BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC., a Colorado Corporation,	)	
Petitioner,	)	
v.	)	AS 08-6 (Adjusted Standard - PIMW)
ILLINOIS ENVIRONMENTAL PROTECTION AGENCY,	)	
Respondent.	)	

NOTICE OF FILING

To: Illinois Environmental Protection Agency
Division of Legal Counsel
c/o Kyle Davis, Esq.
1021 North Grand Avenue East
P.O. Box 19276
Springfield, Illinois 62794-9276

PLEASE TAKE NOTICE that I filed with the Office of the Clerk of the Pollution Control Board the foregoing Motion to File *Instanter* Amended Petition for Adjusted Standard of BioMedical Technology Solutions, Inc., a copy of which is herewith served upon you.

Dated: January 7, 2008

Jason B. Elster

Neal H. Weinfield
Jason B. Elster
GREENBERG TRAURIG, LLP
Firm No. 36511
77 West Wacker Drive, Suite 2500
Chicago, Illinois 60601
312-456-8400 (Telephone)
312-456-8435 (Facsimile)
weinfieldn@gtlaw.com
elsterj@gtlaw.com

BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC., a Colorado Corporation,	)	
Petitioner,	)	
v.	)	AS 08-6
	)	(Adjusted Standard - PIMW)
ILLINOIS ENVIRONMENTAL PROTECTION AGENCY,	)	
Respondent.	)	

CERTIFICATE OF SERVICE

I, Jason B. Elster, an attorney, certify that I have caused a true and correct copy of the foregoing MOTION TO FILE *INSTANTER* AMENDED PETITION FOR ADJUSTED STANDARD and NOTICE OF FILING to be served before 5:00 p.m. via First Class Express Mail, overnight delivery, postage pre-paid, on the following:

Illinois Environmental Protection Agency
Division of Legal Counsel
c/o Kyle Davis, Esq.
1021 North Grand Avenue East
P.O. Box 19276
Springfield, Illinois 62794-9276

Dated: January 7, 2008

Jason B. Elster

BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC., a Colorado Corporation, Petitioner,	)	
v.	)	AS 08-6 (Adjusted Standard - PIMW)
ILLINOIS ENVIRONMENTAL PROTECTION AGENCY, Respondent.	)	

MOTION TO FILE *INSTANTER*
AMENDED PETITION FOR ADJUSTED STANDARD

Petitioner BioMedical Technology Solutions, Inc. ("BMTS"), by and through its undersigned attorneys, hereby files *instanter* its Amended Petition for Adjusted Standard pursuant to the Illinois Pollution Control Board's (the "Board") order of December 20, 2007 (the "Order"), and states as follows:

1. On November 28, 2007, BMTS filed a petition for a statewide adjusted standard of 35 Ill. Adm. Code 1422.Appendix A, Table B (the "Petition"). Shortly thereafter, BMTS filed the proof of timely publication of notice of the Petition's filing, as well as certificates of publication stating that notice was published in both the *Chicago Tribune* and the *State Journal Register* on December 6, 2007. *See* Order at 1.

2. On December 20, 2007, the Board entered the Order accepting the Petition and "finding that it meets the content requirements of Section 104.406 of the [Environmental Protection] Act." Order at 1.

3. Because of a discrepancy in preferred nomenclature, the Board directed BMTS to clarify which designation of the same indicator microorganism, *Bacilllus atrophaeus* (ATCC 9372) or *Bacillus subtilis* var *niger* (ATCC 9372), that BMTS is

requesting be substituted in 35 Ill. Adm. Code 1422.Appendix A, Table B by filing an amended petition on or before January 7, 2008. *See* Order at 2.

4. While both designations refer to the same microorganism, the designation *Bacillus atrophaeus* (ATCC 9372) is preferable to *Bacillus subtilis* var *niger* (ATCC 9372).

5. Therefore, pursuant to the Board's Order, BMTS respectfully submits the following substantive amendment to its Petition for Adjusted Standard:

> **IX. Narrative Description of the Proposed Adjusted Standard**
>
> 35 IAC 104.406(f) requires that the Petition provide a narrative description of the proposed adjusted standard as well as proposed language for a Board order that would impose the standard. The Adjusted Standard would simply involve formally recognizing the appropriateness of both the Certified and Chemical Indicators in Table B of 35 IAC 1422 for the validation of dry heat and chemical sterilization processes, respectively. The proposed language for a Board order would involve amending Item 1 of Table B from "1. Bacillus subtilis (ATCC 19659)" to "1. Bacillus subtilis (ATCC 19659) or Bacillus atrophaeus (ATCC 9372)". This language recognizes the recent change in classification of this particular isolate of Bacillus subtilis.
>
> 35 IAC 104.406(f) further requires the Petition to describe efforts necessary to achieve this proposed standard and the corresponding costs must also be presented. BMTS has already completed an Initial Efficacy Test demonstrating a 6 $\log_{10}$ reduction of *B. atrophaeus* (ATCC 9372) under varying load conditions. Thus, no additional efforts are required by the Petitioner if the proposed standard is adopted.

Amended Petition for Adjusted Standard, attached hereto as **Exhibit 1**.[1]

WHEREFORE, Petitioner BioMedical Technology Solutions, Inc. hereby files *instanter* its Amended Petition for Adjusted Standard and respectfully requests that this Board, pursuant to its authority under Section 35 of the Act and the Board's regulations

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[1] Per the Board's Order, the Amended Petition clarifies that BMTS is requesting that Bacillus *atrophaeus* (ATCC 9372) be substituted into 35 Ill. Adm. Code 1422.Appendix A, Table B. Aside from revisions to

under 35 IAC 104, grant BMTS an Adjusted Standard from the provisions of 35 IAC 1422.Table B recognizing *Bacillus atrophaeus* (ATCC 9372) as the most appropriate biological indicator organism for the validation of dry heat sterilization technologies, and grant BMTS any other relief the Board deems just.

Respectfully Submitted,

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC.

By: _____
One of Its Attorneys

Dated: January 7, 2008

Neal H. Weinfield
Jason B. Elster
GREENBERG TRAURIG, LLP
Firm No. 36511
77 West Wacker Drive, Suite 2500
Chicago, Illinois 60601
312-456-8400 (Telephone)
312-456-8435 (Facsimile)
weinfieldn@gtlaw.com
elsterj@gtlaw.com

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ensure consistency, the above-excerpted language is the only substantive change to the Petition. References to any exhibits in the Amended Petition are identical to those submitted with the Petition.

