U.S. FOOD & DRUG ADMINISTRATION

Welcome To Today's Webinar

Thanks for joining us!
We'll get started in a few minutes

Today's Topic:
Medical Device Sterilization Town Hall:
Premarket Submission Expectations and Additional Considerations for Sterility Review

February 7, 2024

Medical Device Sterilization Town Hall:

Premarket Submission Expectations and Additional Considerations for Sterility Review

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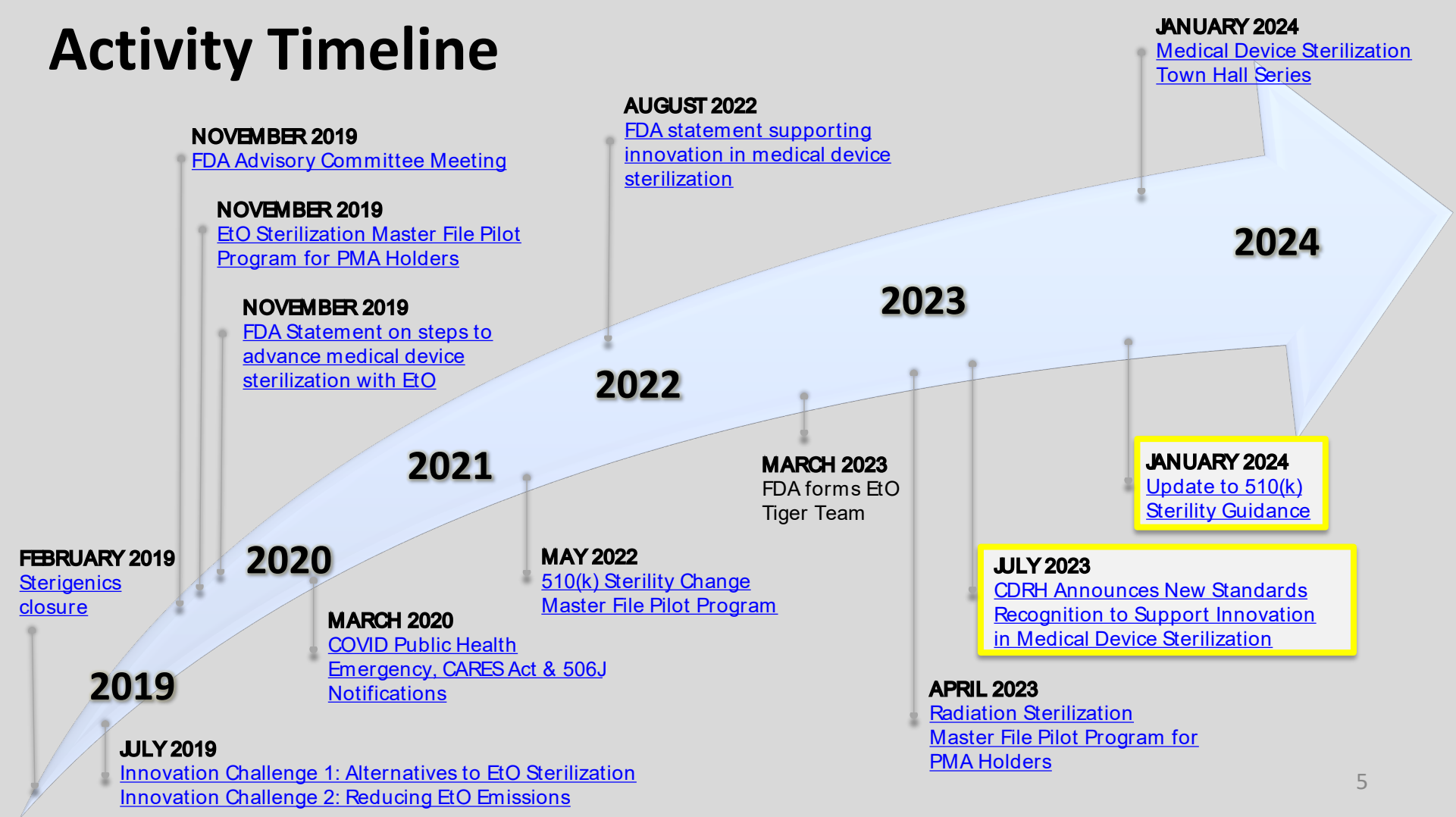
What we heard from you last time

