U.S. FOOD & DRUG ADMINISTRATION

Welcome To Today's Program

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

Today's Topic:
Medical Device Sterilization Town Hall: FDA Modifications (Mods) Guidances and the use of Device Master Files in Reviews

February 29, 2024

Town Halls on Medical Device Sterilization:

FDA Modifications (Mods) Guidances and the use of Master Files in Reviews

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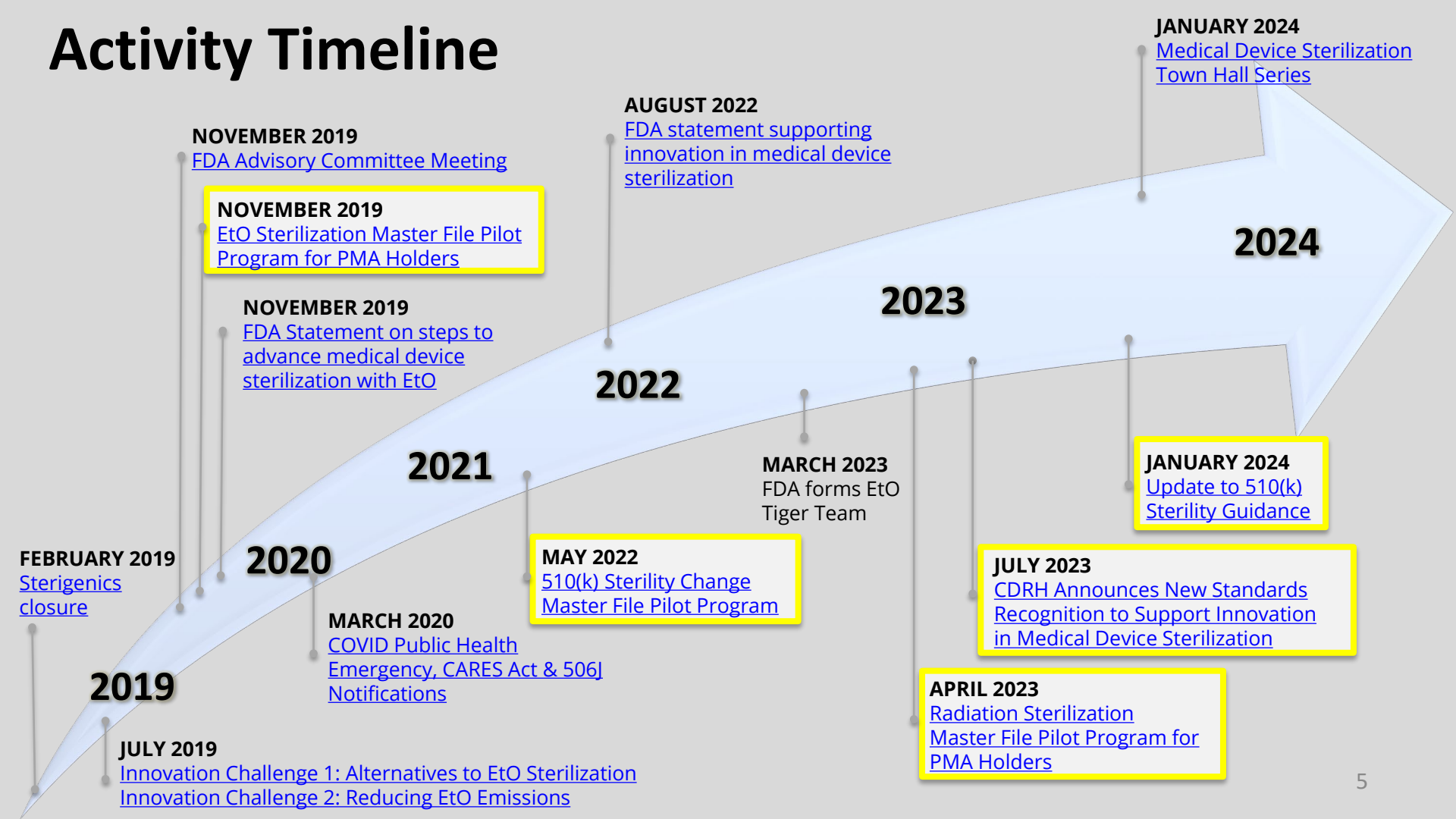
What we heard from you last time