Exhibit 1

EXHIBIT 1

BEFORE THE ILLINOIS POLLUTION CONTROL BOARD

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC., a Colorado Corporation,	)	
Petitioner,	)	
v.	)	AS 08-6
	)	(Adjusted Standard - PIMW)
ILLINOIS ENVIRONMENTAL PROTECTION AGENCY,	)	
Respondent.	)	

AMENDED PETITION FOR ADJUSTED STANDARD

Petitioner BioMedical Technology Solutions, Inc. ("BMTS"), by and through its undersigned attorneys, hereby petitions the Illinois Pollution Control Board (the "Board") for an Adjusted Standard from a provision of 35 IAC 1422. BMTS, which manufactures a countertop medical waste treatment device, the Demolizer® technology, seeks a technology-specific Adjusted Standard from 35 IAC 1422, which requires the use of a particular microorganism, *Bacillus subtilis* (ATCC 19659), to determine the initial efficacy of the technology. In conducting the initial efficacy test required under the Board's regulations, BMTS seeks permission to use a subspecies of *Bacillus subtilis* commonly referred to as *Bacillus atrophaeus* (recently reclassified from *Bacillus subtilis* var. *niger*) that is the preferred and most appropriate biological indicator organism for the validation of dry heat sterilization processes. The proposed Adjusted Standard exhibits superior dry heat resistance and can be distinguished from the generic *Bacillus subtilis* primarily through differences in color or pigmentation response to certain media. Importantly, the proposed Adjusted Standard is nationally and internationally recognized by microbiologists and governing standards organizations as the preferred and most

appropriate biological indicator organism for the validation of dry heat sterilization technologies, the underlying technology of the Demolizer® system. Further, it is the only *Bacillus subtilis* organism available in a tested, certified carrier form. This petition for an Adjusted Standard (the "Petition") is brought pursuant to Section 35 of the Illinois Environmental Protection Act (the "Act"), 415 ILL. COMP. STAT. 5/35, and Part 104 of Chapter 35 of the Illinois Administrative Code, 35 IAC 104. In support of its Petition, BMTS states as follows:

I. Introduction

BMTS manufactures medical waste treatment devices that, employing Demolizer® technology, destroy potentially infectious microorganisms through the use of dry-heat. Prior to conducting a treatment cycle, medical wastes, including "sharps," are placed into the device, which is approximately the size of the common microwave. Through the course of a treatment cycle, the waste is sterilized and rendered into a non-recognizable solid waste that can then be disposed of as any other refuse. Businesses that generate relatively low volumes of medical waste such as nursing homes, medical, dental and veterinary offices, and pharmacies can use BMTS devices on-site as a safe and efficient method of treating and disposing these materials. It also avoids having to ship medical waste off-site for treatment and disposal. In fact, BMTS devices can be found throughout the United States and BMTS has begun marketing the technology world-wide. The technology is formally approved or meets statutory requirements in 46 states.

In order to sell its devices in Illinois, the Board's regulations require that BMTS demonstrate that its Demolizer® technology is effective in eliminating potentially harmful microorganisms by performing an Initial Efficacy Test ("IET"). The purpose of

an IET is to validate the sterilization efficacy of a treatment device. Currently, the Board's regulations specify that a particular microorganism, ATCC 19659 *Bacillus subtilis* ("Chemical Indicator"), must be used in the IET. However, ATCC 19659[1] is not commercially available in a certified form, and the procedure for growing and certifying ATCC 19659 to the same standards achieved using the most appropriate *Bacillus subtilis* certified microorganism could take close to two and a half years and cost upwards of $320,000 - which would require that BMTS sell numerous additional Demolizer® units just to cover these costs. [Exhibit J]

The alternative to ATCC 19659 is a variant of the same species, ATCC 9372 *Bacillus atrophaeus*, also known as *Bacillus subtilis* var. *niger* ("Certified Indicator" or "Dry Heat Indicator"), which is commercially available in a certified form and is the scientifically-recognized standard in 46 states as well as the international community for the validation of dry heat sterilization processes due to its superior growth and heat resistance properties.

The Certified and Chemical Indicator organisms are very similar organisms. The Chemical Indicator, *Bacillus subtilis,* is commonly used for the validation of chemical disinfectants and is, therefore, most appropriate for the validation of alternative technologies employing a chemical sterilization agent. The Chemical Indicator is not recognized by international standards organizations or in the scientific literature for the validation of dry heat sterilization technologies.

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[1] The American Type Culture Collection, commonly known as the ATCC, is an international nonprofit organization that provides biological products and technical services to the scientific community. The biological samples deposited with the ATCC are used internationally as the reference standard for biological materials. *See* ATCC, http://www.atcc.org/About/AboutATCC.cfm (last visited June 20, 2007).

The Certified Indicator, *Bacillus subtilis* var. *niger* (reclassified as *Bacillus atrophaeus* in 2004), exhibits enhanced resistance in dry heat applications compared to a generic *Bacillus subtilis* organism, typical of the Chemical Indicator. In a definitive study conducted by Gurney and Quesnel, the dry heat resistance performance of a generic *Bacillus subtilis* and *Bacillus subtilis* var. *niger* were compared at dry heat treatment temperatures ranging form 140 to 170°C. At all temperatures, *Bacillus subtilis* var *niger* demonstrated superior dry heat resistance. The study definitively found that "the var. *niger* strain is clearly the organism of choice as an indicator of dry heat sterilization..." *See* Group Exhibit H, Gurney, T.R. & Quesnel, L.B., *Thermal Activation and Dry-heat Inactivation of Spores of Bacilus subtilis MD2 and Bacillus subtilis var. niger,* J. APPLIED BACTERIOLOGY, 48, 231-247 (1980).

Based on these findings and the preponderance of evidence in the scientific community, the Certified Indicator has been universally adopted as the preferred and most appropriate biological indicator organism for the validation of dry heat sterilization. The following international standards organizations specify the proposed Adjusted Standard, *Bacillus subtilis* var. *niger* (ATCC 9372) as the preferred biological indicator organism for dry-heat processes. Each standards organization convenes an expert panel of microbiologists and specialists in sterilization assurance that review the body of scientific evidence to substantiate their recommendations and published standards. Manufacturers of certified biological indicators must then test each production lot against these standards meeting stringent performance requirements for resistance as measured in D-values and z-values.[2]

[2] The D-value is the time required to destroy 90% (1 log10 reduction) of cells under specified conditions while the z-value is the increase in temperature required to reduce the thermal death time by a factor of 10.

1. **US Pharmacopoeia**. USP28-NF23 USP. Monographs: Biological Indicator for Dry-Heat Sterilization, Paper Carrier; Rockville, MD; 2005.
2. **FDA**. Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities. Infection Control Devices Branch, Division of General and Restorative Devices (March 1993).
3. **FDA**. Premarket Notifications [510(k)] for Biological Indicators Intended to Monitor Sterilizers Used in Health Care Facilities; Draft Guidance for Industry and FDA Reviewers; U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, Infection Control Devices Branch (March 2001).
4. **British Pharmacopoeia Commission**. Methods of sterilization. London, UK: British Pharmacopoeia Commission; British Pharmacopoeia Appendix XVIII (2003).
5. **European Pharmacopoeia Commission**. Biological indicators of sterilization. Strasbourg, France: European Pharmacopoeia Commission; European Pharmacopoeia EP 5.1.2 (1997).
6. **Japanese Pharmacopoeia**. JP14e.partII.15 JP. Terminal Sterilization and Sterilization Indicators.
7. **ISO and ANSI.** Sterilization of health care products – Biological indicators; Part 4: Biological indicators for dry heat processes. Geneva (Switzerland): International Organization for Standardization/ANSI; ISO 11138-4:2006.

BMTS is requesting relief from the Board's requirement of using the Chemical Indicator in the IET and seeks permission to demonstrate the effectiveness of its devices by conducting the IET using the Certified Indicator. Currently, out of the 46 states that have approved the Demolizer® or for which the Demolizer® meets statutory requirements, Illinois is the only state that has required use of the Chemical Indicator in the IET for the Demolizer® technology rather than the Certified or Dry Heat Indicator for the validation of the dry heat sterilization technology.

