701 Pennsylvania Avenue, NW
Suite 800
Washington, DC 20004-2654
Tel: 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org

AdvaMed
Advanced Medical Technology Association

March 11, 2009

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rm 1061
Rockville, MD 20852

RE: Response to Docket No. FDA-2008-D-0611

Dear Sir or Madam:

On behalf of AdvaMed, the Advanced Medical Technology Association, I am pleased to submit these comments in response to the United States Food and Drug Administration publication of "*Draft* Guidance for Industry and FDA Staff –Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled As Sterile."

AdvaMed member companies produce the medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. Our members produce nearly 90 percent of the health care technology purchased annually in the United States and more than 50 percent purchased annually around the world. AdvaMed members range from the largest to the smallest medical technology innovators and companies. AdvaMed member companies are dedicated to ensuring the safety and efficacy of the products they manufacture.

Thank you for the opportunity to provide comments on the draft guidance. AdvaMed fully supports FDA's efforts to update and clarify the procedures for reviewing premarket notification submissions (510(k)) for devices labeled as sterile and for pyrogenicity information to be included in 510(k) submissions. However, AdvaMed member companies do have recommendations for changes to the current draft document. These recommended changes to the draft guidance are provided in Attachment A. The line number references are related to the line-numbered copy of the draft guidance (Attachment B).

Of major concern is the requirement listed in section III.A.3. : *"The reviewer should document that all blood contacting devices, permanent implants, devices that contact cerebrospinal fluid, and devices labeled pyrogen free or non- pyrogenic are, in fact, non-pyrogenic."* This statement represents a significant change in current FDA policy as experienced by AdvaMed member companies and as stated in the current FDA guidance "Updated 510(k) Sterility Review Guidance K90-1. The current guidance states *"If the product is labeled "pyrogen free," a description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL)"*. Most device-specific guidances reference K90-1 when discussing sterility and pyrogenicity.

A review of FDA recognized standards related to pyrogen testing shows an inconsistency of scope that does not support the wording in the draft guidance:

> USP31:2008<161> Transfusion and Infusion Assemblies and Similar Medical Devices (Transfusion and infusion assemblies and similar devices that require end-product endotoxin testing or that claim to be non-pyrogenic)
>
> USP31:2008<151> Pyrogen Test (USP Rabbit Test) (All devices that need to limit, to an acceptable level, the risk of a febrile reaction in the patient.)
>
> ANSI/AAMIST72:2002 Bacterial Endotoxin Testing Methodologies, Routine Monitoring, and Alternative to Batch Testing ("...apply to sterile and non-pyrogenic assemblies or devices in contact directly or indirectly with the cardiovascular system, the lymphatic system or cerebrospinal fluid")
>
> USP31:2008<85> Bacterial Endotoxin Test (LAL) ("Devices that contact patient blood, cerebrospinal fluid, or other normally sterile body fluids or tissues; implantable devices; and products labeled as non-pyrogenic.")

The specific requirements stated in the draft guidance will result in testing devices that have not warranted non-pyrogenic claims in the past and for which FDA has not required non-pyrogenic claims. As always, increased testing incurs increased cost to produce medical devices. AdvaMed member companies are more than willing to conduct appropriate and necessary testing to ensure device safety; however, they are reluctant to conduct testing that is unnecessary and does not improve or contribute to device safety.

AdvaMed recommends that the wording relating to pyrogen testing in the revised guidance be the same as stated in the K90-1. This wording allows decisions related to appropriate pyrogen testing of individual device types to be determined by FDA through guidances, standards recognition, and discussions with industry.

If you have questions or would like clarification, please feel free to contact me at 202-434-7220 or rdempsey@advamed.org.

