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August 19, 2001

Dockets Management Branch
Division of Management and Systems Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, Maryland 20852

RE: Docket No. 01D-0193

Dear Sir or Madame:

This correspondence is in response to the notice published in the Federal Register on May 21, 2001, regarding the availability of a draft guidance titled "Premarket Notifications [510(k)] for Biological Indicators Intended to Monitor Sterilizers Used in Health Care Facilities; Draft Guidance for Industry and FDA Reviewers". FDA has requested that comments regarding this document may be submitted within 90 days of publication. STERIS Corporation wishes to file the following comments in response to this request from FDA. The comments herein represent STERIS Corporation's position regarding the content of the guidance document for filing of Premarket Notifications for Biological Indicators.

STERIS Corporation, a Mentor, Ohio based company, is a leading provider of infection prevention, contamination prevention, microbial reduction, and therapy support systems, products, services and technologies to health care, scientific, research, food and industrial customers throughout the world.

STERIS Corporation believes that the proposed guidance document for Premarket Notifications for Biological Indicators is generally appropriate to establish the safety and efficacy of Biological Indicators. We do, however, have concerns related to several of the testing requirements and definitions identified in the document. These concerns and our recommendations are outlined below.

I. Comments on "I. Introduction"

C. Definitions:

The Definition for BIER vessels should be modified to meet the current definition proposed in the AAMI guidelines drafted in 1999.

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C9

D. Regulatory Authority and Classification of Biological Indicators:

In paragraph three liquid chemical sterilants should be referenced as a recognized new technology. Biological indicators developed to monitor performance of liquid chemical sterilants may be developed based on this guidance document.

E. Device Modifications:

In the examples of significant modifications that require a new 510(k) submission (p. 5), the reference to "a change in spore species and strain" should be modified to strictly "a change in species". A change in the strain of organism may not in all circumstances be considered a significant modification that could effect the safety and effectiveness of the device.

III. Premarket Notification (510(k)) Format and Content:

D. Comparison of the New Biological Indicator to the Predicate:

In Table I, the comparison of Resistance Characteristics, "Z-value (steam only)" should be modified to "Z-value (thermal processes only)". A Z-value may also be utilized for dry heat sterilization processes. See definition for Z-Value (AAMI, 1999b).

E. Description and Specifications of the Biological Indicator:

Resistance characteristics (#2) should be modified to change "(steam only)" to "(thermal processes only)".

An additional requirement for device design should include identification of the growth and culture conditions for non-self contained biological indicators.

G. Labeling:

The reference to shelf life (#8) should be limited to expiration date only to provide clarity to the end user.

The guidance document should provide clarification to #10 "C. Describe user quality assurance procedures."

H. Efficacy Data:

The following are recommended changes to Table 2 (p.16). The recommended changes are in bold.

Sterilizer Type:	Indicator Organism/Spore:
Steam	Bacillus stearothermophilus (ATCC 7953 or 12980) **or (NCTC 10003 or 10007) or (DSM 494 or 22 or 5934) or (CIP 52.81)**
Dry Heat	Bacillus subtilis var.niger (ATCC 9372) **or (NCTC 10073) or (CIP 7718)**
Ethylene Oxide	Bacillus subtilis var.niger (ATCC 9372) **or (NCTC 10073) or (CIP 7718)**
Peracetic Acid	Bacillus stearothermophilus (ATCC 7953 or 12980) **or (NCTC 10003 or 10007) or (DSM 494 or 22 or 5934) or (CIP 52.81)**
Hydrogen Peroxide	Bacillus stearothermophilus (ATCC 7953 or 12980) **or (NCTC 10003 or 10007) or (DSM 494 or 22 or 5934) or (CIP 52.81)**

The additional recognized strains accepted for use in monitoring sterilization processes are based on approved strains identified in ISO Standard 11138, "Sterilization of health care products- Biological Indicators" (Reference Numbers ISO11138-2 and ISO 11138-3).

Peracetic Acid and Hydrogen Peroxide are both recognized methods of sterilization which can be monitored using the species and strains referenced above.

3. Efficacy Studies

a) Viable spore population assay:

The reference to USP 24 and ANSI/AAMI ST-59-1999 Annex A should be for "examples of assay methods" instead of "for information on assay methods". Additional language should be added to clarify that alternative methodologies for establishing spore population other than those used in USP 24 and ST-59-1999 may also be utilized.

b) Resistance characteristics:

In Table 3 minimum recommended populations and resistance characteristics are identified. STERIS Corporation recommends that when multiple cycle temperatures are indicated for a biological indicator to monitor steam sterilization, that D-values for indicated temperatures of 132 C or higher not be specified but be calculated based on a Z-value constant. The Z-value constant can be generated from conducting D-value testing at lower temperatures. The most common temperature is 121°C. At this temperature, the resistance profile gives several fractional cycles

(cycles exhibiting some surviving biological indicators). The accuracy of the D-value calculation at this temperature is good due to typically high numbers of fractional cycles. As temperature increases, fewer fractional points are obtained reducing the accuracy of the test. In fact, some high temperatures may lead to no fractional cycles during the D-value test. Lower temperatures may be utilized in the calculation of Z-value, this allows for temperatures of 121°C or lower to be tested thus avoiding the accuracy problem associated with testing high temperature steam (132°C or higher). The resistance at 132°C or higher can be dictated by controlling the Z-value constant.

The footnote on page 19 should be changed to refer to Table 3.

XIII. Appendix H – The Center for Devices and Radiological Health, FDA Guidance for Validation of Biological Indicator Incubation Time

Under the methodology recommended by FDA for validation of reduced incubation times a recommendation is made in step #2 to expose biological indicators in 3 partial sterilization cycles (100 per partial cycle). In some instances, it may not be possible to test all 100 samples in a single BIER vessel cycle. STERIS Corporation requests the following change in this recommended methodology be made to clarify that more than one cycle may be run to achieve the 100 samples per lot.

> " Using predefined sterilization parameters, expose the biological indicators in partial sterilization cycles (100 per lot tested). This may be accomplished by running more than one cycle to achieve 100 processed biological indicators per lot".

The NOTE in #5 should refer only to new sterilization technologies. This should not be necessary with more common technologies such as steam or ethylene oxide.

#10 should be modified to change "partial cycles" to "lots" to account for limitations in BIER vessel capacities. The reference to "partial cycle incubation times" should be deleted.

The example provided on p. 37 should be modified to address the above comment regarding BIER vessel cycle limitations to achieve 100 samples per lot. The example should take into consideration that more than one partial cycle could be run to obtain 100 samples per lot. In addition, the example should reflect acceptable and non-acceptable conditions assuming a partial cycle fails to meet the 30%-80% positive indicator criteria.

Thank you for the opportunity to comment on this draft guidance document. If you have any questions or require additional information regarding these comments, please do not hesitate to contact Donna Haire at 440-392-7812 or Raymond Ursick at 440-392-7016.

Sincerely,
STERIS Corporation

Mike Ebers
Manager, Regulatory Affairs

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