Activity Timeline



Learning Objectives

- Understand FDA expectations for submission (510(k), PMA) modifications
  - Leveraging the “When to Submit a 510(k) for a Change to an Existing Device” (AKA “Mods”) and “Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process” guidances.
- Understand the use of Device Master Files (MAFs) for sterility review and what it means to use MAFs. Understand the Sterility MAF Pilot Programs and the difference between the MAF Pilots as compared to traditional MAFs.

Christopher Dugard, MS
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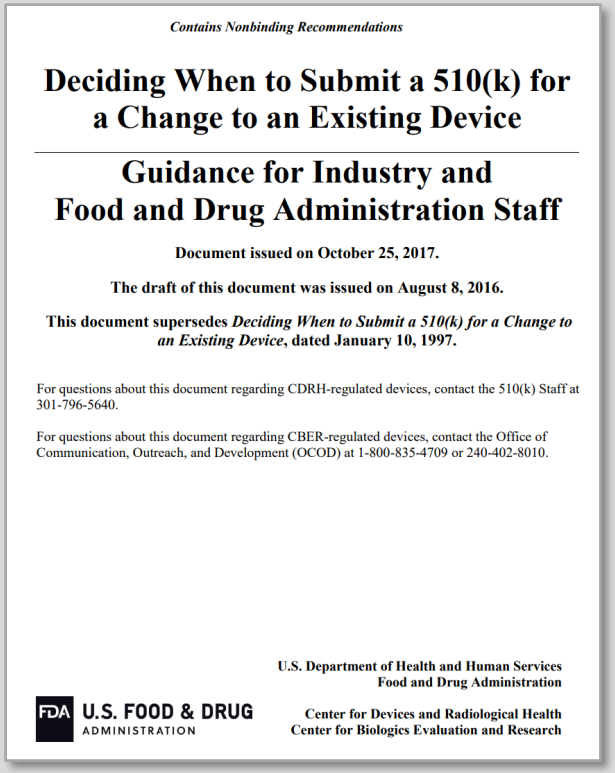
FDA Expectations for Submission Modifications

Premarket Considerations for Modifications to Existing Devices



Contains Nonbinding Recommendations

Deciding When to Submit a 510(k) for a Change to an Existing Device

Guidance for Industry and Food and Drug Administration Staff

Document issued on October 25, 2017.

The draft of this document was issued on August 8, 2016.

This document supersedes *Deciding When to Submit a 510(k) for a Change to an Existing Device*, dated January 10, 1997.

For questions about this document regarding CDRH-regulated devices, contact the 510(k) Staff at 301-796-5640.

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

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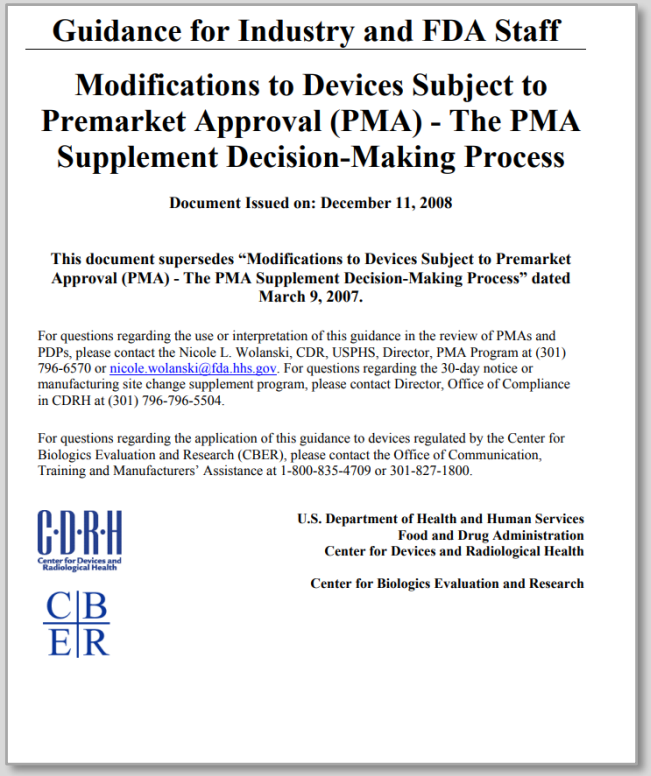
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

[510(k) Modifications Guidance]



Guidance for Industry and FDA Staff

Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process

Document Issued on: December 11, 2008

This document supersedes "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" dated March 9, 2007.

