MesaLabs

LABELING CHANGE NOTIFICATION

06 August 2018

Notification ID: CN-180601
Notification Type: Product Labeling Change

Dear Customer,

We wish to notify you that the purity specification has been removed from the certificates of analysis for the catalog numbers provided in the attachment to this letter. The change is being made effective immediately, beginning with the next lots to be manufactured for any given product line.

A change was made in August 2016 to the United States Pharmacopeia, when the Official Monograph for Biological Indicators was deleted and relevant ISO standards for testing were added to Chapter <55>. The purity specification, upon which our claim was based, is no longer required per the USP.

Mesa has made no changes to in-process or release testing for our biological indicators, nor have we changed any processes which have the potential to impact purity. We continue to confirm purity at several points in the manufacturing process, as we always have. The only change is to remove the claim from our certificates of analysis, because it is no longer required per the USP. We will continue to ensure our labeling is in compliance with the requirements of Section 4.3 of ISO 11138:2017.

We have attached a copy of the Mesa SporeNews Volume 13, No. 1 in which we discussed other changes made to the USP. If you have any questions regarding this change, please contact your Mesa Laboratories representative.

06 Aug 2018
Date

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06 Aug 2018
Date

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Attachments:

- List of impacted catalog numbers
- Mesa SporeNews Volume 13, No. 1

CN-180601
Attachment 1

1B-6100AT	Stainless Steel BI (5230)
1-1000	Spore Strip (*B. atrophaeus*) Log 6 (1000 ct)
1-4100	Spore Strip (*B. atrophaeus*) Log 4 (100 ct)
1-6100	Spore Strip (*B. atrophaeus*) Log 6 (100 ct)
1-6500	Spore Strip (*B. atrophaeus*) Log 6 (500 ct)
3-1000	Spore Strip (*G. stearothermophilus*) Log 5 (1000 ct)
3-4100	Spore Strip (*G. stearothermophilus*) Log 4 (100 ct)
3-5100	Spore Strip (*G. stearothermophilus*) Log 5 (100 ct)
3-6100	Spore Strip (*G. stearothermophilus*) Log 6 (100 ct)
5-1000C	Spore Strip (Dual)
5-1000T	Spore Strip (Dual)
5-5100T	Spore Strip (Dual)
PS-4-10	ProSpore Log 4 (10 ct)
PS-4-50	ProSpore Log 4 (50 ct)
PS-5-10	ProSpore Log 5 (10 ct)
PS-5-50	ProSpore Log 5 (50 ct)
PS-6-50	ProSpore Log 6 (50 ct)
3-1000PB	Spore Disc (*G. stearothermophilus*) 9 mm
1-10006MM	Spore Disc (BATR) 6 mm
1-1000PB	Spore Disc (BATR) 9 mm
1-6100TT	Spore Cotton Thread
1-6100YT	Thread/Poly Suture
1-6100YTHW	Thread/Poly Suture
3-6100PB	Spore Disc (*G. stearothermophilus*) 9 mm
3-6100YT	Thread/Poly Suture
3-6100YTC2	Poly Suture Log 6
PL-3-6-15	ProLine Process Challenge Device
A1X25/6	MesaStrip (*B. atrophaeus*) 1x25 mm
A1X25/6G	MesaStrip (*B. atrophaeus*) 1x25 mm In glassine
A2X10/6	MesaStrip (*B. atrophaeus*) 2x10 mm
A2X10/6G	MesaStrip (*B. atrophaeus*) 2x10 mm In glassine
AOZ/3T	MesaStrip (*B. atrophaeus*) Log 3 Ozone
AOZ/6T	MesaStrip (*B. atrophaeus*) Log 6 Ozone
DH/50	DriAmp
DPSSC/3	MesaDisc (*G. stearothermophilus*) Log 3
DS6R/5	MesaDisc (*G. stearothermophilus*) Log 5
DS6R/6	MesaDisc (*G. stearothermophilus*) Log 6
DS6R/6G	MesaDisc (*G. stearothermophilus*) Log 6 In glassine
EZG/6	EZTest Gas 100 ct
EZG/625	EZTest Gas 25 ct
EZH/5	EZTest H2O2 Log 5
EZH/5I	EZTest H2O2 Log 5 International
EZH/6	EZTest H2O2 Log 6
EZH/6I	EZTest H2O2 Log 6 International
EZS/5	EZTest Steam Log 5
EZS/525	EZTest Steam Log 5 (25 ct)
EZS/6	EZTest Steam Log 6

