REGULATORY CONSIDERATIONS AND OPPORTUNITIES FOR COLLABORATION IN MEDICAL DEVICE STERILIZATION

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FERMILAB MEDICAL DEVICE WORKSHOP

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Presentation Outline

- Framing the Issue and Background
- 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
- >50% of devices that require sterilization use EtO
- EPA regulates EtO emissions from commercial sterilizers
- US commercial sterilizers of medical devices:
  - 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
- Facility closures have the potential to result in device shortages

Background: Chronology of Closures

Trigger: On February 15, 2019, the Illinois Environmental Protection Agency (EPA) issued a Seal Order to stop the Sterigenics facility in Willowbrook, Illinois, from sterilizing medical products and other products with ethylene oxide (EtO) due to concerns about the facility's emissions

Facility Closures:

- Sterigenics-
  - Smyrna GA facility - closed temporarily -- announced in Aug. 2019; allowed to conduct limited business due to COVID-19 in March 2020
  - Willowbrook IL- permanent closure announced by firm on Sept. 2019
- Becton Dickinson, in GA -- closed temporarily -- announced in Oct. 2019; reopened Nov 2019
- Medline Industries, in Waukegan IL-- voluntarily closed Dec. 2019 to undertake facility changes (i.e., abatement); reopened March 2020
- Viant, in Grand Rapids MI -- permanently closed (end of 2019)

Identified Shortage

- Smiths Medical Bivona tracheostomy tubes due to Willowbrook closure

https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-facility-updates

Background: FDA Communications & Actions

- Communications
  - Launch of FDA webpages
  - FDA Commissioner's Statements
    - Steps the Agency is taking to prevent potential medical device shortages and ensure safe and effective sterilization amid shutdown of a large contract sterilization facility (March 2019)
    - Statement on concerns with medical device availability due to certain sterilization facility closures (October 2019)
- Actions
  - Hosted November 2019 Advisory Committee Meeting
  - Launched and maintain 2 EtO Innovation Challenges
  - Launched and maintain the EtO Master File Pilot Program
  - Continued Shortage Assessments
  - Continued Stakeholder Engagement

Outcomes: November 2019 Advisory Committee Meeting Key Take-Aways

- Patients would suffer from abrupt unavailability of devices sterilized using EtO
- The current EtO ecosystem cannot absorb additional facility shut downs
- E-labeling could decrease the amount of paper that is sterilized and help optimize EtO cycle time and reduce emissions
- Alternative methods have significant challenges due to material compatibility, scalability, packaging
- Moving completely away from EtO could take 10 years

Advisory Committee Meeting announcement:
https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-7-2019-general-hospital-and-personal-use-devices-panel-medical-devices-advisory-committee

Outcomes: EtO Innovation Challenge and EtO Master File Pilot Program

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

EtO 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
- 2 participants: Boston Scientific and Becton Dickinson

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: 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

Q-Submission: Informational Meetings

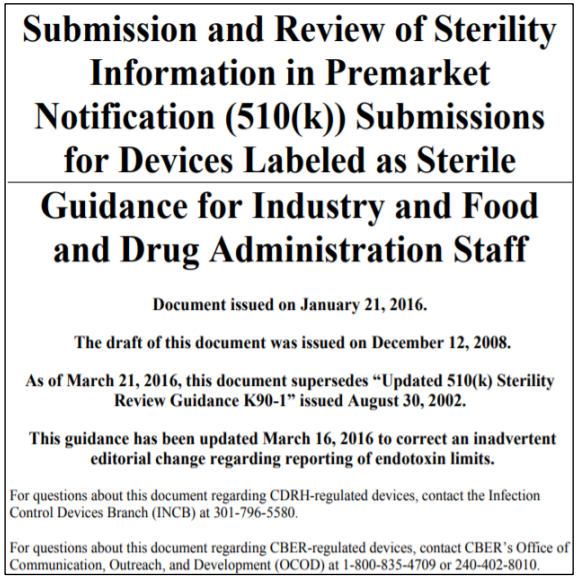
Meeting intended to share information with the FDA

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

TOOLS, RESOURCES AND OTHER WAYS TO ENGAGE WITH FDA

510(k) and PMA 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.

