Premarket Notification [510(k)] Submissions for Medical Sterilization Packaging Systems in Health Care Facilities; Draft Guidance for Industry and FDA

Draft Guidance – Not for Implementation

This guidance document is being distributed for comment purposes only.

Draft released for comment on March 7, 2002

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Infection Control Devices Branch
Division of Dental, Infection Control, and General Hospital Devices
Office of Device Evaluation

Preface

Public Comment:

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

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Premarket Notification [510(k)] Submissions for Medical Sterilization Packaging Systems in Health Care Facilities; Draft Guidance for Industry and FDA

This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

Background

FDA regulates sterilization packaging medical devices intended for use in health care facilities. The term, "medical sterilization packaging systems" used in this document refers to sterilization wraps, sterilization packs, sterilization pouches, sterilization containers, sterilization trays, and sterilization cassettes, including related components such as trays, holders or mats, used by health care facilities to package and sterilize medical devices intended for either single use or reuse. This document was drafted by FDA following our interaction with industry, government, academia, and health care professionals.

A person intending to market a sterilization packaging system intended for the terminal sterilization of medical devices in health care facilities must submit to FDA, and have cleared, a premarket notification submission prior to introduction of the product into interstate commerce, in accordance with section 510(k) of the Federal Food, Drug, and Cosmetic Act (the act).

Regulations governing the general content and format of 510(k) submissions for packaging are codified under 21 Code of Federal Regulations, Part 807. These and other regulatory requirements pertaining to the marketing of a new medical device are discussed in guidance documents available from CDRH, Division of Small Manufacturers, International, and Consumer Assistance (DSMICA). These requirements are also explained on the Internet in CDRH Device Advice, http://www.fda.gov/cdrh/devadvice.

This guidance document is intended to provide specific recommendations to 510(k) submitters about information that they should include in 510(k)s for medical sterilization packaging systems for health care facilities.

This guidance includes sterilization trays and cassettes used for sterilization in health care facilities, because they are intended to enclose medical devices for terminal sterilization and they are considered a medical sterilization packaging system. Therefore, they are Class II devices requiring the submission of a premarket notification [510(k)]. On February 18, 1998, the CDRH Office of Compliance sent a letter to the manufacturers and initial distributors of sterilization trays and cassettes reminding them that if these devices are used for the sterilization of medical devices, they are considered Class II medical devices subject to 510(k) requirements. A copy of this letter is attached as Appendix A.

The proper use and adequate performance of medical sterilization packaging systems used in health care facilities is important to prevent nosocomial infections. The selection of packaging material is a critical step in developing suitable packaging for terminally sterilized medical devices. The process of designing and developing packaging systems for terminally sterilized medical devices is a complicated, critical endeavor. The use of comprehensive, scientifically sound criteria to evaluate medical sterilization packaging systems helps ensure the safety and effectiveness of these products. We recognize that providing FDA reviewers, 510(k) submitters, and other interested parties information on the 510(k) review process can promote a more consistent and efficient regulatory process.

I. INTRODUCTION

A. Scope

This document provides guidance concerning the content and format of 510(k) submissions for medical sterilization packaging systems intended for the sterilization of medical devices in health care facilities. This guidance also covers reusable cassettes and trays provided by instrument manufacturers that are intended to be reused by the health care facility.

Medical sterilization packaging systems encompass:

- Sterilization wraps
- Sterilization pouches and packs
- Sterilization containers and cassettes, including trays, mats, holders, or any other component that is used for sterilization of medical devices.

These devices are regulated under 21 CFR §880.6850, Sterilization wrap, which reads:

> A sterilization wrap (pack, sterilization wrapper, bag, or accessories) is a device intended to be used to enclose another medical device that is to be sterilized by a health care provider. It is intended to allow sterilization of the

enclosed medical device and also to maintain sterility of the enclosed device until used.

Sterilization containers, cassettes, trays, etc., intended to be used for sterilization are considered accessories to a sterilization wrap. FDA encourages you to contact DSMICA or Division of Dental, Infection Control, and General Hospital Devices (DDIGD) representatives with any questions before submitting a 510(k) for medical sterilization packaging systems for health care facilities.

B. Exclusions

This document does not cover the medical device packaging products listed below:

1. Trays and cassettes intended to be used only for storage or transportation, and not for sterilization.

2. Packaging systems used in industrial settings by manufacturers to enclose their medical devices for sterilization for commercial distribution.

3. Cassettes or trays used for the packaging of single use devices that are not intended to be reused.

4. Process indicators printed on the packaging systems or incorporated in a sterilization container system. (Process indicators are themselves medical devices subject to 510(k) requirements. See Appendix G. 510(k) Checklist for Through-Put Process Indicators.)

5. Packaging intended for aseptically produced devices.

C. Definitions

Cassettes, Sterilization: No consensus definition available. FDA defines cassettes as sterilization containers that have perforations to allow the sterilant to penetrate. To maintain sterility, they are enclosed in a sterilization wrap.

Containers, Rigid sterilization: Packaging systems designed to contain items for sterilization, storage, transportation, aseptic presentation of contents, and return of contaminated items to the decontamination area. Note — The system generally consists of a bottom or base with carrying handles and a lid that is secured to the base by means of a latching mechanism. A basket or tray to hold instruments or other items to be sterilized is placed inside. A filter or valve system is incorporated into the lid and/or base to provide for air evacuation and sterilant penetration

during the sterilization cycle and to act as a barrier to microorganisms during storage. (AAMI, 1996)

Closure: Means used to close a package where no seal is formed; for example, by repeated folding to construct a tortuous path. (AAMI, 1997)

Closure integrity: Condition of the closure, which ensures that the closure presents a microbial barrier to at least the same extent as the rest of the packaging. (AAMI, 1997)

Health care facility: Hospitals, nursing homes, extended-care facilities, freestanding surgical centers, clinics, and medical and dental offices.

