Sterilization for Medical Devices

Medical devices are sterilized in a variety of ways including using moist heat (steam), dry heat, radiation, ethylene oxide gas, vaporized hydrogen peroxide, and other sterilization methods (for example, chlorine dioxide gas, vaporized peracetic acid, and nitrogen dioxide).

June 2022 Radiation Sterilization Update: The FDA is considering a master file pilot program for premarket approval (PMA) holders whose approved devices are sterilized using radiation, including gamma radiation.

The FDA is considering this pilot program due to global supply chain constraints and to support sterilization supply chain resiliency. If implemented, this program would help medical device manufacturers advance alternative ways to sterilize their approved medical devices, including changing radiation sources, in a least burdensome regulatory approach.

The FDA is working actively with sterilization experts, medical device manufacturers, and other government agencies to advance alternative ways to sterilize medical devices, including using lower levels of currently used sterilizing agents and using new sterilizing agents or alternatives, while maintaining device safety and effectiveness.

Learn more about FDA's Sterilization Master File Pilot Programs.

On this page:

- Ethylene Oxide
  - Why Is Ethylene Oxide Used to Sterilize Medical Devices?
  - What Devices Are Sterilized with Ethylene Oxide?
  - How Does the FDA Help Ensure that Medical Devices Sterilized with Ethylene Oxide Are Safe?

    - EPA's Role in Ethylene Oxide Sterilization
- FDA's Actions to Advance Medical Device Sterilization
    - Sterilization Master File Pilot Programs
    - FDA Innovation Challenges
    - Advisory Committee Meetings
- Report Sterilization Site Changes to the FDA
- Medical Device Supply Chain Issues

Related pages:

- Ethylene Oxide Sterilization Facility Updates (/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-facility-updates)
- FDA Innovation Challenge 1: Identify New Sterilization Methods and Technologies (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-1-identify-new-sterilization-methods-and-technologies)
- FDA Innovation Challenge 2: Reduce Ethylene Oxide Emissions (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions)

Ethylene Oxide

Why Is Ethylene Oxide Used to Sterilize Medical Devices?

Medical devices are sterilized in a variety of ways including using moist heat (steam), dry heat, radiation, ethylene oxide gas, vaporized hydrogen peroxide, and other sterilization methods (for example, chlorine dioxide gas, vaporized peracetic acid, and nitrogen dioxide). Ethylene oxide sterilization is an important sterilization method that manufacturers widely use to keep medical devices safe. Learn more about sterilization methods in the Submission and Review of Sterility Information in

Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile Guidance (/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled).

For many medical devices, sterilization with ethylene oxide may be the only method that effectively sterilizes and does not damage the device during the sterilization process. Medical devices made from certain polymers (plastic or resin), metals, or glass, or that have multiple layers of packaging or hard-to-reach places (for example, catheters) are likely to be sterilized with ethylene oxide.

What Devices Are Sterilized with Ethylene Oxide?

Literature shows that about fifty percent[1,2,3] of all sterile medical devices in the U.S. are sterilized with ethylene oxide. The types of devices that are sterilized with ethylene oxide range from devices used in general health care practices (for example, wound dressings) to more specialized devices used to treat specific areas of the body (for example, stents).

How Does the FDA Help Ensure that Medical Devices Sterilized with Ethylene Oxide Are Safe?

Before most sterile medical devices are on the market, the FDA reviews premarket submissions to determine if the sterility information (for example, the method the manufacturer is choosing to sterilize their device and validation activities used to show that the device can be effectively sterilized) is in accordance with internationally agreed upon voluntary consensus standards that the FDA recognizes. An important element of our regulatory framework is a robust standards program. The FDA encourages medical device sponsors to use FDA-recognized voluntary consensus standards in their submissions, as conformity to relevant standards streamlines regulatory review and fosters quality. Learn more about the FDA's Recognized Standards Program (/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/standards-and-conformity-assessment-program).

For ethylene oxide sterilization, two voluntary consensus standards (ANSI AAMI ISO 11135:2014 and ANSI AAMI ISO 10993-7:2008(R)2012) describe how to develop, validate, and control ethylene oxide sterilization processes for medical devices and the acceptable levels of residual ethylene oxide and ethylene chlorohydrin left on a device after it has undergone ethylene oxide sterilization. These standards help ensure levels of ethylene oxide on medical devices are within safe limits since long-

term and occupational exposure to ethylene oxide has been linked to cancer. Learn more about the risks of ethylene oxide on the National Institutes of Health web page on ethylene oxide (https://www.cancer.gov/about-cancer/causes-prevention/risk/substances/ethylene-oxide).

If a medical device manufacturer changes the method, process, or the facility identified in its original PMA submission for sterilizing its devices, the manufacturer generally needs to submit a PMA supplement so that the agency can review these changes and determine if they also meet internationally agreed-upon voluntary standards that the FDA recognizes. For manufacturers that are 510(k) holders, sterilization method, process or site modifications can be assessed with the FDA guidance document: "Deciding When to Submit a 510(k) for a Change to an Existing Device (/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device)" for determination on whether the sterilization modifications would trigger the need for resubmission.