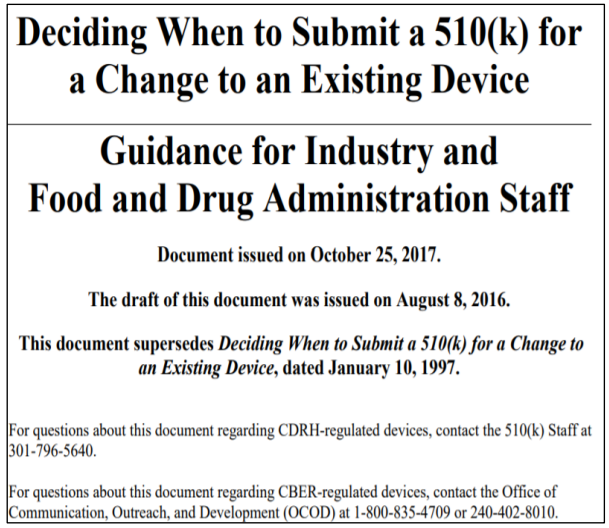
This guidance has been updated March 16, 2016 to correct an inadvertent editorial change regarding reporting of endotoxin limits.

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.

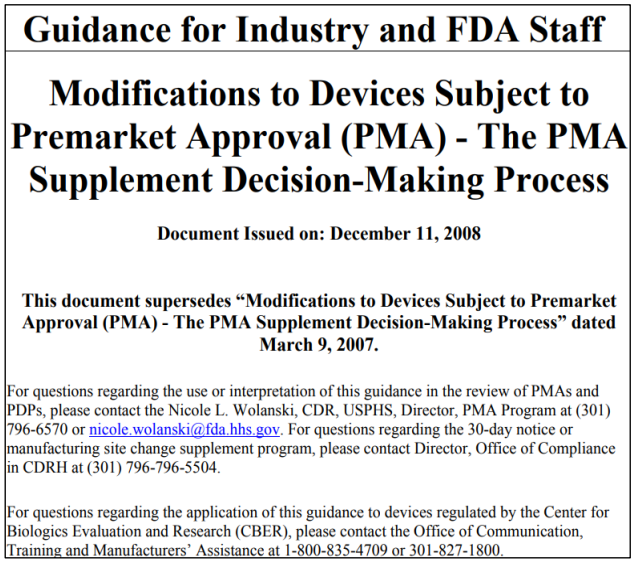
This document supersedes *Deciding When to Submit a 510(k) for a Change to an Existing Device*, dated January 10, 1997.

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 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

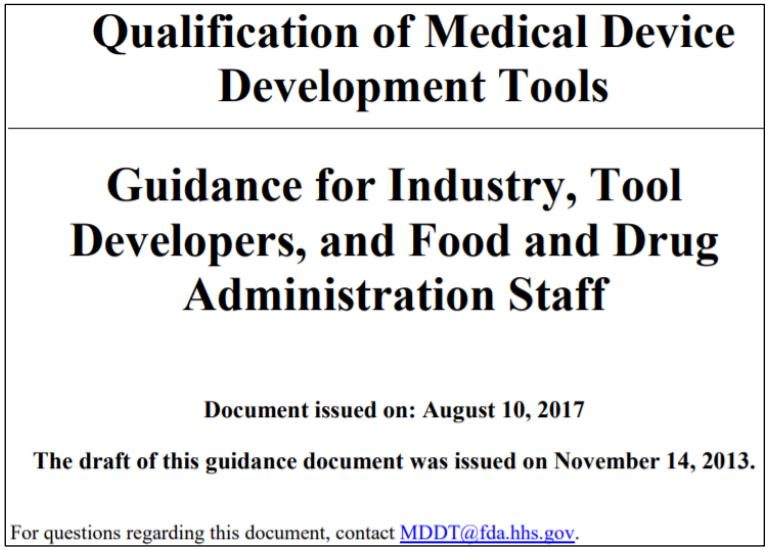
This document supersedes "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" dated March 9, 2007.

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.

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

Encouraging Innovation & Collaboration in Medical Device Sterilization

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