For questions regarding the use or interpretation of this guidance in the review of PMAs and PDPs, please contact the Nicole L. Wolanski, CDR, USPHS, Director, PMA Program at (301) 796-6570 or nicole.wolanski@fda.hhs.gov. For questions regarding the 30-day notice or manufacturing site change supplement program, please contact Director, Office of Compliance in CDRH at (301) 796-796-5504.

For questions regarding the application of this guidance to devices regulated by the Center for Biologics Evaluation and Research (CBER), please contact the Office of Communication, Training and Manufacturers' Assistance at 1-800-835-4709 or 301-827-1800.

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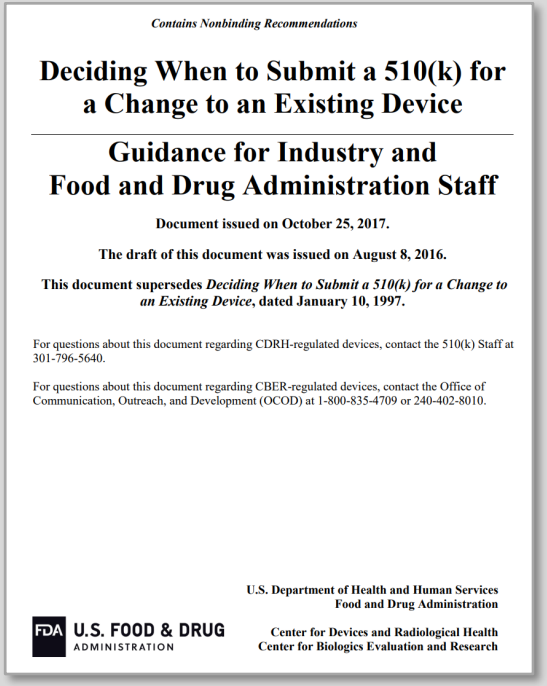
Food and Drug Administration
Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

[PMA Modifications Guidance]

Guidance: Deciding When to Submit a 510(k) for a Change to an Existing Device Guidance for Industry and Food and Drug Administration Staff



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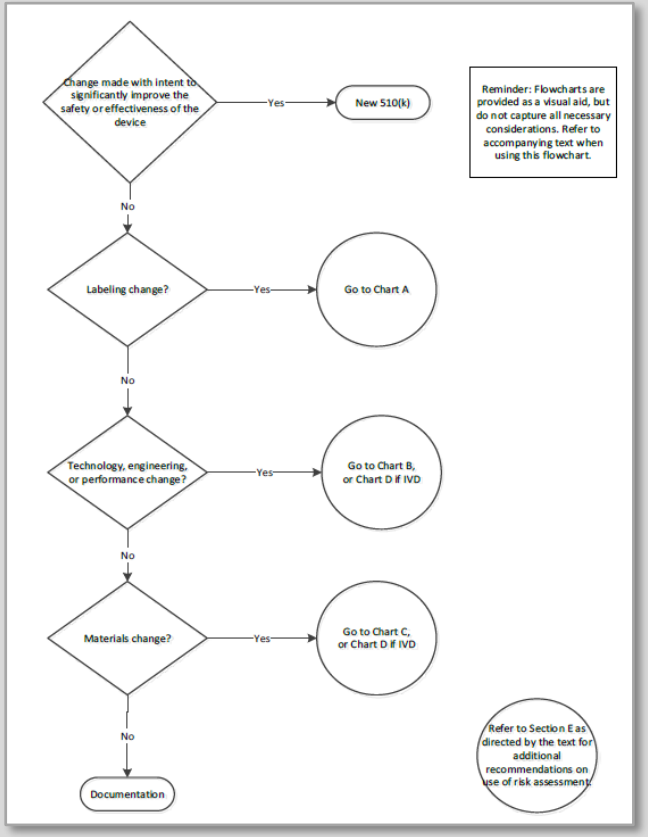
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- Provides recommendations to aid manufacturers who intend to modify a 510(k)-cleared device or other device subject to 510(k) requirements in:
  - Deciding whether a change requires a new 510(k) under 21 CFR 807.81(a)(3)
- Changes requiring a new 510(k) submission may not be introduced into the market until FDA has reviewed and cleared
- Does not address changes to devices that are 510(k) exempt or require a PMA
- Limited to medical devices and not other FDA-regulated products

