affords structure, by which facilities must operate consistent with governing rules and regulations. Reporting, record keeping, and monitoring is also required. The records within the Illinois EPA are generally readily available to the public.

220. The facility has not proposed any "community benefits agreement" or made efforts to reach out to community.

Community benefits agreements are often executed between community groups and the developer of a project and delineate measures that the developer will afford the community that are not otherwise required. These agreements are often used in low-income and communities of color. Such agreements are not a requirement under the Environmental Protection Act.

221. Why can't the Illinois EPA mandate that GIII employees live within 5-10 miles of the source?

State laws and regulations concerning environmental protection generally address sources of pollution and not ancillary issues related to the residency of employees.

222. Nowhere does the FPOP attempt to demonstrate how the proposed measures in fact will ensure that fugitive sources will not cause levels of air contaminants that are injurious to human, plant, or animal life. The program solely focuses on the prohibition of visible emissions beyond the fence line, which is at best a very rough proxy for PM or air toxics particles in the air.

As discussed elsewhere, the prohibitions reflected in the Act and Board regulations are an enforcement tool separate from the FPOP's implementation of measures designed to assure compliance with Part 212. There is no direct means of measuring enforcement with the prohibitions through a permit evaluation.

223. Illinois EPA must impose conditions that prevent odors. Illinois EPA should include specific odor management provisions in the Draft Permit, including use of available odor monitoring systems.

General III is subject to the statutory prohibition against air pollution. In simplest terms, the statute prohibits General III from causing, threatening or allowing air pollution that would cause a violation of a Pollution Control Board regulation or create a nuisance.

224. Neither the Draft Permit nor the fugitive particulate operating program nor the yet-to-be- submitted Contingency Plan contain any practicably enforceable limits on fugitive emissions that demonstrate compliance with the prohibitions on air pollution.

The fugitive emissions from sources such as General III are addressed by state standards. Specifically, they are addressed by provisions within Part 212 Visible and Particulate Matter Emissions of the Pollution Control Board's regulations. These regulations address fugitive emissions by way of limitation on opacity from material handling and processing activities and by way of a prohibition on visible fugitive emissions beyond the plant property line. These regulations also address fugitive emissions through a fugitive particulate operating program, however, General III is not subject to same. Notwithstanding, the Illinois EPA has required General III to develop and implement a fugitive emissions operating program, that was submitted for Agency review, the current version of which is incorporated into the permit. This is the means by which the source ensures compliance with 212.301.

The Contingency Plan that is regulatorily required to be submitted but not at this time, will later be reviewed by the Agency and available to the public. However, it is of limited relevance as it is only activated in the event of a violation of the National Ambient Air Quality Standard for PM10.

The Board's Part 212 regulations were developed with an eye toward the protection of human health and the environment, and the goal of ensuring compliance with the National Ambient Air Quality Standard for Particulate Matter. Indeed, the entire state of Illinois is in compliance with this standard.

Attachment 1: Listing of Significant Changes Between the Draft Construction Permit and the Issued Construction Permit

1. Added a Miscellaneous Fugitive Sources category in the equipment listing to clarify these units are part of the permit.
2. Clarified the requirements for VOM emissions capture from the Hammermill Shredder System.
3. Clarified that the Miscellaneous Fugitive Sources are subject to 35 Ill. Adm. Code 212.123.
4. Clarified that the Ferrous Material Separation System, Non-Ferrous Material Separation System, and Miscellaneous Fugitive Sources are to be operated under the provisions of a Fugitive Emissions Operating Program.
5. Clarified the emission sources in the Ferrous and Non-Ferrous Material Separation equipment listing.
6. Clarified emission testing for Fine Processing Building and Hammermill Shredder System.
7. Added a requirement for the development of and operation under a Feedstock Management Plan for the Hammermill Shredder System.
8. Added a requirement for the development of and operation under an Operation and Maintenance Plan for the control systems.
9. Added a condition to monitor the pressure differential for the Roll-media filter associated with the Hammermill Shredder System and recordkeeping for the differential pressure to ensure proper operation of the control.
10. Added a condition to monitor the pressure differential for Dust Collector (DC-01) associated with the Fines Processing Building to ensure proper operation of the control.
11. Added a requirement for opacity observations from the Hammermill Shredder System stack, each emission unit in the Ferrous Material Separation System, the Fines Processing Building (DC-01), each emission unit in the Non-Ferrous Material Separation System, and Miscellaneous Fugitive Sources.
12. Added recordkeeping for Scrubber differential pressure, scrubbant flow rate, and scrubbant PH monitoring data to ensure proper operation of the control.
13. Added recordkeeping requirement for hours of operation.
14. Added recordkeeping requirement for material receipts.
15. Added recordkeeping requirement for type and amount of material processed by the Hammermill Shredder System.
16. Added recordkeeping requirement for amount of fluff shipped offsite.
17. Added LEL Monitoring system to the exhaust from the capture system associated with the Hammermill Shredder System and associated recordkeeping, and reporting requirements.
18. Added reporting requirement for initial startup for Hammermill Shredder System
19. Added quarterly reporting requirement for type and amount of material received, type and amount of material processed by the Hammermill Shredder System, throughput for the Ferrous Material Separation Process, Non-Ferrous Material Process, and Fines Processing Building, PM, PM_{10}, and HAPs emissions from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System with supporting calculations, VOM emissions from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System with supporting calculations, and amount of non-metallic materials (fluff) shipped offsite.
20. Reconciled the records retention requirements for all records required by the permit requiring retention for at least 5 years.

Exhibit 220

ILLINOIS ENVIRONMENTAL PROTECTION AGENCY
1021 NORTH GRAND AVENUE EAST, P.O. BOX 19276, SPRINGFIELD, ILLINOIS 62794-9276 · (217) 782-3397
JB PRITZKER, GOVERNOR JOHN J. KIM, DIRECTOR

217/785-1705

CONSTRUCTION PERMIT

PERMITTEE

General III, LLC
Attn: Jim Kallas
11600 South Burley Avenue
Chicago, Illinois 60617

Application No.: 19090021 I.D. No.: 031600SFX
Applicant's Designation: Date Received: September 25, 2019
Subject: Scrap Metal Recycling Facility
Date Issued: June 25, 2020
Location: 11600 South Burley Avenue, Chicago, Cook County, 60617

This permit is hereby granted pursuant to the above-referenced application to the above-designated Permittee to CONSTRUCT a Scrap Metal Recycling Facility consisting of the following emission source(s) and/or air pollution control equipment:

Hammermill Shredder System:

One (1) Hammermill Shredder with Integral Water Injection System equipped with capture hood and Cyclone, and controlled by a Roll-Media Filter, 15.0 mmBtu/hour Natural Gas-Fired Regenerative Thermal Oxidizer (RTO), and Quench/Packed Tower Scrubber with feed and takeaway conveyors;
One (1) Vibratory Conveyor; and
One (1) Shredder Infeed Conveyor

Ferrous Material Separation System:
70 Material Transfer Points including:
- Seven (7) Magnetic Separators;
- Two (2) Z-Box Separators with Cyclones;
- Two (2) Ferrous Metal Stacking Conveyors;
- One (1) Auto Shredder Residue (ASR) Stacking Conveyor

2 Truck/Rail Loading Area
1 Barge Loading Point
7 material stockpiles including:
- 2 Poker Picker Stockpiles
- 2 Ferrous Metal Stockpiles
- 1 ASR Stockpile
- 1 Raw Material Stockpile
- 1 Fluff Stockpile (bin).

Non-Ferrous Material Separation System:
88 Uncontrolled Transfer Points including:
- Fifty-three (53) Conveyors;
- Twenty (20) Magnetic Separators;
- Fourteen (14) Eddy Current Separators (ECS) located in Enclosures;
- One (1) Low Speed Shredder for Size Reduction of Clean Non-Ferrous Material;

11 Controlled Transfer Points including:
Nine (9) Conveyors;
One (1) Air Vibe (Air Classifier) with Cyclone;
One (1) Vibratory Batch Feeder;
13 Uncontrolled Screening Points including:
Five (5) Polishers (Air Classifiers) with Cyclone;
One (1) Vibratory Feeder;
Three (3) Tec Screeners;
12 Controlled Screening Points including:
Six (6) Wind Sifters (Air Classifiers) with Cyclones;
Three (3) Tec Screeners;
Six (6) AEI Ecostar Screeners;
2 Truck Loading Points including:
One (1) ASR Feed Hopper with Vibratory Batch Feeder;
13 Stockpile Loading Points
Fines Processing Building - with All Equipment in Building Controlled by Dust Collector DC-01

Miscellaneous Fugitive Sources

Raw Material Unloading/Handling;
Intermediate Ferrous Material and Product Stockpiles;
Fluff Storage and Loadout;
Material Loadout;
Roadways-Paved and unpaved; and
Parking Areas

This Permit is subject to standard conditions attached hereto and the following special condition(s):

1a. This permit is issued based on the emissions of Hazardous Air Pollutants (HAP) as listed in Section 112(b) of the Clean Air Act from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System being less than 10 tons/year of any single HAP and 25 tons/year of any combination of such HAPs. As a result, this permit is issued based on the emissions of all HAPs from the above-listed equipment not triggering the requirements of Section 112(g) of the Clean Air Act.

b. This permit is issued based on the construction of the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System not constituting a new major source or major modification pursuant to Title I of the Clean Air Act, specifically 40 CFR 52.21 (Prevention of Significant Deterioration (PSD)). The source has requested that the Illinois EPA establish emission limitations and other appropriate terms and conditions in this permit that limit the emissions of Particulate Matter (PM), Particulate Matter less than 10 microns (PM_{10}), Particulate Matter less than 2.5 microns ($PM_{2.5}$), and Lead (Pb) from the above-listed equipment below the levels that would trigger the applicability of these rules.

c. This permit is issued based on the construction of the Hammermill Shredder System not constituting a new major source or major

modification pursuant to Title I of the Clean Air Act, specifically 35 Ill. Adm. Code Part 203 (Major Stationary Sources Construction and Modification). The source has requested that the Illinois EPA establish emission limitations and other appropriate terms and conditions in this permit that limit the emissions of Volatile Organic Material (VOM) from the above-listed equipment below the levels that would trigger the applicability of these rules.

d. This permit is issued based on the analysis of the data from the dispersion modeling of the source's Lead (Pb) emissions, that relate to the expected emissions from the project to the maximum off-site ambient air impacts not to exceed the primary and secondary National Ambient Air Quality Standards (NAAQS) for Lead, specifically 40 CFR 50.16. Furthermore, this permit is also issued based on the analysis of the data from the dispersion modeling of emissions of Manganese (Mn) and other metal HAPs, that relate the expected emissions from the project to corresponding maximum off-site ambient air impacts not to exceed the Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels, hazardous air contaminant air quality standards in the Wisconsin Department of Natural Resources air toxics rule (Wisconsin Administrative Code, Chapter NR 445 - Control of Hazardous Pollutants), and an inhalation risk greater than 1 in 1,000,000 for carcinogenic metals with a unit risk factor established by the United States Environmental Protection Agency (USEPA) or the California Air Resources Board (CARB).

e. For purposes of this permit, General III, LLC is considered a single source with South Chicago Property Management, Ltd. (I.D. No. 031600GYI, located at 11600 South Burley Ave, Chicago).

f. Operation of the Scrap Metal Recycling Facility listed above is allowed under this construction permit for a period of twelve (12) months from the date that raw material is first processed through the Hammermill Shredder. This condition supercedes Standard Condition 1 of this construction permit

g. The operation of the emission units under this Construction Permit shall not begin until construction of the associated air pollution control equipment is complete and reasonable measures short of actual operation have been taken to verify proper operation of the air pollution control equipment.

2a. Pursuant to 40 CFR 50.16(a), the national primary and secondary ambient air quality standards for Lead (Pb) and its compounds are 0.15 micrograms per cubic meter, arithmetic mean concentration over a 3-month period, measured in the ambient air as Pb either by:

i. A reference method based on Appendix G of 40 CFR Part 50 and designated in accordance with 40 CFR Part 53;

ii. An equivalent method designated in accordance with 40 CFR Part 53.

b. Pursuant to 40 CFR 50.16(b), the national primary and secondary ambient air quality standards for Pb are met when the maximum arithmetic 3-month mean concentration for a 3-year period, as determined in accordance with Appendix R of 40 CFR Part 50, is less than or equal to 0.15 micrograms per cubic meter.

3a. The Hammermill Shredder System, Ferrous Material Separation System, Non-Ferrous Material Separation System, and Miscellaneous Fugitive Sources are subject to 35 Ill. Adm. Code Part 212 Subpart B (Visible Emissions). Pursuant to 35 Ill. Adm. Code 212.123(a), no person shall cause or allow the emission of smoke or other particulate matter, with an opacity greater than 30 percent, into the atmosphere from any emission unit other than those emission units subject to 35 Ill. Adm. Code 212.122.

b. Pursuant to 35 Ill. Adm. Code 212.123(b), the emission of smoke or other particulate matter from any such emission unit may have an opacity greater than 30 percent but not greater than 60 percent for a period or periods aggregating 8 minutes in any 60 minute period provided that such opaque emissions permitted during any 60 minute period shall occur from only one such emission unit located within a 305 m (1000 ft) radius from the center point of any other such emission unit owned or operated by such person, and provided further that such opaque emissions permitted from each such emission unit shall be limited to 3 times in any 24 hour period.

c. This source is subject to 35 Ill. Adm. Code Part 212 Subpart K (Fugitive Particulate Matter). Pursuant to 35 Ill. Adm. Code 212.301, no person shall cause or allow the emission of fugitive particulate matter from any process, including any material handling or storage activity, that is visible by an observer looking generally toward the zenith at a point beyond the property line of the source.

d. The Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System are subject to 35 Ill. Adm. Code Part 212 Subpart L (Particulate Matter Emissions from Process Emission Units). Pursuant to 35 Ill. Adm. Code 212.321(a), except as further provided in 35 Ill. Adm. Code Part 212, no person shall cause or allow the emission of particulate matter into the atmosphere in any one hour period from any new process emission unit which, either alone or in combination with the emission of particulate matter from all other similar process emission units for which construction or modification commenced on or after April 14, 1972, at a source or premises, exceeds the allowable emission rates specified in 35 Ill. Adm. Code 212.321(c).

e. Pursuant to 35 Ill. Adm. Code 212.321(b), interpolated and extrapolated values of the data in 35 Ill. Adm. Code 212.321(c) shall be determined by using the equation:

$$E = A(P)^B$$

where:

P = Process weight rate; and
E = Allowable emission rate; and,

i. Up to process weight rates of 408 Mg/hr (450 T/hr):

	Metric	English
P	Mg/hr	T/hr
E	kg/hr	lbs/hr
A	1.214	2.54
B	0.534	0.534

ii. For process weight rate greater than or equal to 408 Mg/hr (450 T/hr):

	Metric	English
P	Mg/hr	T/hr
E	kg/hr	lbs/hr
A	11.42	24.8
B	0.16	0.16

f. Pursuant to 35 Ill. Adm. Code 212.321(c), Limits for Process Emission Units for Which Construction or Modification Commenced on or After April 14, 1972:

