What's Your Five-Year Device Sterilization Plan Look Like?

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Agenda

- Navigating Sterilization Validation Requirements
- Regulatory Understanding
- Novel Methods
- Gamma/E-beam/Xray
- Steam
- Ethylene Oxide

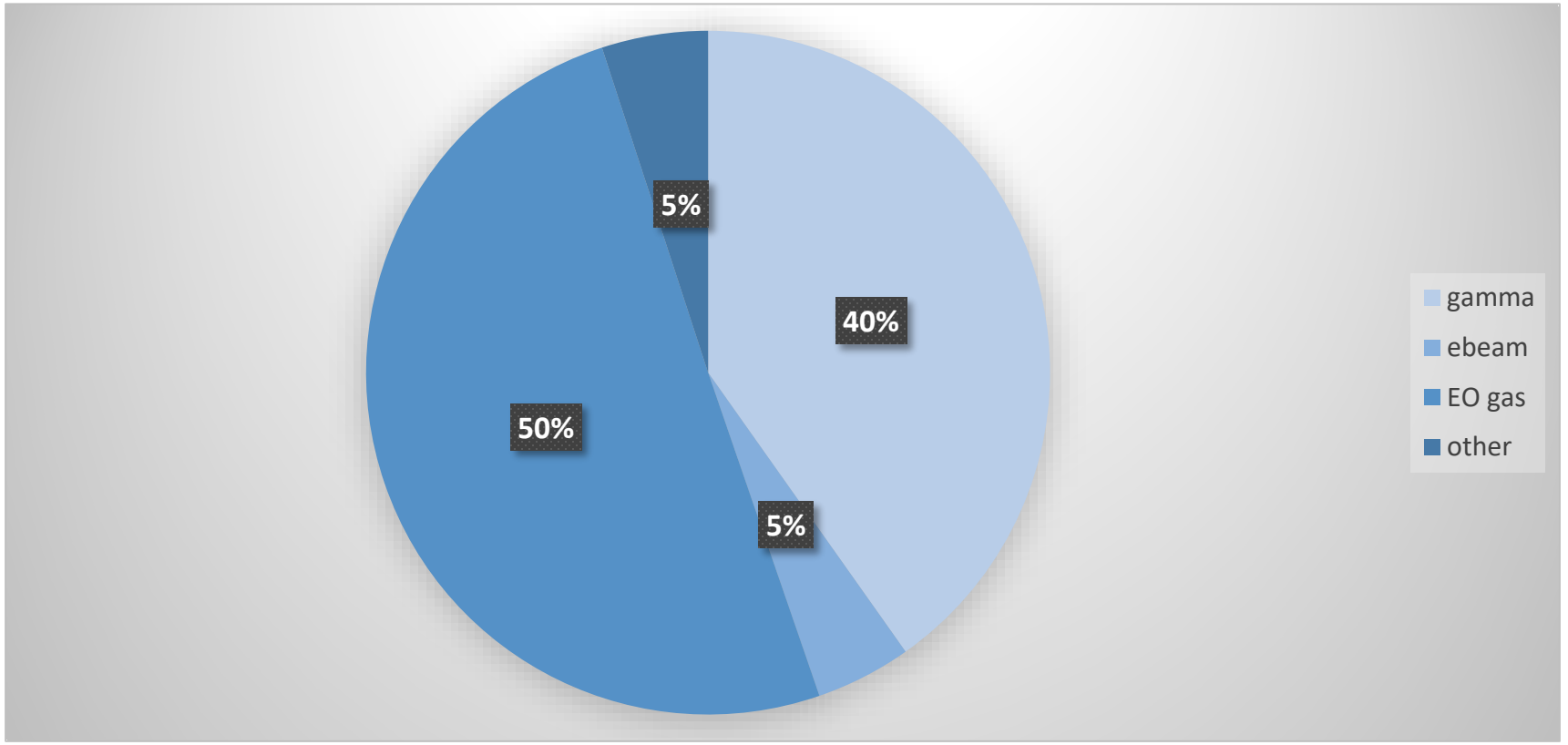
Navigating Sterilization Validation Requirements

- Sterilization is a processing step within the overall healthcare manufacturing process
- Testing on the device allows the Manufacturer to determine the level of microbial load on a device and thereby define the probability of a viable microorganism commonly referred to as Sterility Assurance Level (SAL).