Medical device: As defined in the act:

> …an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is
>
> 1. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
>
> 2. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
>
> 3. intended to affect the structure or any function of the body of man or other animals, and
>
> which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. 21 USC §321(h).

Meltblown: A material that is similar to spunbonded material in that it is formed from a polymer by in-line melt spinning, but the fibers are finer and may not be continuous. (ASTM, 1997)

Microbial barrier: Attribute of the packaging systems that prevents the ingress of microorganisms under specified conditions. (AAMI, 1997)

Seal: The result of joining of the layers, e.g., by use of adhesives or thermal fusion. (AAMI, 1997)

Seal integrity: Condition of the seal, which ensures that it presents a microbial barrier to at least the same extent as the rest of the packaging. (AAMI, 1997)

Seal strength: Mechanical strength of the seal. (AAMI, 1997)

Spunbond/meltblown/spunbond: A fabric consisting of three thermally or adhesively bonded layers. Spunbonded materials are made up of continuous filaments, which are formed by in-line melt spinning. Meltblown materials are similar in that they are formed from a polymer by in line melt spinning, but the fibers are finer and may not be continuous. (ASTM, 1997)

Spunbonded: A material made up of continuous filaments, which are formed by in-line melt spinning. (ASTM, 1997)

Sterilization Medical Packaging Systems: No consensus definition available. FDA defines sterilization packaging systems as sterilization wraps, packs, pouches, or accessories (e.g., containers, cassettes, trays, holders, etc.) that are intended to enclose another medical device that is to be sterilized by a health care provider. They are intended to allow sterilization of the enclosed device.

Surgical kraft paper: High-strength virgin pulp, with minimal ingredients that may serve as nutrients to microorganisms. Paper formation is closely controlled to provide optimum porosity and effective bacterial barrier. (Wiley, 1997).

Trays: No consensus definition is available. FDA defines trays as baskets with perforated sides and bottom that hold instruments and are either enclosed in sterilization wrap or placed inside a container for sterilization.

Wet Laid: A nonwoven fabric consisting of wood pulp or a blend of polyester and wood pulp fibers. The fibers are suspended in water to obtain a uniform dispersion and are then separated from the slurry by draining the water through a fine mesh screen. For medical-grade fabrics, a chemical binder is often used to bond the fibers together. A chemical treatment can be used to improve liquid penetration resistance. (ASTM, 1997)

D. Regulatory Authority And Classification

FDA classified medical devices that were in commercial distribution prior to the 1976 medical device amendments into one of three regulatory classes: class I, II, or III. The class establishes the regulatory controls that are necessary to provide reasonable assurance of the device safety and effectiveness. Class I devices are subject to general controls. Class II devices are subject to general controls and any FDA-established special controls (as amended by the Safe Medical Devices Act of 1990.) Class III devices are subject to general controls and premarket

approval procedures. See DSMICA's Device Advice at http://www.fda.gov/cdrh/devadvice/ for guidance on general controls.

A medical sterilization wrap or packaging systems is a class II device (product code FRG or KCT) subject to premarket notification 510(k) requirements (21 CFR §880.6850.) Medical sterilization packaging systems also include pouches, rigid sterilization containers, sterilization cassettes, sterilization trays (also referred to as instrument trays) and accessories. No performance standards were promulgated for this device.

E. The 510(k) Paradigm: Alternate Approaches to Demonstrating Substantial Equivalence

Section 510(k) of the act requires a person who intends to introduce a device into commercial distribution to submit a premarket notification, or 510(k), to FDA at least 90 days before commercial distribution is to begin. Section 513(i) of the act stipulates that FDA may issue an order of substantial equivalence upon making a determination that the device to be introduced into commercial distribution is as safe and effective as a legally marketed device. FDA guidance, "A New 510(k) Paradigm - Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance," http://www.fda.gov/cdrh/ode/parad510.html, describes alternative approaches to the traditional methods to demonstrate substantial equivalence.

F. Device Modification

FDA guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device," www.fda.gov/cdrh/ode/510kmod.html explains when to submit a new 510(k) for a change to a legally marketed device.

The following modifications are examples of changes to a 510(k) cleared medical sterilization packaging system that do not significantly affect the safety and effectiveness of the modified device and therefore, do not require the submission of a new 510(k)[1].

1. Changes to the process indicator contained in the packaging system (as long as it is a previously cleared process indicator).

[1] Under 21 CFR §807.85(b), a distributor who places a device into commercial distribution for the first time under his own name and a repackager who places his own name on a device and does not change any other labeling or otherwise affect the safety and effectiveness of the device, is not required to submit a 510(k) if 1) The device was in commercial distribution before May 28, 1976; or a premarket notification submission was filed by another person.

2. The addition of new sizes of sterilization containers to a family of 510(k)-cleared sterilization containers, as long as the configuration and perforations remain the same.

3. Incremental changes in perforations to the 510(k)-cleared sterilization container for better sterilant penetration that do not adversely affect the maintenance of sterility.

4. Changes in the directions for use that make them clearer or more user friendly.

5. Extension of shelf life based on FDA-accepted protocols in the original 510(k).

Device modifications that impact safety and effectiveness, but do not change the intended use or fundamental device technology, may be eligible for review as a Special 510(k). The criteria and content for a special 510(k) are discussed in guidance on the new 510(k) paradigm, cited above.