Sincerely,

Ruey C. Dempsey

Ruey C. Dempsey
Director
Technology and Regulatory Affairs

Attachment A-AdvaMed Comments
Attachment B-Draft Guidance with line numbers

ATTACHMENT A

ADVAMED Comments

Draft Guidance for Industry and FDA Staff Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile

No. – Edit number
Line(s) No. – Line or lines numbers of the guidance (see line numbered copy Attachment B)
Change – Proposed change to the guidance
Reason – Reason for proposed change

No.	Line(s) No.	Change	Reason
1	112-113	Therefore, we intend to inspect the ***sterilization facility*** before clearing a 510(k) for a device that is sterilized by a novel non-traditional sterilization process.	The manufacturing facility may not be the site of the sterilization operation (e.g., contract sterilizer facility).
2	113-114	Sentence is incomplete	
3	115	Clarify the *Scope* of the guidance (or state in another section of the guidance) to specify that changing sterilization methods to a non-traditional method does not require a new 510(k) to be filed as long as the SAL remains the same.	Updated 510(k) Sterility Review Guidance K90-1, dated August 30, 2002 makes this provision.
4	122-127	…Examples of microbial exclusion processes include sterilizing filtration methods and aseptic processing, commonly used in pharmaceutical manufacturing. Heparin and saline lock flush solutions, which are regulated as medical devices,[8] belong to this category ***if in non-heat stable containers*** and, therefore, are excluded. ***Proof of incompatibility with terminal sterilization process should be provided and reviewed.***	Heparin and saline lock flush solutions are heat-stable and are suitable for terminal sterilization. As a result, heparin and saline lock flush solutions should not be categorically excluded from the guidance if they are terminally sterilized
5	154	Traditional Sterilization Methods: methods that have a ***demonstrated*** safe and effective use as documented by …	"long history" is vague.
6	163	Add to the definition of *non-traditional sterilization methods* a statement that a sterilization method that was previously cleared by a 510(k) for use as a Sterilizer in a Health Care facility qualifies the method as non-traditional for an industrial sterilization application.	

ATTACHMENT A

ADVAMED Comments

Draft Guidance for Industry and FDA Staff Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile

7	209-211	Delete phrase ***"or uses a long gas dwell time (e.g., greater than 8 hours)"***	The length of EO exposure is not in any way 'Novel" or non-traditional. It is not uncommon to have long gas dwell times in traditional fixed chamber sterilization, based upon package and device configuration. Including this example in the guidance document may lead to confusion regarding what defines a novel sterilization method.
8	250-251	FDA recommends an SAL of 10^{-3} for devices intended only for contact with the skin, or ***with no direct patient contact.***	Many devices are sterilized even though there is no intent that the device will contact the patient. Examples are needle connection devices for use in surgical suites and collection bags for used surgical sponges. It would be unnecessarily burdensome to impose more stringent requirements on these types of non-patient contact sterile devices than for devices that are intended for contact with intact skin.
9	252-256	If the product is labeled "pyrogen free," a description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL).	Retain current language in K90-1. See discussion in the cover letter.
10	258	A description of the method ***to be*** used…	In many cases, the product that is the subject of a 510(k) submission has not yet been manufactured in the final manufacturing setting; therefore, actual finished product testing has not been completed so the method has not been used at the time of the 510(k).
11	259-261	…e.g., bacterial endotoxins test (BET), also known as the *limulus* amebocyte lysate (LAL) test; ***or USP Pyrogen Test (Rabbit) or equivalent test…***	Expand the list of examples to include rabbit and equivalent test.
12	262-263	b. identification of the ***endotoxin limit***; and	"endpoint" is not typically used when referring to a product endotoxin limit. The FDA LAL Guideline document (1987), USP<161>, and ANSI/AAMI ST72:2002 all use the term "endotoxin limit" when describing how to calculate the product endotoxin limit.

ATTACHMENT A

ADVAMED Comments

Draft Guidance for Industry and FDA Staff Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile

13	264-284	c. an explanation supporting the selected ***endotoxin limit***. We recommend the following ***endotoxin limit***: 0.5 EU/ml for general medical devices (e.g., blood contacting) and 0.06 EU/ml for devices that contact cerebrospinal fluid. These ***endotoxin limits***…	See comment above
14	281	Add reference: ***United States Pharmacopeia (USP) <161> Transfusion and Infusion Assemblies and Similar Medical Devices***	USP <161> provides guidelines for performing extractions of medical devices for the purposes of LAL testing, as well as the formula used to calculate the product endotoxin limits for medical devices.
15	293-301	Provide requirements for information on methods used for novel non-traditional sterilization methods. What information is needed?	Requirements for information for information traditional methods are listed in III A.; the requirements for non-traditional are stated in III B. **No** requirements are listed for novel non-traditional in III C.
16	380	Describe how manufacturers will be made aware that a previously novel non-traditional sterilization method has been redefined as a non-traditional method.	It will be important for companies who are submitting 510(k)s to know that a previously novel non-traditional method has been re-classified as non-traditional.
17	435-437	Footnote 12 Provide more specific information on the requirement for "whole package integrity test and one seal strength test". List FDA recognized standards for package integrity testing.	