Navigating Sterilization Validation Requirements

- Sterilization refers to any process that removes, kills or deactivates all forms of life and other biological agents present in or on a surface, object or fluid.
- The sterilization modality depends on several factors:
  - Materials
    - Compatible with repeated exposures
  - Packaging
    - Maintains SBS and Shelf life
  - Design/Complexity
  - Process availability, location and capacity
  - Cost and time

Sterilization Market Breakdown



Source: www.iia.com

Regulatory Understanding

FDA - Sterilization modalities are segregated into two categories.

Category A

- Dry heat
- EO with devices in a fixed, rigid chamber
- Moist heat or steam
- Radiation (gamma, e-beam, Xray)
- Vaporized Hydrogen Peroxide (H_2O_2)

Category B

- Ozone (O_3)
- Flexible bag systems (e.g., EO in a flexible bag system, diffusion method, injection method

Novel Sterilization Methods

"The specific process does not appear to have been evaluated by FDA, either because the parameters of an FDA-cleared sterilizer have been altered, or because process validation data have not been evaluated and found to be adequate in previous cleared or approved submissions"

Novel Sterilization Methods

Flexible bag systems (EO in a flexible bag system, diffusion method, injection method)

- TIR 56 Guidance for the development and routine control of an EO process using Flexible Bag Systems.

Ozone (O_3)
Chlorine Dioxide (chamber/flexible bag system)
Ultraviolet

www.sterility.com

Sterilization Modalities - Gamma

Source is Cobalt 60, ~3-6 hours processing

High penetration capability

Compatible with high density products

On certain materials, embrittlement, discoloration, change in viscosity due to irradiation

Sterilization Modalities - Gamma

Requirements outlined in ISO 11137

- Part 1: Requirements for validation and routine control
- Part 2: Establishing the dose
- Part 3: Dosimetry and Process Control

IQ/OQ are performed by the contract facility

Bioburden based approach

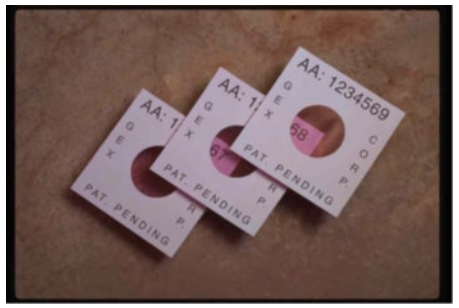
- Based on inactivation probability model

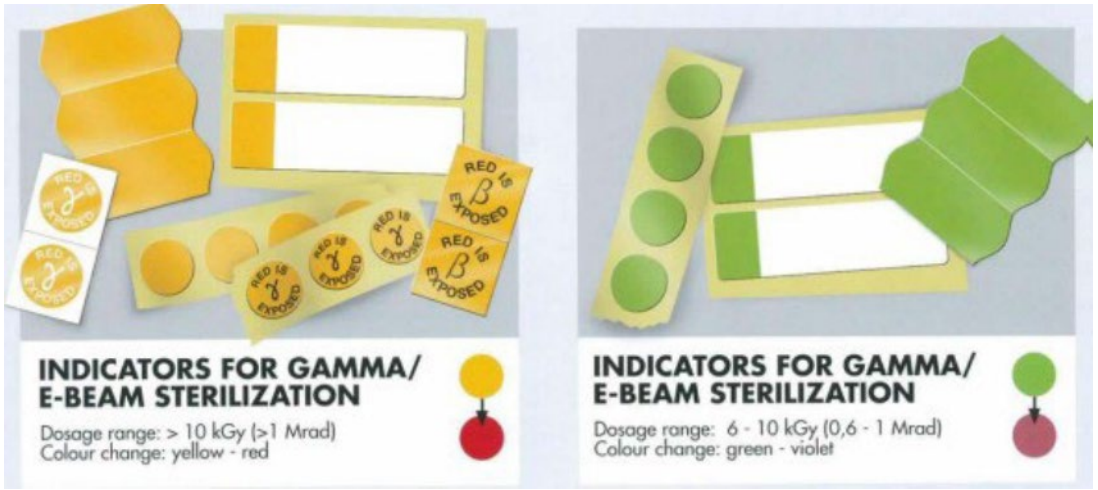
Density of load, can penetrate up to 0.40 g/cm^2

Pallets or boxes can be processed

Sterilization Modalities – Gamma

- Each ‘product family’ is dose mapped by placing dosimeters throughout the product load.
- This verifies that the minimum specified dose is applied to the product, within the product packaging, and that the maximum specified dose is not exceeded.
- Performed using Radiochromic film or Alanine Dosimeters - measures absorbed dose using a spectrophotometer
- Radiation indicator is not the same as a Dosimeter – go /no go tool