G. Premarket Notification 510(k) Procedures

If you determine that it is necessary to submit a 510(k) for a sterilization packaging system intended for use in a health care setting, you should include all of the data or information outlined in this guidance document. You should explain, if you omit some of the elements or if you provide alternative data. If we determine that the 510(k) submission is grossly incomplete, we will refuse to accept the document and notify you in writing. See also, FDA guidance, "510(k) Refuse to Accept Procedures 5/20/94 (K94-1)" http://www.fda.gov/cdrh/k941.html**.**

This guidance document is intended to supplement FDA guidance, "Premarket Notification 510(k): Regulatory Requirements for Medical Devices" http://www.fda.gov/cdrh/manual/510kprt1.html. You should use both to prepare your 510(k).

II. 510(k) CONTENT

A. Cover Letter and Introductory Information

The cover letter in the 510(k) should contain the following information.

1. Trade name or proprietary name of the device

2. Common, usual, or classification name of the device, e.g., sterilization wrap, sterilization containers, sterilization cassettes.

3. Establishment registration number, if applicable, of the owner or operator submitting the 510(k)

4. FDA product code:

   FRG - wrap

   KCT- pack, container, cassettes and components

5. FDA review panel code: INCB (Infection Control Devices Branch)

6. Classification: Class II

7. Name and 510(k) number of the legally marketed predicate

8. Name, address, and telephone number of an official contact person for the 510(k) submission

B. Table of Contents

The document should include a table of contents that notes the section titles and pages.

C. Information Required

A 510(k) must include either:

A summary of the safety and effectiveness information upon which an equivalence determination could be based. 21 CFR §807.92.

or

A statement that safety and effectiveness information will be made available to interested persons upon request. 21 CFR §807.93(a)(1).

A person submitting a 510(k) must also provide a Truthful and Accurate Statement, which affirms that to the best of his or her knowledge, all information submitted in the premarket notification is truthful and accurate and no material fact has been omitted. 21 CFR §807.87(k).

In addition, each 510(k) submission should include an Indication for Use Statement for the device. An Indication for Use Statement for a sterilization packaging systems should include the type of sterilization method and the cycle parameters for which the packaging systems are intended to be used.

Examples of the following administrative documents are attached as follows:

- Truthful and Accurate statement (Appendix B)
- 510(k) Statement (Appendix C)
- Indication for Use statement (Appendix D)

D. Comparison of the New Device with the Predicate

A 510(k) submission should include a detailed summary table comparing the new device to the predicate device. You should identify a predicate and compare the characteristics of the new device to the predicate. The following table is an example of the information that you should provide.

Table 1. Comparison with the Predicate

ELEMENT	NEW DEVICE	PREDICATE
Intended use		
Material Composition		
Physical Properties		
Chemical Properties		
Configurations/Dimensions		
Air permeance		
Percent of surface perforations		
PERFORMANCE	**NEW DEVICE**	**PREDICATE**
Sterilant Penetration		
Microbial Barrier Properties (Packaging Integrity)		
Material Compatibility		
Toxicological Properties (Biocompatibility, including Sterilant Residue Limits)		
Shelf Life		
Drying time		
Aeration time		

At a minimum, the performance characteristics above should be supported by the following information:

- Sterilant Penetration - You should submit performance data comparing the characteristics of sterilant penetration of your device with the predicate. Your device should be porous enough to allow adequate sterilant penetration or conductance.

- Microbial Barrier Properties - You should submit performance data comparing the packaging integrity properties of your device with the predicate. To maintain sterility, your device should be impermeable to microorganisms.

- Material Compatibility - You should submit data comparing the material compatibility characteristics of your device with the predicate, using the sterilization process(es) for which it is intended. Your device should not be degraded by any sterilant used to sterilize it.

- Toxicological Properties - You should submit comparative biocompatibility information on the level of any toxic by-product, including the sterilant residues that may pose health risk to patients.

- Shelf Life - You should compare the shelf life claimed for your device with the predicate, if applicable.

- Drying Time - You should submit comparative information on the drying time needed to allow drying of the enclosed devices. Your device should permit adequate drying of the enclosed devices.

- Aeration Time - You should submit comparative information on the aeration time needed to allow removal of sterilant residues. Your device should permit adequate aeration of the sterilant, i.e., removal of sterilant residues.

E. Device Description

The device description for the sterilization medical packaging system should include the general characteristics regarding the device design and manufacturing specifications as follows. The examples given below are for illustrative purposes. They are not exhaustive lists of all possibilities.

1. Material Composition

    - Wraps - e.g., spunbonded polyolefin, spunbond/meltblown/spunbonded laminates, woven.

    - Pouches - e.g., tyvek/plastic, surgical kraft paper/plastic, spunbonded/plastic.

- Sterilization containers, cassettes or trays - e.g., polymer, anodized aluminum, stainless steel.

2. Specifications and Tolerances

    - Wraps - sizes, thickness, burst strength, tensile strength, linting, air permeability.

    - Pouches – various sizes, configurations, process indicators, burst strength, tensile strength, air permeability, seal strength, seal integrity.

    - Containers – design, percentage of open area or perforations, process indicators, accessories, detailed description of filters, gaskets, bottom/lid alignment, baskets, holders, mats.

    - Cassettes – design, percentage of open area or perforations, identification of sterilization wrap, mats.

3. Toxicological properties of the material, including sterilant residues

4. Compatibility of the material with the recommended sterilization processes and cycle parameters

5. Description of the recommended sterilization process and cycle parameters

6. Limits of reuse

F. Intended Use

The 510(k) should clearly state the intended use of the sterilization wrap, container, or cassette. According to 21 CFR §880.6850, a sterilization wrap (pack, sterilization wrapper, bag, or accessories) is a device intended to be used to enclose another medical device that is to be sterilized by a health care provider. A sterilization wrap is intended to allow sterilization of the enclosed medical devices and to maintain sterility of the enclosed device until it is used. Accessories refer to containers, cassettes, trays, baskets, mats, holders, etc. that are used with sterilization packaging systems.