Metric		English	
P	E	P	E
Mg/hr	kg/hr	T/hr	lbs/hr
0.05	0.25	0.05	0.55
0.1	0.29	0.10	0.77
0.2	0.42	0.20	1.10
0.3	0.64	0.30	1.35
0.4	0.74	0.40	1.58
0.5	0.84	0.50	1.75
0.7	1.00	0.75	2.40
0.9	1.15	1.00	2.60
1.8	1.66	2.00	3.70
2.7	2.1	3.00	4.60
3.6	2.4	4.00	5.35
4.5	2.7	5.00	6.00
9.	3.9	10.00	8.70
13.	4.8	15.00	10.80
18.	5.7	20.00	12.50
23.	6.5	25.00	14.00
27.	7.1	30.00	15.60
32.	7.7	35.00	17.00
36.	8.2	40.00	18.20
41.	8.8	45.00	19.20
45.	9.3	50.00	20.50
90.	13.4	100.00	29.50
140.	17.0	150.00	37.00

Metric		English	
P	E	P	E
Mg/hr	kg/hr	T/hr	lbs/hr
180.	19.4	200.00	43.00
230.	22.	250.00	48.50
270.	24.	300.00	53.00
320.	26.	350.00	58.00
360.	28.	400.00	62.00
408.	30.1	450.00	66.00
454.	30.4	500.00	67.00

where:

P = Process weight rate in metric or T/hr, and
E = Allowable emission rate in kg/hr or lbs/hr.

g. The Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System are subject to 35 Ill. Adm. Code 212.324 (Process Emission Units in Certain Areas). Pursuant to 35 Ill. Adm. Code 212.324(b), except as otherwise provided in 35 Ill. Adm. Code 212.324, no person shall cause or allow the emission into the atmosphere, of PM_{10} from any process emission unit to exceed 68.7 mg/scm (0.03 gr/scf) during any one-hour period.

h. This source is subject to 35 Ill. Adm. Code Part 212 Subpart U (Additional Control Measures). Pursuant to 35 Ill. Adm. Code 212.700(a), 35 Ill. Adm. Code 212 Subpart U (Additional Control Measures) shall apply to those sources in the areas designated in and subject to 35 Ill. Adm. Code 212.324(a)(1) or 212.423(a) and that have actual annual source-wide emissions of PM_{10} of at least fifteen (15) tons per year.

4. The RTO associated with Hammermill Shredder System is subject to 35 Ill. Adm. Code Part 214 Subpart K (Process Emission Sources). Pursuant to 35 Ill. Adm. Code 214.301, except as further provided by 35 Ill. Adm. Code Part 214, no person shall cause or allow the emission of sulfur dioxide into the atmosphere from any process emission source to exceed 2000 ppm.

5a. The Hammermill Shredder System is subject to 35 Ill. Adm. Code Part 218 Subpart G (Use of Organic Material). Pursuant to 35 Ill. Adm. Code 218.301, no person shall cause or allow the discharge of more than 3.6 kg/hr (8 lbs/hr) of organic material into the atmosphere from any emission unit, except as provided in 35 Ill. Adm. Code 218.302, 218.303, or 218.304 and the following exception: If no odor nuisance exists the limitation of 35 Ill. Adm. Code Part 218 Subpart G shall only apply to photochemically reactive material.

b. Pursuant to 35 Ill. Adm. Code 218.302(a), emissions of organic material in excess of those permitted by 35 Ill. Adm. Code 218.301 are allowable if such emissions are controlled by one of the following methods:

Flame, thermal or catalytic incineration so as either to reduce such emissions to 10 ppm equivalent methane (molecular weight 16) or less, or to convert 85 percent of the hydrocarbons to carbon dioxide and water.

c. The Hammermill Shredder System is subject to 35 Ill. Adm. Code Part 218 Subpart TT (Other Emission Units). Pursuant to 35 Ill. Adm. Code 218.980(a):

i. A source is subject to 35 Ill. Adm. Code Part 218 Subpart TT if it contains process emission units not regulated by 35 Ill. Adm. Code Part 218 Subparts B, E, F (excluding 35 Ill. Adm. Code 218.204 (l)), H (excluding 35 Ill. Adm. Code 218.405), Q, R, S, T (excluding 35 Ill. Adm. Code 218.486), V, X, Y, Z or BB of this Part, which as a group both:

A. Have maximum theoretical emissions of 90.7 Mg (100 tons) or more per calendar year of VOM, and

B. Are not limited to less than 90.7 Mg (100 tons) of VOM emissions per calendar year in the absence of air pollution control equipment through production or capacity limitations contained in a federally enforceable permit or a SIP revision.

ii. If a source is subject to 35 Ill. Adm. Code Part 218 Subpart TT as provided in 35 Ill. Adm. Code Part 218 Subpart TT, the requirements of 35 Ill. Adm. Code Part 218 Subpart TT shall apply to a source's VOM emission units which are not included within any of the categories specified in 35 Ill. Adm. Code Part 218 Subparts B, E, F, H, Q, R, S, T, V, X, Y, Z, AA, BB, PP, QQ, or RR or which are not exempted from permitting requirements pursuant to 35 Ill. Adm. Code 201.146.

d. Pursuant to 35 Ill. Adm. Code 218.986(a), every owner or operator of an emission unit subject to 35 Ill. Adm. Code 218 Subpart TT shall comply with the requirements of 35 Ill. Adm. Code 218.986(a), (b), (c), (d), or (e) below.

Emission capture and control equipment which achieves an overall reduction in uncontrolled VOM emissions of at least 81 percent from each emission unit.

6. This permit is issued based on the Scrap Metal Recycling Facility not being subject to the New Source Performance Standards (NSPS) for Metallic Mineral Processing Plants, 40 CFR 60 Subpart LL because the Raw Material Receiving and Handling System, Hammermill Shredder System, Ferrous Material Separation System, Non-Ferrous Material Separation System, and Fines Processing System at this source are not used to produce metallic mineral concentrates from ore.

7a. This permit is issued based on the Scrap Metal Recycling Facility not being subject to the National Emission Standards for Hazardous Air

Pollutants (NESHAP) from Off-Site Waste and Recovery Operations, 40 CFR 63 Subpart DD, because the plant site is not a major source of HAP emissions as defined in 40 CFR 63.2.

b. This permit is issued based on the Scrap Metal Recycling Facility not being subject to the NESHAP for Primary Nonferrous Metals Area Sources–Zinc, Cadmium, and Beryllium, 40 CFR 63 Subpart GGGGGG, because the source will not be engaged in primary zinc production or primary beryllium production.

c. This permit is issued based on the Scrap Metal Recycling Facility not being subject to the NESHAP for Secondary Nonferrous Metals Processing Area Sources, 40 CFR 63 Subpart TTTTTT, because the source will not be engaged in secondary nonferrous metals processing as defined in 40 CFR 63.11472.

d. This permit is issued based on the Scrap Metal Recycling Facility not being subject to the NESHAP for Nine Metal Fabrication and Finishing Source Categories, 40 CFR 63 Subpart XXXXXX, because the source will not be primarily engaged in the operations in one of the nine source categories listed in 40 CFR 63.11514(a)(1) through (9).

8a. Pursuant to 35 Ill. Adm. Code 212.314, 35 Ill. Adm. Code 212.301 shall not apply and spraying pursuant to 35 Ill. Adm. Code 212.304 through 212.310 and 35 Ill. Adm. Code 212.312 shall not be required when the wind speed is greater than 40.2 km/hr (25 mph). Determination of wind speed for the purposes of 35 Ill. Adm. Code 212.314 shall be by a one-hour average or hourly recorded value at the nearest official station of the U.S. Weather Bureau or by wind speed instruments operated on the site. In cases where the duration of operations subject to 35 Ill. Adm. Code 212.314 is less than one hour, wind speed may be averaged over the duration of the operations on the basis of on-site wind speed instrument measurements.

b. Pursuant to 35 Ill. Adm. Code 212.324(d), the mass emission limits contained in 35 Ill. Adm. Code 212.324(b) and (c) shall not apply to those emission units with no visible emissions other than fugitive particulate matter; however, if a stack test is performed, 35 Ill. Adm. Code 212.324(d) is not a defense finding of a violation of the mass emission limits contained in 35 Ill. Adm. Code 212.324(b) and (c).

9a. Pursuant to 35 Ill. Adm. Code 212.324(f), for any process emission unit subject to 35 Ill. Adm. Code 212.324(a), the owner or operator shall maintain and repair all air pollution control equipment in a manner that assures that the emission limits and standards in 35 Ill. Adm. Code 212.324 shall be met at all times. 35 Ill. Adm. Code 212.324(f) shall not affect the applicability of 35 Ill. Adm. Code 201.149. Proper maintenance shall include the following minimum requirements:

i. Visual inspections of air pollution control equipment;

ii. Maintenance of an adequate inventory of spare parts; and

iii. Expeditious repairs, unless the emission unit is shutdown.

b. Pursuant to 35 Ill. Adm. Code 212.701(a), those sources subject to 35 Ill. Adm. Code Part 212 Subpart U shall prepare contingency measure plans reflecting the PM_{10} emission reductions set forth in 35 Ill. Adm. Code 212.703. These plans shall become federally enforceable permit conditions. Such plans shall be submitted to the Illinois EPA by November 15, 1994. Notwithstanding the foregoing, sources that become subject to the provisions of 35 Ill. Adm. Code Part 212 Subpart U after July 1, 1994, shall submit a contingency measure plan to the Illinois EPA for review and approval within ninety (90) days after the date such source or sources became subject to the provisions of 35 Ill. Adm. Code Part 212 Subpart U or by November 15, 1994, whichever is later. The Illinois EPA shall notify those sources requiring contingency measure plans, based on the Illinois EPA's current information; however, the Illinois EPA's failure to notify any source of its requirement to submit contingency measure plans shall not be a defense to a violation of 35 Ill. Adm. Code Part 212 Subpart U and shall not relieve the source of its obligation to timely submit a contingency measure plan.

c. Pursuant to 35 Ill. Adm. Code 212.703(a), all sources subject to 35 Ill. Adm. Code Part 212 Subpart U shall submit a contingency measure plan. The contingency measure plan shall contain two levels of control measures:

i. Level I measures are measures that will reduce total actual annual source-wide fugitive emissions of PM_{10} subject to control under 35 Ill. Adm. Code 212.304, 212.305, 212.306, 212.308, 212.316(a) through (e), 212.424 or 212.464 by at least 15%.

ii. Level II measures are measures that will reduce total actual annual source-wide fugitive emissions of PM_{10} subject to control under 35 Ill. Adm. Code 212.304, 212.305, 212.306, 212.308, 212.316(a) through (e), 212.424 or 212.464 by at least 25%.

d. Pursuant to 35 Ill. Adm. Code 212.703(b), a source may comply with 35 Ill. Adm. Code Part 212 Subpart U through an alternative compliance plan that provides for reductions in emissions equal to the level of reduction of fugitive emissions as required at 35 Ill. Adm. Code 212.703(a) and which has been approved by the Illinois EPA and USEPA as federally enforceable permit conditions. If a source elects to include controls on process emission units, fuel combustion emission units, or other fugitive emissions of PM_{10} not subject to 35 Ill. Adm. Code 212.304, 212.305, 212.306, 212.308, 212.316(a) through (e), 212.424 or 212.464 at the source in its alternative control plan, the plan must include a reasonable schedule for implementation of such controls, not to exceed two (2) years. This implementation schedule is subject to Illinois EPA review and approval.

e. Pursuant to 35 Ill. Adm. Code 212.704(b), if there is a violation of the ambient air quality standard for PM_{10} as determined in accordance with 40 CFR Part 50, Appendix K, the Illinois EPA shall notify the source or sources the Illinois EPA has identified as likely to be

causing or contributing to one or more of the exceedances leading to such violation, and such source or sources shall implement Level I or Level II measures, as determined pursuant to 35 Ill. Adm. Code 212.704(e). The source or sources so identified shall implement such measures corresponding to fugitive emissions within ninety (90) days after receipt of a notification and shall implement such measures corresponding to any nonfugitive emissions according to the approved schedule set forth in such source's alternative control plan. Any source identified as causing or contributing to a violation of the ambient air quality standard for PM_{10} may appeal any finding of culpability by the Illinois EPA to the Illinois Pollution Control Board pursuant to 35 Ill. Adm. Code 106 Subpart J.

f. Pursuant to 35 Ill. Adm. Code 212.704(e), the Illinois EPA shall require that sources comply with the Level I or Level II measures of their contingency measure plans, pursuant 35 Ill. Adm. Code 212.704(b), as follows:

i. Level I measures shall be required when the design value of a violation of the 24-hour ambient air quality standard, as computed pursuant to 40 CFR 50, Appendix K, is less than or equal to 170 ug/m^3.

ii. Level II measures shall be required when the design value of a violation of the 24-hour ambient air quality standard, as computed pursuant to 40 CFR 50, Appendix K, exceeds 170 ug/m^3.

10a. The Scrap Metal Recycling Facility shall be operated under the provisions of a Fugitive Emissions Operating Program. This operating program was submitted by the Permittee and designed to limit fugitive particulate matter emissions to ensure compliance with 35 Ill. Adm. Code 212.301.

b. The Fugitive Emissions Operating Program, as submitted by the Permittee pursuant to Condition 10(a) dated June 25, 2020, is incorporated herein by reference. The source shall comply with the provisions of this Program and any amendments to the Program submitted pursuant to Condition 10(c).

c. The Fugitive Emissions Operating Program shall be amended from time to time by the Permittee so that the operating Program is current. Such amendments shall be consistent with Condition 10(a) and shall be submitted to the Illinois EPA within thirty (30) days of amendment. Any future revision to the Program made by the Permittee during the permit term is automatically incorporated by reference unless expressly disapproved by the Illinois EPA within thirty (30) days of submission. In the event that the Illinois EPA notifies the Permittee that further information regarding the revision to the Program is needed, the Permittee shall respond to the notice within thirty (30) days of receipt of notification.

d. The Hammermill Shredder System shall be operated under the provisions of a Feedstock Management Plan. This plan shall be submitted to the

Illinois EPA for review and approval at least ninety (90) days prior to initially receiving recycling materials at the facility. At a minimum, this plan must contain the following:

i. Incoming material restrictions;

ii. Load inspection procedures;

iii. List of materials accepted requiring special handling;

iv. Procedures for each of the materials requiring special handling;

v. Personnel training procedures.

