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2021 Midwest Medical Device Sterilization Workshop

Medical Device Sterilization: Continuing the Conversation

Summary Report

Fermi National Accelerator Laboratory

Organizing Committee: Debbie Cotton[1], Dr. Thomas Kroc[2], Vu Le[3], Mark Pasmore[1], John Williams[4]

Authors: Dr. Thomas Kroc[2], Aaron Sauers[2]

Workshop hosted by: Fermi National Accelerator Laboratory

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[1] Baxter International

[2] Fermi National Accelerator Laboratory

[3] Abbott

[4] Medtronic

About Fermi National Accelerator Laboratory

Fermilab is a U.S. Department of Energy laboratory managed by Fermi Research Alliance, LLC under contract DE-AC02-07CH11359. The Laboratory is located outside Chicago at Kirk Road and Pine Street, Batavia, Illinois, 60510-5011. For information about Fermilab and its pioneering science and technology programs, see www.fnal.gov .

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ABBREVIATIONS AND ACRONYMS

510k	A premarket submission to the FDA for a device that is substantially equivalent to an existing device
AAMI	Association for the Advancement of Medical Instrumentation
ASTM	Formerly the American Society for Testing and Materials; it is an international standards organization.
DOE	U.S. Department of Energy
DUR	Dose Uniformity Ratio
E-beam	Electron beam
EO	Ethylene oxide
FDA	Food and Drug Administration
IFU	Instructions for Use
ISO11137-1	International Organization for Standardization standard, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*. Note: gamma, e-beam and x-ray radiation sterilization are in scope.
ISO11137-3	Sterilization of health care products — Radiation — Part 3: Guidance on dosimetric aspects of development, validation and routine control. Note: gamma, e-beam and x-ray radiation sterilization are in scope.
MDIC	Medical Device Innovation Consortium
NNSA	National Nuclear Security Administration
PDA	The Parenteral Drug Association
PMA	premarket approval to the FDA for a new medical device
PNNL	Pacific Northwest National Laboratory
The Panel	The Panel on Gamma and Electron Irradiation (https://www.irradiationpanel.org/)
R&D	Research and development
TIR	Technical Information Report; designation for an AAMI guidance document
AAMI TIR104	Guidance on transferring health care products between radiation sterilization sites or modalities; early draft
Method VD_{max}	An ISO/EN/AAMI method for establishing radiation sterilization dose using the dose substantiation methodology.
X-ray	High-energy electromagnetic radiation