Materials intended to wrap, containerize, or seal articles being sterilized need to permit the penetration of sterilant or conductance of thermal energy within a reasonable period of time. Sterilization cassettes and trays require sterilization wrap. Sterilization containers require filters that are usually made of the same material as sterilization wrap.

Sterilization containers and cassettes are enclosed systems. To permit sterilant penetration, sterilization containers and cassettes require perforations in the lid, bottom, or both. Sterilization cassettes need to be completely enclosed in sterilization wrap to maintain sterility. The sterilization wrap used should be legally marketed and used according to its intended use.

Sterilization trays are not enclosed systems. Generally, trays do not have lids. Instead, they may be entirely open. Therefore, sterilization trays need sterilization wrap to maintain sterility.

Sterilization cassettes and trays are reusable devices, therefore you should provide their limits of reuse.

If process indicators are included in medical sterilization packaging systems, you should provide the information recommended in Appendix G. A process indicator is also a class II device, 21 CFR §880.2800 (sterilization process indicator), requiring 510(k) clearance. The process indicator may be cleared in the same 510(k) as the medical sterilization packaging system.

G. Consensus Standards

You should identify any consensus standards that the medical sterilization packaging system meets. FDA will accept declarations or statements of conformity to recognized standards which address descriptive or performance recommendations in this document in lieu of the information or performance data. (See also Appendix F for a sample format of a Declaration of Conformity to a recognized standard.) FDA maintains a list of recognized standards at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm. For additional information on the use of standards in 510(k) submissions, see "Guidance on the Use of Standards in Substantial Equivalence Determinations," http://www.fda.gov/cdrh/ode/guidance/1131.html.

III. PERFORMANCE INFORMATION AND TESTING

You should provide verification and validation data for the parameters listed in under **II. 510(k) Content**, **D. Comparison of the New Medical Device with the Predicate** and **E. Device Description**.

You should provide validation data for the accessories and the instruments that are to be used with the sterilization packaging system. You should also provide information on the sealing properties of the seals, gaskets, and filters used in the packaging system.

If the new device includes a number of sizes and configurations, the samples selected for obtaining performance information should adequately represent all of the sizes and configurations that will be considered cleared under the 510(k).

Protocols submitted in the 510(k) should provide sufficient information to allow FDA to evaluate efficacy claims.

The protocol should contain the following information.

- The objective of the testing
- Detailed information about the sterilization methods used, e.g., steam, ethylene oxide (EO)
- The sterilization cycles tested
- Detailed information about materials (porous or nonporous), devices
- Description of the sterilizer used and the cycle parameters
- Medical devices sterilized
- Sterilization loads, e.g., size and representative products used
- Load configuration, including stacking
- Biological and chemical indicators
- Positive and negative controls
- Results obtained from the study
- Analysis of results
- Conclusions drawn from the study

The following are the recommended performance data that need to be provided in the 510(k) submission:

A. Sterilant Penetration

1. Penetration and Contact

You should provide performance information demonstrating that the sterilant is able to penetrate the sterilization wrap, pouch, cassette, container, or tray and sustain direct contact with the medical instruments inside the package for each sterilization method claimed in labeling. The information should be in a form that allows for comparison with the predicate in order to determine substantial equivalence.

2. Device Families, Product Lines, and Accessories

The submission should include information that supports using the selected packaging system(s) to demonstrate the substantial equivalence of all of the packaging devices that will be marketed upon clearance of the submission. This should include devices or accessories such as mats, holders, and dividers.

3. Loads and Configurations

You should use the maximum recommended loads of instruments and configurations in performance testing. If you recommend stacking the packaging devices during sterilization, testing should include stacked configurations. Testing should show how stacking affects air evacuation, sterilant penetration, and drying of contents.

4. Biological Indicators

Biological indicators (BIs) should be placed in the most difficult areas to reach inside the packaging and in or on instruments to demonstrate adequate sterilant penetration to these areas by the lethality of the BIs. In addition, we recommend performing half cycle determinations to demonstrate the minimum exposure time, i.e., the exposure time resulting in no BI survivors. The labeled exposure time for the sterilization packaging systems should be at least double the minimum exposure time. The established sterilization cycle time should be within the standardized cycle time of the sterilizers routinely used in the health care setting.

5. Steam Sterilant

For steam sterilant penetration testing of containers and cassettes, you should obtain temperature profiles by placing (thermocouple) temperature probes in the chamber, in the container, on the instruments, and near the chamber drain. The temperature probes can be used to assess steam penetration by showing how long it takes for the temperature inside the container to reach the temperature in the sterilizer chamber. To show adequate steam penetration, the temperature profile inside the container should be the same as the temperature profile inside the sterilizer chamber. Sterilization cassettes and trays are usually wrapped for sterilant penetration testing. If you also plan to market baskets, trays, or other components with your sterilization containers, you should conduct additional testing to show that these components do not impede steam sterilant penetration.

B. Package Integrity

1. Physical Properties

You should conduct performance testing to show the physical properties of the material. For sterilization wrap and pouches, testing demonstrating tensile strength, thickness

variation, tear resistance, air permeance, burst strength, etc. should be conducted, in addition to performance testing, both before and after sterilization. This type of testing should also be conducted on the filter material used for sterilization containers.

2. Microbial Barrier Properties

You should conduct performance testing demonstrating the microbial barrier properties of the medical device packaging system after sterilization. Microbial barrier properties of the sterilization packaging system may be determined by the microbial challenge test or physical test methods. FDA believes physical test methods that are scientifically sound and properly validated are better suited to demonstrate sterile package integrity and maintenance of sterility.