Sterilization Modalities - Gamma

MAXIMUM DOSE TESTING

- Validate product to max dose plus 5-10 kGy

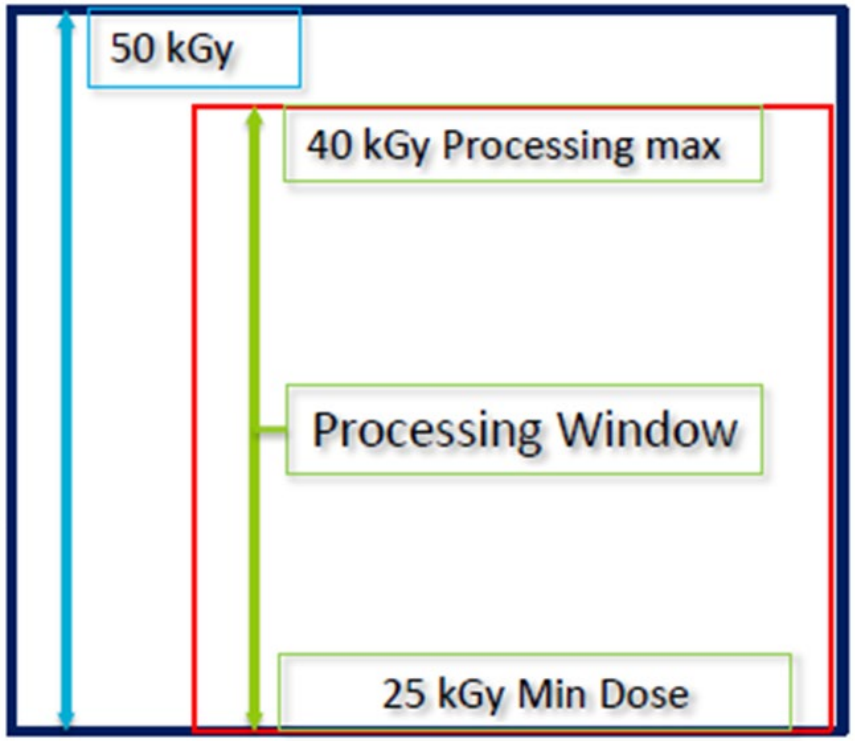
Sterilization at 25-40 kGy

Irradiate samples at 50 kGy

- Perform product functionality testing

Also package, biocompatibility, tox… testing

- Allows for dose augmentation or accidental overdose



Sterilization Modalities - Gamma

Choosing the "**right**" method

VDmax most common (ISO 13004)

- Uses fewest test articles

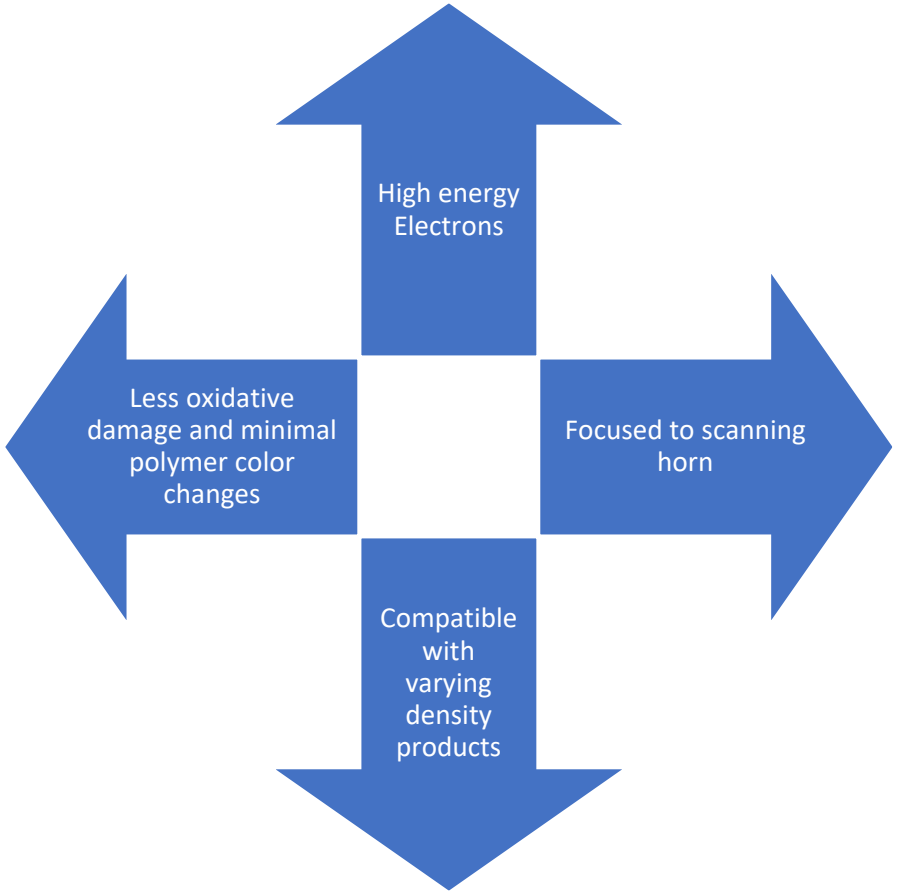
Method 1 - dose directly correlates to bioburden amount–lower dose