The FDA also inspects industrial facilities that sterilize medical devices and medical device manufacturing facilities to make sure that they have validated sterilization processes that meet FDA-recognized standards.

State health departments inspect health care facilities that use ethylene oxide to sterilize medical devices. Learn more about guidelines for sterilization in health care facilities on the Centers for Disease Control and Prevention web page (https://www.cdc.gov/infectioncontrol/guidelines/disinfection/sterilization/ethylene-oxide.html).

EPA's Role in Ethylene Oxide Sterilization

The US Environmental Protection Agency (EPA) reviews and enforces the Clean Air Act regulations for sterilization facilities that emit ethylene oxide to ensure that they protect the public from significant risk. Learn more about the EPA's Regulations for Ethylene Oxide on EPA's website (https://www.epa.gov/hazardous-air-pollutants-ethylene-oxide/agency-actions-ethylene-oxide#regulations).

FDA's Actions to Advance Medical Device Sterilization

The FDA is actively working with sterilization experts, medical device manufacturers, and other government agencies to advance innovative ways to sterilize medical devices with lower levels of currently used agents, and employ new agents or alternatives, while maintaining device safety and effectiveness.

Sterilization Master File Pilot Programs

The FDA developed the Sterilization Master File Pilot Programs to help ensure patients have access to safe medical devices and encourage new, innovative ways to sterilize medical devices that reduce the potential impact of EtO on the environment and on public health.

Radiation Sterilization Update for PMA Holders

On June 7, 2022, the FDA announced it was considering a master file pilot program for premarket approval (PMA) holders whose approved devices are sterilized using radiation, including gamma radiation. The FDA is considering this pilot program due to global supply chain constraints and to support sterilization supply chain resiliency. If implemented, this program would help medical device manufacturers advance alternative ways to sterilize their approved medical devices, including changing radiation sources, in a least burdensome regulatory approach.

Note: This pilot program would not include 510(k)-cleared devices. For 510(k)-cleared devices, radiation is an established category A sterilization method per the Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile (/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled). Per the Deciding When to Submit a 510(k) for a Change to an Existing Device (/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device), changes from one established category A method to another established category A method, including a change from gamma to another radiation source, would generally not need a new 510(k) if the change could not significantly affect the performance or biocompatibility of the device, or constitute a major change or modification in the intended use of the device.

510(k) EtO Sterility Change Master File Pilot Program

The FDA announced (https://www.federalregister.gov/public-inspection/2022-10925/medical-devices-510k-sterility-change-master-file-pilot-program), in May 2022, a Sterility Change Master File Pilot Program for sterilization changes to 510(k) cleared medical devices for sterilization providers with an Established Category B or Novel Sterilization Method, as described in the FDA guidance Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile (/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled).

The 510(k) Sterility Change Master File Pilot Program is **open to all current 510(k) holders** and is intended to help with changes to a cleared medical device's sterilization method from a fixed chamber EtO sterilization cycle to the sterilization method described in the Master File. Under certain conditions, medical device manufacturers can reference the Master File rather than submitting a new 510(k) for the sterilization change.

The pilot program is **not** limited to the sterilization Innovation Challenge participants (Identify New Sterilization Methods and Technologies (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-1-identify-new-sterilization-methods-and-technologies) or Reduce Ethylene Oxide Emissions (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions)). However, the FDA encourages Innovation Challenge participants to consider participation in the pilot program, because they may benefit from it as a part of their Innovation Challenge interactions. The pilot program may be an impactful endpoint for Innovation Challenge participants with Established Category B or Novel Sterilization Methods.

If you have questions about the 510(k) Sterility Change Master File Pilot Program, email cdrh-innovation-sterilization@fda.hhs.gov (mailto:cdrh-innovation-sterilization@fda.hhs.gov).

EtO Sterilization Master File Pilot Program for PMA holders

On November 25, 2019, the FDA announced its EtO Sterilization Master File Pilot Program for PMA holders. This voluntary program is intended to allow companies that sterilize single-use medical devices using fixed chamber EtO to submit a Master File when making certain changes between sterilization processes and facilities that reduces the amount of EtO concentrations on medical devices.

Under this voluntary program, PMA holders of Class III medical devices may reference the Master File submitted by their sterilization provider in a post approval report rather than submitting a PMA supplement.