11a. The Roll-Media Filter, RTO, Quench/Packed Tower Scrubber, and Dust Collectors (DC-01 through DC-04) shall be in operation at all times when the associated emission units are in operation and emitting air contaminants.

b. The RTO combustion chambers shall be preheated to at least the manufacturer's recommended temperature, but no less than the temperature at which compliance was demonstrated in the most recent compliance test, or 1,400°F in the absence of a compliance test. This temperature shall be maintained during operation of the Metal Shredder System and calculated as a three-hour block average.

c. The RTO shall only be operated with natural gas as the fuel. The use of any other fuel in the RTO may require that the Permittee first obtain a construction permit from the Illinois EPA and then perform stack testing to verify compliance with all applicable requirements.

d. The RTO associated with the Hammermill Shredder System shall be equipped with a temperature monitoring device that is installed, calibrated, operated, and maintained, in accordance with vendor/manufacturer specifications and 35 Ill. Adm. Code 218.105(d)(2).

e. The Quench/Packed Tower Scrubber associated with the Hammermill Shredder System shall be equipped with a monitoring device for pressure differential, scrubbant liquid flow rate, and pH of the scrubbant liquid. These monitoring devices shall be installed, calibrated, operated, and maintained, in accordance with vendor/manufacturer specifications. The data measured by this device shall be automatically recorded on at least a 15 block minute averages basis and on an hourly average in an electronic database.

f. The Roll-Media Filter associated with the Hammermill Shredder System shall be equipped with a monitoring device for pressure differential. This monitoring device shall be installed, calibrated, operated and maintained, in accordance with vendor/manufacturer specifications. The data measured by this device shall be automatically recorded on at least a 15-block minute average basis and on an hourly average in an electronic database.

g. The Dust Collector (DC-01) associated with the Fines Processing Building shall be equipped with a monitoring device for pressure differential. This monitoring device shall be installed, calibrated, operated, and maintained, in accordance with vendor/manufacturer specifications. The data measured by this device shall be automatically recorded on at least an hourly basis in an electronic database.

h. The monitoring devices required in conditions 11(e)-(h) shall be installed and fully operational at prior to first processing material through the Hammermill Shredder System.

i. The Permittee shall operate the capture system, Roll-Media Filter, RTO and the Quench/Packed Tower Scrubber associated with the Hammermill Shredder System, Dust Collectors (DC-01 through DC-04) and equipment used for the control of fugitive dust identified in the Fugitive Emissions Operating Program under the provisions of an Operation and Maintenance Plan. At least thirty (30) days prior to first processing material through the Hammermill Shredder System, the Permittee shall submit to the Illinois EPA for review and approval an Operation and Maintenance Plan for the capture system, Roll-Media Filter, RTO and the Quench/Packed Tower Scrubber associated with the Hammermill Shredder System, Dust Collectors (DC-01 through DC-04) and equipment used for the control of fugitive dust identified in the Fugitive Emissions Operating Program. This plan shall provide specific operating parameters and inspection, and maintenance practices and procedures for the for each system or control device identified in this condition, including frequencies of such specific activities and actions and associated recordkeeping procedures.

j. The Permittee shall install, operate, and maintain a continuous gas flammability monitoring device for the shredder exhaust gas stream. This device shall measure the percent of the Lower Explosive Limit (% LEL) or percent of the Lower Flammability Limit (% LFL) of the shredder exhaust gas. This monitoring device shall have an accuracy of at least +/-3 percent of full scale. Values measured by this device shall be automatically recorded at least once per second and stored in an electronic data base.

k. The Permittee shall install, operate and maintain a continuous monitoring device for the control train for the Hammermill Shredder System for one of the following operational parameters. This monitoring device shall make measurements at least every minute and have an accuracy of at least ± 5 percent. The data measured by this device shall be automatically recorded on at least a minute by minute basis and on an hourly average in an electronic database. The Permittee shall determine the gas flow rate to be used to calculate VOM emissions from a Bypass Event using data collected by this monitoring system.

    i. The amperage or usage of electrical power by the motor for the Roll Media Filter fan;

ii. The shredder exhaust gas flow rate; or.

iii. Other operational parameter(s) approved by the Illinois EPA.

l. The Permittee shall install, operate, and maintain a continuous monitoring device for the status of the emergency bypass damper for the RTO in the control train for the Hammermill Shredder System, i.e., whether this damper is closed or open. The data collected by this device shall be automatically recorded in an electronic database.

m. The Permittee shall operate the continuous monitoring devices required by Condition 11(j), (k) and (l) at all times that the Hammermill Shredder System is in operation.

12a. Operation of the source's emission units and activities shall not exceed the following limits:

i. Hours of operation:

Site Operation	Monday to Friday		Saturday	
Ferrous System Operation (includes Hammermill Shredder RTO/Scrubber Stack and Rail and Truck Loading)	7:00 AM - 7:00 PM	12 hrs/day	7:00 AM - 5:00 PM	10 hrs/day
Barge, Loading	7:00 AM - 3:00 PM	8 hrs/day	7:00 AM - 3:00 PM	8 hrs/day
Non-Ferrous System Operation	5:00 AM - 11:00 PM	18 hrs/day	5:00 AM - 11:00 PM	18 hrs/day
Roadway Fugitive Emissions (Facility Vehicle Traffic)*	5:00 AM - 7:00 PM	14 hrs/day	5:00 AM - 5:00 PM	12 hrs/day

* The roadway fugitive emissions (Facility Vehicle Traffic) operation limitations in the table above is only intended to reflect haul truck traffic (semi-trailers) on specified road segments accompanying deliveries of metal scrap and removal of waste material.

ii. The limitations on hours of operation for the source are based upon the meteorological hours modeled for each operation as specified on Table 1 of the modeling analysis and page 1 of supplement No. 1 to the Air Dispersion Modeling Report, dated January 24, 2020, for assessment of metal emission impacts.

b. Emissions from and operation of the Hammermill Shredder System shall not exceed the following limits:

i. VOM emissions:

Emission Unit	Process Rate (Tons/Mo)	Process Rate (Tons/Yr)	Uncontrolled Emission Factor (lb/Ton)	VOM Emission (Tons/Mo)	VOM Emission (Tons/Yr)
Hammermill Shredder RTO/Scrubber Stack	100,000	1,000,000	0.5119	0.51	5.12

These limits are based on maximum shredder material throughput, an uncontrolled emission factor derived from a stack test at the inlet of the RTO in November 2019 at GII, LLC (I.D. # 031600BTB), and 98% removal efficiency by the RTO/Scrubber. All measured total hydrocarbon (THC) emissions are assumed to be VOM.

ii. HAP emissions:

Emission Unit	Lead (Pb) (T/Mo)	Lead (Pb) (T/Yr)	Manganese (Mn) (T/Mo)	Manganese (Mn) (T/Yr)	Hydrochloric Acid (HCl) (T/Mo)	Hydrochloric Acid (HCl) (T/Yr)	Combined HAPs[1] (T/Mo)	Combined HAPs[1] (T/Yr)
Metal Shredder RTO/Scrubber Stack	0.000138	0.00138	0.000199	0.00199	0.08	0.77	0.13	1.33

[1] Combined HAPs means the total of all individual HAPs (as defined in Section 112(b) of the Clean Air Act) that are emitted from the Hammermill Shredder System.

These limits are based on the maximum shredder material throughput in Condition 12(b)(i) above and measured emission rates from the November 2019 stack test at GII, LLC (I.D. # 031600BTB) adjusted by safety factor of 2.0.

iii. PM, PM_{10}, and $PM_{2.5}$ emissions:

Emission Unit	Process Rate (Tons/Mo)	Process Rate (Tons/Yr)	Emission Factor (lb/Ton)	PM, PM_{10}, and $PM_{2.5}$ Emissions (Tons/Mo)	PM, PM_{10}, and $PM_{2.5}$ Emissions (Tons/Yr)
Metal Shredder RTO/Scrubber Stack	100,000	1,000,000	0.0047	0.47	4.70

These limits are based on maximum shredder material throughput in Condition 12(b)(i) above, emission factors derived from the May/June 2018 stack test at GII, LLC (I.D. # 031600BTB) adjusted by a safety factor of 2.0, and all measured filterable PM assumed to be PM_{10} and $PM_{2.5}$.

c. Emissions from fuel combustion in the RTO associated with the Hammermill Shredding System shall not exceed the following limits:

i. Natural gas usage: 6.57 mmscf/month, 51.47 mmscf/year

ii. Emissions from the combustion of natural gas:

Pollutant	Emission Factor (lbs/mmscf)	Emissions (Tons/Mo)	(Tons/Yr)
Carbon Monoxide (CO)	583.55	1.50	15.02
Nitrogen Oxides (NO_x)	100.0	0.26	2.57
Particulate Matter (PM, PM_{10}, and $PM_{2.5}$)	7.6	0.02	0.20
Sulfur Dioxide (SO_2)	0.6	0.01	0.09

These limits are based on the maximum firing rate of the RTO burner (15.0 mmBtu/hour), maximum natural gas usage, 12.86 tons/year of CO emissions and 0.05 tons/year of SO_2 emissions based on data from the November 2019 stack test at GII, LLC (I.D. # 031600BTB), and standard emission factors (Tables 1.4-1 and 1.4-2, AP-42, Fifth Edition, Volume I, Supplement D, July 1998).

d. Emissions from and operation of the Ferrous Material Separation Process shall not exceed the following limits:

i. Material process rates and Particulate Matter (PM) Emissions:

Emission Unit	Process Rate (Tons/Mo)	(Tons/Yr)	Emission Factor (lb/Ton)	PM Emissions (Tons/Mo)	(Tons/Yr)
70 Conveyor Transfer Points	1,444,050	14,440,500	0.00014	0.10	0.96
2 Rail/Truck Loading areas and 1 Barge loading point	137,600	1,376,000	0.000204	0.01	0.14
7 Stockpile Loading Points	300,000	3,000,000	0.00122	0.18	1.83
				Total:	2.93

ii. PM_{10} and $PM_{2.5}$ Emissions:

Emission Units	PM_{10} Emission Factor (lb/Ton)	PM_{10} Emissions (Tons/Mo)	(Tons/Yr)	$PM_{2.5}$ Emission Factor (lb/Ton)	$PM_{2.5}$ Emissions (Tons/Mo)	(Tons/Yr)
70 Conveyor Transfer Points	0.000046	0.03	0.31	0.000013	0.01	0.09
2 Rail/Truck Loading areas and 1 Barge loading point	0.00010	0.01	0.07	0.000015	0.01	0.01
7 Stockpile Loading Points	0.00058	0.09	0.87	0.000087	0.01	0.13
		Totals:	1.25			0.23

iii. HAP emissions:

Emission Unit	Lead (Pb) Emissions (Tons/Mo)	(Tons/Yr)	Manganese (Mn) Emissions (Tons/Mo)	(Tons/Yr)	Combined HAP Emissions[2] (Tons/Mo)	(Tons/Yr)
Ferrous Material Separation Process	0.0007	0.0069	0.0004	0.0042	0.0015	0.0143

[2] Combined HAPs means the total of all individual HAPs (as defined in Section 112(b) of the Clean Air Act) that are emitted from the Ferrous Material Separation Process.

iv. The above limits for PM, PM_{10}, and $PM_{2.5}$ are based on the maximum material throughput, standard emission factors from AP-42 (Table 11.19.2-2, Fifth Edition, Volume I, Update 2004, August 2004) for conveyors transfer points and Truck/Barge Loading, stockpile loadings emission factor derived using AP-42, Section 13.2.4.3 (Table 13.2.4, AP-42, Fifth Edition, Volume I, November 2006) using coefficients of K=0.74 (PM), K=0.35 (PM_{10}), and K=0.053 ($PM_{2.5}$); U (mean windspeed) = 9.0 mph, and M (minimum moisture content) = 1.5% applied to light material stockpile, 5.4% applied to raw scrap metal handling, 10% applied to ASR stockpile loading. The above limits for HAP emissions limits are based upon total metal HAPs being 0.49% of the estimated total PM emissions based on metal HAP analyses performed on a site-specific sample of material at GII representing anticipated characteristics of Ferrous Material Processing.

e. Emissions from and operation of the Non-Ferrous Material Separation Process and Fines Processing System shall not exceed the following limits:

i. PM, PM_{10}, and $PM_{2.5}$ emissions for Fines Separation System emission units and activities inside a building controlled by Dust Collector DC-01 shall not exceed 0.15 tons/month and 1.44 tons/year. This limit is based on PM, PM_{10}, and $PM_{2.5}$ emissions being calculated by using the stack flow rate (12,000 cfm) and grain loading of 0.005 gr/dscf and hours of operation.

ii. Emissions from and operation of other Non-Ferrous Separation System emission units shall not exceed the following limits:

A. Material process rates and Particulate Matter (PM) Emissions:

Emission Units	Process Rate (Tons/Mo)	Process Rate (Tons/Yr)	Emission Factor (lb/Ton)	PM Emission (Tons/Mo)	PM Emission (Tons/Yr)
88 Conveyor Transfer Points (Uncontrolled)	333,876	3,338,757	0.00300	0.43	4.34
11 Conveyor Transfer Points (Controlled)	57,210	572,103	0.00014	0.01	0.04
13 Screening Points (Uncontrolled)	13,670	136,702	0.02500	0.17	1.71
12 Screening Points (Controlled)	42,209	422,085	0.00220	0.04	0.41
2 Truck Loading Points	45,847	458,466	0.00020	0.01	0.05
13 Stockpile Loading Points	23,338	233,378	0.00737	0.09	0.86
				Total:	7.40

B. PM_{10} and $PM_{2.5}$ emissions from outdoor emission units:

Emission Units	PM_{10} Emission Factor (lb/Ton)	PM_{10} Emissions (Tons/Mo)	PM_{10} Emissions (Tons/Yr)	$PM_{2.5}$ Emission Factor (lb/Ton)	$PM_{2.5}$ Emission (Tons/Mo)	$PM_{2.5}$ Emission (Tons/Yr)
88 Conveyor Transfer Points (Uncontrolled)	0.0011	0.16	1.59	0.000167	0.02	0.24
11 Conveyor Transfer Points (Controlled)	0.000046	0.01	0.01	0.000013	0.01	0.01
13 Screening Points (Uncontrolled)	0.0087	0.06	0.59	0.001317	0.01	0.09
12 Screening Points (Controlled)	0.00074	0.01	0.14	0.00005	0.01	0.01
2 Truck Loading Points	0.0001	0.01	0.02	0.000015	0.01	0.01
13 Stockpile Loading Points	0.00351	0.04	0.41	0.00051	0.01	0.06
		Totals:	2.76			0.41

C. The above limits for PM, PM_{10}, and $PM_{2.5}$ are based on the maximum material throughput, Standard emission factors from AP-42 (Table 11.19.2-2, Fifth Edition, Volume I, Update 2004, August 2004) for conveyors transfer points screening and Truck Loading, stockpile loading emission factor derived using AP-42, Section 13.2.4.3 (Table 13.2.4, AP-42, Fifth Edition, Volume I, November 2006) using coefficients of K=0.74 (PM), K=0.35 (PM_{10}), and $PM_{2.5}$ U (mean windspeed) = 9.0 mph, and M (minimum moisture content) = 1.5% applied to light material stockpile loading.

iii. HAP emissions from Non-Ferrous Material Separation Process shall not exceed the following limits:

Emission Unit	Lead (Pb) Emissions (Tons/Mo)	(Tons/Yr)	Manganese (Mn) Emissions (Tons/Mo)	(Tons/Yr)	Combined HAP Emissions[3] (Tons/Mo)	(Tons/Yr)
Non-Ferrous Material Separation Process	0.0042	0.0417	0.0016	0.0156	0.01	0.07

[3] Combined HAPs means the total of all individual HAPs (as defined in Section 112(b) of the Clean Air Act) that are emitted from the Non-Ferrous Material Separation Process.