- 100 sample sterility test

Method 2 - dose directly correlates to bioburden resistance–lowest dose possible, incremental

- Uses the most samples for validation

Sterilization Modalities – E-beam



~30 minutes processing time

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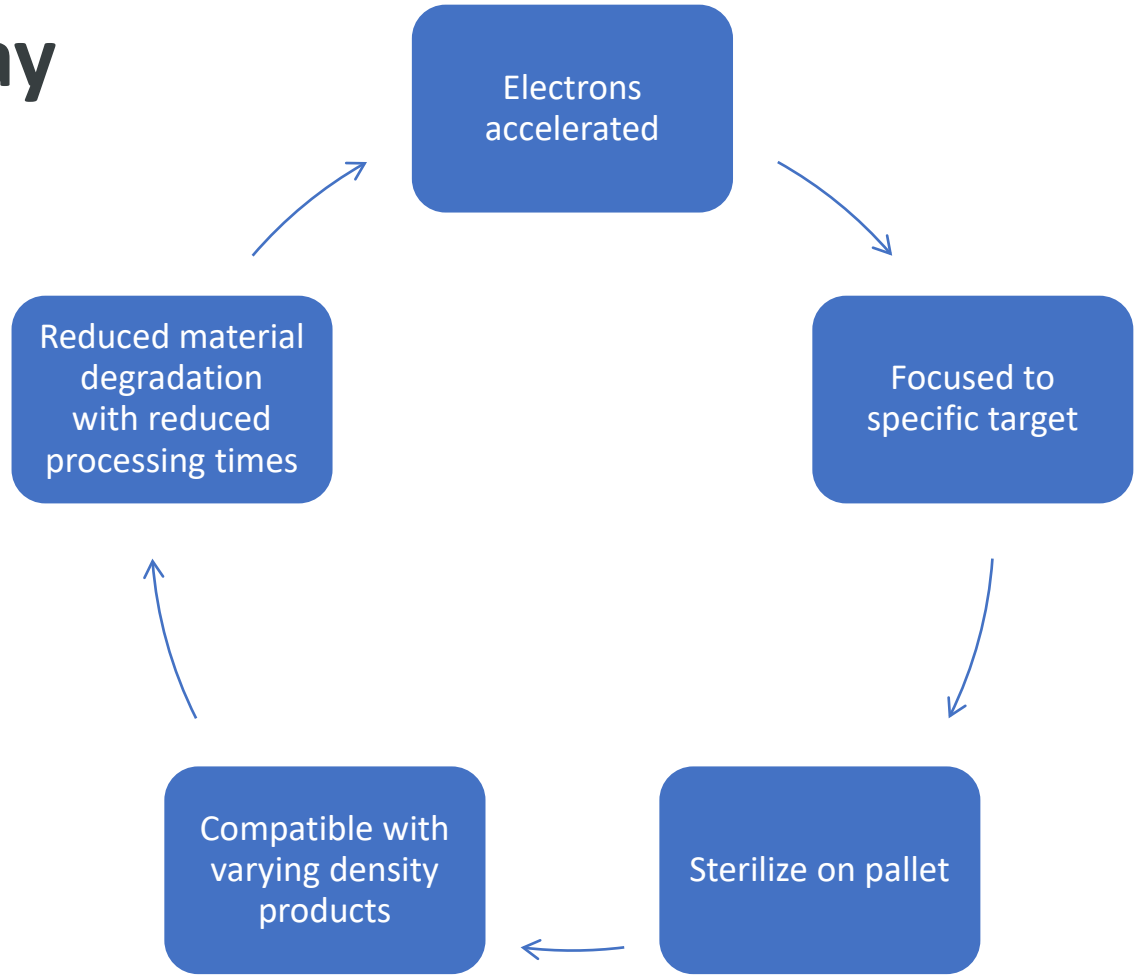
Sterilization Modalities - Xray