Activity Timeline



Learning Objectives

- Understand FDA expectations for initial premarket submissions based on the 510(k) Sterility Guidance, including recent guidance changes, sterilization modality categories, and what to include in a submission.
- Understand additional device and submission considerations for sterility that impact FDA review.

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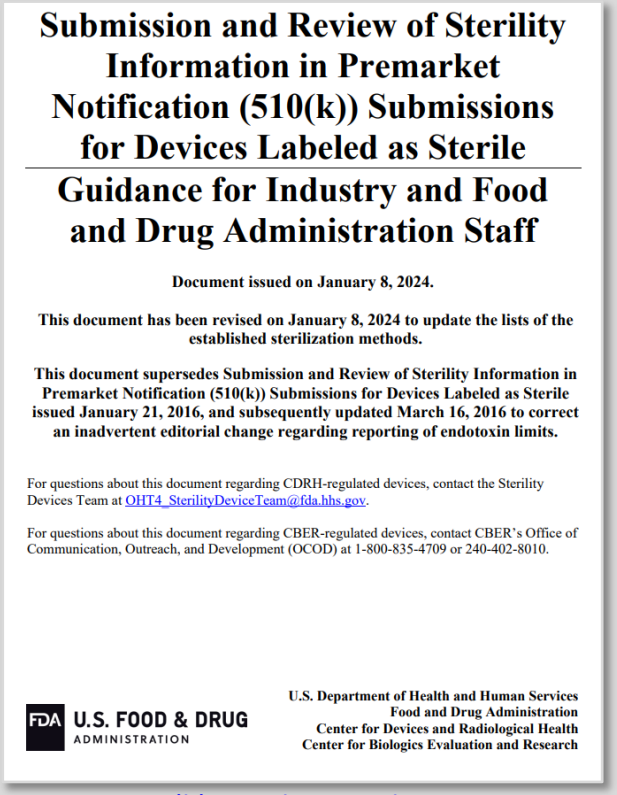
FDA Expectations in New Submissions

Scope of the 510(k) Sterility Guidance



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

Guidance for Industry and Food and Drug Administration Staff

Document issued on January 8, 2024.

This document has been revised on January 8, 2024 to update the lists of the established sterilization methods.

This document supersedes Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile issued January 21, 2016, and subsequently updated March 16, 2016 to correct an inadvertent editorial change regarding reporting of endotoxin limits.

For questions about this document regarding CDRH-regulated devices, contact the Sterility Devices Team at OHT4_SterilityDeviceTeam@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact CBER's Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

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

510(k) Sterility Guidance

- Within the scope of the guidance:
  - 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
- Outside the scope of the guidance:
  - Sterilizers that are themselves medical devices subject to 510(k)
  - Microbial exclusion processes (e.g., filtration, aseptic processing), rather than microbial inactivation processes
  - Processes intended to sterilize medical devices that incorporate materials of animal origin
  - Processes that incorporate the use of liquid chemical sterilants
  - Processes intended to be used by reprocessors of single-use devices
  - Cleaning, disinfecting, and sterilizing information for reusable devices that are reprocessed at healthcare facilities

New for 2024

- Vaporized Hydrogen Peroxide (VHP) is a now an Established Category A Sterilization method
- The VHP standard, ISO 22441:2022, was completely recognized by the Agency in July 2023, Supplementary Information Sheet

Categories of Sterilization Modalities

- Established Category A Sterilization
- Established Category B Sterilization
- Novel Sterilization