The microbial challenge test is a whole package test that consists of placing the packaging system inside a chamber and exposing it to a defined aerosol of microorganisms and conducting sterility testing on the contents. FDA is not aware of data demonstrating that the microbial challenge test has been validated or standardized. If you use the microbial challenge test for package integrity, you should submit a detailed protocol along with the data from the testing.

3. Physical Test Methods

FDA will accept data from these physical test methods:

- Physical test methods developed by standard setting bodies, set forth in consensus standards that are recognized by the Agency

- Physical test methods published in peer-review journals and performed under well-controlled conditions. (You should demonstrate that the use of one of these methods is sensitive and appropriate for your packaging materials, and that your data are not statistically different in reproducibility and repeatability from the published data.)

- Physical test methods developed by manufacturers, if properly validated for the manufacturer's device and packaging system

The American Society for Testing and Materials (ASTM) has published several standards for package integrity testing using physical test methods. The following are recognized by FDA:

- Standard Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission D3078:1994

- Standard Practice for Performance Testing of Shipping Containers and Systems D4169:1999
- Standard Test Method for Seal Strength of Flexible Barrier Materials F88:1999
- Standard Test Methods for Failure Resistance of Unrestrained and Nonrigid Packages for Medical Application F1140:1996
- Standard Terminology Relating to Barrier Materials for Medical Packaging F1327:1998
- Standard Guide for Integrity Testing of Porous Barrier Medical Packaging F1585:1995
- Standard Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method) F1608:1995
- Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection F1886:1998
- Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration F1929:1998
- Standard Guide for Accelerated Aging of Sterile Medical Device Packages F1990:1999

Please note that the "Standard Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission" is the only standard for physical testing of whole package integrity.

Physical test methods published in peer-review journals or developed by manufacturers should be validated against methods from the standards cited above. The validation process includes, at a minimum, the following elements:

- Select the most appropriate tests for the packaging materials
- Establish pass/fail criteria
- Establish test sensitivity
- Determine method repeatability
- Demonstrate reproducibility

4. Sterilization Pouch Integrity

You should provide data demonstrating both seal strength, seal integrity, and whole package integrity. You should use the standard test methods from the standards cited above or validated test methods. Data should show that the seals are impermeable and continuous and there are no tears, punctures, material delamination, separation channels, or open seals. Whole package integrity data may be obtained from either physical or microbial barrier testing.

5. Sterilization Cassette Integrity

The data should show that the enclosed devices are sterile. The cassette itself cannot maintain sterility. No claims can be made for maintenance of sterility unless the cassette is wrapped with sterilization wrap.

6. Sterilization Container Integrity

You should provide data on the microbial barrier properties of the filter material and gaskets, in addition to performance data demonstrating package integrity. The data should demonstrate that they have tamper evident closure systems, matching lids and bottoms, and gaskets and filters that provide a microbial barrier.

C. Maintenance of Package Integrity

An important characteristic of a medical sterilization packaging system is its ability to maintain the sterility of the enclosed medical device under labeled shelf life, transport, and storage conditions. Microbial barrier properties of sterilization packaging should be evaluated after exposure to storage conditions and environmental stresses expected for finished packaging systems. Data should demonstrate that the enclosed devices are sterile and the integrity of the packaging systems during shelf life, transport, and storage is maintained.

Performance testing should be conducted to evaluate the stability of the packaging systems after stressing by simulating labeled shelf life, transport, and storage conditions. After stressing the packaging system, physical testing or microbial challenge testing should be conducted to determine the microbial barrier properties. Physical test data for pouches should show that the physical parameters for seal strength and whole package integrity are still within the original package integrity specifications.

D. Drying and Aeration

1. Drying Time

Testing should demonstrate that the sterilization packaging system permits drying of the medical instruments inside the package and aeration of the sterilant. Drying time for a steam sterilizer is usually 25 minutes. Drying of the medical devices inside the containers or cassettes is necessary to prevent contamination during storage. Certain plastic containers require longer than the standard drying time. You should explain any longer drying times observed in testing. The labeling should state whether the drying time is over 25 minutes; how long the drying time is; and that this drying time is required to prevent wet packs.

2. Non-Woven Materials Effect on Drying Time

Containers or cassettes with non-woven inner mats and liners should be tested to show that these materials do not interfere with drying or extend the drying time. A woven material in contact with a hot metal container is more likely to dry faster than a synthetic or non-woven material. Non-woven material can interfere with the drying process by occluding the perforations, impeding the drainage of condensate. Adding a higher percentage of perforations may be necessary to prevent this.

3. Plastic Containers

A plastic container with a non-woven liner may extend the drying time significantly, creating the risk of contamination due to moisture retention. FDA believes data are needed to support the use of a plastic container with a non-woven liner, except in circumstances when extended drying times and moisture retention have no effect, such as when the sterilized contents will be used immediately.

4. Containers With Valves

Recondensation can occur with containers with valves. For containers with valves, you should explain how recondensation has been resolved. You should also include instructions in the labeling if the user needs to act because of recondensation, e.g., extend the drying time or use woven material to reabsorb the recondensation.

5. Aeration Time and EO Residuals

Aeration time is the time needed to remove EO residuals. You should provide the EO residuals and the method for measuring the level of EO residuals, in addition to the aeration time. The aeration time for health care EO sterilizers is usually 8 hours at 60°C (141°F) or

12 hours at 48°C (120°F). You should explain any extended aeration times. Labeling should reflect any extended aeration time. For reusable packaging systems such as plastic containers, the aeration of EO residuals should be performed after the limits of reuse, because retention or build-up of EO residuals in the plastic may affect the container or its contents. Since these containers are reusable, the amount of EO residuals that remain on the containers after the limits of reuse may be above the levels otherwise acceptable for single use devices.