II. Regulatory Requirements For Conducting An Initial Efficacy Test

35 IAC 104.406(a) requires that the Petition contain a statement describing the regulation from which an Adjusted Standard is sought. Pursuant to 35 IAC 1422.124, "[t]he manufacturer, owner or operator of a treatment unit shall conduct an Initial Efficacy Test, pursuant to Appendix A of this Part, for each model prior to its operation." 35 IAC 1422.124(a). The IET is a scientifically-controlled demonstration that the treatment unit does in fact eliminate the infectious potential from potentially infectious medical waste. Section 1422.Appendix A ("Appendix A"), titled Initial Efficacy Test Procedures, sets forth the procedures for conducting an IET for three classes of treatment units. *See* 35 IAC 1422.Appendix A.

The IET procedure that applies to BMTS involves placing carriers of indicator microorganisms inside the device, conducting a treatment cycle, and then measuring the number of indicator microorganisms that remain viable. *See id.* Appendix A identifies three indicator microorganisms to be used in an IET for treatment units that use thermal treatment and maintain the integrity of the container of indicator microorganisms (*e.g.*, incinerators, autoclaves, and radiation-based processes): 1) *Bacillus subtilis* (ATCC 19659); 2) *Bacillus stearothermophilus* (ATCC 7953); and 3) *Bacillus pumilus* (ATCC 27142). *See* 35 IAC 1422.Table B ("Table B"). The Agency has agreed that the second and third indicator microorganisms are not scientifically appropriate for verifying the efficacy of the Demolizer® system because they are not recognized for the validation of dry heat systems. The effective date of the regulation is March 1993.

III. Statement of Applicability

As required by 35 IAC 104.406(b), the regulation of general applicability was not promulgated to implement, in whole or in part, the requirements of the CWA (33 USC 1251 et seq.), Safe Drinking Water Act (42 USC 7401 et seq.), or the State programs concerning RCRA, UIC, or NPDES [415 ILCS 5/28.1].

IV. Level of Justification

35 IAC 104.406(c) requires the Petitioner to state whether a specific level of justification is provided in the regulation of general applicability. 35 IAC 1422 does not specify a level of justification or other requirements.

V. Description of the Nature of the Petitioner's Activity

35 IAC 104.406(d) requires a complete and concise description of the nature of BMTS' activity that is the subject of the proposed Adjusted Standard. BMTS was incorporated in 2005 as a Colorado corporation. BMTS produces medical waste treatment devices that employ Demolizer® technology, which is based on a dry-heat treatment process that was developed and broadly approved throughout the United States in the mid-1990s. The technology heats one gallon of medical waste to a minimum treatment temperature of 350°F for a minimum of 90 minutes. The Demolizer® technology has demonstrated broad-scale efficacy under these treatment conditions through studies at Stanford University, Kansas State University, and various private laboratories. BMTS has customers in almost every state and has begun marketing the technology world-wide. Further, the temperature profile completely destroys sharps waste through a slow-melting of the plastic components of used syringes. The resulting

melted mass is further contained in the bottom of the metal collector for final disposal as ordinary solid waste.

A. BMTS' Initial Efficacy Test Using the Certified Indicator

In 2006, BMTS commissioned Dr. James Marsden, Regent's Distinguished Professor at Kansas State University, to conduct an initial efficacy test for its updated Demolizer® technology that could be used to secure regulatory approval both in the United States and internationally (the "KSU Efficacy Test"). In selecting an appropriate indicator microorganism, Dr. Marsden conducted a comprehensive review of the scientific literature prior to initiating the efficacy trial.

In his preparations for the KSU Efficacy Test, Dr. Marsden discovered that the Chemical Indicator was not commercially available in a certified spore carrier form. However, the scientifically similar Certified Indicator, which is the industry standard for validating dry-heat sterilization technologies due to superior heat resistance, was readily available from multiple certified manufacturers including STERIS Corporation, NAMSA, Raven Laboratories, STS, and Charles River Laboratories, to name a few. Through his literature review, Dr. Marsden concluded that the Chemical and Certified Indicators are essentially equivalent with primary differentiation based on pigmentation response to certain media. In fact, over 99.8% of their genetic material is *identical* - meaning that, but for their color, the Chemical and Certified Indicators are indistinguishable.[3]

Most importantly, Dr. Marsden determined that the international scientific community, including many of the world's most prestigious standards organizations, recognizes the Certified Indicator as the preferred and most appropriate biological

[3] *See* Group Exhibit H, *infra*, K.S. Blackwood, C.Y. Tureene, D. Harmsen, and A.M. Kabini,, *Reassessment of Sequence-Based Targets for the Identification Bacillus Species*, J. CLINICAL MICROBIOLOGY, 42, No. 2 (2004).

indicator for the validation of dry heat processes. As cited in the previously, *Bacillus subtilis* var. *niger,* the Certified Indicator, exhibits enhanced resistance in dry heat applications compared to a generic *Bacillus subtilis* organism, typical of the Chemical Indicator.

Therefore, it was the recommendation of Dr. Marsden, consistent with the overwhelming body of scientific literature, to use the commercially available Certified Indicator in the KSU Efficacy Test. This approach poses the most rigorous challenge for the Demolizer® technology and relies on the use of tested and standardized indicator spore carriers.

The results from the KSU Efficacy Test conclusively established that the Demolizer® technology is an effective sterilization treatment for potential infectious medical waste. Since complete elimination or destruction of all forms of microbial life is difficult to prove, sterilization is usually expressed as a probability function in terms of the number of microorganisms surviving a particular treatment process. Under the Board's regulations, a valid sterilization process must demonstrate a one-millionth survival probability in the indicator microorganism population.[4] The Demolizer® devices used in the KSU Efficacy Test unequivocally demonstrated their ability to meet Illinois' requirements for sterilization devices.

B. Historical Classification and Subsequent Sub-Classification of the *Bacillus Subtilis* Species

The following provides a discussion of the subspecies reclassification of the *Bacillus* genus that affects *Bacillus subtilis* organisms.

[4] The Board's regulations express this probability function is a 6 Log_{10} reduction, *i.e.*, a 99.9999% reduction in microbial life.

Until 1989, the scientific community recognized the Chemical and Certified Indicators as members of the *Bacillus* family commonly referred to as *Bacillus subtilis*. Migula first described the species now know as *Bacillus subtilis* in 1900. *See* Migula, W., *System der Bakterien*, vol. 2. JENA: GUSTAV FISCHER (1990). In 1952, Smith *et al.* noted that certain strains of *Bacillus subtilis* produced different colored pigments when exposed to varying culture conditions, but otherwise found no other discriminatory property between the strains other than pigmentation. *See* Smith, N.R., Gordon, R. E. & Clark, F.E., *Aerobic Spore-forming Bacteria*, AGRICULTURE MONOGRAPH NO. 16, Washington, DC: United States Department of Agriculture (1952). In that same work, Smith *et al.* allocated certain strains into a subspecies variety called *Bacillus subtilis* var. *niger*. *See id.*

However, in 1973, these different varieties were once again subsumed into the broader species designation *Bacillus subtilis* through the work of Gordon *et al.* due to the lack of differentiation between varieties. *See* Gordon, R.E., Haynes, W.C. & Pang, C. H.-N., *The Genus Bacillus*, AGRICULTURE HANDBOOK NO. 427, Washington, DC: United States Department of Agriculture (1973). In 1989, Nakamura re-examined the pigment-producing strains of *Bacillus subtilis* and, just like Smith *et al.*, once again differentiated certain subspecies based on pigmentation. *See* Group Exhibit H, *infra*, Nakamura, L.K., *Taxonomic Relationship of Black-Pigmented* Bacillus Subtilis *Strains and a Proposal for* Bacillus Atrophaeus *sp. nov.*, INT. J. SYST. BACTERIOLOGY 39, 295-300 (1989).