510(k) Mods Guidance – Guiding Principles

- Changes made with intent to significantly affect safety or effectiveness of the device will likely need a 510(k)
- Risk-based assessment should be conducted to determine whether a change or modification could significantly affect safety or effectiveness
- Should also consider unintended consequences of change
- Use of risk management to conduct a risk-based assessment of changes
- Testing to evaluate whether a change could significantly affect safety and effectiveness
- Impact of simultaneous changes should be made -- includes assessment of each change individually as well as in aggregate
- Use of appropriate comparative device to assess cumulative effect of changes
- Documentation of device changes is required by the quality system regulation
- New 510(k) should fully describe all changes and their impacts
- Substantial equivalence determination is up to FDA

Decision Making - Main Flowchart



- Labeling change?
- Technology, engineering or performance change?
- Materials change?

Labeling Changes

- Change to indications for use?
  - Single use to reusable?
  - Rx to OTC?
  - Change to device name?
  - New disease, condition, or patient population?
  - Identification of any new risks or significantly modified existing risks?
- Add/delete contraindication?
- Change to warnings/precautions?
- Affect directions for use?

Technology, Engineering, and Performance Changes

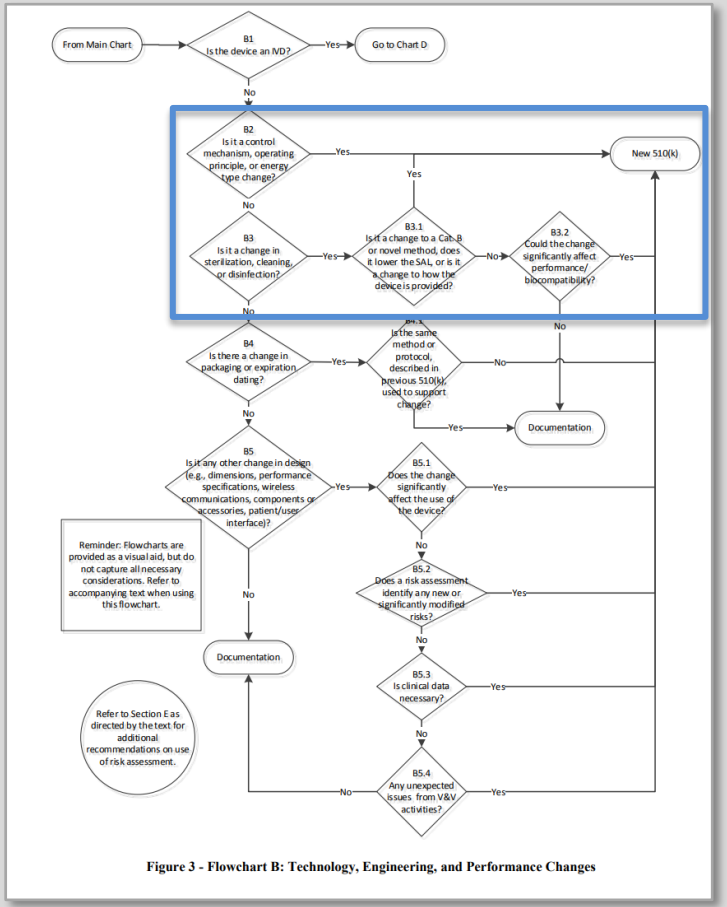


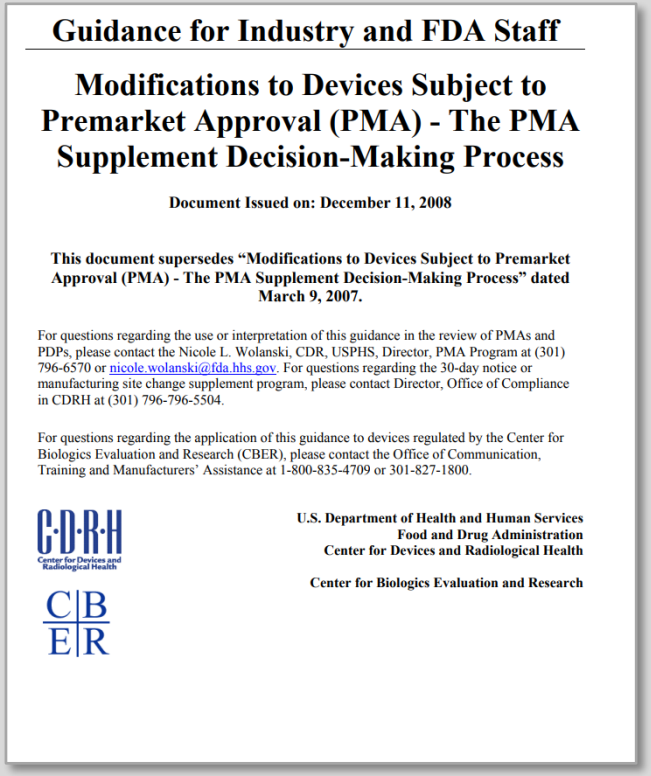
Figure 3 - Flowchart B: Technology, Engineering, and Performance Changes

- Is the device an IVD?
- Control mechanism, operating principle, or energy type change?
- Change in sterilization, cleaning, or disinfection?
  - Which category?
  - Could change significantly affect performance/biocompatibility?
- Change in packaging/expiration date?
  - Same method as previously described?
- Change in design?
  - Affect use of the device?
  - Does risk assessment identify any new/significantly modified risks?
  - Clinical data necessary?
  - Any unexpected issues during V&V testing?