ADVAMED COMMENTS

ATTACHEMENT B

Draft Guidance for Industry and FDA Staff: Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: December 12, 2008

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Alternatively, electronic comments may be submitted to http://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding devices regulated by the Center for Devices and Radiological Health, contact Steven Turtil at (240) 276-3747, or by e-mail at steven.turtil@fda.hhs.gov, or Chiu Lin, Ph.D. at (240) 276-3747, or by e-mail at chiu.lin@fda.hhs.gov. For questions regarding devices regulated by the Center for Biologics Evaluation and Research (CBER), contact Leonard Wilson at 301-827-0373 or by email at leonard.wilson@fda.hhs.gov.

When final, this document will supersede Updated 510(k) Sterility Review Guidance K90-1, dated August 30, 2002.

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

Center for Biologics Evaluation and Research

Preface

Additional Copies

Additional Copies

Additional copies are available from the Internet at:
http://www.fda.gov/cdrh/ode/guidance/xxxx.html. You may also send an e-mail request to dsmica@fda.hhs.gov to receive an electronic copy of the guidance or send a fax request to 240-276-3151 to receive a hard copy. Please use the document number (1615) to identify the guidance you are requesting. Copies of the guidance are also available from:

Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448
Phone: 800-835-4709 or 301-827-1800

Contains Nonbinding Recommendations
Draft - Not for Implementation

Table of Contents

Draft Guidance for Industry and FDA Staff

Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA'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 FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Introduction

This draft guidance document updates and clarifies the procedures for reviewing premarket notification submissions (510(k)s) for devices labeled as sterile, particularly with respect to sterilization technologies FDA considers novel, and provides details about the pyrogenicity information that we recommend you include in your 510(k) submissions.[1] This draft guidance document also addresses the information regarding sterilization processes that we recommend you include in 510(k)s for devices labeled as sterile.

This draft guidance document does not apply to sterilizers that are themselves medical devices subject to 510(k).[2] ,[3]This draft guidance document also does not address 510(k) submissions for reusable medical devices that are reprocessed in health care settings,[4] 510(k) submissions for reprocessed single-use devices,[5] or information to be included in 510(k)s for devices that contain animal tissue.[6] Finally, FDA notes that the sterilization methods used in manufacturing settings are subject to FDA's Quality System (QS) regulation requirements, 21 CFR Part 820.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

A. The Least Burdensome Approach

This draft guidance document reflects our careful review of what we believe are the relevant issues related to review of devices labeled as sterile (including those regulated by the Center for Biologics Evaluation and Research (CBER)) and what we believe would be the least burdensome way of addressing these issues. If you have comments on whether there is a less burdensome approach, however, please submit your comments as indicated on the cover of this document.

B. Background

In recent years, FDA has received an increased number of 510(k)s for devices labeled as sterile that use **non-traditional** sterilization methods in their manufacture. FDA has experience with some types of **non-traditional** methods of sterilization. We recognize, however, there may be **novel non-traditional** sterilization technologies used in the manufacture of class I and class II devices. (The terms **non-traditional** and **novel non-traditional** are defined in Section II.A. below.)

Under section 513(f)(5) of the Federal Food, Drug, and Cosmetic Act (the act), FDA may not withhold 510(k) clearance for failure to comply with any provision of the act unrelated to a substantial equivalence decision, including failure to comply with Good Manufacturing Practice (GMP),[7] unless FDA finds that there is a substantial likelihood that failure to comply with the provision "will potentially present a serious risk to human health." We believe that using **novel non-traditional** sterilization technologies carries a substantial risk of inadequate sterility assurance and that, consequently, devices sterilized using **novel non-traditional technologies** may not comply with GMP. Failure to assure sterility presents a serious risk to human health because of the risk of infection.

Therefore, we intend to inspect the manufacturing facility before clearing a 510(k) for a device that is sterilized by a **novel non-traditional** sterilization process. We believe inspecting devices sterilized using novel

C. Scope

The scope of this guidance is limited to the review of 510(k)s for devices labeled as sterile that are subject to industrial terminal sterilization processes based on microbial inactivation. Examples of these processes include radiation, steam, ethylene oxide (EtO), and new technology sterilization processes.