This time, Nakamura created a new subspecies designation, *Bacillus atrophaeus*, which included 21 of the 25 strains that had previously been designated as *Bacillus subtilis* var. *niger*. *See id.* Henceforth, the Certified Indicator belonged to the subspecies

atrophaeus while the Chemical Indicator remained part of the subspecies *subtilis*. In making this distinction between strains, Nakamura noted that the species descriptions of *Bacillus subtilis* and *Bacillus atrophaeus* are not affected by the re-classification because, "except for the colour of the soluble pigment, all of the strains were indistinguishable by the standard characterization method; *i.e.* they exhibited the traits typical of *B. subtilis*." *Id.*; *see also* Fritze, D. and Pukall, R., *Reclassification of Bioindicator Strains* Bacillus Subtilis *DSM 675 and* Bacillus Subtilis *DSM 2277 as* Bacillus Atrophaeus, INT'L. J. SYSTEMATIC EVOLUTIONARY MICROBIOLOGY, 51, 35-37 (2001).

Since Nakamura's 1989 re-classification of *Bacillus subtilis* strains, the scientific community has consistently and unanimously found that members of the *Bacillus subtilis* and *Bacillus atrophaeus* are phenotypically identical except for color. *See generally*, Group Exhibit H, *infra*.

C. BMTS' Regulatory Approval Efforts

As part of the KSU Efficacy Test, extensive trials were conducted on the updated Demolizer® technology utilizing an array of organisms under varying conditions as required by the Illinois statutes and other state agencies across the United States. These results have been exhaustively reviewed by many of the states that formally approve such technologies and resulted in the issuance of technology approval letters. Only three states specifically identify the Chemical Indicator in their regulations for use in validation procedures: Arizona, Illinois, and Delaware. In fact, both Arizona and Delaware have reviewed the KSU Efficacy Test that used the Certified Indicator and issued approval for the technology based on its findings. To date, BMTS' Demolizer® technology is either approved or meets statutory requirements in 46 states. Historically, the technology has

been reviewed favorably by over 75 federal, state, and local agencies, and it meets statutory requirements for treatment across the United States and throughout the international community. Exhibit I contains regulatory approval documentation from select states, including the States of Arizona and Delaware, which have accepted the Certified Indicator as equivalent to the Chemical Indicator. This information has been previously provided to the Illinois Bureau of Land in September 2007 in support of the Agency's review of this petition.

In mid-October 2006, BMTS contacted the Illinois Environmental Protection Agency (the "Agency") to request that the Agency consider a continuous monitoring system as an alternative to biological testing consistent with the provisions of 35 IAC 1422.125(a)(3).[5] After speaking with an Agency representative, BMTS submitted a formal request that included the KSU Efficacy Test results on October 19, 2006. Over the next few months, BMTS periodically contacted the Agency to check on the status of its request and was told that a response would be issuing shortly. In January 2007, BMTS received a formal response from the Agency stating that, in the Agency's opinion, the KSU Efficacy Test did not conform with the IET requirements. A true and correct copy of the Agency's January 5, 2007 Letter is attached hereto as Exhibit A.

After receiving the Agency's January 5, 2007 letter, BMTS agreed to provide the Agency with additional information to resolve the issue regarding the IET, which was transmitted on January 10, 2007. A true and correct copy of BMTS' January 10, 2007 Correspondence is attached hereto as Exhibit B. Over the next four months, BMTS periodically contacted the Agency to inquire as to its review of the additional information

[5] Formal approval from the Agency is required in order for a manufacture like BMTS to use a continuous monitoring approach to periodic verification initiatives.

BMTS provided. On May 7, 2007, BMTS received a response from the Agency that reiterated its prior position.[6] A true and correct copy of the Agency's April 4, 2007 Letter is attached hereto as Exhibit C. The Agency's representative referred BMTS to Agency attorney Bill Ingersoll, who in turn referred BMTS to the Agency Attorney, Kyle Davis.

From May 8, 2007 through early June 2007, BMTS exchanged correspondence with Mr. Ingersoll regarding the IET. A true and correct copy of the e-mail correspondence between BMTS and Mr. Ingersoll is attached hereto as Exhibit D. Mr. Ingersoll recognized that the Chemical Indicator was not commercially available.[7] Even so, Mr. Ingersoll stated that "it seems that we are unable to help you . . ." *See* Exhibit D. Pursuant to the suggestion of Mr. Ingersoll, BMTS filed a Variance Petition on or about June 24, 2007. (The Variance Petition was subsequently dismissed on July 26, 2007).

On August 24, 2007, BMTS and IEPA and Agency Attorney Kyle Davis, discussed concerns related to the pending Variance Petition. Dr. Marsden participated in this teleconference to try to answer specific technical questions on the appropriateness of the use of the Certified Indicator in the KSU Efficacy Study. As an outcome of this conference, BMTS agreed to provide additional information supporting the assertion that the Certified Indicator is the preferred and most appropriate biological indicator organism for the validation of dry heat sterilization processes.

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[6] Although the Agency's letter was dated April 4, 2007, which appears in a different type-font than the rest of the letter, BMTS received the letter on May 7, 2007.

[7] The Chemical Indicator cannot be purchased in a certified form. However, it is available in freeze-dried form, which would require the purchaser to grow a viable population. However, this method necessitates that the purchaser conduct rigorous testing to certify that the custom-grown population has the proper resistance properties to validate a treatment process. In most cases, the purchaser will have to grow and test several populations in order to certify a custom-grown population.

Dr. Daniel Y.C. Fung, an internationally known food, environmental and public health microbiologist, and authority in the field of sterility control, reviewed the body of scientific literature and provided an assessment on the appropriateness on the use of the proposed Adjusted Standard for the validation of the Demolizer® technology. Specifically, Dr. Fung concludes:

> "Based on the overwhelming evidence, it is my expert opinion that *Bacillus subtilis var. niger* (ATCC 9372, also known as *Bacillus atrophaeus)* is the *most appropriate* biological indicator organism for the validation of dry heat sterilization technologies. This specific subspecies of *Bacillus subtilis* demonstrates excellent growth and dry heat resistance characteristics. Standards for performance have been established by USP, ISO, and others to ensure that certified biological indicators for dry heat sterilization deliver predictable and standardized resistance.
>
> The Demolizer® technology is an alternative infectious waste treatment system that employs dry heat as the sterilization agent. As such, the most appropriate biological indicator organism for the validation of the efficacy of the Demolizer® technology is the ISO and USP recognized standard, *Bacillus subtilis* var. *niger* (also known as *Bacillus atrophaeus*). Further, certified carriers manufactured under rigorous quality standards should be used, wherever possible, since such carriers are tested for purity and performance meeting defined D-value and z-value performance criteria."

Letter from Dr. Daniel Y. C. Fung to Diane Gorder, August 27, 2007, a true and correct copy of which is attached hereto as Exhibit G.