Materials Changes

- Is device an IVD?
- Change in material type, formulation, composition, or processing?
- Will changed material directly or indirectly contact body tissues/fluids?
- Does risk assessment identify any new or increased biocompatibility concerns?
  - Are the same materials used in a similar legally marketed device?
- Could change affect device's performance specification?

Changes in PMAs and IVDs



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- Changes that require a new PMA Supplement are described under 21 CFR 814.39(a)
- Considerations are similar (operating principle, applicable guidance, risk assessment, V&V activities)
- Changes to PMAs will need different submissions based on the change
  - New PMA, Panel-Track, 180-day, Real-Time, 30-Day Notice, Special PMA Supplement – Changes being Effected, and Manufacturing Site Change Supplement
  - Master file pilots may impact which submissions are needed

Ryan Ortega, PhD
Regulatory Advisor
Regulatory Policy and Combination Products Staff

Office of Product Evaluation and Quality

Device Master File (MAF) use in Sterility Review & FDA's Sterility MAF Pilot Programs

Traditional MAFs vs Sterility MAF Pilots

Traditional MAFs: Can be submitted by anyone

- No review outside of its use in a specific submission
- No limits to what can be submitted
- Cannot be used to reduce the need for a new submission/supplement

Sterility MAF Pilots: Submitted by sterilization providers (up to 9 per pilot)

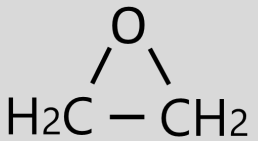
- Undergo review as described in FR notice
- Specific information should be included per FR notice
- 6-month reports updating any changes needed
- Can impact whether a new submission/supplement for devices in-scope is submitted

Device Master Files webpage

Ethylene Oxide Master File Pilot

Sterilization providers that sterilize single-use, PMA approved devices with EtO may submit a MAF when making certain changes between sterilization sites or when making certain changes to sterilization processes that utilize reduced EtO concentrations.

