MEDICAL DEVICE STERILIZATION: INCREASING UNDERSTANDING AND OUTREACH BETWEEN FDA AND STAKEHOLDERS

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FERMILAB MEDICAL DEVICE WORKSHOP

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Presentation Overview

- Framing the Issue and Background
- Sterilization Innovation
- Engaging with FDA - Qsub Process
- Tools, Resources and Other Ways to Engage with FDA
- Conclusion

Framing the Issue

- FDA's role is to assure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices
  - FDA regulates devices which need to demonstrate adequate sterilization using method chosen by manufacturer
- Of the medical devices that require sterilization
  - ~50% use EtO
  - ~40% use gamma irradiation
  - ~5% use e-beam radiation
  - ~5% use other modalities (e.g., x-ray, steam)

Framing the Issue (cont.)

- Challenges with EtO
  - Operating at near max capacity (24 hour/day, 7 days/week except for servicing)
  - Little ‘room’ to absorb more product if facilities are forced to shut down
- Challenges with Gamma irradiation
  - Security, environmental, and regulatory risks regarding its use
  - Isotope availability
- Device shortages could result from
  - Temporary or permanent EtO facility closures
  - Unavailability of cobalt 60

Background: Recent EPA & Regional Air Agency Activities

- **EPA**
  - As part of its EtO proposed rulemaking activities, EPA conducted a risk assessment which identified 23 commercial sterilizers in several states that were found to emit high levels of ethylene oxide
  - EPA is engaging with impacted communities
- **Regional Air Agency South Coast Air Quality Management District (SCAQMD)**
  - Currently investigating facilities that emit EtO
  - As a result of the investigation, Parter Medical Inc., voluntarily shut down its EtO operations until additional pollution controls can be implemented

Background: Recent FDA Communications & Actions

- Communications
  - Updating FDA webpages
  - CDRH Center Director Statement
    - FDA Continues Efforts to Support Innovation in Medical Device Sterilization(August 2022)
- Actions
  - Maintain 2 EtO Innovation Challenges
  - Maintain the PMA Master File Pilot Program
  - Launched the 510(k) EtO Master File Pilot Program
  - Announced consideration of a Radiation Master File Pilot Program
  - Continued Shortage Assessments
  - Continued Stakeholder Engagement

Outcomes: EtO Innovation Challenge

Challenge 1: Alternatives to EtO sterilization

- Selected 5 submissions that include:
  - Supercritical Carbon dioxide
  - Nitrogen dioxide
  - Accelerator-based radiation
  - Hydrogen peroxide
  - Hydrogen peroxide-ozone
- Identifying high volume or essential devices that can be sterilized by these technologies

Challenge 2: Reducing EtO emissions

- Selected 8 participants in these categories:
  - Enhanced EO cycle design and processes
  - Flexible chamber
  - Reduced sterilant concentration
  - Abatement

Encouraging Progress :

- Early observations suggest that some facilities have cut emissions ranging from 20-35%, with the potential to impact millions of devices
- Generally, manufacturers are targeting an ethylene oxide cycle concentration that is 11-66% less than the typical ethylene oxide concentration range
- Manufacturers' are working collaboratively with contract sterilizers to validate new or different sterilization methods as well as the feasibility for scale up

Outcomes: EtO Master File Pilot Program

EtO PMA Master File Pilot Program:

- Intended to streamline the regulatory processes for fixed chamber EtO sterilizers and PMA holders to make certain process changes:
  - Changing sterilization sites
  - Certain changes to sterilization processes that utilize reduced EtO concentrations
- 5 participants: Boston Scientific, Becton Dickinson, Steris Corporation, Oscor Inc., and Medtronic Inc.
- 11 sites and 28 class III devices included in the pilot

EtO 510(k) Sterility Change Master File Pilot Program

- Exponentially expands the number of medical devices eligible for pilot participation
- Helps to facilitate the change from fixed EtO chamber to established "Category B" or "Novel" sterilization methods*