E. Additional Information for Reusable Containers and Cassettes

For reusable containers and cassettes, data should be provided as described in FDA guidance "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance," http://www.fda.gov/cdrh/ode/198.pdf. The following information should also be provided.

- The limits of reuse
- The procedure for reprocessing including the cleaning parameters (time, temperature, etc.), cleaning action (e.g., ultrasonic, automatic washer), cleaning detergent, cleaning endpoint, tracking, etc.
- Data to demonstrate that after processing the container or cassette maintain the original specifications

The labeling for reusable sterilization containers or wraps should contain validated instructions for reprocessing the device. You should provide instructions for reprocessing, limits of reuse, and method for tracking the device in the labeling. (Please note that tracking refers only to the facility's tracking system, not device tracking as defined in 21 CFR Part 821.) EO residuals are cumulative. EO residual studies should be performed on plastic containers or cassettes after the limits of reuse have been met.

F. Material Compatibility

You should provide data demonstrating that the package material is compatible with the sterilization process for which it is intended. For polymeric composites, you should include a table in the 510(k) comparing the physical and chemical properties of the sterilization packaging materials, before and after sterilization. The properties evaluated should include:

- tensile strength
- thickness variations

- durability
- tear resistance
- air permeance
- burst strength

G. Biocompatibility

You should provide data in the 510(k) demonstrating that the sterilization packaging material is not toxic. Data should also demonstrate that the sterilization packaging material is compatible with the sterilization process for which it is intended. FDA recommends that, at the minimum, you conduct one of the following tests on polymeric materials:

- Primary Dermal Irritation
- Dermal Sensitization
- Blood Hemolysis

In addition, woven materials for wraps should be free of particulate or loose fiber.

IV. LABELING

The labeling for a medical sterilization packaging system must meet the general requirements outlined in 21 CFR Part 801. You are required to submit proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for use. 21 CFR §807.87(e). Where applicable, photographs or engineering drawings should also be submitted. FDA recommends including performance data in the labeling, so users can determine whether the sterilization packaging system will meet their needs.

The following references may also provide further FDA guidance for labeling.

- Labeling - Regulatory Requirements for Medical Devices. This document provides information on false and misleading labeling, and advertising material (FDA 89-4203) http://www.fda.gov/cdrh/dsma/470.pdf.

- Device Labeling Guidance #91-1 (Office of Device Evaluation Blue Book Memorandum) http://www.fda.gov/cdrh/g91-1.html. This guidance provides detailed information on labeling and applicable labeling regulations.

These publications are available on the Internet at the addresses shown or by calling DSMICA at (800) 638-2041.

For sterilization wraps, pouches, containers, and cassettes the following information should be included in the labeling:

- The intended use, e.g., the types of instruments recommended to be used with the packaging system
- Manufacturer's name and address
- Description of the device (e.g., medical sterilization packaging systems)
- The sterilization method and types of cycles, e.g., gravity, prevacuum, EO
- The recommended sterilization load, stacking, configuration
- The aeration times for the device and contents, if any, for EO sterilization
- Instructions for use
- Shelf-life
- A statement that complex instruments (e.g., air-powered instruments, endoscopes, and instruments with lumens or channels) should be prepared and sterilized according to the instrument manufacturer's instructions.

We recommend including additional labeling information, as shown, for the following devices:

Sterilization wrap

- Instructions for wrapping
- A precaution if the sterilization is performed by an outside contract facility, that the wrapped devices should be protected from contamination by an additional covering.

Sterilization Pouches

- Instruction for sealing, e.g., heat-sealing, self-sealing, etc.

Sterilization Containers

- A precaution that small baskets, trays, other types of accessories, especially with cover or lids, should only be used with the sterilization container, if the sterilization container has been specifically designed and tested for that purpose.

- Instructions for a validated method for reprocessing, with acceptance criteria for reuse, limits of reuse, and a tracking system.

- Instructions for closures, gaskets, type, sizes, and placement of filters or valve assembly weight

- Instructions for density and distribution of contents, stacking patterns, etc.

- A precaution that the use of nonabsorbent tray liners (e.g., plastic/silicone-fingered organizing mats) can cause condensate to pool.

Sterilization Cassettes

- A precaution that only legally marketed, FDA cleared sterilization wrap should be used to wrap the cassettes.

- Instructions for a validated method for reprocessing with acceptance criteria for reuse, limits of reuse, and a tracking system.

- A statement that small baskets, trays, other types of accessories, especially with cover or lids, should be used with the sterilization cassettes only if the sterilization containers have been specifically designed and tested for this purpose.

- A recommendation that only legally marketed, FDA cleared sterilization wrap be used with the cassette.

- A precaution that the use of nonabsorbent tray liners (e.g., plastic/silicone-fingered organizing mats) can cause condensate to pool.

V. STERILIZATION PACKAGING SYSTEMS CHECKLIST

Date: **510(k) #:**

Yes	No	N/A	510(k) Elements (see guidance for details)
			Cover Letter (Signed and Dated)
			Trade name or proprietary name of device
			Common, usual, or classification name of the device
			Establishment registration number, if applicable
			Product Code: FRG or KCT
			Panel Code: 880 Infection Control Devices Branch
			Classification: Class II
			The name and 510(k) number of the predicate device
			Name, address, and telephone number of the contact person
			510(k) Summary or Statement
			Indication for Use Statement
			Truthful and Accurate Statement
			Device Description
			Intended use
			Material composition, physical and chemical properties
			Specifications, configuration, % of surface perforations or openings
			Microbial barrier properties of the material
			Toxicological properties of the material
			Compatibility with the recommended sterilization cycle
			Sterilization methods and cycles
			Forming and seal properties (seals, gaskets, filters)
			Limits of reuse (reusables)
			The type of devices that are to be sterilized with the device
			Identification of any accessories
			Equivalency table (see Table 1. Comparison with the Predicate)