D. Exclusions

1. Processes that rely on microbial exclusion, rather than microbial inactivation, are outside the scope of this guidance. Examples of microbial exclusion processes include sterilizing filtration methods and aseptic processing, commonly used in pharmaceutical manufacturing. Heparin and saline lock flush solutions, which are regulated as devices,[8] belong to this category and, therefore, are excluded.
2. Processes intended to sterilize medical devices that incorporate materials of animal origin (i.e., human or animal tissues) are outside the scope of this guidance. We intend to address in a future guidance the processing of these devices and the sterilization methods used (including the use of liquid chemical sterilants). The branch responsible for the review of your device is available to discuss your questions about devices that contain materials of human or animal origin.
3. Processes intended to be used by reprocessors of single-use devices are outside the scope of this document. See "**Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices**."[9]
4. Information on the cleaning, disinfecting, and sterilizing of reusable devices that are reprocessed at healthcare facilities (and for single-use devices that are provided non-sterile for further sterilization at healthcare facilities) are outside the scope of this document. Please refer to "**Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance**.[10]

II. Methods of Sterilization

A. Definitions

FDA recognizes three categories of sterilization methods currently used to sterilize medical devices in manufacturing settings – **Traditional, Non-traditional, and Novel Non-traditional**. These processes are defined as:

1. **Traditional Sterilization Methods** : methods that have a long history of safe and effective use as demonstrated by ample literature, clearances of 510(k)s or approvals of premarket approval applications, and satisfactory QS inspections, and for which there are voluntary consensus standards for validation that are recognized by FDA.
2. **Non-traditional Sterilization Methods** : methods that do not have a long history of safe and effective use and for which there are no FDA-recognized standards, but for which published information on validation of these methods exists and for which FDA has previously evaluated data as part of a QS evaluation and determined the methods to be adequate.
3. **Novel Non-traditional Sterilization Methods** : newly developed methods for which there are no FDA recognized standards, there is no FDA inspectional history, or there is little or no published information on validation, and for which there is no history of comprehensive FDA evaluation of sterilization validation data. A **Novel Non-traditional Sterilization Method** is also a method that has not been evaluated by FDA as part of a QS evaluation and that employs sterilization methods that FDA has not reviewed and determined to be adequate to provide reasonable assurance of safe and effective use.

B. Examples of Sterilization Methods (as of the date of this guidance)

1. **Traditional**
    1. Dry Heat
    2. Ethylene Oxide (EtO) with devices in a fixed chamber
    3. Moist Heat or Steam

4. Radiation (e.g., gamma, electron beam)

2. **Non-traditional**
    1. Hydrogen Peroxide (H 2O 2) Gas Plasma
    2. Ozone (O 3)

- **Novel non-traditional**

    1. Chlorine Dioxide (ClO 2)
    2. Ethylene Oxide-in-a-Bag (EtO-in-a-Bag, Diffusion method, or Injection method)
       This method differs from **traditional** EtO methods in that Ethylene Oxide-in-a-Bag specifies a volume of EtO instead of a concentration (e.g., 7.2 grains instead of 500-600 mg/L), uses an EtO cartridge or capsule, uses humidichips, or uses a long gas dwell time (e.g., greater than 8 hours).
    3. High Intensity Light or Pulse Light
    4. Microwave Radiation
    5. Sound Waves
    6. Ultraviolet Light
    7. Vaporized Chemical Sterilant Systems (e.g., hydrogen peroxide or peracetic acid).

III. Sterilization Information for Devices Labeled as Sterile

A. ODE and CBER scientific reviewers should evaluate **traditional** sterilization methods submitted in 510(k)s for the following information. ODE and CBER scientific reviewers should also document that this information was provided.

1. For the sterilant, the reviewer should document the following:
    a. a description of the sterilization method;
    b. in the case of radiation sterilization, the radiation dose; and
    c. the maximum levels of sterilant residuals that remain on the device, and an explanation of why those levels are acceptable for the device

type and the expected duration of patient contact.

In the case of EtO sterilization, CDRH has accepted EtO residuals information based on the recognized standard, "ANSI/AAMI/ISO 10993-7:1995 Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals."