These limits are based on total metal HAPs being 0.83% of the estimated total PM emissions based on metal HAP analyses performed on a site-specific sample of material at GII representing anticipated characteristics of Non-Ferrous Material Processing.

f. Compliance with the annual limits of this permit shall be determined on a monthly basis from the sum of the data for the current month plus the preceding 11 months (running 12-month total).

13a. Pursuant to 35 Ill. Adm. Code 201.282, every emission source or air pollution control equipment shall be subject to the following testing requirements for the purpose of determining the nature and quantities of specified air contaminant emissions and for the purpose of determining ground level and ambient air concentrations of such air contaminants:

i. Testing by Owner or Operator. The Illinois EPA may require the owner or operator of the emission source or air pollution control equipment to conduct such tests in accordance with procedures adopted by the Illinois EPA, at such reasonable times as may be specified by the Illinois EPA and at the expense of the owner or operator of the emission source or air pollution control equipment. The Illinois EPA may adopt procedures detailing methods of testing and formats for reporting results of testing. Such procedures and revisions thereto, shall not become effective until filed with the Secretary of State, as required by the APA Act. All such tests shall be made by or under the direction of a person qualified by training and/or experience in the field of air pollution testing. The Illinois EPA shall have the right to observe all aspects of such tests.

ii. Testing by the Illinois EPA. The Illinois EPA shall have the right to conduct such tests at any time at its own expense. Upon request of the Illinois EPA, the owner or operator of the emission source or air pollution control equipment shall provide, without charge to the Illinois EPA, necessary holes in stacks or ducts and other safe and proper testing facilities, including scaffolding, but excluding instruments and sensing devices, as may be necessary.

14a. Pursuant to 35 Ill. Adm. Code 212.107, for both fugitive and nonfugitive particulate matter emissions, a determination as to the presence or absence of visible emissions from emission units shall be conducted in accordance with Method 22, 40 CFR Part 60, Appendix A, except that the length of the observing period shall be at the discretion of the observer, but not less than one minute. 35 Ill. Adm. Code 212 Subpart A shall not apply to 35 Ill. Adm. Code 212.301.

b. Pursuant to 35 Ill. Adm. Code 212.109, except as otherwise provided in 35 Ill. Adm. Code Part 212, and except for the methods of data reduction when applied to 35 Ill. Adm. Code 212.122 and 212.123, measurements of opacity shall be conducted in accordance with Method 9, 40 CFR Part 60, Appendix A, and the procedures in 40 CFR 60.675(c) and (d), if applicable, except that for roadways and parking areas the number of readings required for each vehicle pass will be three taken at 5-second intervals. The first reading shall be at the point of maximum opacity and second and third readings shall be made at the same point, the observer standing at right angles to the plume at least 15 feet away from the plume and observing 4 feet above the surface of the roadway or parking area. After four vehicles have passed, the 12 readings will be averaged.

c. Pursuant to 35 Ill. Adm. Code 212.110(a), measurement of particulate matter emissions from stationary emission units subject to 35 Ill. Adm. Code Part 212 shall be conducted in accordance with 40 CFR Part 60, Appendix A, Methods 5, 5A, 5D, or 5E.

d. Pursuant to 35 Ill. Adm. Code 212.110(b), the volumetric flow rate and gas velocity shall be determined in accordance with 40 CFR Part 60, Appendix A, Methods 1, 1A, 2, 2A, 2C, 2D, 3, and 4.

e. Pursuant to 35 Ill. Adm. Code 212.110(c), upon a written notification by the Illinois EPA, the owner or operator of a particulate matter emission unit subject to 35 Ill. Adm. Code Part 212 shall conduct the applicable testing for opacity or visible emissions at such person's own expense, to demonstrate compliance. Such test results shall be submitted to the Illinois EPA within thirty (30) days after conducting the test unless an alternative time for submittal is agreed to by the Illinois EPA.

15. Pursuant to 35 Ill. Adm. Code 218.988(a), when in the opinion of the Illinois EPA it is necessary to conduct testing to demonstrate compliance with 35 Ill. Adm. Code 218.986, the owner or operator of a VOM emission unit subject to the requirements of 35 Ill. Adm. Code Part 218 Subpart TT shall, at his own expense, conduct such tests in accordance with the applicable test methods and procedures specified in 35 Ill. Adm. Code 218.105.

16a. Within sixty (60) days after the date raw material is first processed through the Hammermill Shredder, the Permittee shall:

i. Conduct opacity observations from the Hammermill Shredder System stack, each emission unit in the Ferrous Material Separation

System, Fines Processing Building (DC-01), each emission unit in the Non-Ferrous Material Separation System, and Miscellaneous Fugitive Sources during conditions which are representative of maximum emissions in order to demonstrate compliance with 35 Ill. Adm. Code 212.123 and Condition 3(a) of this permit. Thereafter, this testing shall be conducted once every five (5) years from the preceding testing date.

ii. Measure and quantify (gr/dscf and lb/hr) the emissions of PM, PM_{10}, and $PM_{2.5}$ from the Fines Processing Building (DC-01) during conditions which are representative of maximum emissions in order to demonstrate compliance with 35 Ill. Adm. Code 212.321, 35 Ill. Adm. Code 212.324(b), and Conditions 3(d)-(g), and 12(e)(i) of this permit. Thereafter, this testing shall be conducted once every five (5) years from the preceding testing date.

iii. Measure and quantify the emissions of PM (gr/dscf and lb/hr), PM_{10} (gr/dscf and lb/hr), $PM_{2.5}$ (gr/dscf and lb/hr), SO_2 (ppmv and lb/hr), CO (ppmv and lb/hr), HCl (ppmv and lb/hr), and Metals (ppmv and lb/hr) emissions from the Hammermill Shredder System during conditions which are representative of maximum emissions in order to demonstrate compliance with 35 Ill. Adm. Code 212.321, and Conditions 3(d)-(g), 12(b)(ii), (b)(iii) and (c) of this permit.

iv. Measure (ppmv) and quantify (lb/hr) from the inlet and outlet emissions of VOM from the RTO, measure VOM capture efficiency of capture system, determine the destruction efficiency of the RTO, and calculate overall VOM control efficiency for the capture system and RTO, during conditions which are representative of maximum emissions in order to demonstrate compliance with 35 Ill. Adm. Code 218.986(a), and Condition 12(b)(i) of this permit. If VOM capture efficiency meets the criteria of a PTE as determined by USEPA Method 204 or an alternate method adopted by the USEPA to demonstrate capture efficiency, testing under this condition shall be conducted once every five (5) years from the preceding testing date. However, if the VOM capture efficiency does not meet the criteria of a PTE, subsequent testing shall be conducted within twelve (12) months from the preceding testing.

b. The following methods and procedures shall be used for testing of emissions, unless another method is approved by the Illinois EPA:(refer to 40 CFR 51, Appendix M and 40 CFR 60, Appendix A for USEPA test methods).

Sample and Velocity Traverses for Stationary Sources	USEPA Method 1
Sample and Velocity Traverses for Stationary Sources with Small Stacks or Ducts	USEPA Method 1A
Determination of Stack Gas Velocity and Volumetric Flow Rate (Type S Pitot Tube)	USEPA Method 2
Direct Measurement of Gas Volume through Pipes and Small Ducts	USEPA Method 2A

Determination of Gas Velocity and Volumetric Flow Rate in Small Stacks or Ducts (Standard Pitot Tube)	USEPA Method 2C
Measurement of Gas Volume Flow Rates in Small Pipes and Ducts	USEPA Method 2D
Gas Analysis for the Determination of Dry Molecular Weight	USEPA Method 3
Gas Analysis for the Determination of Dry Molecular Weight-Instrumental Method	USEPA Method 3A
Determination of Moisture Content in Stack Gases	USEPA Method 4
Determination of Particulate Matter from Stationary Sources	USEPA Method 5
Determination of Sulfur Dioxide from Stationary Sources	USEPA Method 6
Determination of Sulfur Dioxide Emissions from Stationary Sources (Instrumental Analyzer Procedure)	USEPA Method 6C
Visual Determination of the Opacity of Emissions from Stationary Sources	USEPA Method 9
Determination of Carbon Monoxide from Stationary Sources	USEPA Method 10
Determination of Inorganic Lead Emissions from Stationary Sources	USEPA Method 12
Visual Determination of Fugitive Emissions from Material Sources	USEPA Method 22
Determination of Total Gaseous Nonmethane Organic Emissions as Carbon	USEPA Method 25
Determination of Total Gaseous Organic Concentration Using a Flame Ionization Analyzer	USEPA Method 25A*
Determination of Hydrogen Halide and Halogen Emissions from Stationary Sources—Isokinetic Method	USEPA Method 26A
Determination of Metals Emissions from Stationary Sources	USEPA Method 29**
Determination of PM_{10} and $PM_{2.5}$ Emissions from Stationary Sources (Constant Sampling Rate Procedure)	USEPA Method 201A
Dry Impinger Method for Determining Condensable Particulate Emissions from Stationary Sources	USEPA Method 202
Criteria for and Verification of a Permanent or Temporary Total Enclosure	USEPA Method 204, 204(A-F)

* USEPA Method 25A may only be used if outlet VOM concentration is less than 50 ppm as carbon (non-methane).

** USEPA Method 29 may be used as an alternate to USEPA Method 12 for lead emissions.

c. Within sixty (60) days prior to the actual date of testing, the Permittee shall submit a written test plan to the Illinois EPA, Bureau of Air, Compliance Section Manager. This plan shall include at a minimum:

i. The name (or other identification) of the emission unit(s) to be tested and the name and address of the facility at which they are located;

ii. The name and address of the independent testing service(s) performing the tests, with the names of the individuals who may

be performing sampling and analysis and their experience with similar tests;

iii. The specific determinations of emissions and/or performance which are intended to be made, including the site(s) in the ductwork or stack at which sampling will occur;

iv. The specific conditions under which testing will be performed, including a discussion of why these conditions will be representative of the maximum emissions, maximum operating rate, minimum control performance, the levels of operating parameters for the emission unit, including associated control equipment, at or within which compliance is intended to be shown, and the means by which the operating parameters will be determined;

v. The test method(s) which will be used, with the specific analysis method, if the method can be used with different analysis methods. The specific sampling, analytical and quality control procedures which will be used, with an identification of the standard methods upon which they are based;

vi. Any minor changes in standard methodology proposed to accommodate the specific circumstances of testing, with justification;

vii. Any proposed use of an alternative test method, with detailed justification; and

viii. The format and content of the Source Test Report.

d. The Permittee shall provide the Illinois EPA with written notification of testing at least thirty (30) days prior to testing and again five (5) days prior to the testing to enable the Illinois EPA to have an observer present. This notification shall include the name of emission unit(s) to be tested, scheduled date and time, and contact person with telephone number.

e. If testing is delayed, the Permittee shall promptly notify the Illinois EPA by e-mail or facsimile, at least five (5) days prior to the scheduled date of testing or immediately, if the delay occurs in the five (5) days prior to the scheduled date. This notification shall also include the new date and time for testing, if set, or a separate notification shall be sent with this information when it is set.

f. The Permittee shall submit the Final Source Test Report(s) for these tests accompanied by a cover letter stating whether or not compliance was shown, to the Illinois EPA, Bureau of Air, Compliance Section Manager within thirty (30) days after the test results are compiled, but no later than sixty (60) days after the date of testing or sampling. The Final Source Test Report shall include as a minimum:

i. General information describing the test, including the name and identification of the emission source, which was tested, date of testing, names of personnel performing the tests, and Illinois EPA observers, if any;

ii. A summary of results;

iii. Description of test procedures and method(s), including description and map of emission units and sampling points, sampling train, testing and analysis equipment, and test schedule;

iv. Detailed description of test conditions, including:

A. List and description of the equipment (including serial numbers or other equipment specific identifiers) tested and process information (i.e., mode(s) of operation, process rate or throughput, fuel or raw material consumption rate, and heat content of the fuels);

B. Control equipment information (i.e., equipment condition and operating parameters) during testing; and

C. A discussion of any preparatory actions taken (i.e., inspections, maintenance and repair).

v. Data and calculations, including copies of all raw data sheets and records of laboratory analyses, sample calculations, and data on equipment calibration. Identification of the applicable regulatory standards and permit conditions that the testing was performed to demonstrate compliance with, a comparison of the test results to the applicable regulatory standards and permit conditions, and a statement whether the test(s) demonstrated compliance with the applicable standards and permit conditions;

vi. An explanation of any discrepancies among individual tests, failed tests or anomalous data;

vii. The results and discussion of all quality control evaluation data, including a copy of all quality control data; and

viii. The applicable operating parameters of the pollution control device(s) during testing (temperature, pressure drop, scrubbant flow rate, etc.), if any.

17a. Pursuant to 35 Ill. Adm. Code 218.105(d)(2)(A)(i), an owner or operator: That uses an afterburner or carbon adsorber to comply with any Section of 35 Ill. Adm. Code Part 218 shall use Illinois EPA and USEPA approved continuous monitoring equipment which is installed, calibrated, maintained, and operated according to vendor specifications at all times the control device is in use except as provided in 35 Ill. Adm. Code 218.105(d)(3). The continuous monitoring equipment must monitor the following parameters:

For each afterburner which does not have a catalyst bed, the combustion chamber temperature of each afterburner.

b. Pursuant to 35 Ill. Adm. Code 218.105(d)(2)(B), an owner or operator: Must install, calibrate, operate and maintain, in accordance with manufacturer's specifications, a continuous recorder on the temperature monitoring device, such as a strip chart, recorder or computer, having an accuracy of ± 1 percent of the temperature measured in degrees Celsius or ± 0.5° C, whichever is greater.

18. Pursuant to 40 CFR 63.10(b)(3), if an owner or operator determines that his or her stationary source that emits (or has the potential to emit, without considering controls) one or more hazardous air pollutants regulated by any standard established pursuant to section 112(d) or (f) of the Clean Air Act, and that stationary source is in the source category regulated by the relevant standard, but that source is not subject to the relevant standard (or other requirement established under 40 CFR Part 63) because of limitations on the source's potential to emit or an exclusion, the owner or operator must keep a record of the applicability determination on site at the source for a period of 5 years after the determination, or until the source changes its operations to become an affected source, whichever comes first. The record of the applicability determination must be signed by the person making the determination and include an analysis (or other information) that demonstrates why the owner or operator believes the source is unaffected (e.g., because the source is an area source). The analysis (or other information) must be sufficiently detailed to allow the USEPA and/or Illinois EPA to make a finding about the source's applicability status regarding the relevant standard or other requirement. If relevant, the analysis must be performed in accordance with requirements established in relevant subparts of 40 CFR Part 63 for this purpose for categories of stationary sources. If relevant, the analysis should be performed in accordance with USEPA guidance materials published to assist sources in making applicability determinations under Section 112 of the Clean Air Act, if any. The requirements to determine applicability of a standard under 40 CFR 63.1(b)(3) and to record the results of that determination under 40 CFR 63.10(b)(3) shall not by themselves create an obligation for the owner or operator to obtain a Title V permit.