Established Category A Methods

- Long history of safe and effective use
- Multiple sources of information
  - Ample literature
  - Clearances of 510(k)s or approvals of PMAs
  - Satisfactory Quality System (QS) inspections
- Voluntary consensus standards for development, validation, and routine control that are recognized by FDA

Established Category A - Examples

- Dry heat (ISO 20857)
- Moist heat or steam (ISO 17665)
- Ethylene Oxide (EO or EtO) with devices in a fixed, rigid chamber (ISO 11135)
- Radiation (Gamma, E-beam, X-ray) (ISO 11137)
- Vaporized Hydrogen Peroxide (ISO 22441)

Established Category B Methods

- Established methods for which there are no FDA-recognized dedicated consensus standards, but for which published information on development, validation, and routine control is available, and
- FDA has previously evaluated sterilization development and validation data for specific sterilizers using discrete cycle parameters and determined the validation methods to be adequate.

Novel Sterilization Methods

These are newly developed methods for which there exists:

- little or no published information,
- no history of FDA evaluation of sterilization development and validation data through a cleared 510(k) or approved PMA for devices sterilized with such methods, and
- no FDA-recognized dedicated consensus standards on development, validation, and routine control.

A novel sterilization method is a method that FDA has not reviewed and determined to be adequate to effectively sterilize the device for its intended use.

Novel Sterilization Methods - Examples

- Chemical(s) that have not been cleared or approved by FDA as a sterilant or has not been identified in scientific literature as a sterilant
- A novel combination of chemicals
- Modified cycles of an FDA cleared healthcare sterilizer that have not been previously reviewed
- Examples may include: vaporized peracetic acid, high intensity light or pulse light, microwave radiation, sound, or UV light

Sterility Information in a 510(k)

- Summary level information needed for Established Category A:
  - Sterilization method
  - Maximum level of residuals remaining on device with associated limit (if applicable)
  - Radiation dose (if applicable)
  - Standards followed and validation method used (e.g., overkill, BI/Bioburden)
  - Sterility Assurance Level (SAL)
  - Pyrogen information
  - Packaging description
  - Shelf-life and validation method
- Additional information needed for Established Category B:
  - 510(k) clearance number, make, and model of sterilizer, and cycle information, if applicable
  - Identification of prior premarket review in which the sterilization method/cycles were evaluated
- Full test reports needed for novel sterilization methods

Sterility Information in a PMA/De Novo/IDE

- PMA/De Novo
  - Full test reports needed (Installation Qualifications/Operational Qualifications/Performance Qualifications)
- IDE
  - Full test reports may be needed
  - Batch release is typically acceptable
  - Minimum information needed to support safety (i.e., patients in the study will be receiving a sterile device)

Shani Haugen, PhD
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Additional Device and Submission Considerations for Sterility Review

Additional Device Considerations: EtO Residuals

ISO 10993-7* and related guidance information

- Residual (EtO and Ethylene Chlorohydrin (ECH)) limits are impacted by contact classification
  - Permanent contact
  - Prolonged exposure (≥ 24 hours, ≤ 30 days)
  - Limited exposure (<24 hours)
  - Tolerable contact limits for surface contacting devices/implants
- Allowable limits for neonates and infants (see ISO 10993-7 Second edition 2008-10-15 Amendment 1 (2019))
- Some devices have specific EtO and ECH limits (see device specific guidance as applicable)
- The standard also includes recommended testing

*ISO 10993-7 Second edition 2008-10-15 Amendment 1 (2019)

Additional Device Considerations: Pyrogens

- The following types of devices should include pyrogen testing:
  - Implants
  - Devices in contact directly or indirectly with the cardiovascular system, the lymphatic system, or cerebrospinal fluid, including devices that are present for similar systemic exposure
  - Devices labeled non-pyrogenic
- Endotoxin limit needed and an explanation supporting the limit
- Recommended testing: USP <161>, ANSI/AAMI ST72, or USP <85>

Additional Device Considerations: Packaging and Shelf Life

- Confirms the integrity of the sterile package throughout the shelf-life period
- Typical testing (AAMI/ANSI/ISO 11607 series):
  - Simulated Shipping: Packaging testing (e.g., seal strength, bubble leak) conducted after simulated shipping / transportation
  - Shelf-Life Validation: Accelerated or real time aging before packaging testing (e.g., seal strength, bubble leak)

Additional Submission Considerations

Question: My 510(k) device is provided sterile for single-use only. What sterility attachments should I provide in eSTAR?