			Performance data
			Sterilant penetration for each sterilization method claimed
			Package integrity testing
			For wraps and pouches, data on the microbial barrier properties of the material
			For containers, data on the microbial properties of the filter
			Maintenance of sterility and/or shelf life
			Material sterilization compatibility data
			Drying time or aeration time
			Biocompatibility data
			Labeling
			Intended use
			Manufacturer's name and address
			Description of device
			Sterilization method and types of cycles
			Sterilization load and configuration
			Drying and aeration times
			Instruction for use Pouches - instructions for sealing Wraps - instructions for wrapping Containers - instructions on closures, gaskets, filters, or valve assembly weight, Density and distribution of contents, stacking patterns, etc
			Shelf-life
			A statement that complex instruments should be prepared and sterilized according to the manufacturer's written instructions.
			For sterilization wrap, a statement that if sterilization is performed by an outside contract facility, the wrapped devices should be protected from contamination by an additional covering.
			For reusables, instructions for a validated method of reprocessing with acceptance criteria for reuse, limits of reuse, and a tracking system.
			For sterilization containers, small baskets, trays, other types of accessories, especially with cover or lids, should be used with the sterilization containers only if the sterilization containers have been specifically designed and tested for this purpose.

VI. REFERENCES

ANSI/AMMI ST33-1996. Association for Advancement of Medical Instrumentation. Guidelines for the Selection and Use of Reusable Rigid Sterilization Container Systems for Ethylene Oxide Sterilization and Steam Sterilization in Health Care Facilities.

ANSI/AMMI/ISO 11607 - 1997. Association for Advancement of Medical Instrumentation. Packaging for Terminally Sterilized Medical Devices.

AORN Standards. Association of Operating Room Nurses. Recommended Practices, and Guidelines; Recommended Practices for Selection and Use of Packaging Systems.

ASTM F1670 –1997. American Society for Testing & Materials. Standard Test Method for Resistance of materials Used In Protective Clothing to Penetration by Synthetic Blood.

ASTM F1671 – 1997. American Society for Testing & Materials. Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-Borne Pathogens Using PHI- X174 Bacteriophage Penetration as a Test System.

BS EN 868-1:1997. British Standard. Packaging Materials and Systems for Medical Devices which are to be Sterilized - Part 1: General Requirements and Test Methods.

BS EN 868-2:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 2: Sterilization Wrap Requirements and Test Methods.

BS EN 868-3:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 3: Paper for Use in the Manufacture of Paper Bags (specified in EN868-4) and in the Manufacture of Pouches and Reels (specified in EN 868-5) – Requirements and Test Methods.

BS EN 868-4: 1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 4: Paper Bags – Requirements and Test Methods.

BS EN 868-5:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 5: Heat and Self-sealable Pouches and Reels of Paper and Plastic Film Construction—Requirements and Test Methods.

BS EN 868-6:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 6: Paper for the Manufacture of Packs for Medical Use for Sterilization by Ethylene Oxide or Irradiation—Requirements and Test Methods

BS EN 868-7:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized – Part 7: Adhesive Coated Paper for the Manufacture of Heat Sealable Packs for Medical Use for Sterilization by Ethylene Oxide or Irradiation – Requirements and Test Methods.

BS EN 868-8:1999. Packaging Materials and Systems for Medical Devices which are to be Sterilized—Part 8: Re-usable Sterilization Containers for Steam Sterilizers Conforming to EN285—Requirements and Test Methods.

BS EN 868-9:2000. Packaging Materials and Systems for Medical Devices which are to be Sterilized—Part9: Uncoated Nonwoven Materials of Polyolefines for use in the Manufacture of Heat Sealable Pouches, Reels and Lids—Requirements and Test Methods.

BS EN 868-10:2000. Packaging Materials and Systems for Medical Devices which are to be Sterilized—Part 10: Adhesive Coated Nonwoven Materials of Polyolefines for use in the Manufacture of Heat Sealable Pouches, Reels and Lids—Requirements and Test Methods.

FDA: A New 510(k) Paradigm - Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications; Final Guidance

FDA: ODE Blue Book Memorandum #91-1, August 29, 1991, "Device Labeling Guidance."

FDA: "Labeling: Regulatory Requirements for Medical Devices" (HHS Publication FDA 89-4203)

FDA: "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance

FDA: ODE Blue Book Memorandum #K97-1, January10, 1997, "Deciding When to Submit a 510(k) for a Change to an Existing Device."

ISO-10993: 1995 "Biological Evaluation of Medical Devices Part I: Evaluation and Testing"

The Wiley Encyclopedia of Packaging Technology, 1997, P.611

Appendix A. February 18, 1998 Letter to Sterilization Cassette Manufacturers

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 18 1998

6850

Ref.: CFR 880.~~6580~~
Sterilization Wrap

Dear Sir/Madam:

The purpose of this letter is to inform you that sterilization cassettes are devices as that term is defined by Section 201(h) of the Federal Food, Drug and Cosmetic act (the Act). The Federal Register, dated October 21, 1980, Vol. 45, No. 202, page 69732, sterilization wrap, states, in part, "...Identification; sterilization wrap pack, sterilization wrapper bag or accessories, is a device intended to be used to enclose another medical device that is to be sterilized by a health care provider. It is intended to allow sterilization of the enclose medical device and also to maintain sterility of enclose device until used. Classification: Class II device (performance standards). Effective date: This regulation shall be effective November 20, 1980..." Sterilization cassettes are included in this class.