19a. Pursuant to 35 Ill. Adm. Code 212.110(e), the owner or operator of an emission unit subject to 35 Ill. Adm. Code Part 212 shall retain records of all tests which are performed.

b. i. Pursuant to 35 Ill. Adm. Code 212.324(g)(1), written records of inventory and documentation of inspections, maintenance, and repairs of all air pollution control equipment shall be kept in accordance with 35 Ill. Adm. Code 212.324(f).

ii. Pursuant to 35 Ill. Adm. Code 212.324(g)(2), the owner or operator shall document any period during which any process emission unit was in operation when the air pollution control

equipment was not in operation or was malfunctioning so as to cause an emissions level in excess of the emissions limitation. These records shall include documentation of causes for pollution control equipment not operating or such malfunction and shall state what corrective actions were taken and what repairs were made.

iii. Pursuant to 35 Ill. Adm. Code 212.324(g)(3), a written record of the inventory of all spare parts not readily available from local suppliers shall be kept and updated.

iv. Pursuant to 35 Ill. Adm. Code 212.324(g)(5), the records required under 35 Ill. Adm. Code 212.324 shall be kept and maintained.

20a. Pursuant to 35 Ill. Adm. Code 218.991(a)(2), any owner or operator of a VOM emission unit which is subject to the requirements of 35 Ill. Adm. Code Part 218 Subpart PP, QQ, RR or TT and complying using emission capture and control equipment shall comply with the following:

On and after a date consistent with 35 Ill. Adm. Code 218.106, or on and after the initial start-up date, the owner or operator of a subject VOM source shall collect and record all of the following information each day:

i. Control device monitoring data.

ii. A log of operating time for the capture system, control device, monitoring equipment and the associated emission source.

iii. A maintenance log for the capture system, control device and monitoring equipment detailing all routine and non-routine maintenance performed including dates and duration of any outages.

21a. The Permittee shall maintain records of the following items so as to demonstrate compliance with the conditions of this permit:

i. Records addressing use of good operating practices for the RTO and Quench/Packed Tower Scrubber associated with the Hammermill Shredder System and Dust Collectors (DC-01 through DC-04) associated with Non-Ferrous Material Separation System:

A. Records for periodic inspection of the Roll Media Filter, RTO, Quench/Packed Tower Scrubber, and Dust Collectors (DC-01 through DC-04) with date, individual performing the inspection, and nature of inspection; and

B. Records for prompt repair of defects, with identification and description of defect, effect on emissions, date identified, date repaired, and nature of repair.

ii. A copy of the Fugitive Emissions Operating Program, any amendments or revisions to the Fugitive Emissions Operating

Program, and a record of activities completed according to the Fugitive Particulate Operating Program.

iii. A. Daily records demonstrating the temperature for the RTO;

B. Daily records demonstrating pressure differential across inlet and outlet of the Quench/Packed Tower Scrubber

C. Daily records demonstrating scrubbant liquid flow rate of the Quench/Packed Tower Scrubber;

D. Daily records demonstrating the pH of the scrubbant of the Quench/Packed Tower Scrubber;

E. Daily records demonstrating inlet gas stream to the control train for the Hammermill Shredder System for the flammability of this gas stream as a percentage of the lower explosive limit (LEL) of this stream

F. Daily records demonstrating amperage or usage of electrical power by the motor for the fan in the control train or inlet gas flow rate of the control train.

G. Daily records demonstrating status of the emergency bypass vent on the RTO in the control train for the Hammermill Shredder System, i.e., whether this vent is closed or open.

iv. Records of daily visual inspections of the Hammermill Shredder operations containing the date, time, individual performing the observation, observation details including operation of associated control systems, and any corrective actions taken.

v. Natural gas usage for RTO (mmscf/month and mmscf/year).

vi. Hours of operation for Non-Ferrous System, Barge loading, Hammermill Shredder System, RTO, and Quench/Packed Tower Scrubber (hours/day, hours/month and hours/year).

vii. Type and amount material received by the facility (tons/month and tons/year).

viii. Type and amount material processed by Hammermill Shredder System (tons/month and tons/year).

ix. Material throughput (tons/month and tons/year) for the Ferrous Material Separation Process, Non-Ferrous Material Process, and Fines Processing Building.

x. Amount of non-metallic materials (fluff) shipped offsite (tons/month and tons/year).

xi. Hours of operation for Dust Collector DC-01 (hours/month and

hours/year).

xii. For each event when the emergency bypass vent on the RTO is open while feed material is being sent to or being processed in the Hammermill Shredder System, the Permittee shall maintain records that include: the date, starting time and duration of the event; a description of the event; the monitored flammability of the gas stream at the start of the event; an estimate of the additional VOM emissions attributable to the event, with supporting data; the likely explanation for the event.; and, if the stoppage of feed to the Hammermill Shredder System when this vent opens is not automated, the time that feed to this system ceased.; and

xiii. Monthly and annual emissions of PM, PM_{10}, CO, NOx, SO_2, VOM, and HAPs from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System with supporting calculations (tons/month and tons/year).

b. All records and logs required under this permit shall be retained at a readily accessible location at the source for at least five (5) years from the date of entry and shall be made available for inspection and copying by the Illinois EPA or USEPA upon request. Any records retained in an electronic format (e.g., computer storage device) shall be capable of being retrieved and printed on paper during normal source office hours so as to be able to respond to an Illinois EPA or USEPA request for records during the course of a source inspection.

22a. Pursuant to 35 Ill. Adm. Code 212.110(d), a person planning to conduct testing for particulate matter emissions to demonstrate compliance shall give written notice to the Illinois EPA of that intent. Such notification shall be given at least thirty (30) days prior to the initiation of the test unless a shorter period is agreed to by the Illinois EPA. Such notification shall state the specific test methods from 35 Ill. Adm. Code 212.110 that will be used.

b. Pursuant to 35 Ill. Adm. Code 212.324(g)(6), upon written request by the Illinois EPA, a report shall be submitted to the Illinois EPA for any period specified in the request stating the following: the dates during which any process emission unit was in operation when the air pollution control equipment was not in operation or was not operating properly, documentation of causes for pollution control equipment not operating or not operating properly, and a statement of what corrective actions were taken and what repairs were made.

23a. Pursuant to 35 Ill. Adm. Code 218.991(a), any owner or operator of a VOM emission unit which is subject to the requirements of 35 Ill. Adm. Code Part 218 Subpart PP, QQ, RR or TT and complying by the use of emission capture and control equipment shall comply with the following:

i. By a date consistent with 35 Ill. Adm. Code 218.106, or upon initial start-up of a new emission unit, the owner or operator of the subject VOM emission unit shall demonstrate to the Illinois EPA that the subject emission unit will be in compliance on and

after a date consistent with 35 Ill. Adm. Code 218.106, or on and after the initial start-up date by submitting to the Illinois EPA all calculations and other supporting data, including descriptions and results of any tests the owner or operator may have performed.

ii. On and after a date consistent with 35 Ill. Adm. Code 218.106, the owner or operator of a subject VOM emission source shall notify the Illinois EPA:

A. Of any violation of the requirements of 35 Ill. Adm. Code Part 218 Subpart PP, QQ, RR or TT by sending a copy of any record showing a violation to the Illinois EPA within 30 days following the occurrence of the violation;

B. At least 30 calendar days before changing the method of compliance with 35 Ill. Adm. Code Part 218 Subpart PP or TT from the use of capture systems and control devices to the use of complying coatings, the owner or operator shall comply with all requirements of 35 Ill. Adm. Code 218.991(a)(1). Upon changing the method of compliance with 35 Ill. Adm. Code Part 218 Subpart PP or TT from the use of capture systems and control devices to the use of complying coatings, the owner or operator shall comply with all requirements of 35 Ill. Adm. Code 218.991(a).

24a. The Permittee shall submit a written notification to the Illinois EPA, Bureau of Air, Compliance Section Manager of the initial receipt date of material to be processed in the Hammermill Shredder within seven (7) calendar days after the initial receipt date.

b. The Permittee shall submit a written notification to the Illinois EPA, Bureau of Air, Compliance Section Manager within seven (7) calendar days from the date that raw material is first processed through the hammermill shredder.

c. If, during a Bypass Event, the feed to the hammermill shredder continues for 30 seconds or more after the start of a Bypass Event, the Permittee shall notify the Illinois EPA within 3 hours of the start of the event, with this notification made by email to the Manager of the Compliance Section in the Illinois EPA, Bureau of Air. For all other Bypass Events, the Permittee shall submit to the Illinois EPA, Bureau of Air, Compliance Section Manager, within seven (7) calendar days of such event, a report for detailing the following information for each event when feed to the shredder was interlocked due to the LEL system: % of LEL detected, duration of the event, and VOM emissions with supporting documentation.

25a. The Permittee shall submit a quarterly report containing the following information for each month of the quarter:

i. Type and amount material received by the facility;

ii. Type and amount material processed by Hammermill Shredder System;

iii. Throughput for the Ferrous Material Separation Process, Non-Ferrous Material Process, and Fines Processing Building;

iv. PM, PM_{10}, and HAPs emissions from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System, with supporting calculations;

v. A summary of all bypass events that occur during the quarter and for each event, this summary shall include the date, time, duration, description, likely explanation and estimated additional VOM emissions due to the event.

vi. VOM emissions from the Hammermill Shredder System, Ferrous Material Separation System, and Non-Ferrous Material Separation System, with supporting calculations; and

vii. Amounts of "fluff" and other non-metallic materials shipped offsite (truckloads/month).

b. The Permittee shall submit this quarterly report to the Illinois EPA, Bureau of Air, Compliance Section Manager within thirty (30) calendar days of the end of a calendar quarter.

26a. If there is an exceedance of or a deviation from the requirements of this permit as determined by the records required by this permit or otherwise, the Permittee shall submit a report to the Illinois EPA's Bureau of Air Compliance Section in Springfield, Illinois within thirty (30) days after the exceedance or deviation. The report shall identify the duration and the emissions impact of the exceedance or deviation, a copy of the relevant records and information to resolve the exceedance or deviation, and a description of the efforts to reduce emissions from, and the duration of exceedance or deviation, and to prevent future occurrences of any such exceedance or deviation.

b. One (1) copy of required reports and notifications shall be sent to:

Illinois Environmental Protection Agency
Bureau of Air
Compliance Section (#40)
P.O. Box 19276
Springfield, Illinois 62794-9276

and an electronic copy of test protocols and test results to epa.boa.smu@illinois.gov

If you have any questions on this permit, please call German Barria at 217/785-1705.

Raymond E. Pilapil
Manager, Permit Section
Bureau of Air

REP:GB:tan

STATE OF ILLINOIS
ENVIRONMENTAL PROTECTION AGENCY
DIVISION OF AIR POLLUTION CONTROL
P. O. BOX 19506
SPRINGFIELD, ILLINOIS 62794-9506

STANDARD CONDITIONS FOR CONSTRUCTION/DEVELOPMENT PERMITS ISSUED BY THE ILLINOIS ENVIRONMENTAL PROTECTION AGENCY

July 1, 1985

The Illinois Environmental Protection Act (Illinois Revised Statutes, Chapter 111-1/2, Section 1039) authorizes the Environmental Protection Agency to impose conditions on permits which it issues.

The following conditions are applicable unless superseded by special condition(s).

1. Unless this permit has been extended or it has been voided by a newly issued permit, this permit will expire one year from the date of issuance, unless a continuous program of construction or development on this project has started by such time.

2. The construction or development covered by this permit shall be done in compliance with applicable provisions of the Illinois Environmental Protection Act, and Regulations adopted by the Illinois Pollution Control Board.

3. There shall be no deviations from the approved plans and specifications unless a written request for modification, along with plans and specifications as required, shall have been submitted to the Agency and a supplemental written permit issued.

4. The Permittee shall allow any duly authorized agent of the Agency upon the presentation of credentials, at reasonable times:

   a. to enter the Permittee's property where actual or potential effluent, emission or noise sources are located or where any activity is to be conducted pursuant to this permit,

   b. to have access to and copy any records required to be kept under the terms and conditions of this permit,

   c. to inspect, including during any hours of operation of equipment constructed or operated under this permit, such equipment and any equipment required to be kept, used, operated, calibrated and maintained under this permit,

   d. to obtain and remove samples of any discharge or emission of pollutants, and

   e. to enter and utilize any photographic, recording, testing, monitoring or other equipment for the purpose of preserving, testing, monitoring, or recording any activity, discharge, or emission authorized by this permit.

5. The issuance of this permit:

   a. shall not be considered as in any manner affecting the title of the premises upon which the permitted facilities are to be located,

   b. does not release the Permittee from any liability for damage to person or property caused by or resulting from the construction, maintenance, or operation of the proposed facilities,

   c. does not release the Permittee from compliance with the other applicable statues and regulations of the United States, of the State of Illinois, or with applicable local laws, ordinances and regulations,

   d. does not take into consideration or attest to the structural stability of any units or parts of the project, and

e. in no manner implies or suggests that the Agency (or its officers, agents or employees) assumes any liability, directly or indirectly, for any loss due to damage, installation, maintenance, or operation of the proposed equipment or facility.

6. a. Unless a joint construction/operation permit has been issued, a permit for operation shall be obtained from the Agency before the equipment covered by this permit is placed into operation.

b. For purposes of shakedown and testing, unless otherwise specified by a special permit condition, the equipment covered under this permit may be operated for a period not to exceed thirty (30) days.

7. The Agency may file a complaint with the Board for modification, suspension or revocation of a permit:

a. upon discovery that the permit application contained misrepresentations, misinformation or false statements or that all relevant facts were not disclosed, or

b. upon finding that any standard or special conditions have been violated, or

c. upon any violations of the Environmental Protection Act or any regulation effective thereunder as a result of the construction or development authorized by this permit.

Exhibit 221

From: Geertsma, Meleah
To: Pressnall, Chris; Dowson, Sharon; Frost, Brad
Cc: Peggy Salazar (peggy_setf@sbcglobal.net) (peggy_setf@sbcglobal.net); EXT Harley, Keith
Subject: [External] RE: IEPA FOIA request - 11600 S Burley air application
Date: Thursday, December 19, 2019 1:02:40 PM

A quick update – I just spoke to Bob Bernoteit, the FESOP coordinator in air permitting, and he gave me these facility ID and application #s for the early December application covered by our Dec 13 request:

ID #031600GYI
Application #12020006

Hopefully that helps in tracking down the records so that IEPA can fulfill the FOIA.

Thanks so much,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

NATURAL RESOURCES
DEFENSE COUNCIL
20 N. WACKER DRIVE, SUITE 1600
CHICAGO, IL 60606
T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

From: Geertsma, Meleah
Sent: Thursday, December 19, 2019 12:38 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; sharon.dowson@illinois.gov; brad.frost@illinois.gov
Subject: IEPA FOIA request - 11600 S Burley air application

Hi Sharon – I received your email stating that IEPA would not be able to respond within 5 days to our Dec 13 FOIA request, because the agency cannot find the referenced documents through a routine search. I believe Chris is out until Jan 1 so can't help directly, but I'm sharing his email in case it helps locate the document.