Consideration of a Radiation Master File Pilot

- Attempt to mitigate against global supply constraints and support supply chain resiliency:
  - If implemented, would help medical device manufacturers change radiation sources in a least burdensome way

*FDA's guidance, *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile*

ENGAGING WITH FDA - QSUB PROCESS

Way to Collaborate Early: Q-Submission Program

- Provides a mechanism to request interactions with FDA related to medical device submissions
  - Different topics for interactions
  - Different type of feedback. There are many different types of Q-subs

Relevant Q-Submission Types

Q-sub guidance document:
https://www.fda.gov/media/114034/download

Q-Submission: Informational Meetings

Meeting intended to share information with the FDA

- No official feedback
- Interactive dialogue
- Topics can include:
  - Device development
  - New technologies
  - Topics outside the scope of other Q-Submissions

Q-Submission: Pre-submission

Requests for feedback from the FDA regarding future premarket submissions, Accessory Classification Requests, or CLIA Waivers

Pre-Submission Meeting

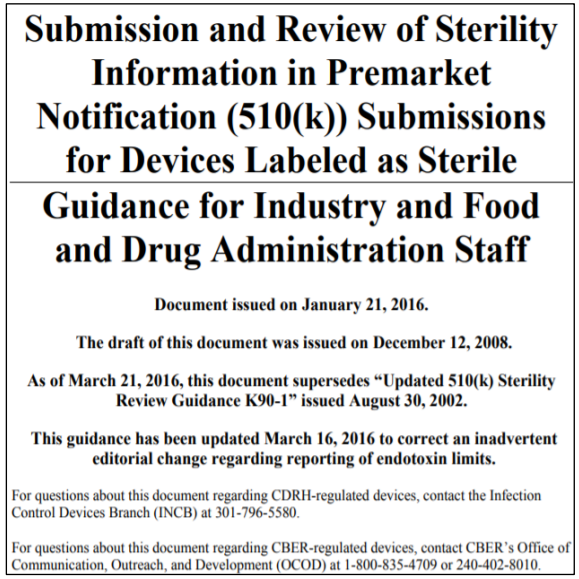
Pre-Submission Written Feedback

- Specific questions
- Recommend 3-4 substantial topics
- Help guide product development, develop protocols, prepare premarket applications

TOOLS, RESOURCES AND OTHER WAYS TO ENGAGE WITH FDA

510(k) Guidances

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 21, 2016.

The draft of this document was issued on December 12, 2008.

As of March 21, 2016, this document supersedes "Updated 510(k) Sterility Review Guidance K90-1" issued August 30, 2002.

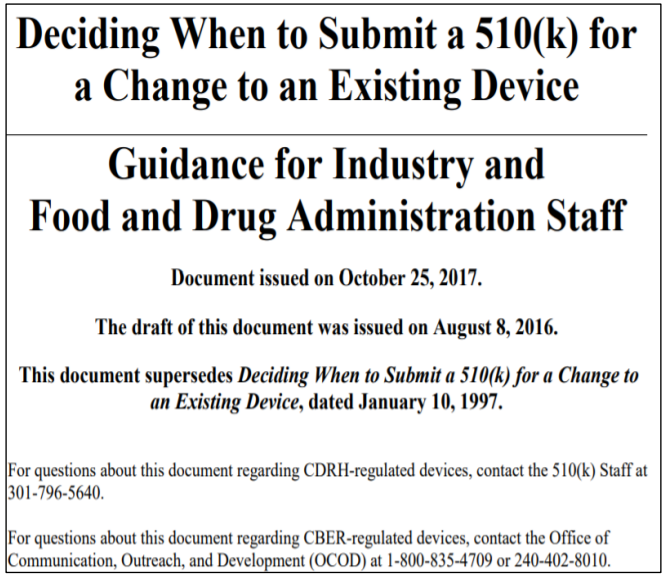
This guidance has been updated March 16, 2016 to correct an inadvertent editorial change regarding reporting of endotoxin limits.