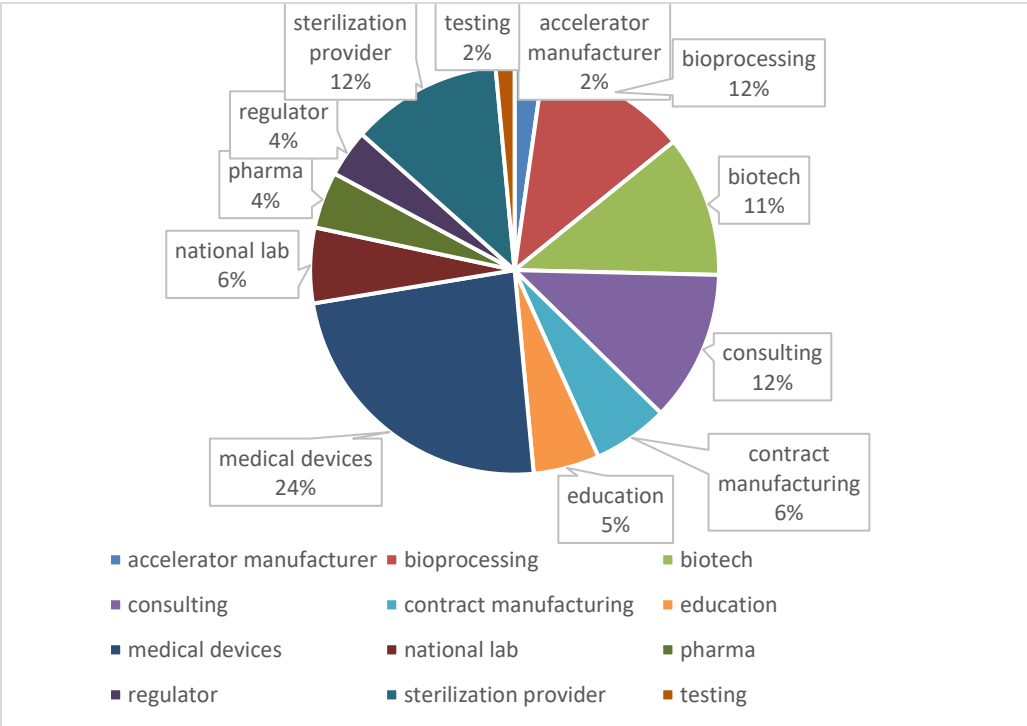
Workshop Background and Overview

On September 22-24, 2021, Fermi National Laboratory hosted the third annual Medical Device Sterilization Workshop convened as a virtual meeting for cross industry stakeholders to share learnings and discussions on accelerator-based sterilization.

Over three half-days, the workshop built on the work presented in the past two years to work towards fostering collaboration and partnership under the common goal of patient safety. The event provided:

- Updates on previous topics such as the performance of materials tested in all three radiation modalities.
- Information on how modeling and simulation can assist in the adaptation of radiation sterilization.
- Interactions with the FDA to help overcome the Regulatory apprehension that many organizations experience in contemplating unfamiliar technologies.
- Multiple Q&A opportunities and breakout sessions

Technical advancements are making accelerator-based sources of radiation viable candidates for sterilization of medical devices. Electron beams and x-rays are becoming more cost-competitive and new facilities are being built to provide needed capacity and redundancy. As the industry becomes more receptive to these modalities, there is a need for information and data to enable prospective users to evaluate these options for their products. The workshops offered in 2019, 2020, and now 2021, were designed to foster conversation between device manufacturers, regulators, consultants, equipment and service providers on needs, capabilities, and knowledge. Over 300 people registered to attend the workshop— a record attendance for the Medical Device Sterilization Workshop.



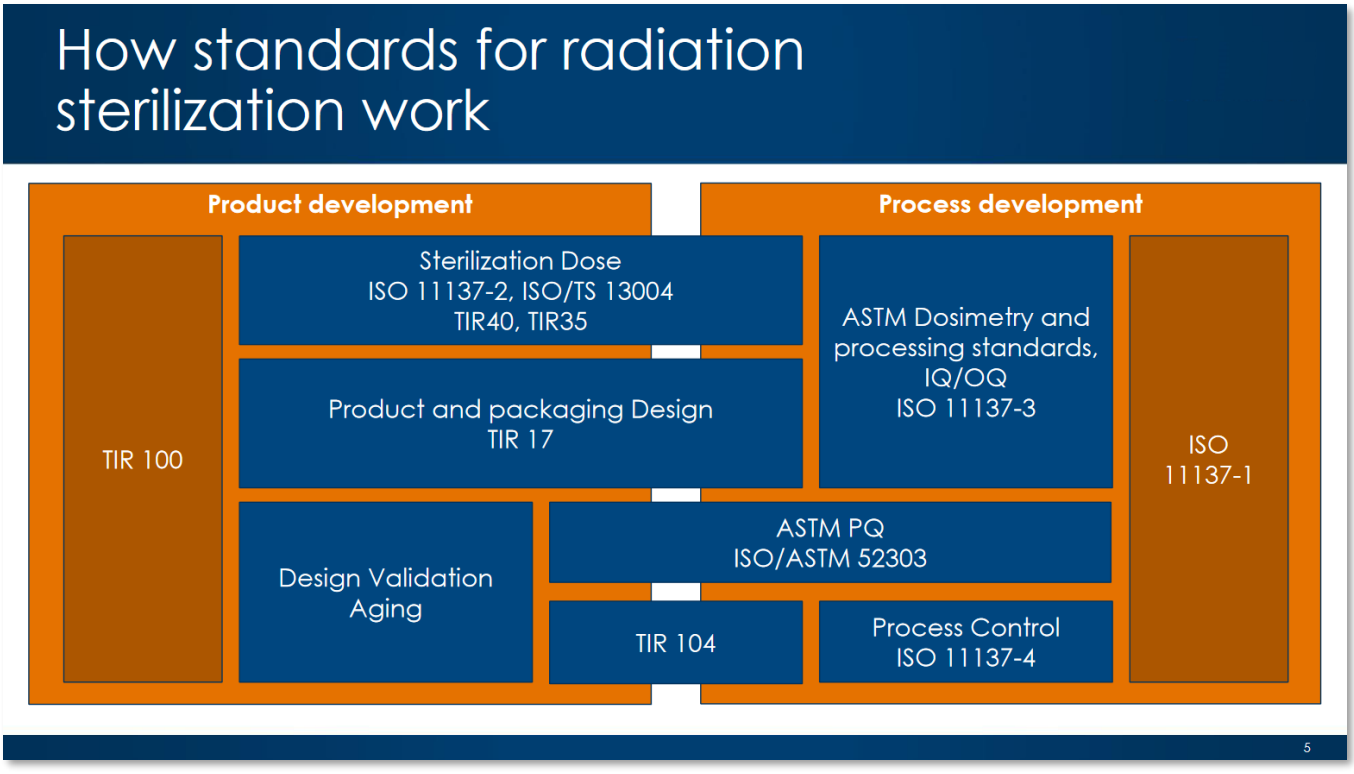
DAY 1[1]