EZS/625	EZTest Steam Log 6 (25 ct)
GRS-090	Apex BI *B. atrophaeu* s 9372
HMV-091	Apex BI *G. stearothermophilus* 12980
KCD-404	Apex BI *G. stearothermophilus* 12980
LAU-196	Apex Suspension
LOG-456	Apex Triscale BI
LPT-606	Apex Suspension
MA/4	MagnaAmp Log 4
MA/5	MagnaAmp Log 5
MA/6	MagnaAmp Log 6
NAS-152	Apex BI *G. stearothermophilus* 7953
RG/100	Releasat Biological Culturing Set
S1X25/6	MesaStrip (*G. stearothermophilus*) 1x25 mm
S1X25/6G	MesaStrip (*G. stearothermophilus*) 1x25mm In glassine
S2X10/6	MesaStrip (*G. stearothermophilus*) 2x10mm
S2X10/6G	MesaStrip (*G. stearothermophilus*) 2x10mm In glassine
SA/4	SterilAmp II Log 4
SA/5	SterilAmp II Log 5
SA/6	SterilAmp II Log 6
SA18/6	SterilAmp II 18 mm Log 6
SA18/NC50	SterilAmp II Log 6 (NC 50 count)
SASU/6	SterilAmp II 5230 Log 6
SBC-327	Apex BI *G. stearothermophilus* 12980
SEZS/5	Smart-Read EZTest Log 5
SEZS/525	Smart-Read EZTest Log 5 (25 ct)
SEZS/6	Smart-Read EZTest Log 6
SEZS/625	Smart-Read EZTest Log 6 (25 ct)
SGMG/3	MesaStrip Gas/DH Log 3
SGMG/6	MesaStrip Gas/DH Log 6
SGMG/6R	MesaStrip Gas/DH Log 6 for Releasat
SGMR/6	MesaStrip Radiation Log 6
SGMR/7	MesaStrip Radiation Log 7
SGMS/3	MesaStrip Steam Log 3
SGMS/5	MesaStrip Steam Log 5
SGMS/6	MesaStrip Steam Log 6
SGMSU/6	MesaStrip 5230
SRSP6/25BI	Smart-Read Test Pack Bulk
SS5230A/7	Suspension 5230 Aqueous
SS5230E/4	Suspension 5230 Ethanol
SS5230E/5	Suspension 5230 Ethanol
SS5230E/6	Suspension 5230 Ethanol
SS5230E/7	Suspension 5230 Ethanol
SS5230E/8	Suspension 5230 Ethanol
SS6633A/7	Supension 6633 Aqueous
SS6633E/4	Suspension 6633 Ethanol
SS6633E/5	Suspension 6633 Ethanol
SS6633E/6	Suspension 6633 Ethanol

SS6633E/7	Suspension 6633 Ethanol
SS6633E/8	Suspension 6633 Ethanol
SSGE/4	Suspension *B. atrophaeus* Ethanol
SSGE/5	Suspension *B. atrophaeus* Ethanol
SSGE/6	Spore Suspension (*B. atrophaeus*) Log 6
SSGE/7	Spore Suspension (*B. atrophaeus*) Log 7
SSGE/8	Spore Suspension (*B. atrophaeus*) Log 8
SSRE/4	Suspension *B. pumilis* Ethanol
SSRE/5	Suspension *B. pumilis* Ethanol
SSRE/6	Suspension *B. pumilis* Ethanol
SSRE/7	Suspension *B. pumilis* Ethanol
SSRE/8	Suspension *B. pumilis* Ethanol
SSSA/7	Suspension *G. stearothermophilus* Aqueous
SSSE/4	Suspension *G. stearothermophilus* Ethanol
SSSE/5	Suspension *G. stearothermophilus* Ethanol
SSSE/6	Suspension *G. stearothermophilus* Ethanol
SSSE/7	Suspension *G. stearothermophilus* Ethanol
SSSME/7	Suspension *Bacillus smithii* Ethanol
STP/25BI	EZTest Steam Test Pack
SU1X25/6	MesaStrip 5230 1x25mm
SU2X10/6	MesaStrip 5230 2x10mm

MesaLabs

SporeNews

biological indicators newsletter

Volume 13, No. 1

Biological Indicators and the United States Pharmacopeia

by Kurt McCauley and Nicole Robichaud

Mesa Labs manufactures its biological indicators (BIs) in accordance with several standards. In a previous edition of Spore News, we discussed the AAMI/ISO standards which pertain to BIs manufactured for the medical device industry (Spore News Vol 12, no 1). This edition covers BIs manufactured for use in the pharmaceutical industry as detailed in the United States Pharmacopeia (USP). As is the case with any standard that is designed to remain relevant, the USP undergoes periodic revisions. The most recent revision of the USP contains significant changes pertaining to biological indicators and their use in the industry and these will be discussed in this Spore News edition.