Cc'ing Brad, too, since he's the EJ contact point while Chris is out, and this is a time-sensitive request that it would be great to get taken care of asap.

Best,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

NATURAL RESOURCES
DEFENSE COUNCIL
20 N. WACKER DRIVE, SUITE 1600
CHICAGO, IL 60606
T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

From: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Sent: Thursday, December 12, 2019 4:54 PM
To: Geertsma, Meleah <mgeertsma@nrdc.org>
Subject: RE: 11600 S Burley updated permit application

Hello Meleah –

The permit application referenced did indeed arrive after the FOIA. I believe the application was dated December 2 (or date stamped, not sure). So it is in-house now.

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Geertsma, Meleah <mgeertsma@nrdc.org>
Sent: Thursday, December 12, 2019 2:24 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Subject: [External] 11600 S Burley updated permit application

Hi Chris –
Thanks again for the updates on air permitting of the proposed new metals facility on Burley. I see from the Nov 1 document that the applicant anticipated submitting a permit application for the multiple entities at the site within 30 days of that Nov 1 document. Can you confirm whether that

application has been submitted? In general I'm wondering whether it would have gotten picked up by Keith's/our 11/25 FOIA or not.

Thanks,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

NATURAL RESOURCES
DEFENSE COUNCIL
20 N. WACKER DRIVE, SUITE 1600
CHICAGO, IL 60606
T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

From: Pressnall, Chris
To: Frost, Brad; Armitage, Julie
Cc: Nifong, Heather
Subject: FW: [External] General III: Request for Public Participation and Environmental Justice Analysis
Date: Wednesday, October 30, 2019 1:21:01 PM
Attachments: SETF NRDC Ban Petcoke General III IL EPA PP and EJ Request.docx

---

FYI

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA
(217) 524-1284
(217) 785-8346 (fax)
chris.pressnall@illinois.gov

From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Wednesday, October 30, 2019 1:18 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Subject: [External] General III: Request for Public Participation and Environmental Justice Analysis

Hi Chris -

The attached letter is being sent to Director Kim today by the Southeast Environmental Task Force, my client, as well as the Chicago South East Side Coalition to Ban Petcoke and the Natural Resources Defense Council.

Thank you for assistance in making sure this request receives the Director's attention. If you, Director Kim and/or others at the IL EPA would like to discuss this matter, please feel free to contact me and I will coordinate with my co-counsel.

Keith Harley, Attorney for SETF
Chicago Legal Clinic, Inc.
211 W. Wacker, Suite 750
Chicago, IL 60606
(312) 726-2938

October 30, 2019

John Kim, Director
Illinois Environmental Protection Agency
1021 Grand Avenue East
P.O. Box 19276
Springfield, IL 62794-9276

Re: General III, LLC, 11600 S. Burley, Chicago, IL 60617: Request for an Environmental Justice Analysis, a Public Hearing and a Subsequent Written Comment Period

To the Director,

We are writing on behalf of the Southeast Environmental Task Force ("SETF")[1] and the Chicago South East Side Coalition to Ban Petcoke[2], community-based organizations that are dedicated to the health, safety and welfare of the people who live, work and recreate in the Calumet region. We are also writing on behalf of the Natural Resources Defense Council ("NRDC") and our thousands of members and activists in the City of Chicago, including those who reside on Chicago's southeast side.[3] For purposes of this letter, these groups will be referred to as the NGO coalition.

On October 1, 2019, the Illinois EPA distributed a notice that General III, LLC submitted a Construction Permit application to construct a scrap metal recycling facility at 11600 S. Burley, Chicago Illinois 60617. This facility would operate at this location with four existing, affiliated businesses – Reserve Marine Terminals, South Chicago Recycling, LLC, Napauk Salvage of Waupaca, LLC and RSR Partners, LLC doing business as Regency Technologies. General III, LLC, which is wholly owned by RMG Investment Group, will be a fifth RMG-related operation on the site. General III will be located on an approximately 23 acre portion of the site that extends from the intersection of 116th and Burley to the Calumet River. General III will purchase the "business and substantially all of the assets" of General Iron Industries, which currently processes 740,000 tons of scrap per year.

The NGO coalition is making a formal request that IL EPA incorporate a public hearing and a subsequent written comment period into its permitting activities. The NGO coalition is asking IL EPA to post current information during the duration of this permitting transaction on its document explorer website. Moreover, considering the characteristics of the immediately surrounding area, the NGO coalition is formally requesting IL EPA to conduct an environmental justice analysis as part of its permitting process.

There is a strong justification for an environmental justice analysis and for a full and complete opportunity for public participation. According to information derived from the demographic feature of U.S. EPA's ECHO database, there are 68,947 people living within a three-mile radius of General III's proposed facility. 49% of the people who live in that three-mile radius are Hispanic, and 30% are African American. The ECHO database also indicates that there are

[1] http://setaskforce.org/
[2] https://www.facebook.com/SSCBP60617/
[3] https://www.nrdc.org/

26,624 households in this area as well as 19,051 minors younger than 18. Nearby residential communities include the East Side, South Deering and Hegewisch. The facility would operate immediately adjacent to the Calumet River. In addition, the facility is less than one mile from a school, Washington High School. This area scores above 90% in eleven categories assessed by U.S. EPA's EJ screening tool, including PM 2.5, diesel PM, NATA air toxics cancer risk, NATA respiratory hazard index, traffic proximity, lead paint indicator, superfund proximity, risk management plan proximity, hazardous waste proximity and wastewater discharge proximity.

The Southeast Environmental Task Force obtained a copy of General III's construction permit application through a FOIA request. After reviewing this application, the NGO coalition is concerned about the cumulative impact of this new facility in combination with the existing, affiliated facilities that already operate at this location. In light of the nearby residential neighborhoods and the existing environmental problems they face, the NGO coalition is concerned that this facility could cause and contribute to pollution that creates a significant, adverse and disproportionate impact on public health and safety, the use and enjoyment of property, children's health and environmental quality. The NGO coalition is concerned that new emissions produced by the facility are not accurately characterized, particularly in light of the use of outdoor storage piles.

IL EPA, as a federally funded entity, has a legal obligation to consider environmental justice issues in compliance with Title VI. [4] As articulated in Title VI, recipients of federal funds have an affirmative obligation to ensure non-discrimination. Because IL EPA is a state agency that receives funding from a federal entity, the U.S. Environmental Protection Agency (U.S. EPA), it has a legal duty to ensure non-discrimination in this case. [5] IL EPA will violate its legal responsibilities under Title VI if it allows the permitting of the facility in question without an environmental justice analysis, and without providing a full and complete opportunity for public participation. Because the area surrounding the proposed facility is disproportionately minority, it is exactly the type of area that is meant for protection under Title VI and Illinois environmental justice policies.

In the resolution of United States Environmental Protection Agency Administrative Complaint Number 13R-10-R5, IL EPA made a commitment to revise its environmental justice public participation policy "…so that permitting activities in areas identified as potential EJ communities will be given an appropriate level of outreach…". As part of its subsequently revised Environmental Justice Public Participation Policy, IL EPA identified a series of public participation initiatives that apply to "all permitting transactions." These commitments include:

1. providing early and meaningful public involvement throughout the permitting process;

2. making a determination of the appropriate outreach based on factors like the type of permit, potential impact of the project, type of source or level of interest;

[4] "No person in the United States shall, on the ground of race, color or national origin, . . . be subjected to discrimination under any program or activity receiving Federal financial assistance." Title VI of the Civil Rights Act of 1964, 42 U.S.C. 2000d.

[5] Illinois EPA's obligations also include the commitments it made to resolve three previous Title VI Complaints, which are documented at: http://www.epa.illinois.gov/topics/environmentaljustice/grievances/index

3. encouraging the permit applicant to meet with community stakeholders, to provide notice and information about the project or to develop a Community Relations Plan;

4. providing the community with information via mailed EJ notifications;

5. making and distributing fact sheets or project summaries;

6. developing and publishing a Public Notice;

7. conducting an informational meeting or a public hearing;

8. publishing a draft permit for public review;

9. conducting a public written comment period on the permit; and,

10. prior to issuing a permit, making an effort to make information available to residents in a timely and efficient manner.

There is a final factor that is important evidence of the need for public participation and an environmental justice analysis. This permitting process represents a vital juncture for IL EPA to provide public engagement to ensure that this facility operates in manner which meets federal, state and local environmental standards, and to take steps to avoid any significant, adverse and disproportionate effects that could occur. Consequently, there is a high degree of public interest regarding General III and IL EPA's permitting activities in relation to the proposed facility.

Thank you for your consideration of this request. Please contact us if you have any questions or comments. I look forward to your response.

Sincerely,

Keith Harley

Keith Harley, Attorney for Southeast Environmental Task Force
Chicago Legal Clinic, Inc.
211 W. Wacker Drive, Suite 750
Chicago, IL 60606
Tel: (312) 726-2938
E-Mail: kharley@kentlaw.iit.edu

/s/ Nancy C. Loeb
Attorney for Chicago South East Side Coalition to Ban Petcoke
Clinical Associate Professor of Law
Director, Environmental Advocacy Clinic
Bluhm Legal Clinic
Northwestern Pritzker School of Law
375 East Chicago Avenue, Chicago, IL 60611-3069

Tel: 312-503-0052
E-Mail: n-loeb@northwestern.edu

/s/Meleah Geertsma
Senior Attorney, Natural Resources Defense Council
20 N. Wacker Drive, Suite 1600
Chicago, IL 60606
Tel: 312-651-7904
E-Mail: mgeertsma@nrdc.org

cc Chris Pressnall, Illinois EPA Environmental Justice Officer via E-Mail

From: DoNotReply.EJRequest@illinois.gov
To: Bernoteit, Bob; Frost, Brad; Frost, Brad; Pressnall, Chris; Lenkart, Maggie; Barria, German
Subject: Request for EJ Review for General III LLC | 031600SFX | 19090021 | Air
Date: Friday, September 27, 2019 11:01:39 AM

A new request has been submitted to the EJ Outreach database.

Source Name: General III LLC

Activity/Subactivity Type: Permit / Construction

Decision Due Date: 12/24/2019

Reviewer - When the permit is ready to be issued, click this link to view the request. When viewing the request, click the button labeled 'Ready for issuance' to mark the record for EJ Release.

From: Herr, Alane
To: Frost, Brad
Subject: General III Oct 1 2019
Date: Wednesday, June 17, 2020 1:02:21 PM
Attachments: General III LLC Contact List .xlsx
General III LLC 031600SFX 19090021.pdf

Alane Herr
EJ Office Associate
Illinois Environmental Protection Agency
(217) 524-3735
M-F 8:00am-4:00pm

Name	Title	Address	City	State	Zip Code			
Southeast Environmental Task Force	Peggy Salazar	13300 S. Baltimore Ave.	Chicago	IL	60633		9	
Lori Lightfoot, Mayor	City of Chicago	121 N. LaSalle Street, 4th Floor	Chicago	IL	60602	letterforthemayor@cityofchicago.org		3
								10
								11
								14
Email Contacts								15
Veterans Park Improvement Association	Janey Zavala	janzav34@gmail.com					17	
General III LLC	Jim Kallas	jim@general-iron.com						
U.S. Representative Robin Kelly*	U.S. Congressional District #2	rick.bryant@mail.house.gov						
Senator Elgie R. Sims, Jr.	State Senate District #33	esims@senatorelgiesims.com					1	
Representative Marcus C. Evans, Jr.	State Representative District #33	Repevans33@gmail.com	Chicago	IL	60619		2	
Alderwoman Susan Sadlowski Garza	City of Chicago	ward10@cityofchicago.org						4
Chicago Southside Branch NAACP	Rose Joshua	chicagossnaacp@gmail.com						8

Illinois Environmental Council	Colleen Smith	colleen@ilenviro.org
University of Chicago Law School	Elizabeth Lindberg	elindberg@uchicago.edu
Natural Resource Defense Council	Meleah Geertsma	mgeertsma@nrdc.org
N/A	Cristina Guerrero	crguerrer@gmail.com
N/A	Sarah Richmond	sarahelizabethrichmond@gmail.com
Natural Resource Defense Council	Ivan Moreno	imoreno@nrdc.org
Chicago Legal Clinic	Keith Harley	Kharley@kentlaw.iit.edu
N/A	Kelly E. Nichols	kellynichols1@gmail.com
Grumman/Butkus Associates	Sumeta Medicherla	smedicherla@grummanbutkus.com
IDOT*	John Sherrill*	John.Sherrill@illinois.gov
Friends of the Chicago River	Adam Flickinger	aflickinger@chicagoriver.org
County Board of Commissioners	N/A	cookcounty.board@cookcountyIL.gov
Dept. of Environment and Sustainability	N/A	environment@cookcountyil.gov
N/A	Samira Hanessian	Samira.hanessian@cityofchicago.org
CPI	Natalie Warkenthien	nwarkenthien@cpilink.com
N/A	Sam Cardik	samuel.cardick@illinois.gov
Illinois Environmental Protection Agency	Sabrina Bailey	Sabrina.Bailey@illinois.gov

Delta Institute	Mila Marshall	mmarshall@delta-institute.org
N/A	Wendy Stark-Riemer	Wendystarkriemer@gmail.com
N/A	Alexis Winter	lexmwinter@gmail.com
Bridgeport Alliance	Anna Schibrowsky	anna.schibrowsky@gmail.com
N/A	Sarah Buchhorn	sarah.buchhorn@gmail.com
Chicago DPH	Alfonso Martel	alfonso.martel@cityofchicago.org
Indian Creek E.E.C.	Jayme Boberek	indiancreekeec@outlook.com
City of Chicago	Liliana Escarpita	Liliana.escarpita@cityofchicago.org
NAAEE		arturo@naaee.org
Sims Metal Manageme	Deborah Hays	debbie.hays@simsmm.com
Delta Institute	Emily Rhodes	erhodes@delta-institute.org
N/A	Andre M. Joyce	Ajoycegolden@student.ccc.edu
N/A	Loreen Targos	ltargos@gmail.com
N/A	Erica Knox	eknox@clccrul.org