Dr. Fung has published extensively in Food Microbiology, Applied Microbiology and Rapid Methods with more than 700 Journal articles, meeting abstracts, proceeding papers, book chapters and books in his career. He has served as the major professor for more than 90 M.S. and Ph.D. graduate students. The Kansas State University Rapid Methods and Automation in Microbiology Workshop, directed by Dr. Fung, has attracted more than 3,500 participants from 60 countries and 46 states to the program in the past 27 years. Dr. Fung is a Fellow in the American Academy of Microbiology, Institute of Food Technologists (IFT), International Academy of Food Science and Technology and Institute for Food Science and Technology (UK). He has won more than 30 professional awards which included the International Award from IFT (1997), Waksman Outstanding Educator Award from The Society of Industrial Microbiology (2001), KSU College of Agriculture Excellence in Graduate Teaching Award (2005), and the Exceptional Achievement and Founder of the KSU International Workshop on Rapid Methods and Automation in Microbiology Award given by the Director of the Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration, 2005. Dr. Fung received the B.A. degree from International Christian University, Tokyo, Japan in 1965, M.S.P.H. at University of North Carolina-Chapel Hill in 1967, and the Ph.D. in Food Technology from Iowa State University in 1969. He is currently a Professor of Food Science, Professor of Animal Sciences and Industry and Ancillary Professor of Biology at Kansas State University and Distinguished Professo,r Universitat Autonama de Barcelona, Spain.

Based on all of this information, the Agency has agreed to recommend to the Board that it grant this Petition for an Adjusted Standard.

VI. Difficulties Meeting 35 IAC § 1422.Table B

In developing the specific protocol used for demonstrating treatment efficacy, BMTS attempted to acquire the Chemical Indicator in a certified carrier form. Unfortunately, this subspecies is not available commercially in a certified carrier form.

With the help of researchers at Kansas State University, BMTS reviewed a comprehensive scientific literature survey and identified an equivalent subspecies, the Certified Indicator, as the industry standard for the validation of dry-heat sterilization processes. The overwhelming use of the Certified Indicator as the preferred and most appropriate indicator organism for dry-heat processes stems from its demonstrated excellent dry heat resistance compared to dry heat sterilization compared to other *B. subtilis* organisms. *See* Exhibit G, Letter from Dr. Daniel Fung, and Group Exhibit H, Gurney, et al for expanded discussion on the appropriateness of the Certified Indicator for the validation of dry heat sterilization processes. The Certified Indicator is cited in numerous national and international standards including the U.S. Pharmacopoeia, the International Standards Organization, and over three dozen scientific papers related to the validation of sterilization processes. *See* Group Exhibit H, *infra.*

BMTS made the decision to use the Certified Indicator because: 1) the indicators are phenotypically identical with the exception of pigmentation response; 2) the Certified Indicator is nearly universally recognized as the appropriate indicator microorganism to demonstrate the effectiveness of dry-heat treatment processes, the underlying treatment technology of the Demolizer® system; and 3) use of a Certified Indicator comports with the best practices of the scientific community since Custom Indicator populations must be grown in more non-controlled laboratory environments where it is possible to

inadvertently compromise the resistance and growth properties. Each manufacture must test all production lots against stringent dry heat resistance performance standards as expressed in D-values and z-values. Since the Certified Indicator is indisputably recognized as the most appropriate *Bacillus* indicator organism for dry heat sterilization processes and considered superior, from a heat resistance perspective, to the Chemical Indicator and, unlike the Chemical Indicator, is available in a certified form that comports with the industry's best practices, BMTS used the Certified Indicator in the KSU Efficacy Test.

VII. Description of Efforts Necessary for BMTS to Achieve Immediate Compliance

35 IAC 104.406(e) requires that the Petition contain a description of the efforts required to come into immediate compliance. Under the Agency's current interpretation of the Board's regulations, it is impossible for BMTS to achieve immediate compliance, which could take as long as two and a half years due to the time and resources required to grow and certify a Chemical Indicator to the same standards already demonstrated in the KSU Efficacy Test. However, BMTS has already conducted a successful IET using the preferred and most appropriate *Bacillus subtilis* indicator microorganism with a dry heat resistance, understood in the scientific community, to be superior to that of the specific species identified in the regulations. Therefore, if the Board were to accept the proposed Adjusted Standard recognizing the overwhelming evidence in the scientific community, BMTS would be in immediate compliance with the Board's regulations.

VIII. Immediate Compliance Would Impose an Arbitrary and Unreasonable Hardship

35 IAC 104.406(e) requires that BMTS set forth reasons why immediate compliance with the regulation would impose arbitrary and unreasonable hardship. Table B's requirement of using a Chemical Indicator over a Certified or Dry Heat Indicator is inappropriate and would impose an arbitrary and unreasonable hardship because it does not take into consideration the body of scientific evidence that unequivocally supports the claim that the Certified Indicator is most appropriate due to enhanced heat resistance under dry heat conditions.

Further, 35 IAC 1422 has not been updated to include the Certified Indicator as an equivalent alternative *B. subtilis* organism for the validation of dry heat and gas sterilization technologies consistent with the market availability of such sterilization technologies and the consensus within the standards and scientific community. At the time of the adoption of 35 IAC 1422, prevalent sterilization technologies included incineration, steam sterilization, chemical disinfection and radiation. The selection of the specific subspecies in Table B are appropriate and consistent with scientifically recognized indicator organisms for these traditional sterilization processes but are inconsistent with domestic and international standards for the qualification of dry heat treatment processes. These international standards promulgated by the US Pharmacopoeia, International Standards Organization, the U.S. Food and Drug Administration, the European Pharmacopoeia Commission, and others are the primary reason why *B. subtilis* is only available commercially both domestically and internationally as the Certified Indicator used in the KSU Efficacy Study.

Most states modeled their statutes and regulations off of a report titled *Technical Assistance Manual: State Regulatory Oversight of Medical Waste Treatment Technologies* that was prepared by the State and Territorial Association on Alternate Treatment Technologies (the "STAATT Report").[8] True and correct portions of the STAATT Report are attached hereto as Exhibit E. The STAATT Report identified the Chemical Indicator strain as a representative example of *Bacillus subtilis*. However, the STAATT Report stressed that the Chemical Indicator spore was only a representative strain of the species and was not selected based on any special resistance properties. Further, the STAATT Report stated that "the guidelines developed through this series of meetings should serve only to provide guidance to states in the development of a review and approval process for medical waste treatment technologies." Exhibit E, STAATT Report at p. 3.

As explained by Dr. Nelson S. Slavik, the primary author of the STAATT Report, BMTS' "selection of *B. subtilis* ATCC 9372 spores is consistent with the criteria provided by STAATT in their publication. This strain [the Certified Indicator] provides the dry-heat resistance which is appropriate for your treatment process." Letter from Nelson S. Slavik to Diane Gorder, June 11, 2007, a true and correct copy of which is attached hereto as Exhibit F.

This opinion is supported by Dr. Daniel Y. C. Fung, internationally renowned microbiologist. *See* Section V-C of this Petition and Exhibit G for a review of Dr. Fung's analysis on the appropriateness of the Certified Indicator. The 35 IAC 1422 requirements

[8] The STAATT Report was a culmination of conferences and debates beginning in 1992, the conclusions of which were widely disseminated prior the publication of the final STAATT Report in April 1994.

that dry-heat based sterilization processes use the Chemical Indicator as opposed to the Certified or Dry Heat Indicator in the IET is clearly arbitrary.

Moreover, BMTS will incur significant and unreasonable costs if it is required to repeat the KSU Efficacy Test using a different colored indicator microorganism that is likely to exhibit inferior heat resistance in a dry heat sterilization process. After learning of the Agency's position, BMTS requested that KSU prepare an estimate to repeat the KSU Efficacy Test using the Chemical Indicator to the same quality standards as attained in the original KSU Efficacy Study. In preparation of this estimate, BMTS again contacted Dr. Marsden, who would be responsible for repeating the study. Dr. Marsden informed BMTS that, in order to grow a custom indicator and ensure comparable quality standards to the previously conducted study using a certified carrier, the study would require two major phases.