For questions about this document regarding CDRH-regulated devices, contact the Infection Control Devices Branch (INCB) at 301-796-5580.

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.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled

510(k) Modifications Guidance



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.

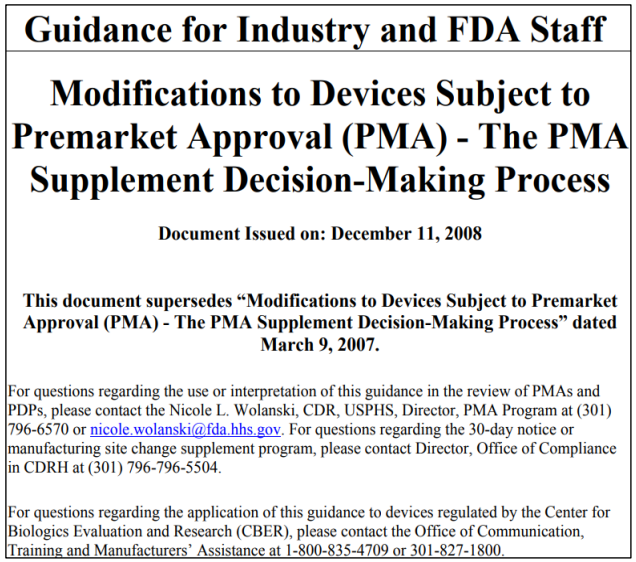
For questions about this document regarding CDRH-regulated devices, contact the 510(k) Staff at 301-796-5640.

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.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device

PMA Guidances

PMA 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

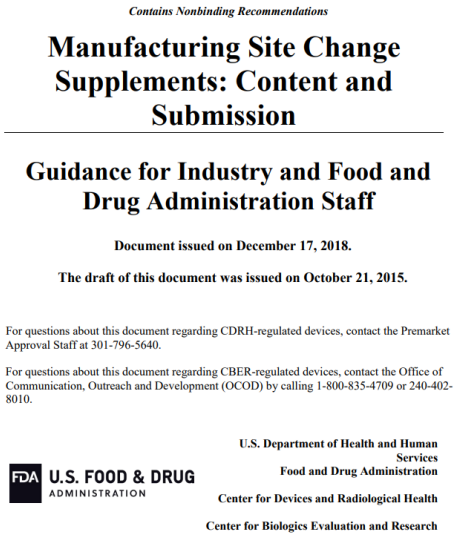
This document supersedes "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" dated March 9, 2007.

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.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process.

Manufacturing Site Change Supplements: Content and Submission



Contains Nonbinding Recommendations

Manufacturing Site Change Supplements: Content and Submission

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 17, 2018.

The draft of this document was issued on October 21, 2015.

For questions about this document regarding CDRH-regulated devices, contact the Premarket Approval Staff at 301-796-5640.

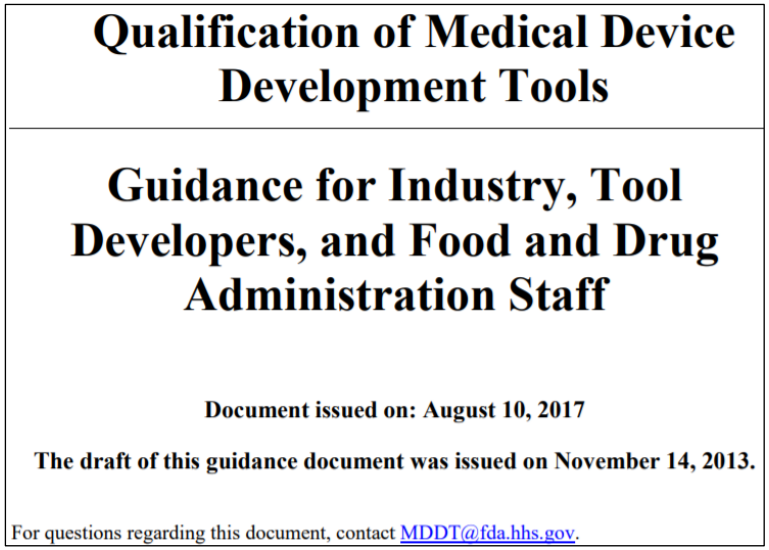
For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD) by calling 1-800-835-4709 or 240-402-8010.