Senator Dick Durbin	N/A	Erica_DeAngelis@durbin.senate.gov
Senator Tammy Duckworth	N/A	info@duckworth.senate.gov
American Lung Association IL	Angela Tin	angela.tin@lung.org
ComEd	Kareena Wasserman	kareena.wasserman@comed.com
Chemical Industry Council of Illinois	Lisa Frede	lfrede@cicil.net
Earthjustice	Debbie Chizewer	dchizewer@earthjustice.org
Earthjustice	Jennifer Cassel	jcassel@earthjustice.org
Environmental Law & Policy Center	Jeffrey Hammons	Jhammons@elpc.org
Environmental Law & Policy Center	Kiana Courtney	KCourtney@elpc.org
Faith in Place	Rev. Brian Sauder	info@faithinplace.org
Illinois Environmental Council	Jennifer Walling	jwalling@ilenviro.org
Illinois Farm Bureau	Lauren Lurkins	Llurkins@ilfb.org
Illinois Environmental Regulatory Group	Alec Davis	iergstaff@ierg.org
Illinois NAACP	Gregory Norris	gnorris@illinoisnaacp.org
Illinois NAACP	Theresa Haley	thaley@illinoisnaacp.org
LVEJO	Juliana Pino	jpino@lvejo.org
N/A	Nick Firmand	nick.firmand@gmail.com
N/A	Stacey Mihallik	Mihallik_Stacey@cat.com
N/A	Loreen Targos	ltargos@gmail.com
N/A	Molly Kordas	mkordas@openlands.org
Prairie Rivers Network	Elliot Brinkman	ebrinkman@prairieriversnetwork.org
Respiratory Health Association	Brian P. Urbaszewski	BUrbaszewski@lungchicago.org
Shawnee Hills & Hollers	Sabrina Hardenbergh	woodlandrunner@gmail.com
Shawnee Hills & Hollers	Georgia de la Garza	shawneehollers247@gmail.com
Sierra Club IL	Christine Nannicelli	christine.nannicelli@sierraclub.org
Sierra Club IL	Jack Darrin	jack.darin@sierraclub.org
Sierra Club IL	Katrina Phillips	katrina.phillips@sierraclub.org
Bluhm Legal Clinic, Northwestern Pritzker Law	Cary Shepard	cary.shepherd@law.northwestern.edu
N/A	Ash Ngu	ash.ngu@propublica.org

U.S. Representative
U.S. Representative Bobby Rush
U.S. Representative Robin Kelly*
U.S. Representative Dan Lipinski*
U.S. Representative Jesús García*
U.S. Representative Mike Quigley
U.S. Representative Sean Casten*
U.S. Representative Danny Davis
U.S. Representative Raja Krishnamoorthi
U.S. Representative Jan Schakosky*
U.S. Representative Brad Schneider*
U.S. Representative Bill Foster
U.S. Representative Mike Bost
U.S. Representative Rodney Davis
U.S. Representative Lauren Underwood*
U.S. Representative John Shimkus
U.S. Representative Adam Kinzinger
U.S. Representative Cheri Bustos*
U.S. Representative Darin LaHood

U.S. Rep Emails
rick.bryant@mail.house.gov (2)
grace.graunke@mail.house.gov (3)
il04.schedule@mail.house.gov (4)
anne.wick@mail.house.gov (6)
leslie.combs@mail.house.gov (9)
Tommy.Brown@mail.house.gov (10)
il14.casework@mail.house.gov (14)
alexandra.fields@mail.house.gov (17)

City/Village
Susie Sunshine, Mayor
Susie Sunshine, Village President

City/Village
Sunnyville City Council
Sunnyville Village Board
Alder[wo]man

Senator w/ email
Senator Martin A. Sandoval
Senator Napoleon Harris, III
Senator Iris Y. Martinez
Senator Laura Murphy
Senator Terry Link
Senator Dave Koehler
Senator Jil Tracy
Senator Dale Righter
Senator Rachelle Crowe

Represntatives w/ email
Rep. Dan Burke
Rep. Theresa Mah
Rep. Mike Fortner
Rep. Michelle Mussman
Rep. Tony McCombie
Rep. Michael Halpin
Rep. Lance Yednok
Rep. Sue Scherer
Rep. Monica Bristow

October 1, 2019

Re: General III LLC (Illinois EPA BOA ID# 031600SFX)
Construction Permit (19090021)

To Distribution List:

In accordance with the Illinois EPA's Environmental Justice Policy, the Illinois EPA wants to provide you with information about a potential Illinois EPA action. The Illinois EPA is sending this letter to notify you of an application received by the Illinois EPA Bureau of Air (BOA).

The Illinois EPA has received a Construction Permit application from General III LLC for a proposed facility located at 11600 South Burley Avenue in Chicago. The application requests the construction of a scrap metal recycling facility.

The application is currently under review by the Illinois EPA's Bureau of Air.

If you are receiving paper notifications and would like to sign up to receive notifications by email instead, please visit the Illinois EPA Environmental Justice webpage: https://www2.illinois.gov/epa/topics/environmental-justice/Pages/EJ-Notice-Sign-up.aspx

If you have questions about the application, please contact Chris Pressnall, Environmental Justice Officer at (217) 524-1284, chris.pressnall@illinois.gov.

Sincerely,

Chris Pressnall
Environmental Justice Officer

Distribution List

General III LLC
State Senator Elgie R. Sims, Jr. - State Senate District #17
State Representative Marcus C. Evans, Jr. - State Representative District #33
U.S. Representative Robin Kelly - U.S. Congressional District #2*
U.S. Senator Richard J. Durbin*
U.S. Senator Tammy Duckworth*
City of Chicago – Lori Lightfoot, Mayor
City of Chicago – Susan Sadlowski Garza, Ward 10
Cook County Board of Commissioners*
Cook County Department of Environment & Sustainability*
Chicago Southside Branch NAACP – Rose Joshua
Illinois NAACP – Gregory Norris*
Illinois NAACP – Teresa Haley*
American Lung Association of Illinois – Angela Tin*
Respiratory Health Association - Brian P. Urbaszewski*
Sierra Club – Jack Darin*
Sierra Club – Christine Nannicelli*
Prairie Rivers Network – Elliot Brinkman*
Faith in Place – Rev. Brian Sauder*
Illinois Environmental Regulatory Group – Alec Davis*
Chemical Industry Council of Illinois – Lisa Frede*
Illinois EPA – Crystal Myers-Wilkins*
Chicago Legal Clinic – Keith Harley*
Natural Resource Defense Council – Meleah Geertsma*
Natural Resource Defense Council – Ivan Moreno*
Illinois Environmental Council – Colleen Smith*
University of Chicago Law School – Elizabeth Lindberg*
Grumman/Butkus Associates – Sumeta Medicherla*
Illinois Dept. of Transportation – John Sherrill*
Friends of the Chicago River – Adam Flickinger*
Shawnee Hills & Hollers – Georgia de la Garza*
Shawnee Hills & Hollers – Sabrina Hardenbergh*
Illinois Environmental Council – Jennifer Walling*
LVEJO – Juliana Pino*
Environmental Law & Policy Center – Jeffrey Hammons*
Environmental Law & Policy Center – Kiana Courtney*
Illinois Farm Bureau – Lauren Lurkins*
ComEd – Kareena Wasserman*
Earthjustice – Jennifer Cassel*
Earthjustice – Debbie Chizewer*
Calumet Area Industrial Commission - David Holmberg*
Bridgeport Alliance - Anna Schibrowsky*
Chicago Dept. of Public Health - Alfonso Martel*
City of Chicago - Liliana Escarpita*
Delta Institute - Mila Marshall*
Indian Creek E.E.C.- Jayme Boberek*
Veterans Park Improvement Association - Janey Zavala*
Southeast Environmental Task Force - Peggy Salazar

***Receiving e-notifications**

From: Frost, Brad
To: EXT Harley, Keith
Subject: RE: [External] General III Public Participation Request
Date: Wednesday, March 25, 2020 3:23:00 PM
Attachments: image001.png
image002.png
image003.png
image005.png

Keith,

Please give me a call at your earliest convenience. It sounds like from the Legal Clinic voicemail that you may not be in the office, possibly working from home, and won't get a voicemail message quickly.

Thanks
Brad

Brad Frost
Manager, Office of Community Relations
217/782-7027

From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Tuesday, March 17, 2020 3:34 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; Frost, Brad <Brad.Frost@Illinois.gov>
Cc: Geertsma, Meleah <mgeertsma@nrdc.org>; Nancy Loeb <n-loeb@northwestern.edu>
Subject: [External] General III Public Participation Request

Hi -

As you know, several organizations including SETF requested a public hearing and a written comment period related to the General III construction permit. On behalf of these organizations, I'm writing to inquire what effect coronavirus state/city policies will have on IL EPA's plans for the requested public hearing and a subsequent written comment period. I've spoken to SETF, NRDC and the Ban Petcoke Coalition members who still want an in-person public hearing and see no substitute for this as a venue for local residents to participate in this permitting process. At the same time, they see no alternative to delaying this until the current public health crisis is resolved and public gatherings are again safe for the community and IL EPA.

Thanks,

Keith Harley, Attorney for Southeast Environmental Task Force
Chicago Legal Clinic (312) 726-2938

From: Frost, Brad
To: Pressnall, Chris
Cc: Nifong, Heather; Armitage, Julie
Subject: General III
Date: Wednesday, March 25, 2020 3:59:00 PM

Don't think you will, but in case you do get a call or e-mail, I called Keith Harley today and let him know that we are planning to move forward with a virtual hearing on General III. Keith was planning on informing SETF and others tomorrow or next day.

From: Pressnall, Chris
To: EXT Harley, Keith; Frost, Brad
Cc: Geertsma, Meleah; Nancy Loeb
Subject: RE: [External] General III Public Participation Request
Date: Thursday, March 19, 2020 12:16:30 PM

Hello Keith –

As you can imagine, we are exploring all options for this matter and others on the horizon. One thing that is strongly being considered is the holding virtual public hearings given that we do not know when people will be able to assemble in large groups and there are statutory deadlines that must be adhered to. Obviously, this does meet the goal of an in-person hearing but where we stand now, there just is not enough clarity as to how things will stand weeks and months from now. Delaying indefinitely is not an option given the aforementioned statutory deadlines.

Any additional thoughts you, your team and your clients have would be welcomed.

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Tuesday, March 17, 2020 3:34 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; Frost, Brad <Brad.Frost@Illinois.gov>
Cc: Geertsma, Meleah <mgeertsma@nrdc.org>; Nancy Loeb <n-loeb@northwestern.edu>
Subject: [External] General III Public Participation Request

Hi -

As you know, several organizations including SETF requested a public hearing and a written comment period related to the General III construction permit. On behalf of these organizations, I'm writing to inquire what effect coronavirus state/city policies will have on IL EPA's plans for the requested public hearing and a subsequent written comment period. I've spoken to SETF, NRDC and the Ban Petcoke Coalition members who still want an in-person public hearing and see no substitute for this as a venue for local residents to participate in this permitting process. At the same time, they see no alternative to delaying this until the current public health crisis is resolved and public gatherings are again safe for the community and IL EPA.

Thanks,

Keith Harley, Attorney for Southeast Environmental Task Force
Chicago Legal Clinic (312) 726-2938

From: EXT Harley, Keith
To: Pressnall, Chris; Frost, Brad
Cc: Geertsma, Meleah; Nancy Loeb
Subject: [External] General III Public Participation Request
Date: Tuesday, March 17, 2020 3:28:52 PM

Hi -

As you know, several organizations including SETF requested a public hearing and a written comment period related to the General III construction permit. On behalf of these organizations, I'm writing to inquire what effect coronavirus state/city policies will have on IL EPA's plans for the requested public hearing and a subsequent written comment period. I've spoken to SETF, NRDC and the Ban Petcoke Coalition members who still want an in-person public hearing and see no substitute for this as a venue for local residents to participate in this permitting process. At the same time, they see no alternative to delaying this until the current public health crisis is resolved and public gatherings are again safe for the community and IL EPA.

Thanks,

Keith Harley, Attorney for Southeast Environmental Task Force
Chicago Legal Clinic (312) 726-2938

From:	EXT Harley, Keith
To:	Pressnall, Chris
Cc:	Nancy Loeb; Geertsma, Meleah (mgeertsma@nrdc.org); Layman, Robb; Frost, Brad; Mohr, Kent; Bernoteit, Bob; Barria, German; Jones, Eric E.
Subject:	[External] General Iron aka GII LLC
Date:	Wednesday, March 11, 2020 12:54:36 PM

Hi -

Thank you for participating in our recent conversation about the active and proposed facilities located at 11600 S. Burley in Chicago.

I'm writing to follow up on our commitment to provide information about the General Iron's operations at its existing location. As we discussed, these operations are one basis for community concerns about the transfer of this business and its operations to 11600 S. Burley. More specifically, our clients are concerned that this business and its operations could be a source of poorly controlled shredder emissions, fugitive particulate matter and releases of auto shredder residue. Moreover, in the context of permitting, our clients are concerned that actual and potential emissions from the shredder and other operations at 11600 S. Burley are not well characterized, and do not form the basis for making fundamental permitting choices.

Part of this concern is based on inspection and enforcement activity which is occuring at the existing General Iron facility. I'm enclosing the results of a city inspection that took place on February 10, 2020 that identifies facility practices that are relevant to assessing actual shredder operations and emissions, the release of fugitive particulate matter, releases of auto shredder residue and the history of compliance at this facility.

Thank you for your attention to this matter and for taking this information into account as part of pending permitting transactions.

Keith Harley, Attorney for Southeast Environmental Task Force
(312) 726-2938

CHICAGO DEPARTMENT OF PUBLIC HEALTH ENVIRONMENTAL RESPONDED TO A CITIZEN?S COMPLAINT REGARDING ODORS AND AN EXPLOSION HEARD IN THE MORNING COMING FROM THE FACILITY AT 1909 N CLIFTON AVE, GENERAL IRON INDUSTRIES (GII, LLC). GII LLC OPERATES A RECYCLING FACILITY PURSUANT TO A CLASS IVB RECYCLING PERMIT (ENVREC1063430) ISSUED BY CDPH.WHILE CANVASSING THE AREA SURROUNDING GII, LLC ON FEBRUARY 10, 2020, ODORS WERE OBSERVED AT THE FOLLOWING LOCATIONS: HOME DEPOT (1232 W NORTH AVE) PARKING LOT, INTERSECTION OF THROOP ST WABANSIA AVE, AND INTERSECTION OF THROOP ST WABANSIA AVE. IT IS A PUNGENT ODOR OF SWEET METAL THAT BURNS MY NOSTRILS. I ALSO OBSERVED AN ODOR OF BURNING MATERIAL. THE SAME ODORS OF SWEET METAL WERE ALSO OBSERVED ONSITE.UNTREATED EMISSIONS WERE OBSERVED ESCAPING THE TOP AND THE SIDES OF THE SHREDDER. I ALSO OBSERVED SMOKE LEAVING THE SHREDDER AND TRAVELING THROUGH THE PROPERTY ACROSS FROM THE NORTH BRANCH CHICAGO RIVER. THE SHREDDER IS NOT AN ENCLOSED PIECE OF EQUIPMENT. IT DOES CONTAIN A HOOD TO CAPTURE THE EMISSIONS AND PROCESS THEM THROUGH A