A Brief History of the USP

The USP was established on January 1, 1820, in the senate chamber of the U.S. capital building. Its purpose was to create a compendium of therapeutic products and provide recipes for their preparation. A comprehensive timeline of changes to the organization can be found on the USP website1 however a few dates of interest include:

- 1830 - a Committee of Revision was created and the USP is revised at 10-year intervals.
- 1900 - USP incorporated as a not-for-profit corporation and the Board of Trustees is created.
- 1938 - The Federal Food, Drug, and Cosmetic Act passed and the USP is recognized as official and is enforced by the FDA.
- 1942 - The USP revision cycle is changed from every 10 years to every 5 years.
- 2002 - The USP is revised and published annually.

Revisions now occur continuously and are presented annually in the USP and twice-annually as Supplements to the USP.

USP Structure

The USP is organized into numerous chapters. General chapters numbered 1 to 999 (i.e. monographs) are considered "enforceable" whereas general chapters numbered greater than 1000 are for informational purposes only.

In the current USP revision, BI content is predominantly in chapters <55> *"Biological Indicators—Resistance Performance Tests"* and <1229.5> *Biological Indicators for Sterilization"*, although most chapters in the <1229> series also contain BI references.

BIs and the USP

Biological Indicators are not pharmaceutical products so why are they included in the USP? The USP mission statement, *"To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods"*, provides the answer. In short, BIs are a tool necessary for assuring the "quality" and "safety" of pharmaceutical products and as such, guidance for their preparation and use are included in the USP.

Chapter <55>, considered enforceable, describes the methods and materials used to determine the resistance of BIs and is intended for both the manufacturer and the user. It sets tighter controls for the manufacturers on the use of replicate units per test, while stating "the end users are not required to use the same number of replicates for verification of those determinations".

A comparison of differences between the current revision and the previous version of chapter <55> is presented in Appendix 1. The most significant change is that all BI information has been deleted from the official monographs section and much of it relocated in chapter <55>. This table is not all inclusive and the reader should refer to the USP for complete details.

New informational chapters to the USP are numbered in the <1229> series and largely replace the deleted chapter <1035> "Biological Indicators for Sterilization". This series provides a well written and easy to understand description of the basic principles for control of a sterilization process including, process development, process validation, and maintenance/monitoring.

As Biological Indicators are tools that are used in each of these steps, they are discussed throughout most of the <1229> series which include:

- <1229> Sterilization of Compendial Articles
- <1229.1> Steam Sterilization by Direct Contact
- <1229.2> Moist Heat Sterilization of Aqueous Liquids
- <1229.3> Monitoring of Bioburden
- <1229.4> Sterilizing Filtration of Liquids
- <1229.5> Biological Indicators for Sterilization
- <1229.6> Liquid Phase Sterilization
- <1229.7> Gaseous Sterilization
- <1229.8> Dry Heat Sterilization
- <1229.9> Physicochemical Integrators and Indicators for Sterilization
- <1229.10> Radiation Sterilization
- <1229.11> Vapor Phase Sterilization
- <1229.12> New Sterilization Methods

A comparison between the <1229> chapters and the deleted chapter <1035> is presented in Appendix 2. This table is not all inclusive and the reader should refer to the USP for complete details.

Discussion

It is our opinion that the latest revision of the USP provides significant improvements in both its organization and presentation of the Biological Indicator subject matter. Some of the values previously presented in the general information chapter (e.g. the D-value ranges in chapter <1035>) were interpreted by many firms to be enforceable, and as such caused some confusion. These have been removed in the latest revision. Additionally, the USP increasingly references existing standards that meet their expectations (e.g. ISO 11138 series-Biological Indicators, and ISO 18472-Resistometers), rather than create a redundant set of standards.

Appendix 1. Comparison of Current Revision of Chapter <55> to Deleted Enforceable Chapters