1. For the sterilization method, the reviewer should document a description of the method used to validate the sterilization cycle (e.g., the half-cycle method) but not the validation data itself. The submission should also identify all relevant consensus standards used and aspects of the standards that were not met.
2. The reviewer should document the sterility assurance level (SAL) of 10^{-6} for devices labeled sterile unless the device is intended only for contact with intact skin. FDA recommends a SAL of 10^{-3} for devices intended only for contact with intact skin.
3. The reviewer should document the testing performed to demonstrate that all blood contacting devices, permanent implants, devices that contact cerebrospinal fluid, and devices labeled pyrogen free or non-pyrogenic are, in fact, non-pyrogenic. The documentation should include the following:

a. a description of the method used to make the determination, e.g., bacterial endotoxins test (BET), also known as the *limulus* amebocyte lysate (LAL) test;
b. identification of the testing endpoint that was reached; and
c. an explanation supporting the selected endpoint. We recommend the following endotoxin endpoint: 0.5 EU/ml for general medical devices (e.g., blood contacting) and 0.06 EU/ml for devices that contact cerebrospinal fluid. These endpoints assume an extraction methodology described in the guidance or standards listed below (i.e., based on a 40 ml extraction volume per device). See:
    - FDA "**Guideline on Validation of the Limulus Amebocyte Lysate Test as an End Product Endotoxin Test for Human and Animal Parenteral Drugs,**

Biological Products, and Medical Devices" (1987)[11]

- United States Pharmacopeia (USP) <85> Bacterial Endotoxins Test
- ANSI/AAMI ST72:2002 Bacterial endotoxins—Test methodologies, routine monitoring, and alternatives to batch testing

1. The reviewer should document a description of the packaging and how it will maintain the device's sterility, and a description of the package test methods, but not package test data.[12]

B. ODE and CBER scientific reviewers should evaluate **non-traditional** sterilization methods in 510(k)s and document the information submitted following the recommendations above for **traditional** sterilization methods.

C. ODE scientific reviewers should refer **novel non-traditional** sterilization methods in 510(k)s to the Infection Control Devices Branch (INCB) for sterility consultation review. INCB should, in coordination with the Lead Review branch, send any requests for clarification or additional data to the Office of Compliance to enable the Agency to fully characterize and assess the method described in the 510(k). CBER lead reviewers should ask for a sterility consultation review from the appropriate CBER and/or CDRH offices.

IV. Review Routing for Sterile Devices

A. In order to maintain consistency in our approach to sterility review in 510(k) submissions, the 510(k) should be reviewed in accordance with the following procedures. A summary table is provided below in section B.

1. The Lead Reviewer should follow the recommendations in **Section III. Sterilization Information for Sterile Devices** for reviewing information in a 510(k) fora device intended to be subjected to **traditional** Sterilization Methods.
2. The Lead Reviewer should follow the recommendations in **Section III. Sterilization Information for Sterile Devices** when reviewing information in a 510(k) submission fora device intended to be subjected to **non-traditional** sterilization methods. Additionally, the Lead Reviewer should notify the appropriate Division of Enforcement Branch Chief within the CDRH Office of Compliance that a 510(k) for a device using a **non-traditional**

sterilization method has been submitted. The notification should also request that Office of Compliance consider a priority QS “Post-Clearance Inspection” after FDA clears the 510(k). For CBER-led reviews, the Lead Reviewer should consult with the CBER Office of Compliance and Biologics Quality, Division of Inspection Surveillance (OCBQ/DIS) on any requests for Post-Clearance inspections.

3. The Lead Reviewer (with the concurrence of his or her Branch Chief) should forward the informationin a 510(k) for a device intended to be subjected to what appears to be a **novel non-traditional** sterilization method to the Branch Chief, INCB, with a formal request for a comprehensive sterility consultation review. Upon receiving the request, the Branch Chief, INCB, and Division Director, Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices, along with the referring ODE Division Director (i.e., the lead review division), should work with the ODE Deputy Director for Science and Review Policy to decide whether the sterilization method is a **novel non-traditional** sterilization method as defined in this guidance. The CBER lead reviewer should consult with appropriate CBER and/or CDRH offices depending on the scientific expertise required to evaluate whether the sterilization method is a novel non-traditional method as defined in this guidance.