Manufacturers and initial distributors of sterilization cassettes need to comply with all requirements of the Act, including registration and listing, obtaining appropriate marketing clearance, assuring conformance with the Good Manufacturing Practices(GMP)for medical devices regulation, as set forth in the Quality Systems Regulation, and to appropriately label the devices to assure they provide adequate directions for safe use.

If your firm introduced sterilization cassettes into commercial distribution for the first time after May 28, 1976, the date of enactment of the device amendments to the Act, or if your firm has significantly modified any device which was commercially marketed prior to that date, you must submit a pre-market notification [510(k)], pursuant to the requirements of 21 CFR 807.81(a)(1). The medical device listing regulations (21 CFR part 807) require certain establishments to list its devices with the FDA and to maintain a historical listing file of labels, labeling, and promotional material for those devices. Paragraph 807.31(e) of the regulations requires the owner or operator of the establishments upon request, to provide FDA with information from those files.

We request that you provide us with your firm's 510(k) clearance number, a set of the current labeling for your sterilization cassettes, including materials such as labels, brochures, instructional materials, user manuals, patient information, promotional and advertising materials, and any other information on the use of your device. I would also

like to request the name and address of the official correspondent for your company, your establishment registration number and lastly, the names of any other medical devices that you manufacturer and distribute. Please send these material within 15 days of receipt of this letter to me at the above address.

In addition, you may obtain a free guidance document on how to prepare a pre-market notification submission [510(k)] by calling our Division of Small Manufacturers Assistance at 1-800-638-2041 or by faxing a request for information to 301-443-8818. Also, ask for any guidance documents specifically relating to sterilization wraps/cassettes.

Should you have any questions regarding this policy, please contact Sandy Waldron, consumer Safety Officer, General Hospital Devices at this address, or you may call me at 301-594-4618 x118. Thank you for your cooperation.

Sincerely,

Sandy Waldron
Consumer Safety Officer
General Hospital Devices Branch
Division of Enforcement II
Office of Compliance
Center for Devices and
Radiological Health

Enclosures: 21 CFR Part 807
21 CFR Part 880.6250
Introduction to Medical Device Regulations
The Division of Small Manufacturers Assistance (DSMA)

Appendix B. Truthful and Accurate Statement

[Refer to 21 CFR §807.87(k)]

I certify, in my capacity as *[Title]*, that I believe, to the best of my knowledge, that all data and information submitted in this 510(k) Premarket Notification Submission is truthful and accurate and that no material fact has been omitted.

[Signature]

_____

[Name]
[Title]

_____

[Date]

_____

Appendix C. 510(k) Statement

[Refer to 21 CFR §807.93]

I certify that, in my capacity as [*the position held in company by person required to submit the premarket notification, preferably the official correspondent in the firm]*, I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification submission is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential commercial information, as defined in 21 CFR §20.61.

Certified: *[Signature]*

_____

[Date]

Appendix D. Indications for Use Statement

Page_____of_____

510(k) Number (if known):

Device Name:

Indications for Use:

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)
Concurrence of CDRH, Office of Device Evaluation (ODE)

Appendix E. Declaration of Conformity with Design Controls

Verification Activities:
To the best of my knowledge, the verification activities, as required by the risk analysis, for the modification were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met.

_____

[Name] *[Date]*

[Title]

[Company]

Manufacturing Facility:
The manufacturing facility, *[Company Name]* is in conformance with the design control requirements as specified in 21 CFR §820.30 and the records are available for review.

_____

Name] *[Date]*

[Title]

[Company]

[NOTE: The above two statements should be signed by the designated individual(s) responsible for those activities.]

Appendix F. Declaration of Conformity with Consensus Standards

This device is certified to comply with the voluntary standards as contained in *[identify standard(s) along with edition date(s)]*, as specified and so stipulated above, unless and where specifically so indicated to be at variance with the standard specification, in which case information, data and analysis, or justification for non-applicability, are provided to fully describe the variance and its impact on the device and to justify said variance.

_____

[Name] *[Date]*

[Title]

[Company]

[Note: When there is a third-party certifying laboratory or certification body, provide the names and addresses and a reference to any accreditation of each laboratory. Certification statements should also be included.]

Appendix G. 510(k) Checklist for Through-Put Process Indicators

510(k):

DATE:

REVIEWER:

Is the listed information included in the 510(k) submission?			
Yes	**No**	**N/A**	
			I. Device description includes:
			A. A description of the chemical reaction that between the chemical indicator and the sterilization process.
			B. Specifies the conditions under which the chemical indicator will exhibit a color change. If the indicator is labeled to change at more than one temperature, provide data to verify that the indicator will change appropriately at the labeled temperature and not at other temperatures.
			C. Identifies conditions other than those associated with the sterilization process that can cause the chemical indicator to change. These conditions should be described and cautions listed in the labeling.
			II. Labeling does not infer that sterilization has occurred. Labeling should include the following information:
			A. Expiration date, if applicable
			B. Storage conditions
			C. Directions for use
			D. Exposure conditions
			E. Parameters measured
			F. Instructions for interpretation of qualitative or quantitative changes in the indicator
			G. A color standard, if the indicator undergoes a color change during processing and the user is required to make a subjective decision regarding whether the color change is complete
			H. Factors affecting shelf-life
			I. Factors affecting performance
			III. Performance testing. The submission should provide information to demonstrate:
			A. Stability of the strip before use (both unopened/shelf-life and opened package/use-life) to validate storage conditions
			B. The lasting quality (stability) of the color change
			C. The completeness and uniformity of the color change
			D. Color change is all or none at the conditions measured, unless a color standard is provided on the indicator.

IV. Required Administrative Information			
			A. 510(k) summary of Safety and Effectiveness or a 510(k) Statement
			B. Indications for Use Statement
			C. Truthful and Accurate Statement