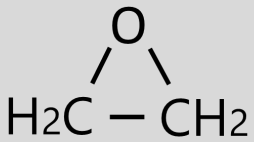
Federal Register: [84 FR 65162 EtO MAF Pilot]



Ethylene Oxide Master File Pilot

Under this voluntary program, manufacturers may reference the Master File submitted by their sterilization provider in a post-approval report in lieu of submitting a premarket approval application (PMA) supplement.

- Provided the MAF holder gives the PMA holder right of reference for the MAF.



Radiation Master File Pilot

Sterilization providers that sterilize single-use, PMA approved medical devices with gamma may submit a MAF when making certain changes between sterilization sites, changes to sterilization methods to utilize non-gamma radiation sources, or reductions in gamma dose.

- Also allows for a change from ethylene oxide to e-beam or x-ray in certain scenarios.

Federal Register: [88 FR 22040 Radiation MAF Pilot]

Radiation Master File Pilot

Under this voluntary program, manufacturers may reference the Master File submitted by their sterilization provider in a post-approval report in lieu of submitting a premarket approval application (PMA) supplement.

- Provided the MAF holder gives the PMA holder right of reference for the MAF.

510(k) Master File Pilot

- Gives companies that terminally sterilize single-use, 510(k) cleared devices using certain sterilization methods (Established Category B or Novel methods) a pathway to submit a MAF for FDA's review.
- FDA will accept a MAF into this pilot when it determines that there is not a likelihood that switching from a fixed chamber ethylene oxide (EtO) sterilization method to the sterilization method described in the MAF could significantly affect the safety or effectiveness of a 510(k)-cleared device that is in-scope of the MAF.

Federal Register: [87 FR 30957 510(k) MAF Pilot]

FDA 510(k)

510(k) Master File Pilot

If a MAF is accepted into the 510(k) Sterility Pilot Program, manufacturers of 510(k)-cleared devices may choose to reference the MAF in internal documentation in support of a justification for not submitting a new premarket notification (510(k)).

- Provided the MAF holder gives the PMA holder right of reference for the MAF.

FDA 510(k)

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	First FDA Medical Device Sterilization Town Hall	www.fda.gov/medical-devices/workshops-conferences-medical-devices/medical-device-sterilization-town-hall-overview-sterilization-landscape-and-role-ethylene-oxide
9	510(k) Modifications Guidance	www.fda.gov/media/99812/download
9	PMA Modifications Guidance	www.fda.gov/media/81431/download

Resources

Slide Number	Cited Resource	URL
19	Device Master Files webpage	www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/device-master-files
20	84 FR 65162 EtO MAF Pilot	www.federalregister.gov/documents/2019/11/26/2019-25631/center-for-devices-and-radiological-health-ethylene-oxide-sterilization-master-file-pilot-program
22	88 FR 22040 Radiation MAF Pilot	www.federalregister.gov/documents/2023/04/12/2023-07598/center-for-devices-and-radiological-health-radiation-sterilization-master-file-pilot-program
24	87 FR 30957 510(k) MAF Pilot	www.federalregister.gov/documents/2022/05/20/2022-10925/medical-devices-510k-sterility-change-master-file-pilot-program

Summary

- We described FDA requirements and recommendations for submission (510(k), PMA) modifications.
- We described how to use the “When to Submit a 510(k) for a Change to an Existing Device” (AKA “Mods“) and “Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process” guidances.
- We compared the difference between a traditional device MAF and a sterility MAF pilot.
- We described the three sterility MAF pilots and how they impact review.

Next Town Hall

Date: Thursday, March 21, 2024

Time: 12:00 – 1:00 pm ET

Potential Topics:

- Value of consensus standards
- Use of standards in premarket review
- FDA standards program

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

Suzanne Schwartz, MD, MBA
Director

Office of Strategic Partnerships and Technology Innovation

Shani Haugen, PhD
Assistant Director

Office of Health Technology 3
Office of Product Evaluation and Quality

Aftin Ross, PhD
Deputy Director
Office of Readiness & 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 CDRH Events (including Town Halls and Webinars)**
  - www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-events

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