   If CDRH believes the sterilization method is a **novel non-traditional** method, INCB should initiate a review. At the same time, and in coordination with the Lead Reviewer of the reviewing Division, INCB should notify the appropriate Division of Enforcement Branch Chief within CDRH Office of Compliance that a 510(k) for a device sterilized using a **novel non-traditional** method has been received.

   The notice should include a formal request that CDRH Office of Compliance initiate a priority QS “Pre-Clearance Inspection” prior to the clearance of the 510(k). The ODE request for a directed inspection may include instructions to collect specific data for evaluation, as recommended by INCB. For CBER-led reviews, the lead reviewer should consult with CBER OCBQ/DIS on any requests for inspections.

Throughout the review process, INCB will be available to provide technical expertise to the Office of Compliance and the Office of Regulatory Affairs.

After FDA issues a 510(k) clearance letter, the Lead Reviewer should notify the Branch Chief, INCB, and the Office of Compliance that FDA has cleared a 510(k) with a newly validated **novel non-traditional** sterilization method. The Branch Chief, INCB, should inform the ODE review staff that FDA now considers the newly validated **novel non-traditional** sterilization method to be a **non-traditional** sterilization method. From that point on, ODE should review new 510(k)s for devices that use the sterilization method following the recommendations in **Section IV. Review Routing for Sterile Devices** subsection A. 2. above. For very unique and/or difficult to validate sterilization procedures, FDA may request that more than one device using the new method be cleared before considering the novel non-traditional sterilization method a non-traditional sterilization method.

B. Summary Table: Recommended Review Routing.[13]

Sterilization Method	INCB Consult	QS Inspection
Traditional	No	Routine Post-Market
Non-traditional	No	“Priority” Post-Clearance
Novel non-traditional	Yes	“Priority” Pre-Clearance

C. INCB is available to provide technical consultation to the CDRH Office of Compliance, and the Office of Regulatory Affairs on both **non-traditional** and **novel non-traditional** sterilization methods.

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[1] When final, this guidance will supersede “Updated 510(k) Sterility Review Guidance K90-1” (available at http://www.fda.gov/cdrh/ode/guidance/361.pdf) issued August 30, 2002, which superseded the Blue Book Memorandum #K90-1, issued on February 12, 1990.

[2] Ethylene oxide gas sterilizer, 21 CFR 880.6860, dry-heat sterilizer, 880.6870, and steam sterilizer 880.6880.

[3] "Guidance on Premarket Notification 510(k) Submissions for Sterilizers Intended for Use in Health Care Facilities," http://www.fda.gov/cdrh/ode/hcfsteril.pdf.

[4] For devices marketed as "non-sterile intended for sterilization at the health care facility," FDA recommends the immediate package label and labeling prominently identify the device as non-sterile. ODE scientific reviewers should consult "Labeling Reusable Medical Devices for Reprocessing in Health Care Facilities: FDA Reviewer Guidance" (available at http://www.fda.gov/cdrh/ode/198.pdf) for additional labeling recommendations.

[5] See the guidance entitled, "Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices" available at http://www.fda.gov/cdrh/ode/guidance/1216.html.

[6] FDA intends to issue a separate draft guidance to address the sterilization of human and animal tissue for use in medical devices because this subject matter involves concerns unique to materials from these sources. The branch responsible for the review of your device (the lead review branch) is available to discuss your questions about 510(k)s for devices that contain human or animal tissue.

[7] The implementing regulations for GMP requirements, section 520(f) of the Federal Food, Drug, and Cosmetic Act, are referred to as Quality System (QS) requirements (see also 21 CFR Part 820).

[8] "Heparin Catheter Lock-Flush Solutions; Transfer of Primary Responsibility from Center for Drug Evaluation and Research to Center for Devices and Radiological Health." 71 FR 47499, August 17, 2006.

[9] http://www.fda.gov/cdrh/ode/guidance/1216.html.

[10] http://www.fda.gov/cdrh/ode/198.pdf.

[11] http://www.fda.gov/cder/guidance/old005fn.pdf.

[12] Package test methods should include simulated distribution followed by one whole package integrity test and one seal strength test.

[13] This recommended procedure is specific for CDRH. CBER has similar review routing procedures that are specific to the offices responsible for various aspects of 510(k)s reviews. Any questions regarding CBER's review routing procedures should be directed to the relevant product offices.

Updated December 11, 2008