9:00 A.M. Welcome from Mark Pasmore, Rick Verhaagen, and Timothy Meyer

Day 1 of the Medical Device Sterilization Workshop was kicked off by welcoming statements from Mark Pasmore, Rick Verhaagen, and Timothy Meyer.

9:15 A.M. Emily Craven, Boston Scientific— How Standards are *Accelerating* the Adoption of Machine Source Radiation Sterilization

In order for the medical device industry to grow, we need to provide more options for radiation sterilization. Craven's talk discussed the standards organizations pertinent to radiation sterilization and how standards can help ease the transfer between sterilization modalities. The talk discussed AAMI TIR100, which will provide a comprehensive framework for ensuring the end-to-end sterility of medical products; AAMI TIR17, which can be used as a resource in new product design when selecting materials for a health care product; and AAMI TIR104, which provides guidance on transferring between radiation sources. To take advantage of machine source radiation, guidance can help organizations understand the fundamentals of designing products for radiation and transferring products from one radiation source to another. The collaboration between industry/regulatory bodies and between standards organizations is helping to fill this gap. New guidance will help accelerate the adoption of machine source radiation sterilization technology. Consideration of end-to-end product lifecycle will make modality transitions easier. Coordination between different standards organizations is key. Standards work is a great example of collaboration to meet the needs of the health care product sterilization community.



[1] Joyce Hansen, originally scheduled to deliver the first presentation of the workshop, delivered on day 3 of the workshop.

10:00 A.M. Randolph Schwarz & Mark Murphy, PNNL, Modeling 1 "User Friendly Fast Interface for Calculating Dose Distribution in Polymer Products"

Significant impediments remain for medical device manufacturers desiring to transition from gamma-ray and ethylene-oxide sterilization modalities to electron-beam or X-ray. These impediments are mostly in the form of data and education gaps and not necessarily a lack in technology. The Office of Radiological Security (ORS) within the National Nuclear Security Administration (NNSA) has been working with government and private entities that utilize high activity gamma-ray irradiators for various applications, which includes medical product sterilization. One aim is to help advance X-ray and electron beam technologies and increase their use. ORS asked PNNL to build a collaborative team that included major players in the medical sterilization industry. The team was charged to focus on data and education gaps, as identified by the Fermilab and IAEA reports. This presentation covers a recently added task, which is to identify gaps in dose distribution modeling tools, and brainstorm ways in which to improve these software tools for use by non-experts.