~3-6 hours processing time

https://www.steris-ast.com/solutions/x-ray-irradiation/



Sterilization Modalities - Changes

TIR35 Product Adoption and alternative sampling plans

Points of Consideration

- Max Dose – does candidate device still function?
- Product Design
  - Surface area
  - Materials –product and packaging
  - Biocompatibility
- Environment
  - Bioburden

Sterilization Modalities - Changes

Paper Justification

- Demonstrates the technical review does not identify significant differences

Bioburden Adoption

- Most common
- Includes technical review and bioburden testing
  - Numbers and types of organisms are similar

Dose Audit Adoption

Sterilization Modalities - Changes

TIR104:2022 Guidance on transferring healthcare products between radiation sterilization sources

25-40 kGy has been “standard” dose for many years

- Coincides with up to 1,000 CFU, “overkill” process
- Consider validations using lower minimum doses
  - 17.5 kGy carries maximum bioburden of 9 CFU
  - 20.0 kGy carries maximum bioburden of 45 CFU
  - Must coordinate with irradiator first – understand processing categories
- Larger dose range allows for more potential availability in scheduling (25-45 to 25-50 kGy)

Sterilization Modalities - Steam

ANSI/AAMI ST79 “Comprehensive guide to steam sterilization and sterility assurance in health care facilities”

- Achieved by exposing items to saturated steam under pressure.
- Low cost, safe, no residues
- Not compatible with oils or lubricants
- IQ/OQ/PQ are performed by the facility

Sterilization Modalities - Steam

3 phase approach

Conditioning – air is removed from the chamber (gravity or dynamic air removal)

Exposure – times and temps can be country-specific

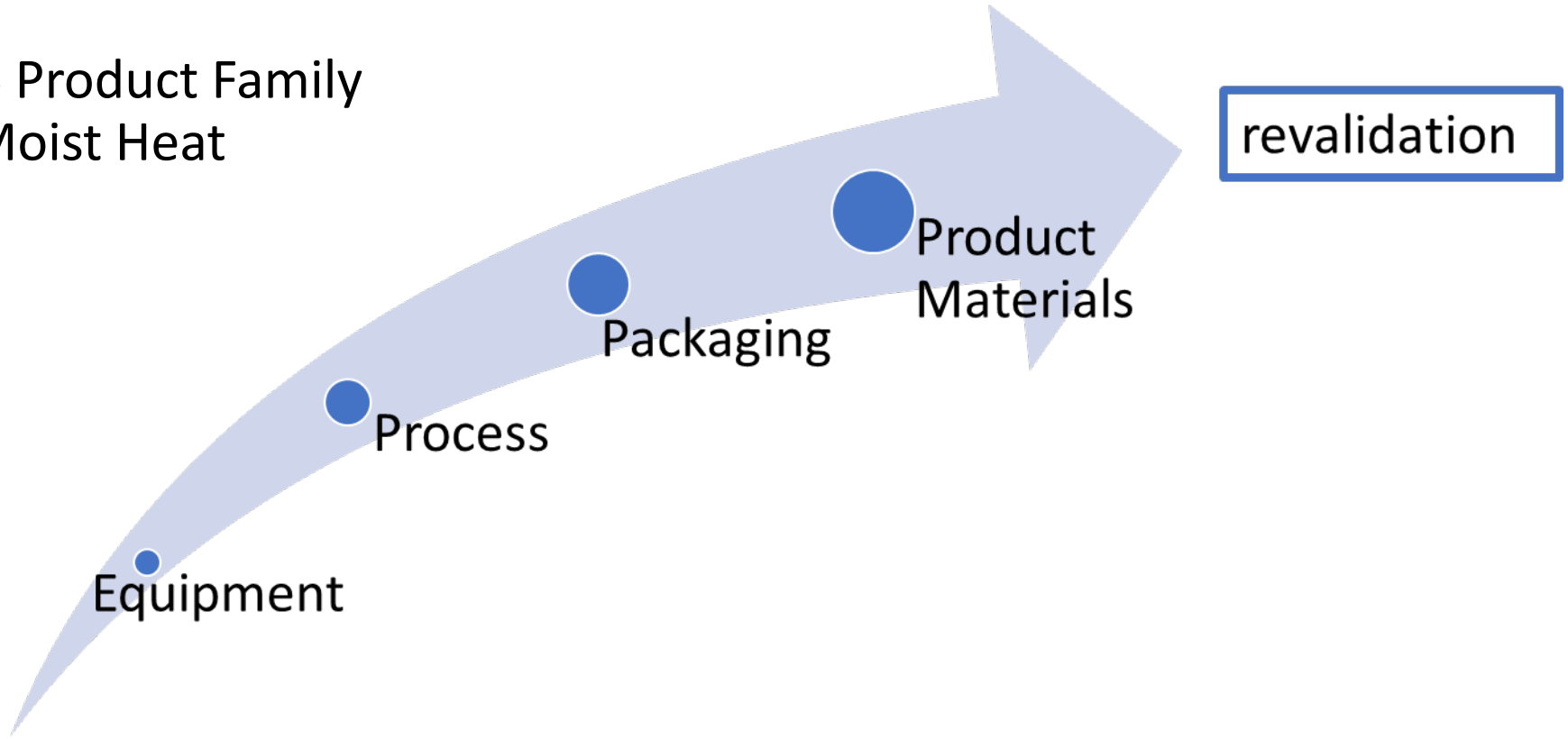
Exhaust – steam is removed from the chamber