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

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/manufacturing-site-change-supplements-content-and-submission

Medical Device Development Tools (MDDT) & Regulatory Science Tools



Qualification of Medical Device Development Tools

Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

Document issued on: August 10, 2017

The draft of this guidance document was issued on November 14, 2013.

For questions regarding this document, contact MDDT@fda.hhs.gov.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/qualification-medical-device-development-tools

MDDT Catalogue

Clinical outcome assessments, biomarker tests, nonclinical assessment models

https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt

- The MDDT program is a way for FDA to qualify tools that device sponsors can use to develop or evaluate medical devices.
  - Complementary to consensus standards
- In addition to MDDTs, the Catalog of Regulatory Science Tools provides a peer-reviewed resource for companies to use where standards and MDDTs do not yet exist.
  - Phantoms, methods, computational models and simulations

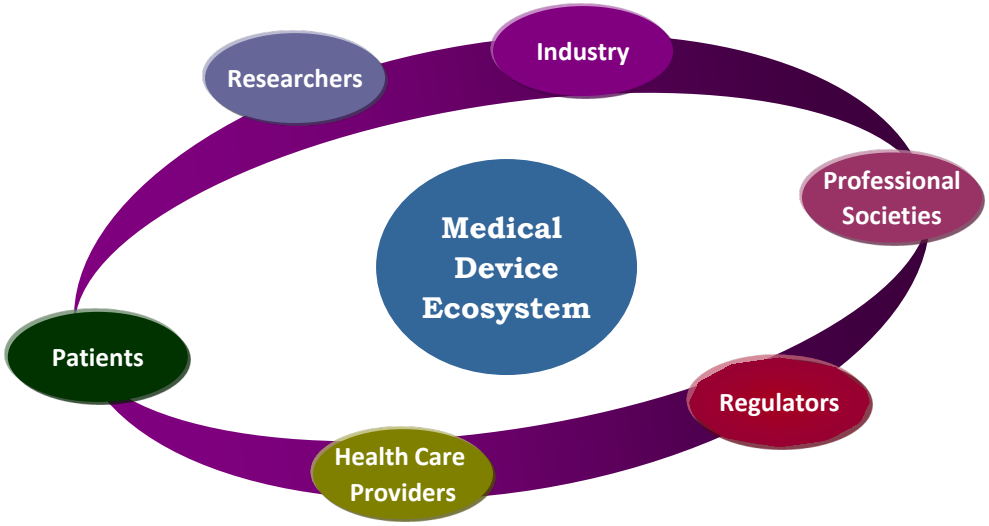
https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

Collaborative Communities

- A collaborative community is a continuing forum in which private and public-sector members work together on medical device challenges to achieve common objectives and outcomes.
  - Convened by interested stakeholders
- Our collaborative community toolkit has:
  - Best practices for establishing a community
  - Considerations for maintaining a community
  - Considerations for communication, transparency, and decision making
  - Frameworks for assessing effectiveness, impact, outcomes, and value of a community

https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together

Questions?



Question for the audience: Are there ways that industry, researchers, and other ecosystem partners can work together more collaboratively?

Shortage Reminder

FDA requests device manufacturers and commercial sterilizers to notify FDA of any potential or known shutdowns of commercial sterilizers and potential shortages of medical devices so we can help minimize supply chain impacts to healthcare stakeholders

Encouraging Innovation & Collaboration in Medical Device Sterilization

FDA contacts:

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