The first phase would involve growing a culture population of the Custom Indicator and certifying its resistance properties through exhaustive D-value studies.[9] Dr. Marsden would use standard protocols for validating the resistance of the culture similar to those used throughout the industry. This study will likely need to be repeated several times until a population is grown to the standards comparable to a Certified Indicator like those obtained from certified manufactures.

Dr. Marsden provided an estimate of a minimum of $60,000 for a single D-value evaluation of a population. It is very possible that repeated trials could result in a **total cost approaching $250,000** to properly certify the population with a **total time frame of up to two years**. These estimates are phase-one costs only.

[9] An organism's D-value is the treatment time required for 90% deactivation (sterilization), *i.e.*, a measure of an organism's resistance to a particular treatment method - here, dry-heat.

Once a Custom Indicator population has been grown and certified, Dr. Marsden would begin the second phase, which involves repeating the Demolizer® efficacy study using appropriate replicates, load conditions, etc. This requires a **minimum of 2-4 months** to coordinate and report the study. Upon completion of both phases, validation results comparable to those already reported could be obtained. The estimate provided by Dr. Marsden for phase two of the validation study using ATCC 19659 is **$40,000**. In addition to these costs, BMTS would incur **direct costs totaling more than $30,000**, which includes the cost of three dedicated systems and the cost of BMTS staff time to be on-site at Kansas State University to facilitate the trial.

Therefore, the total cost for repeating the efficacy study using a Custom Indicator is estimated to be between $130,000 and $320,000 dollars and could take up to two and a half years to complete. A true and current copy of the estimate is found in Exhibit J. This information was also provided to the Illinois Bureau of Land in September 2007 in support of the agency's review of this petition. BMTS would have to sell numerous additional Demolizer® units to make up for the cost of repeating the IET with the Chemical Indicator. Given that the Certified Indicator is reported to demonstrate greater heat resistance than other *Bacilus subtilis* isolates, requiring BMTS to repeat the same efficacy test using a Chemical Indicator is an arbitrary and unreasonable hardship.

Further, BMTS envisions continuous improvements of the technology which may necessitate future IET trials to validate such improvements have not adversely impacted treatment efficacy. The Certified Indicator is the scientifically recognized and widely accepted indicator organism for the validation of the Demolizer® technology. If the Adjusted Standard is not granted, BMTS will continue to incur substantial ongoing costs

to conduct efficacy studies using two similar and likely equivalent organisms, the Certified Indicator and the Chemical Indicator organisms. Such duplicate effort is not scientifically justified and is an arbitrary and unreasonable hardship.

IX. Narrative Description of the Proposed Adjusted Standard

35 IAC 104.406(f) requires that the Petition provide a narrative description of the proposed adjusted standard as well as proposed language for a Board order that would impose the standard. The Adjusted Standard would simply involve formally recognizing the appropriateness of both the Certified and Chemical Indicators in Table B of 35 IAC 1422 for the validation of dry heat and chemical sterilization processes, respectively. The proposed language for a Board order would involve amending Item 1 of Table B from "1. Bacillus subtilis (ATCC 19659)" to "1. Bacillus subtilis (ATCC 19659) or Bacillus atrophaeus (ATCC 9372)". This language recognizes the recent change in classification of this particular isolate of Bacillus subtilis.

35 IAC 104.406(f) further requires the Petition to describe efforts necessary to achieve this proposed standard and the corresponding costs must also be presented. BMTS has already completed an Initial Efficacy Test demonstrating a 6 $\log_{10}$ reduction of *B. atrophaeus* (ATCC 9372) under varying load conditions. Thus, no additional efforts are required by the Petitioner if the proposed standard is adopted.

X. No Environmental Impact

35 IAC 104.406(g) requires that the Petition describe the quantitative and qualitative description of the impact of the petitioner's activity on the environment if the Petitioner were to comply with the regulation of general applicability as compared to the quantitative and qualitative impact on the environment if the Petitioner were to comply only with the proposed Adjusted Standard. BMTS' activities, operating under either the regulation of general applicability or the proposed Adjusted Standard, have no adverse impact on human, plant, or animal life. This is established by the studies described herein. There are no emissions, discharges or releases from the use of the Demolize® technology. All infectious waste treated in a Demolizer® system meets the requirements for sterilization and final disposal outlined in the regulations.

XI. Justification for the Adjusted Standard

35 IAC 104.406(h) requires that the Petition explain how the Petitioner seeks to justify, pursuant to the applicable level of justification, the proposed adjusted standard. As presented in Section IV of this Petition, the regulation of general applicability does not describe a specific level of justification therefore the level of justification outlined in 35 IAC 104.426 applies. The following outlines a statement of justification for each of the four conditions outlined in 35 IAC 104.426.

A. Change in Factors Relied Upon by the are Substantially Different

35 104.426(a)(1) requires that the Petitioner demonstrate that factors relating to that petitioner are substantially and significantly different from the factors relied upon by the Board in adopting the general regulation applicable to that petitioner. At the time the

Illinois regulations were drafted (1992-1993), infectious waste treatment technologies available both domestically and internationally primarily consisted of autoclave or steam sterilization, chemical disinfection, and radiation. The Agency identified scientifically recognized indicator organisms for these classes of sterilization technologies. *Bacillus stearothermophilus* is the internationally recognized indicator organism for the validation of steam sterilization technologies in the same manner that the Certified Indicator is the USP and ISO recognized indicator organism for dry heat. *Bacillus subtilis* (ATCC 19659), the Chemical Indicator, is commonly used for the validation of chemical disinfection processes, disinfectants and handwashing procedures. *Bacillus pumilis* is generally recognized as the appropriate indicator organism for radiation sterilization technologies. During the time period of the adoption of the Illinois regulation, the STAATT committee, a group of state regulatory personnel and infection control scientists, strongly recommended that the specific subspecies (*Bacillus subtilis, Bacillus stearothermophilus, and Bacillus pumilis)* are for example purposes only and should not be integrated directly into regulations since future technologies may warrant the use of better suited indicator organisms. Section VIII and Exhibit F hereto provides additional supporting evidence to this effect.

In the late 1990s, the Demolizer® technology and other dry heat based systems were formally introduced in the United States for the treatment of infectious wastes. The regulations were, in fact, promulgated in 1993 before the Demolizer technology was formally introduced. Further, published standards for the validation of dry heat sterilization technologies both domestically and internationally converged on the selection of the Certified Indicator in the mid to late 1990s as the most appropriate

indicator organism for the validation of such technologies. The specific selection of biological indicators in Table B is consistent with chemical disinfection, steam sterilization, and radiation-based technologies. Table B does not, however, include the Certified Indicator which is specifically optimal for the validation of dry heat sterilization processes.

The Agency acknowledged that an Adjusted Standard may be necessary to address emerging technologies in the Second Notice for Rulemaking (R91-20) published on March 25, 1993. On Pages 19 and 20 of this Notice, the Agency specifically cites the following:

"The record shows that the Study Group and the Agency proposed these provisions to allow easy consideration for new technologies that do not fit the definition of chemical, thermal or irradiation treatment. The Board supports this concept." (Note, dry heat is not specifically listed in the definition of thermal treatment provided in the regulation.)