10:30 A.M. Ludovic Eychenne & Antoine Ghilardi, RayXpert, Modeling 2 "X-ray radiation processing simulation with RayXpert

The presentation discussed RayXpert, a code developed by TRAD Tests & Radiations that associates a 3D modeling tool to a Monte Carlo calculation method to perform radiation simulation and dose rate calculation for the Industry, the Nuclear & Medical fields. The tool can reduce the cost of dosimetry, increase confidence in dose mapping, and increase efficiency (quality/qualification time).

11:00 A.M. BREAK

11:10 A.M. Kevin O'Hara, Sterigenics, Modeling 3 "The Current State of the Mathematical Model in Radiation Processing"

The presentation reviewed the current state of the mathematical model used in radiation processing, focusing on healthcare product sterilization. O'Hara summarized the current tools, including strengths/weaknesses; described the organizations that currently offer a dose calculations service or have in-house capabilities; and described some practical applications of the mathematical method in radiation processing. While expertise in mathematical models exists through numerous organizations (service providers, consultants, equipment manufacturers), the tool has not been universally adopted, and the regulatory/industry mindset will have to change. International standards need to evolve for the mathematical methods to be more universally accepted. Papers/publications/workshops focusing on mathematical models will assist with its adoption.

11:40 A.M. Ileana Pazos, NIST, "Upgrades and Partnerships Enhancing High-Dose Radiation Calibration at NIST

The presentation discussed calibration services, lab renovation and move, acquisition of a new irradiator, consensus value to scale electron-beam, Emergency Radiation Dosimetry System (ERDS) collaboration, and the NIST On A Chip (NOAC) collaboration. The ERDS system is a portable device to rapidly measure the amount of radiation received by exposed individuals in the aftermath of a mass-exposure nuclear event. NOAC is a first step toward a miniaturized version of the conventional calorimetry technique. NOAC operates by measuring the temperature rise in silicon devices due to radiation absorption. The chip-based device detects how heat energy affects the properties of light passing through microscopic channels being irradiated by gamma rays or an electron beam. The new sensor promises highly accurate readings at smaller dimensions.

12:10 P.M. Antoine Ghilardi, Mark Murphy, Kevin O'Hara, Ileana Pazos, Needs (Modeling and Tools) Panel Discussion

12:55 P.M. Recap and Closing

DAY 2

9:00 A.M. John Williams, Welcome: Day 1 Recap / Day 2 Agenda

9:10 A.M. Christiane Beerlage, Zimmer Biomet, Converting Modalities "Product Transfer to Alternative Sterilization Methods: Gamma to X-ray"

This presentation was a case study that presented the experience of converting a product from gamma to x-ray sterilization. It covered establishing the team and product scope, supplier qualification and process qualification, material compatibility and biological evaluation, and regulatory considerations.

9:40 A.M. Aaron Neighbour, Peter Laurence, eBeam: A Global View to Electron-Beam Sterilization

The presentation reviews the current market situation, discusses the need for new modalities with masks as a case study, and concludes that e-beam can supplement sterilization needs. Electron beam sterilization can alleviate systemic PPE shortages, as a topical example.

10:00 A.M. Betty Howard, X-Ray: Future of X-ray Services

The presentation describes the market for gamma services and the projected capacity gap, regulatory pressures, ionizing radiation options, a comparison of gamma, electron beam, and x-ray, and paths forward.