Monitored by mechanical, chemical, and biological monitors.

Quality of the water has requirements

Sterilization Modalities - Changes

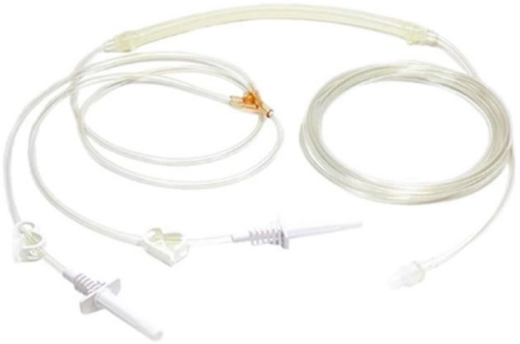
AAMI WD TIR116 Product Family Designation for Moist Heat



Sterilization Modalities - EO

Many medical devices cannot be sterilized by methods other than EO for the following reasons:

- Gamma and e-beam radiation can make plastics brittle or cause certain non-woven materials to disintegrate
- Steam is high temperature and can melt plastics and/or damage products sensitive to heat and/or moisture
- Hydrogen peroxide and gas plasma are intended for small-scale, surface sterilization and have limited penetration with devices that have interior chambers or mated surfaces



Sterilization Modalities - EO

According to FDA “the most commonly used method in the U.S. to sterilize medical devices is ethylene oxide”[1]

The sterilization process typically consists of 3 phases, can be performed in a single chamber

- Preconditioning
- Exposure
- Aeration

Monitored by mechanical, chemical, and biological monitors

Cycles are based on an overkill approach (SAL 10^{-12})

Designed for pallets or boxes

1. Medical Device Sterilization Town Hall: Overview of Sterilization Landscape & Role of Ethylene Oxide

Sterilization Modalities - EO

ISO 11135-1 Sterilization of health care products – Ethylene oxide – Requirements for development, validation, and routine control of a sterilization process for medical devices.

IQ/OQ are performed by the contract facility

PQ

- Microbiological PQ demonstrates that, on application of the sterilization process, the specified requirements for sterility are met.
- Physical PQ demonstrates

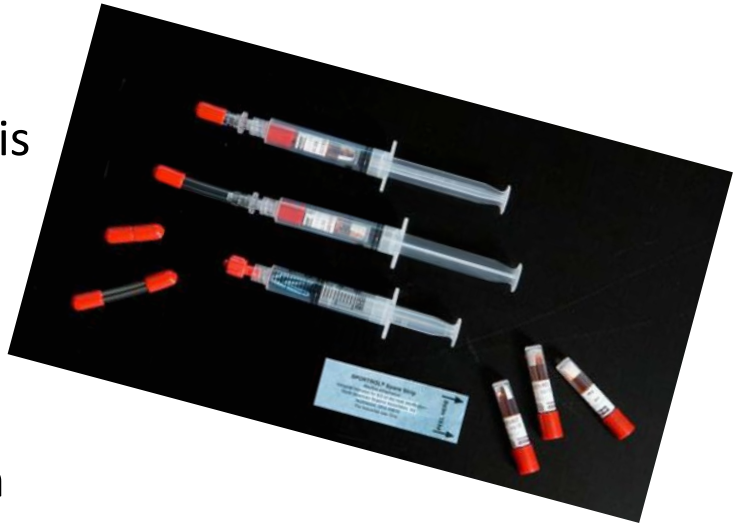
  1) reproducibility of the process (a minimum of three consecutive runs in which all the specified acceptance criteria are met) and

  2) that the specified acceptance criteria are met throughout the load for the duration of the proposed routine process specification.

Sterilization Modalities - EO

Process Challenge Device Selection (PCD)

Evaluates the delivered lethality of the selected process parameters. This is done by placing a biological indicator (BI) within the product at a location where sterilizing conditions are the most difficult to achieve.