- Pyrogen information (if applicable)
- Established B information, Novel sterilization information, Sterility information recommended in device-specific guidance documents
- For 510(k) submissions using an Established Category A sterilization method with a cycle that is validated in accordance with FDA-recognized standards, the information requested in the sterility section of eSTAR is sufficient to address the recommendations of the 510(k) Sterility Guidance Document
- For more information, please consult the eSTAR Program | FDA website

Question: I adopted my **device** into an already established, worst-case family of products with an associated validated process (EO in a rigid chamber) [ISO 11135 and TIR28] or radiation [11137-2, Section 4.2] - what adoption information should I submit in the 510(k)?

- **For most devices**, no additional adoption information is needed in a 510(k) for a device sterilized using an Established A method validated in accordance with an FDA-recognized standard

Resources

Slide Number	Cited Resource	URL
5	Sterigenics closure	www.epa.gov/il/sterigenics-willowbrook-facility
5	Innovation Challenge 1: Alternatives to EtO Sterilization	www.fda.gov/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-1-identify-new-sterilization-methods-and-technologies
5	Innovation Challenge 2: Reducing EtO Emissions	www.fda.gov/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions
5	FDA Advisory Committee Meeting	www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-7-2019-general-hospital-and-personal-use-devices-panel-medical-devices-advisory-committee
5	EtO Sterilization Master File Pilot Program for PMA Holders	www.federalregister.gov/documents/2019/11/26/2019-25631/center-for-devices-and-radiological-health-ethylene-oxide-sterilization-master-file-pilot-program
5	FDA Statement on steps to advance medical device sterilization with EtO	www.fda.gov/news-events/press-announcements/statement-new-steps-advance-innovation-medical-device-sterilization-ethylene-oxide
5	COVID Public Health Emergency, CARES Act & 506J Notifications	www.fda.gov/medical-devices/medical-device-safety/medical-device-supply-chain-and-shortages
5	FDA statement supporting innovation in medical device sterilization	www.fda.gov/news-events/press-announcements/fda-continues-efforts-support-innovation-medical-device-sterilization
5	510(k) Sterility Change Master File Pilot Program	www.federalregister.gov/documents/2022/05/20/2022-10925/medical-devices-510k-sterility-change-master-file-pilot-program

Resources

Slide Number	Cited Resource	URL
5	Radiation Sterilization Master File Pilot Program for PMA Holders	www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-announces-radiation-sterilization-master-file-pilot-program
5	CDRH Announces New Standards Recognition to Support Innovation in Medical Device Sterilization	www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-announces-new-standards-recognition-support-innovation-medical-device-sterilization
5	Update to 510(k) Sterility Guidance	www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled
5	FDA Medical Device Sterilization Town Hall Series	www.fda.gov/medical-devices/general-hospital-devices-and-supplies/sterilization-medical-devices#town-halls
6, 9	510(k) Sterility Guidance	www.fda.gov/media/74445/download
10	ISO 22441 Standard Supplementary Information Sheet	www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?standard__identification_no=44295
22	eSTAR program	www.fda.gov/medical-devices/how-study-and-market-your-device/estar-program

Summary

- We described the sterility information expected for 510(k) and PMA devices
- We shared the recent revisions to our 510(k) Sterility Guidance
- We compared three different categories of sterilization modalities and how that impacts premarket review
- We explained additional device and submission considerations for sterility review

Next Town Hall

Date: Thursday, February 29, 2024

Time: 1:00 – 2:00 pm ET

Potential Topics:

- Premarket considerations for modifications to sterilization-related submissions
- Use of device Master Files (MAFs) and sterility MAF pilot programs in sterility review

See section on our Sterilization for Medical Devices webpage that includes town hall dates and links to town hall materials.