"The Board emphasizes that it is sympathetic with the concerns of the Agency regarding the administrative burden of adjusted standards. An adjusted standard proceeding is resource consuming not only for the Board, but for the Agency and the petitioning party as well. Accordingly, reliance on the adjusted standard process must be contemplated with care that an unnecessary and onerous administrative burden is not created."

"By requiring the Board to grant adjusted standards consistent with Section 27(a), the statute requires the Board to consider the implications of certain site-specific conditions when granting an adjusted standard. As long as information requirements are met to the extent applicable, a technology-specific adjusted standard may be granted."

Therefore, at the time of adoption of the general regulation, dry heat sterilization had not been adapted for the treatment of infectious waste and was not included in the definition of thermal treatment. In the late 1990s, the Demolizer® and other dry heat treatment technologies became available in the U.S. and the international community. The specific organisms listed in Table B of 35 IAC 1422 are consistent with technologies available in the U.S. in the early 1990s. Table B, however, is not consistent with the application of dry heat to treat infectious waste. The Agency and the Board envisioned that adjusted standards may be warranted to include alternative biological indicators on a technology-specific basis. Therefore, the absence of dry heat alternatives at the time of drafting of the regulations is a factor that is substantially and significantly different than factors existing today and warrant adoption of a technology-specific, adjusted standard.

B. Existence of Those Factors Justifies an Adjusted Standard

35 104.406(a)(2) requires that the Petitioner demonstrate that existence of such factors justifies an adjusted standard. As stated above, 35 IAC 1422 is not consistent with the large body of scientific evidence for the selection of appropriate indicator microorganisms for the validation of dry heat medical waste treatment technologies. The scientific consensus in the domestic and international scientific community and the overwhelming body of evidence justify the use of the Certified Indicator for the validation of dry heat sterilization technologies. Use of a different indicator organism, such as *B. stearothermophilus* or *B. pumilis,* are not recognized in the scientific community for the validation of dry heat technologies. The Chemical Indicator, *Bacillus subtilis* (ATCC 19659) is recognized in the scientific literature for the verification of chemical disinfectants, chemical disinfectant processes and hand washing procedures.

The Chemical Indicator is not recognized in the scientific community for the validation of dry heat treatment processes. Similarly, *Bacillus atrophaeus* (ATCC 9372), the Certified or Dry Heat Indicator, is the biological indicator of choice for dry heat sterilization technologies due to its enhanced heat resistance under such conditions.

Further, the use of certified carriers for the validation of sterilization technologies represents best practices in the scientific community since such certified carriers are manufactured under strict international standards for quality and certification. The Chemical Indicator is not commercially available in a certified form, thus insistence on the use of a carrier that is not recognized for the validation of dry heat technologies and must be grown under non-controlled conditions actually results in a lower quality result. For these reasons, the factors presented hereto justify the proposed Adjusted Standard.

C. No Environmental or Health Effects

35 104.406(a)(3) requires that the Petitioner demonstrate that the requested standard will not result in environmental or health effects substantially and significantly more adverse than the effects considered by the Board in adopting the rule of general applicability. The extensive body of scientific evidence presented herein provides proof that the proposed Adjusted Standard has no adverse environmental or health effect compared to the standard stipulated in the regulation of general applicability. In fact, the proposed Adjusted Standard is more beneficial. The proposed Adjusted Standard, the Certified Indicator, poses a more difficult challenge for the Demolizer® technology than the Chemical Indicator. BMTS has demonstrated that the Demolizer® technology delivers a minimum 6 $\log_{10}$ reduction of the Certified Indicator consistent with the regulatory disinfection standard.

D. Consistency with Applicable Federal Law

35 IAC 104.406(a)(4) requires that the Petitioner demonstrate that the adjusted standard is consistent with any applicable federal law. The treatment of infectious waste and the approval of alternative treatment technologies are not regulated at the federal level. However, state, federal, and international authorities recognize the use of the Certified Indicator as an appropriate indicator microorganism for dry heat sterilization validation procedures.

BMTS' Demolizer® devices have been approved or meet statutory requirements in 46 states based on the results of the KSU Efficacy Test. While some of the states that have approved Demolizer® technology do not specify a particular strain of indicator microorganism, *e.g.*, California, New York, Michigan, Connecticut, North Carolina, South Carolina, Georgia, and Louisiana, others such as Florida specify only that the species *B. subtilis* be used to validate sterilization treatments. Of the three states that particularly identify the Chemical Indicator in their regulations, Arizona, Delaware, and Illinois, BMTS has already received approval from both Arizona and Delaware based on the KSU Efficacy Test. The State of New Mexico regulations have recently been updated effective August 2, 2007. The previous draft of the New Mexico Administrative Code, Solid Waste Regulations cited the *B. subtilis* ATCC 19659 (the Chemical Indicator) as an indicator organism to demonstrate initial efficacy of alternative treatment technologies. In the recently amended N.M.A.C. 20.9.8.13, the State of New Mexico specifically recognizes *Geobacillus stearothermophilus* or *Bacillus atrophaeus* (the Certified Indicator) as appropriate and scientifically recognized indicator organisms for

the validation of alternative technologies consistent with the facts and the evidence of scientific consensus described hereto.

The federal government recognizes the appropriateness of using the Certified Indicator to validate sterilization procedures. The U.S. Food and Drug Administration identifies the Certified Indicator as the appropriate test organism for dry-heat based sterilization procedures. *See* Group Exhibit H, *Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities* (March 1993); *Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities; Draft Guidance for Industry and FDA Reviewers* (May 2001), *supra*. In addition, the U.S. Pharmacopeia states that an appropriate biological indicator for dry-heat sterilization should "compl[y] substantially with the morphological, cultural, and biochemical characteristics of the strain of *Bacillus subtilis*, ATCC No. 9372 [the Certified Indicator], designated subspecies *niger* . . ." Group Exhibit H, U.S. Pharmacopeia, Monographs: Biological Indicator for Dry-Heat Sterilization, Paper Carrier, USP28-NF23 USP (2005), *infra*.

Moreover, the international community has identified the Certified Indicator as the standard indicator microorganism for validating dry-heat processes. For example, the British Pharmacopoeia, the European Pharmacopoeia, the Japanese Pharmacopoeia, and the International Organization for Standardization all list the Certified Indicator as the biological indicator to validate dry-heat sterilization treatments. The world-wide acceptance of the Certified Indicator as the industry standard further supports BMTS' assertion that the Certified Indicator is the most appropriate organism for the validation of dry heat sterilization technologies.

XII. Consistency with Federal Law

35 IAC 104.406(i) requires that the Petition provide supporting reasons that the Board may grant the proposed standard consistent with federal Law. Section XI-D of this Petition provides such a statement. Infectious waste treatment standards are not governed at the federal level. There are no procedural requirements applicable to the Board's decision on the petition that are imposed by federal law.