Internal PCDs (iPCDs) are medical products or devices selected by the manufacturer as the most difficult to sterilize products based upon design and material composition and are used for validations. Demonstrates required SAL is delivered.

External PCDs (ePCDs) are placed external to the product during routine processing to facilitate retrieval from the load after processing.

Sterilization Modalities - EO

Reference Load Selection

The reference load is selected that identifies the worst-case load anticipated for routine sterilization

- Product load density – max conditions
- Product volume – max conditions
- Product/packaging/load venting – netting/shrink wrap

Winter Conditions/Preconditioning Study may be done to simulate conditions in a trailer during colder weather months.

Sterilization Modalities - EO

Fractional Cycle

“A cycle of short duration from which survivors can be recovered shall also be run to demonstrate the adequacy of the recovery technique for BIs exposed to EO gas.” ISO 11135:2014 Sec B.1.2

Cycle performance analysis

Product sterility testing

Bacteriostasis/fungistasis testing

BI sterility testing (process challenge devices)

Sterilization Modalities - EO

Microbial PQ- Half Cycles (3 min) to demonstrate repeatability of a 6 SLR of the BI utilizing minimum parameters, including one half of the intended routine exposure time.

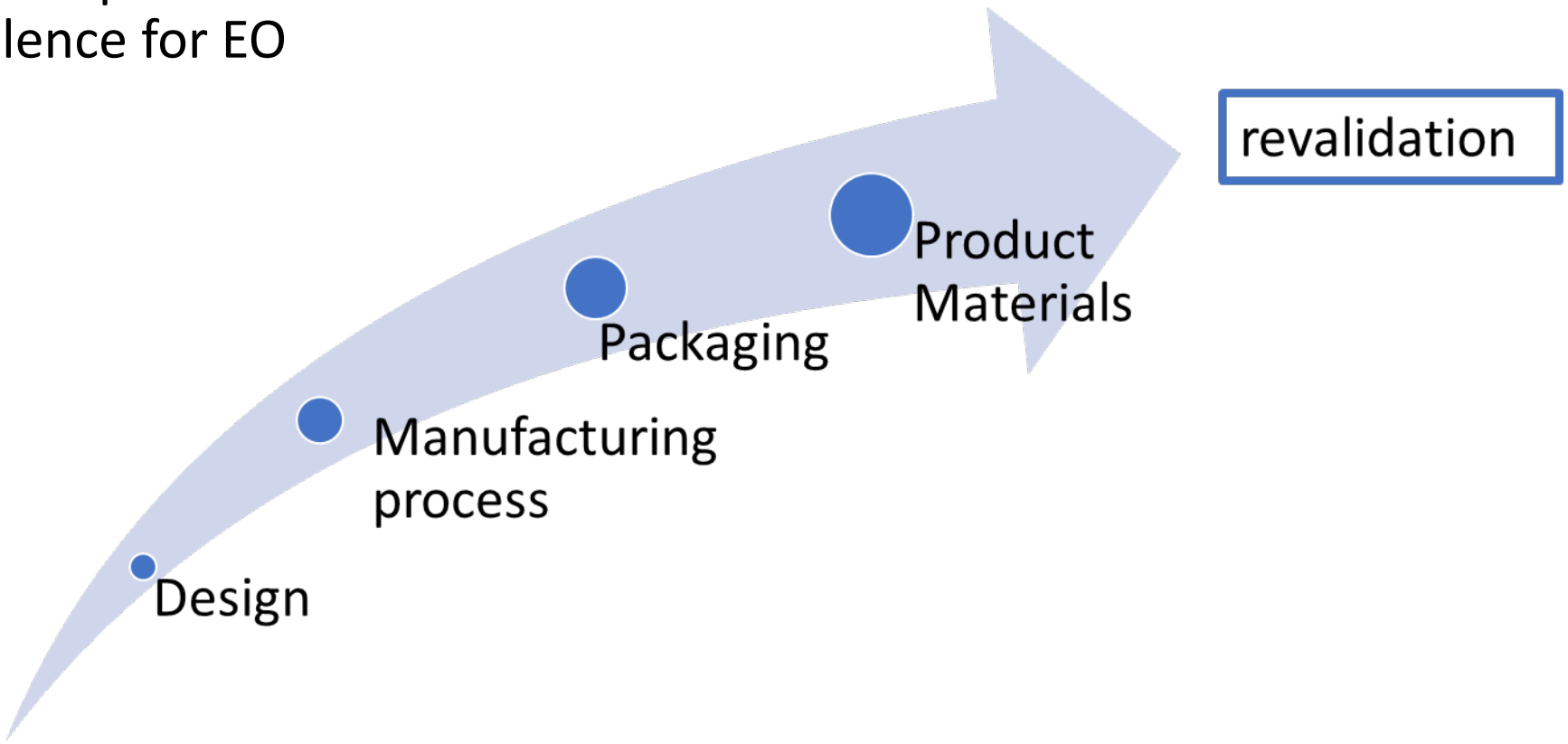
- Cycle performance analysis
- BI sterility testing (PCDs)
- Load temperature/humidity monitoring

Physical PQ- Full Cycles (3) determination (and confirmation) of residues and for product/packaging functionality evaluations.