Subject	Pre-August 1, 2016 Version	Post August 1, 2016 Version
Population – Number of Samples	**Chapter <55>** • three specimens	**Chapter <55>** • manufacturer must use "at least four test samples"
Population - method	**Chapter <55>** • blender cup method.	**Chapter <55>** • does not specify method, only states to "mechanically disrupt to achieve a homogeneous suspension"
Population – test tube size	**Chapter <55>** • screw capped 16 x 125 mm	• Not specified
Population – acceptable range for verification of labeled population	**USP Monographs** • For paper carriers and self-contained: "log average number of viable spores per carrier is not less than 0.3 log of the labeled spore count per carrier and does not exceed the log labeled spore count per carrier by 0.48" • For nonpaper carriers: "the average number of viable spores per carrier are within -50% and +300% of the labeled count per carrier" • For liquid spore suspensions: "within ±1 log of the value stipulated by the manufacturer"	**Chapter <55>** • For vendor supplied BIs: "between 50% and 300% of the manufacturer's stated value" • For spore Suspensions, "within 50% - 300% of the labeled count"
Population – plate counts	**Chapter <55>** • "preferably 30 to 300 colonies, but not less than 6, on each of a pair of plates".	**Chapter <55>** • "30 to 300 colonies on each plate in a pair".
D-value – Number of Samples	**Chapter <55>** • "Take a sufficient number of groups of specimens of biological indicators in their original individual containers, each group consisting of 5 to 10 specimens."	**Chapter <55>** • "Use 20 replicate test sample BIs in their original individual containers, subjected to at least five exposure conditions for a total of 100 tests."
D-value – Verification	**Official Monographs** • "The requirement of the test are met if the determined D value is within 20% of the labeled D value…"	**Chapter <55>** • Not specified in this chapter
Purity	**Official Monographs** • "Purity: By examination of the colonies derived from the spores on a suitable plate culture medium, determine that there is no evidence of contamination with other microorganisms."	**Chapter <55>** • Not specified in this chapter
Survival/Kill	**Official Monographs** • Equations for calculation of Survival and Kill times • Acceptance criteria • Retest procedure if not more than one BI fails the procedure described in Chapter <55> **Chapter <55>** • Procedure for verification of values per the equations presented in the official monographs	**Chapter <55>** • ". . . should be provided by the manufacturer and verified by the end user."

Appendix 2. Comparison of Current Informational Chapter <1229> to Deleted Chapter <1035>

Heading	General Chapter <1035> Biological Indicators for Sterilization	General Chapter <1229.5> Biological Indicators for Sterilization
Introduction/Proper Use of Biological Indicators	• General description of a BI, the organisms used for BIs and the applications of BIs	• General description of a BI, the organisms used for BIs and the applications of BIs
BI Manufacturer's Responsibility	To provide: • Certificate of Analysis • Microbial count and resistance stability throughout shelf-life • D-value and method by which it was determined • Storage conditions • Directions for use, including medium and conditions used for recovery • Disposal instructions	To provide: • Certificate of Analysis • Microbial population • Resistance (D and Z values where appropriate) • Storage conditions • Expiry • Directions for use, including medium and conditions used for recovery • Disposal instructions
BI User's Responsibility	• Should establish suitability for use in a specific sterilization process • Should establish in-house acceptance standards for BIs • Should obtain a Certificate of Performance • Should perform audits of manufacturer • Should verify purity and morphology • Microbial count should be determined • Manufacturer's D-value range, storage conditions, expiration and stability should be observed	• Suitability for use in a specific sterilization process must be established • Should obtain a certificate of analysis • Should verify labeled population • Resistance need not be reconfirmed when used according to manufacturer's directions
User-Prepared Biological Indicators	• Users responsibility to ensure performance requirements met.	• Users responsibility to determine population and resistance.
Characterization of Biological Indicators	• Information located throughout various sections.	End user acceptance and control of BIs • Packaging and Storage • Expiration Date • Identification • Purity • Disposal
Types of Biological Indicators	General descriptions • Spores inoculated onto a carrier in a package • Spore suspension inoculated onto or into product • Self-contained, growth medium in direct contact with spores during sterilization • Self-contained, growth medium placed in direct contact with spores after sterilization	General descriptions • Spores inoculated onto a carrier in a package • Spore suspension inoculated onto or into product • Self-contained, growth medium in direct contact with spores during sterilization • Self-contained, growth medium placed in direct contact with spores after sterilization
Selection for a Specific Process	• Gives general description sterilization modalities, appropriate test organisms, and their typical resistance characteristics.	• Gives general description of sterilization modalities, appropriate test organisms, and directs reader to USP chapters <1229.1 to 1229.11> for further information.

Kurt McCauley has a B.S. in Microbiology and is the Director of R&D and Support Services at the Bozeman manufacturing site. He began work at Mesa Labs (former SGM Biotech) in 1995 and has been involved with all aspects of biological indictor production and development. Mr. McCauley currently serves as Co-chair for AAMI Working Group 91 (Resistometers), and is a member of ISPE.

Nicole Robichaud graduated from Montana State University with a B.S. in Biological Sciences. Nicole has worked for Mesa Labs since 2007 and has held positions in the Spore Cultivation Laboratory, Quality Control and currently is a Scientific and Technical Service Representative.