XIII. Supporting Documents

35 IAC 104.406(k) requires that the Petition cite supporting documents and legal authority. With respect to documents, Exhibits A through I are attached to this Petition and are specifically referenced herein. In addition, for the convenience of the Board, true and correct copies of relevant portions of the scientific authorities cited in this Petition are attached collectively hereto as Group Exhibit H. The scientific literature discussed in this Petition establishes that the Chemical and Certified Indicators are very similar[10], if

[10]In the scientific community, both the Certified and Chemical Indicators have been used to demonstrate efficacy of a particular sterilization technology. The two substrains are very similar with the exception of pigmentation response to certain culture conditions and, prior to 2004, were classified in the same *Bacillus* species. Nakamura and others state that, "[e]xcept for colour of the soluble pigment, all of the strains were indistinguishable by the standard characterization method; i.e., they exhibited the traits typical of *B. subtilis*." Group Exhibit H, Nakamura, *supra*. Blackwood reported that the RNA sequences of various substrains of *B. subtilis* are indistinguishable with a reported sequence mapping of over 99%. *See* Group Exhibit H, Blackwood, *supra*. Moreover, Blackwood also reported that the only way to differentiate between the substrains would be to observe oxidative activity since they are identical with the exception of pigmentation differences. *See id.* In 2000, the European Commission Health and Consumer Protection Directorate-General stated that "*B. atrophaeus* is distinguishable from *B. subtilis* only by pigmentation." Group Exhibit H, European Commission, Health and Consumer Protection Directorate-General, *Opinion of the Scientific Committee on Animal Nutrition on the Safety of Use of Bacillus Species in Animal Nutrition* (Feb. 17, 2000).

Both strains have been used in the validation studies for various oxidative sterilization technologies. In all cases, there was no reported difference in the performance of the two substrains. The Chemical Indicator is broadly used for the validation of disinfectants and chemical disinfection processes. The Certified Indicator is broadly used and recognized as the preferred indicator organism for dry heat sterilization processes due to its demonstrated superior dry heat resistance. The Certified Indicator is also recognized for the validation of certain gas sterilization technologies, including ethylene oxide disinfection. *See generally*, Group Exhibit H; *see Gurney and Quesnel, see* U.S. Food and Drug Administration, *Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities* (March 1993) (listing both the ATCC 9372 and the ATCC 19659 *B. subtilis* samples as

not equivalent, with the Certified Indicator recognized internationally as the *most appropriate* biological indicator for the validation of dry heat sterilization processes.

Most importantly, Gurney and Quesnel established that the Certified Indicator is the preferred biological microorganism for the validation of dry heat treatment processes in a definitive comparative study. This work surveyed the compendium of published literature on dry heat resistance of *Bacillus subtilis* spores. Further, the authors completed extensive comparative resistance studies on the Certified Indicator and a generic *Bacillus subtilis* organism, typical of the Chemical Indicator, over a temperature range of 140 to 170°C. At all temperatures, the Certified Indicator demonstrated superior heat resistance properties. Group Exhibit H, Gurney, T.R. & Quesnel, L.B., *Thermal Activation and Dry-heat Inactivation of Spores of Bacilus subtilis MD2 and Bacillus subtilis var. niger,* J. APPLIED BACTERIOLOGY, 48, 231-247 (1980).

The following domestic and international standards list the Certified Indicator for the validation of dry-heat processes. Each standard is developed by an expert panel of

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equivalent indicator organisms to validate dry-heat sterilizers); *see also* U.S. Food and Drug Administration, *Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities; Draft Guidance for Industry and FDA Reviewers* (May 2001) (updated publication listing only the Certified Indicator (ATCC 9372) to validate dry-heat sterilization treatments).

In a 2004 Environmental Technology Verification Report conducted by Battelle, both the Chemical and Certified Indicators were used to validate the effectiveness of a formaldehyde-based decontamination technology, and there were no reported qualitative differences in the resistance of the two samples. *See* Group Exhibit H, Battelle, *Environmental Technology Verification Report prepared for CERTEK, Inc.* (Aug. 2004).

In a 2001 comparative study by Khadre and Yousef, the resistance of both the Certified and Chemical Indicators were shown to be equivalent during an evaluation of ozone and hydrogen peroxide sterilization technologies. *See* Group Exhibit H, M.A. Khadre, A.E. Yousef, *Sporicidal Action of Ozone and Hydrogen Peroxide: A Comparative Study,* INT'L. J. OF FOOD MICROBIOLOGY, 71, 131-138 (2001). In fact, Khadre and Yousef concluded that "differences among these strains were not significant ($p<0.05$)." *Id.*

Similarly, in a study by Sagripanti, *et al.*, the Chemical and Certified Indicators were evaluated along with other various strains for sporicidal activity against a broad range of oxidative treatment technologies and found to have resistances "within 1 Log_{10} of each other." Group Exhibit H, J-L. Sagripanti, *et al.*, *Virulent Spores of Bacillus Anthracis and other Bacillus Species Deposited on Solid Surfaces Have Similar Sensitivity to Chemical Decontaminants,* J. APPLIED MICROBIOLOGY, 102, 11-21 (2007).

microbiologists and sterility assurance specialists who review the body of scientific and published literature to make recommendations based on overall resistance of organisms to a specific sterilization technology. Manufacturers of certified carriers, such as those used in the KSU Efficacy Study, must test each production lot of carriers to meet specific heat resistance targets, as measured in D-value and z-values under specific conditions, to ensure the proper standardization.

1. **US Pharmacopoeia**. USP28-NF23 USP. Monographs: Biological Indicator for Dry-Heat Sterilization, Paper Carrier; Rockville, MD; 2005.
2. **FDA**. Guidance on Premarket Notification [510(k)] Submissions for Sterilizers Intended for Use in Health Care Facilities. Infection Control Devices Branch, Division of General and Restorative Devices (March 1993).
3. **FDA**. Premarket Notifications [510(k)] for Biological Indicators Intended to Monitor Sterilizers Used in Health Care Facilities; Draft Guidance for Industry and FDA Reviewers; U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, Infection Control Devices Branch (March 2001).
4. **British Pharmacopoeia Commission**. Methods of sterilization. London, UK: British Pharmacopoeia Commission; British Pharmacopoeia Appendix XVIII (2003).
5. **European Pharmacopoeia Commission**. Biological indicators of sterilization. Strasbourg, France: European Pharmacopoeia Commission; European Pharmacopoeia EP 5.1.2 (1997).
6. **Japanese Pharmacopoeia**. JP14e.partII.15 JP. Terminal Sterilization and Sterilization Indicators.
7. **ISO and ANSI.** Sterilization of health care products – Biological indicators; Part 4: Biological indicators for dry heat processes. Geneva (Switzerland): International Organization for Standardization/ANSI; ISO 11138-4:2006.

See Group Exhibit H.

XIV. Affidavit Verifying Facts

The affidavit of BMTS' Director of Regulatory Compliance, Diane Gorder, verifying both that the facts stated in this Petition are true and that the attached exhibits are true and accurate copies, is attached hereto as Exhibit I.

CONCLUSION

BMTS therefore asks that this Board, pursuant to its authority under Section 35 of the Act and the Board's regulations under 35 IAC 104, grant BMTS an Adjusted Standard from the provisions of 35 IAC 1422.Table B recognizing the Certified Indicator as the most appropriate biological indicator organism for the validation of dry heat sterilization technologies.

Specifically, BMTS requests that an Adjusted Standard be granted for the use of *Bacillus atrophaeus* (formerly *Bacillus subtilis var. niger,* also scientifically recognized as ATCC 9372 or NRRL B4418) for the IET of dry heat treatment technologies.

Respectfully Submitted,

BIOMEDICAL TECHNOLOGY SOLUTIONS, INC.

By: _____
One of Its Attorneys

Dated: January 7, 2008

Neal H. Weinfield
Jason B. Elster
GREENBERG TRAURIG, LLP
Firm No. 36511
77 West Wacker Drive, Suite 2500
Chicago, Illinois 60601
312-456-8400 (Telephone)
312-456-8435 (Facsimile)
weinfieldn@gtlaw.com
elsterj@gtlaw.com