Medical Device Sterilization Town Hall Series

www.fda.gov/medical-devices/general-hospital-devices-and-supplies/sterilization-medical-devices#town-halls


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Additional Panelists

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Regulatory Advisor
Regulatory Policy and Combination Products Staff

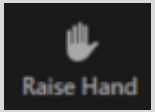
Office of Product Evaluation and Quality

Aftin Ross, PhD
Deputy Director
Office of Readiness and Response

Office of Strategic Partnerships and Technology Innovation

Let's Take Your Questions and Comments

- **To ask a question/share a comment:**
  - Raise your hand in Zoom
  - Moderator will announce your name and invite you to speak
  - Unmute yourself when prompted in Zoom to speak



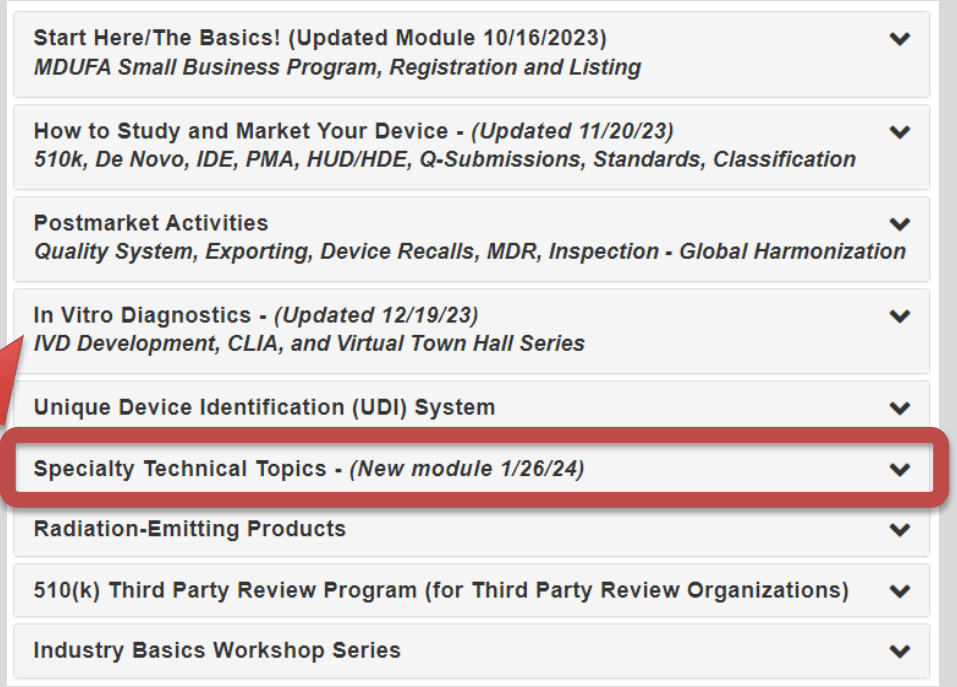
- **When asking a question/sharing a comment:**
  - Keep question/comment as short as possible
  - No questions about specific submissions
- **After question/comment is addressed:**
  - Mute yourself and lower your hand
  - If you have another question/comment - raise your hand again

Additional questions/comments about today's presentation

- Email: MedicalDeviceSterilization@fda.hhs.gov

Thanks for Joining Today!

- **Presentation and Transcript will be available at CDRH Learn**
  - www.fda.gov/Training/CDRHLearn
- **Additional questions/comments about today's presentation**
  - Email: MedicalDeviceSterilization@fda.hhs.gov
- **Upcoming Town Halls & Webinars**
  - www.fda.gov/CDRHWebinar



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