The EtO Sterilization Master File Pilot Program for PMA holders includes the following participants:

Company	Acceptance Date
Boston Scientific	March 18, 2020

Company	Acceptance Date
Becton, Dickinson & Company (BD)	September 11, 2020
Steris Corporation	October 25, 2021
Oscor, Inc.	December 17, 2021
Medtronic, Inc.	February 17, 2022

FDA Innovation Challenges

On July 15, 2019, the FDA announced two public innovation challenges to encourage development of novel sterilization methods, which could include new devices or new modalities that are safe and effective for sterilizing medical devices:

- **Challenge 1: Identify New Sterilization Methods and Technologies (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-1-identify-new-sterilization-methods-and-technologies):** The goal of this challenge is to encourage the development of new approaches to device sterilization methods or technologies for medical devices that do not rely on ethylene oxide.
- **Challenge 2:** (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions)**Reduce Ethylene Oxide Emissions (/medical-devices/general-hospital-devices-and-supplies/fda-innovation-challenge-2-reduce-ethylene-oxide-emissions):** The goal of this challenge is to develop strategies or technologies to reduce emissions to as close to zero as possible from the ethylene oxide sterilization process.

On November 25, 2019, the FDA announced that 46 applications were received and 12 participants selected for the challenges. Refer to each challenge page for details on the selected participants and next steps.

Advisory Committee Meetings

On November 6-7, 2019, the FDA held a meeting of the General Hospital and Personal Use Devices Panel of the Medical Devices Advisory Committee to discuss how best to advance innovations in medical device sterilization. Meeting materials and other event materials are available on the General Hospital and Personal Use Devices Panel of the Medical Devices Advisory Committee Meeting (/advisory-committees/advisory-committee-calendar/november-6-7-2019-general-hospital-and-personal-use-devices-panel-medical-devices-advisory-committee) web page.

One recommendation from the advisory committee meeting is for device manufacturers to begin, as soon as possible, reducing the amount of paper (such as the labeling and instructions for use manuals) that is included in the sterile device package. An ethylene oxide sterilized medical device must be sealed in a carefully designed gas-permeable package that enables the ethylene oxide gas to enter. When the sterilization load (encompassing all the materials inserted into the sterilizer chamber with the device) includes a large amount of paper with the device, it hinders the ethylene oxide getting to the device and generally means that more ethylene oxide is required. Because of this, the FDA is encouraging device manufacturers to move to electronic materials where feasible and safe for device users. We are committed to working with industry to make this change.

In May and November 2019, the FDA engaged the infection control community at the CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC) (https://www.cdc.gov/hicpac/) meeting to update the public on the FDA's work and engagement with industry on sterilization modalities with devices that are normally sterilized using ethylene oxide.

Report Sterilization Site Changes to the FDA

If your products are affected by the stop of operations at a sterilization facility and you are planning to use an alternative facility to sterilize your products:

- **Premarket Approval (PMA) Holders:** You should submit a 180-day site change supplement. However, the FDA intends to review such PMA supplements within 30 days. The FDA issued a final guidance, Manufacturing Site Change Supplements: Content and Submission (/regulatory-information/search-fda-guidance-documents/manufacturing-site-change-supplements-content-and-submission), that PMA holders can refer to for more information about site change supplements. If you have questions about your PMA device or need help with submitting a site change supplement, contact CDRHPremarketProgramOperations@fda.hhs.gov (mailto:CDRHPremarketProgramOperations@fda.hhs.gov).

- **510(k) Holders:** Submitting a new 510(k) is typically not required for this type of change. You should document qualification activities supporting this change in your internal files. However, the FDA recommends that affected 510(k) holders refer to the FDA's guidance, Deciding When to Submit a 510(k) for a Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff (/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device) when determining if a new 510(k) is required.

Medical Device Supply Chain Issues

Contact the FDA about a medical device supply chain issue. (/medical-devices/medical-device-safety/contact-fda-about-medical-device-supply-chain-issue)

Read More:

- Statement from FDA Commissioner Scott Gottlieb, M.D., on 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 (/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-steps-agency-taking-prevent-potential-medical-device) (March 26, 2019)
- Statement on concerns with medical device availability due to certain sterilization facility closures (/news-events/press-announcements/statement-concerns-medical-device-availability-due-certain-sterilization-facility-closures) (October 25, 2019)
- Preventing Medical Device Shortages by Ensuring Safe and Effective Sterilization in Manufacturing (/news-events/fda-voices/preventing-medical-device-shortages-ensuring-safe-and-effective-sterilization-manufacturing) (July 15, 2019)

---

[1] A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products (http://gipalliance.net/wp-content/uploads/2013/01/GIPA-WP-GIPA-iia-Sterilization-Modalities-FINAL-Version-2017-October-308772.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) (2017, August 31).

[2] Blass, C. (2001). The Role of Poly(vinyl Chloride) in Healthcare (https://books.google.com/books?id=vNp3bFNOU_AC&pg=PA47#v=onepage&q&f=false) (http://www.fda.gov/about-fda/website-policies/website-disclaimer). Shawbury, UK: Rapra Technology Limited.

[3] Regulatory Review of the Occupational Safety and Health Administration's Ethylene Oxide Standard (https://www.osha.gov/sites/default/files/ethylene_oxide_lookback.pdf), 29 C.F.R § (2005) 1910.1047