REGENERATIVE THERMAL OXIDIZER (RTO) AND A WET SCRUBBER TO REMOVE VOLATILE ORGANIC COMPOUNDS (VOCS), HAZARDOUS AIR POLLUTANTS (HAPS), AND OTHER AIRBORNE SOLVENTS. BEING ABLE TO OBSERVE EMISSIONS ESCAPING THE SHREDDER LEADS ME TO BELIEVE THAT THE EQUIPMENT CAPTURING THE EMISSIONS IS INSUFFICIENT. CONSEQUENTLY, THIS DOES NOT ALLOW THE RECENTLY INSTALLED AIR POLLUTION CONTROL EQUIPMENT TO PROCESS THE EMISSIONS SINCE THEY ARE ESCAPING AT THE SHREDDER BEFORE THE TREATMENT PROCESS.AUTO FLUFF/AUTO SHREDDER RESIDUE WAS OBSERVED ON THE PROPERTY DIRECTLY SOUTHWEST AND ACROSS THE NORTH BRANCH CHICAGO RIVER. AUTO FLUFF IS A PRODUCT OF SHREDDING OPERATIONS AND IT CONSIST OF FINE PARTICLES OF GLASS, FIBERS, RUBBER, METAL, PLASTIC, DIRT, AND AUTOMOTIVE FLUIDS. FUGITIVE DUST WAS ALSO OBSERVED ONSITE WHEN WORKERS DISTURBED MATERIAL PILES AND MOVED MATERIALS TO AND FROM TRUCK TRAILERS. MISTING CANNONS WERE OBSERVED TO NOT BE IN OPERATION TO CONTROL AIRBORNE PARTICLES AT THE TIME OF THE INSPECTION. OBSERVING AUTO FLUFF IN THE OUTSIDE OF GII, LLC?S PROPERTY AND FUGITIVE DUST WITHOUT OPERATING MISTING CANNONS LEADS ME TO BELIEVE THAT REASONABLE MEASUREMENTS WERE NOT AND ARE NOT BEING TAKEN TO ENSURE DUST, DEBRIS, AND DIRT WON?T MIGRATE OFF SITE AND INTO THE PUBLIC WAY.I SPOKE TO JIM AND HE INFORMED ME THAT THERE WAS AN EXPLOSION IN THE SHREDDER DURING THE MORNING HOURS BETWEEN 7:30AM ? 7:40AM. HE SAID THIS IS A COMMON OCCURRENCE.A NOV CITATION #E0000***** WAS ISSUED FOR AIR POLLUTION PROHIBITED (11-4-730) AND HANDLING OF MATERIAL SUSCEPTIBLE TO BECOMING WINDBORNE (11-4-760[A]). A NOV CITATION #E0000***** WAS ISSUED FOR VIOLATING ANY CONDITION IMPOSED BY THE PERMIT (11-4-030[B]) SPECIAL CONDITION 46 WHICH REQUIRES THE PERMITTEE TO CONTROL AND SUPPRESS DUST AND OTHER MATERIALS TO PREVENT OFF-SITE MIGRATION AND NUISANCE IN CONNECTION WITH BUSINESS (7-28-080). THE HEARING DATE FOR THE CITATIONS WILL BE ON APRIL 30, 2020 AT 1:00 P.M. AT 400 W. SUPERIOR ST. THE CITATION WILL BE SERVED VIA US MAIL TO GENERAL IRON INDUSTRIES (GII, LLC) AGENT LISTED ON THE ILLINOIS SECRETARY OF STATE CORPORATION FILE DETAIL REPORT. THE AGENTS NAME AND ADDRESS ILLINOIS CORPORATION SERVICE C AT 801 ADLAI STEVENSON DRIVE, SPRINGFIELD, IL 62703.

On Mon, Jan 27, 2020 at 10:45 AM Harley, Keith <kharley@kentlaw.iit.edu> wrote:

> Hi -
>
> Thank you for participating in our conversation about the active and proposed facilities located at 11600 S. Burley in Chicago.
>
> I'm writing to follow up on our commitment to provide information about the General Iron's operations at its existing location. As we discussed, these operations are one basis for community concerns about the transfer of this business and its operations to 11600 S. Burley. More specifically, our clients are concerned that this business and its operations could be a source of poorly controlled shredder emissions, fugitive particulate matter and releases of auto shredder residue. Moreover, in the context of permitting, our clients are concerned that actual and potential emissions from the shredder and other operations at 11600 S. Burley are not well characterized, and do not form the basis for making

fundamental permitting choices.

Part of this concern is based on inspection and enforcement activity which is occuring at the existing General Iron facility. I'm attaching a packet which relates to this concern. The packet includes: 1. a Narrative Evaluation prepared by a Chicago Inspector on December 18, 2019; 2. a Narrative Evaluation prepared by a Chicago Inspector on December 23, 2019; and, 3. eight Chicago Notices of Violation issued based on observations that took place on 12/10/19, 12/16/19, 12/18/19 and 12/23/19. As you will see, City Inspectors consistently observed a failure to control and suppress dust to prevent off-site migration, auto fluff that "became scattered by the wind and migrated off-site", and releases of untreated shredder emissions that occurred despite the RTO and scrubber.

Again, thank you for meeting and for engaging the public health, environmental and environmental justice concerns we are expressing on behalf of our clients.

- Keith Harley, Attorney for Southeast Environmental Task Force

From: Geertsma, Meleah
To: EXT Harley, Keith; Pressnall, Chris
Cc: Nancy Loeb; Layman, Robb; Frost, Brad; Mohr, Kent; Bernoteit, Bob; Barria, German; Jones, Eric E.
Subject: [External] RE: General Iron aka GII LLC
Date: Monday, February 10, 2020 4:55:59 PM

All –

With our thanks again for engaging in a discussion around metals recyclers in environmental justice communities, I'm writing with additional follow-up on our commitment to provide information relevant to the various metals recycling permitting actions in Chicago.

First, we draw your attention to comments that our groups submitted to the Chicago Dept. of Public Health (CDPH) with regards to that agency's proposed new local regulations for large recycling facilities: https://www.chicago.gov/content/dam/city/depts/cdph/InspectionsandPermitting/Comment_NRDC_SETF_SSCBP_LVEJO_6-21-19.pdf.

The exhibits to the comments are available at this Dropbox link: https://www.dropbox.com/sh/0wh459ez9iv1lai/AABTdvjK5hxUFg1j5gG0BY6ha?dl=0

In particular, we would like to highlight the following sections:

1. The California study and comment text discussing its findings and other related sources of information on impacts, pages 2-6 (see page 2, Exhibit 2, for the full California study – the link in the footnote is now dead, but the pdf is available via the Dropbox link)
2. The discussion of air emissions in particular, including the Houston study (pages 3-4); grinding emissions and other small facilities emissions (page 15, fnt 43); and the Minneapolis Northern Metals example of dust from ASR processing (page 16, fnt 46). We also note that the actions taken against Northern Metals by the Minnesota Pollution Control Agency contain a number of cautions regarding metals recycling, and we encourage IEPA to familiarize itself with these actions, to the extent the staff has not yet reviewed.
3. The auto shredder residue (ASR) sections at pages 4 and 19-22.

We also are sending our supplemental comments to CDPH on torch cutting and ASR (comments and exhibits are available at this link): https://www.dropbox.com/sh/338rqxbccdxkmx2/AAD99r9AJXYt-xhFeTH_xULza?dl=0

Finally, we are sharing the link to CDPH's inspections database, where as we mentioned on our call IEPA can find descriptions of activities and conditions at the 11600 S Burley facilities, including chronic paving problems and evidence of metallic fines and ASR distributed over the site (there is a small search window at the upper left corner): https://data.cityofchicago.org/widgets/i9rk-duva

Again we thank you for your continued attention to this important issue; please do not hesitate to reach out to our attorney group if you have any questions or comments.

Best,
Meleah

MELEAH GEERTSMA
Senior Attorney, Environmental Justice

NATURAL RESOURCES
DEFENSE COUNCIL
20 N. WACKER DRIVE, SUITE 1600
CHICAGO, IL 60606
T 312.651.7904
F 312.332.1908
mgeertsma@NRDC.ORG
NRDC.ORG

From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Monday, January 27, 2020 10:46 AM
To: Pressnall, Chris <Chris.Pressnall@illinois.gov>
Cc: Nancy Loeb <n-loeb@northwestern.edu>; Geertsma, Meleah <mgeertsma@nrdc.org>; Layman, Robb <Robb.Layman@illinois.gov>; Frost, Brad <Brad.Frost@illinois.gov>; Mohr, Kent <Kent.Mohr@illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@illinois.gov>; Barria, German <German.Barria@illinois.gov>; Jones, Eric E. <Eric.E.Jones@illinois.gov>
Subject: General Iron aka GII LLC

Hi -

Thank you for participating in our conversation about the active and proposed facilities located at 11600 S. Burley in Chicago.

I'm writing to follow up on our commitment to provide information about the General Iron's operations at its existing location. As we discussed, these operations are one basis for community concerns about the transfer of this business and its operations to 11600 S. Burley. More specifically, our clients are concerned that this business and its operations could be a source of poorly controlled shredder emissions, fugitive particulate matter and releases of auto shredder residue. Moreover, in the context of permitting, our clients are concerned that actual and potential emissions from the shredder and other operations at 11600 S. Burley are not well characterized, and do not form the basis for making fundamental permitting choices.

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Again, thank you for meeting and for engaging the public health, environmental and environmental justice concerns we are expressing on behalf of our clients.

- Keith Harley, Attorney for Southeast Environmental Task Force

From: Pressnall, Chris
To: Frost, Brad
Subject: FW: General Iron / South Chicago Property Management
Date: Thursday, January 23, 2020 10:01:39 AM

See below. I just chatted with her and will brief you on the discussion.

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Maria Fattore-Lazzaroni <Maria.Fattore-Lazzaroni@cityofchicago.org>
Sent: Thursday, January 23, 2020 10:01 AM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>
Subject: [External] General Iron / South Chicago Property Management

Hi Chris,

It was a pleasure speaking to you this morning. Thank you for all the information you provided to us about the violations that South Chicago Property Management has.

If there is anything you need from us please don't hesitate to give us a call or email.

Thank you for your assistance,

Maria Fattore-Lazzaroni

Chief of Staff

10th Ward | Alderwoman Susan Sadlowski-Garza

City of Chicago

10th Ward Public Service Office

10500 S Ewing Avenue, Fl 1

Office: 773-768-8138

Fax: 773-768-8176

maria.fattore-lazzaroni@cityofchicago.org

From: Geertsma, Meleah
To: Pressnall, Chris; EXT Harley, Keith; Nancy Loeb; Layman, Robb; Frost, Brad; Mohr, Kent; Bernoteit, Bob; Barria, German; Jones, Eric E.
Subject: [External] Re: 11600 S Burley
Date: Wednesday, January 22, 2020 4:53:02 PM

Thanks again for a very helpful call today - we appreciate all the time taken by multiple IEPA staff. As discussed, I'm sharing a link to CDPH's environmental inspections database, where you can find entries for the 11600 S Burley facilities (to search, click on the very small magnifying glass in the upper left corner):

https://data.cityofchicago.org/widgets/i9rk-duva

Best,
Meleah

From: Pressnall, Chris
Sent: Wednesday, January 22, 2020 2:15 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; EXT Harley, Keith <kharley@kentlaw.iit.edu>; Nancy Loeb <n-loeb@northwestern.edu>; Geertsma, Meleah <mgeertsma@nrdc.org>; Layman, Robb <Robb.Layman@Illinois.gov>; Frost, Brad <Brad.Frost@Illinois.gov>; Mohr, Kent <Kent.Mohr@Illinois.gov>; Bernoteit, Bob <Bob.Bernoteit@Illinois.gov>; Barria, German <German.Barria@Illinois.gov>; Jones, Eric E. <Eric.E.Jones@Illinois.gov>
Subject: 11600 S Burley
When: Wednesday, January 22, 2020 3:00 PM-4:00 PM.
Where: Telephone

-- Do not delete or change any of the following text. --

To join the audio portion of the Personal Conference meeting

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From: Pressnall, Chris
To: EXT Harley, Keith
Cc: Geertsma, Meleah; Nancy Loeb; Daryl Grable; Mohr, Kent; Layman, Robb; Frost, Brad
Subject: RE: [External] Re: Environmental Justice Notification: Napuck Salvage of Waupaca LLC, Chicago
Date: Thursday, January 16, 2020 8:32:20 AM

Good morning Keith –

Thanks for reaching out. I have checked with the Illinois EPA folks working on this issue and we have availability this afternoon. Is there a time that works for you all?

Chris Pressnall
Environmental Justice Coordinator
Illinois EPA

(217) 524-1284
(217) 785-8346 (fax)

chris.pressnall@illinois.gov

From: Harley, Keith <kharley@kentlaw.iit.edu>
Sent: Wednesday, January 15, 2020 3:20 PM
To: Pressnall, Chris <Chris.Pressnall@Illinois.gov>; Lenkart, Maggie <Maggie.Lenkart@illinois.gov>
Cc: Geertsma, Meleah <mgeertsma@nrdc.org>; Nancy Loeb <n-loeb@northwestern.edu>; Daryl Grable <DGrable@clclaw.org>
Subject: [External] Re: Environmental Justice Notification: Napuck Salvage of Waupaca LLC, Chicago

Hi Chris and Maggie -

Please be advised that I represent the Southeast Environmental Task Force which, as you know, has a strong interest in the cluster of existing and proposed facilities located at 11600 S. Burley. The Natural Resources Defense Council (Meleah Geertsma) and Northwestern Law School's Environmental Clinic (Nancy Loeb, on behalf of the Southeast Side Coalition to Ban Petcoke) are working with SETF on this matter.

I'm writing to request your assistance in facilitating a conversation between our organizations and the IL EPA staff members who are now working on permitting and other matters related to the 11600 S. Burley facilities, which include Napuck Salvage, Reserve Marine Terminals, South Chicago Recycling, RSR Partners/Regency Technologies, General III LLC and, perhaps, Calumet Transload. Based on our review of IL EPA documents we acquired using FOIA, it appears that IL EPA concludes that these facilities constitute a single source for purposes of permitting activities pursuant to the Clean Air Act. Despite this, the agency appears to be conducting separate permitting activities for Napuck and, perhaps, General III. We would like to understand how the agency views the air permitting protocols for this cluster of facilities which traditionally have been treated separately but which now appear to be classified as a single source. Our goal in making this request is to gain an understanding that will help avoid misunderstanding, miscommunication and unnecessary conflict.

As you know, this matter triggers the IL EPA's environmental justice responsibilities. My request is also consistent with the invitation Director Kim offered during a phone call with NGOs earlier today, encouraging public interest organizations to communicate early and often with Il EPA.

In this spirit, I look forward to your response and to speaking with you and other relevant IL EPA staff members as soon as possible.

- Keith Harley (312) 726-2938

On Fri, Jan 10, 2020 at 11:50 AM Lenkart, Maggie <Maggie.Lenkart@illinois.gov> wrote:

> Hello,
>
> Thank you for electing to receive e-notifications.
>
> Please find the attached Environmental Justice Notification Letter and Distribution List for **Napuck Salvage of Waupaca LLC**; Reference **12020006.**
>
> The facility is located at **11600 S. Burley Avenue** in **Chicago.**
>
> Sincerely,
>
> Maggie Lenkart
> Illinois Environmental Protection Agency
> Environmental Justice Intern
> 217/558-2693
> Maggie.Lenkart@illinois.gov
> Hours: Tues. – Fri., 8am-1pm
>
>