10:40 A.M. Break, 15 Minutes

11:00 A.M. Live Survey

11:10 A.M. Break-out Sessions: 1. Modeling and Tools 2. Conversion and Capacity

Beau Rollins, James Hathcock, Joern Meissner, John Williams, Mark Pasmore, Peter Baker, Thomas Kroc, Vu Le

MODELING

The survey results for the Modeling session indicated software and tools were used primarily with R&D and innovation. However, there were discussions with interest in the use of these tools as an investigation tool as part of the quality system and referencing results for validations. Participants indicated that they don't see modeling being integrated into their quality system anytime soon. There's a general perception that a theoretical model may not be considered as a tool for a quality decision. Those who have used the tool mentioned it would be helpful if there was additional guidance on how results can be used in parallel with dose mapping such as a method of identifying minimum and maximum dose locations ahead of validations. New and improved tools have become available over the past several years and have become simpler to use but there is still a general perception that these tools are complex and requires a broad set of skillsets to run simulations. This is an opportunity for vendors to provide more general awareness training as well as educational courses to

demystify the difficulties of modeling. The next step with development in this space is bridging the gap between R&D and Operations/Quality. Companies who bring this software and tool in-house will need support from experts or be able to build the needed competency to integrate a model that can be verified and referenced as part of a qualification or even a CAPA tool in the future.

CAPACITY & CONVERSION

The survey results for this section rolled into similar discussions around the regulatory challenges and product testing strategy being the biggest hurdles. The challenges with regulatory can be as difficult internally as external. The publication of AAMI's TIR 104 comes at a critical time as people discussed the need for additional guidance and framework for converting between modalities. There's a need for this to be a step towards harmonization across notified bodies around the world as the position of a modality change can vary from small to substantial when moving between equivalent sources or gamma to electron beam. There's a large portion of products being converted over to electron beam. Simple products with large dose ranges can be prioritized as immediate opportunities to alleviate capacity constraints to allow more time for sensitive combination devices. The capability challenge usually centered around products with limited dose ranges. There's a clear opportunity in these cases where modeling software can infer capability before performing exhaustive DUR studies. Education and awareness can mitigate a lot of the unknowns and hesitation with changing modalities. More case studies and success stories that can be shared can help fill this gap.

SURVEY RESULTS

How did you hear about this workshop?	
8	Attended in a previous year
12	Email from Organizers
2	LinkedIn
18	Referred by a friend or colleague
3	Referred by a professional organization
43	**Total**

Would you recommend the workshop to someone else?	
0	Not likely
0	somewhat not likely
0	neutral
11	somewhat likely
31	very likely
42	**Total**

How likely are you to use the presentations, recordings, or report sometime in the future?	
0	Not likely
2	somewhat not likely
5	neutral
15	somewhat likely
21	very likely
43	**Total**

12:00 P.M. Panel Report Out

12:25 P.M. Recap and Closing

DAY 3

9:05 A.M. Joyce Hansen, Medical Device Sterilization for the Future

Hansen shared a broad perspective from the industry derived from numerous interviews of individuals from the medical device and industrial sterilization community who are executive leaders of R&D organizations from around the world. The presentation reviewed products of today and how they may change in the future, provides a brief overview of current industry strategies, and concluded with a discussion of how the community may shift for the future.

9:35 A.M. Guenther Burgstaller, Regulatory Aspects: Update on standards and other guidance for the industry

The presentation is a detailed discussion of switching to x-ray or e-beam for sterilization of medical devices in the European Union (EU), which includes description of notified bodies, regulations and transition periods, state of the art, standards, documentation for change notification, and deficiencies.

10:00 A.M. Aftin Ross, Clarence Murray, III, Ryan Ortega, Regulatory Aspects - Progressing Sterilization: Regulatory considerations and opportunities for collaboration in device sterilization

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 the method chosen by the manufacturer. The presentation begins with a framing of the issue and background, then proceeds with a description of the Qsub process and how to engage with the FDA. The Qsub is a process for device manufacturers to engage in conversation with the FDA prior to making a formal submission. It allows the manufacturer and FDA to focus the submission on the actual relevant items. The presentation describes tools, resources, and other ways to engage with the FDA before concluding.

10:35 A.M. Break

11:00 A.M. Aftin Ross, Betty Howard, Byron Lambert, Clarence Murray, III, Emily Craven, Guenther Burgstaller, James Hathcock, Joyce Hansen, Ryan Ortega, Panel Discussion: Radiation - Collaboration: Where are we headed as an industry?

12:00 P.M. Closing

LIST OF REGISTRANTS