- Cycle performance analysis
- BI sterility testing (PCDs) - nominal
- EO/ECH residual testing (don’t forget multiple exposures) - max parameters
- Load temperature (minimum)/humidity monitoring

Sterilization Modalities - Changes

- TIR 28 Product adoption and process equivalence for EO



EPA Changes to EO Sterilization & the Impact to Current Validated Cycles

Contract Sterilization Facilities:

- 2.5 to 3.5 years to comply with EPA's requirements instead of 18 months
- need to reduce emissions to levels representative of the tons per year used.

No requirement for MDMs to revalidate to lower concentration levels

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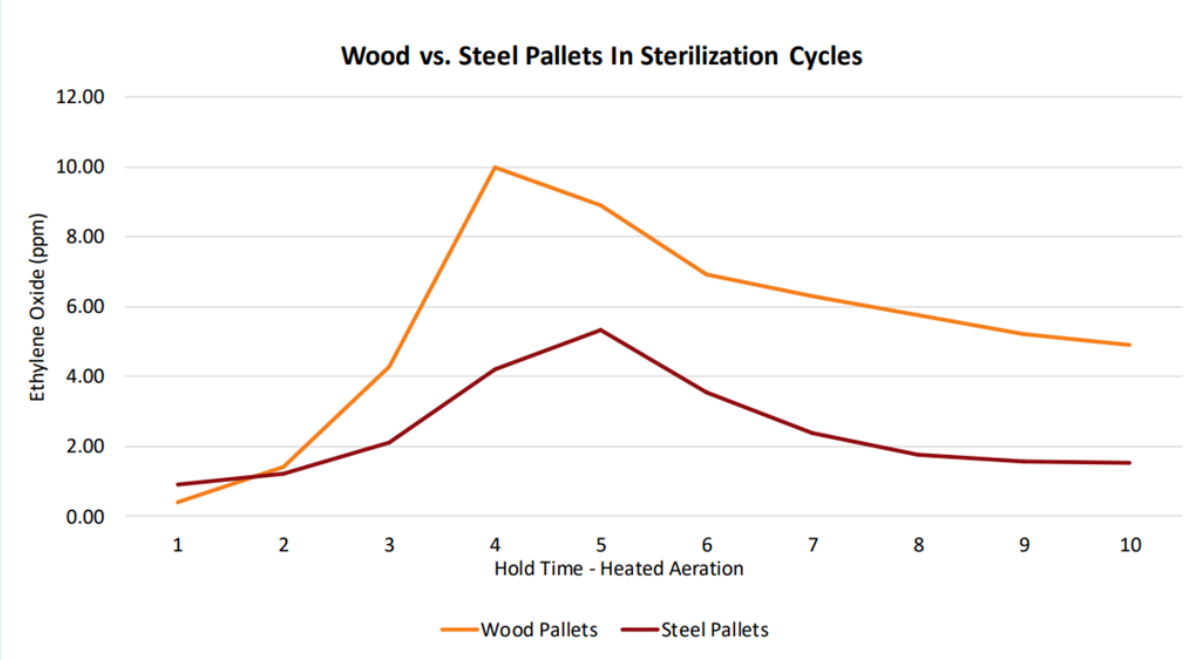
EPA Changes to EO Sterilization & the Impact to Current Validated Cycles

- Material considerations:
  - Pallet options
  - Levels of packaging materials/types
- Process Optimization:
  - Minimize transfer time between chambers
  - Reduced exposure time
  - Reduced concentration
  - Varying vacuum conditions
  - Optimize aeration
- Maximize vessel volume
- Evaluate PCD resistance



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Conclusion

Sterilization plays a crucial role in maintaining health and safety across various sectors, from healthcare facilities to industrial applications.

Traditional sterilization methods will continue to dominate the market based on

- Scalability - (30 pallets)
- Penetration ability
- Material compatibility

Continued focus on alternative methods may provide options for products that may have been pigeonholed.

Thank You

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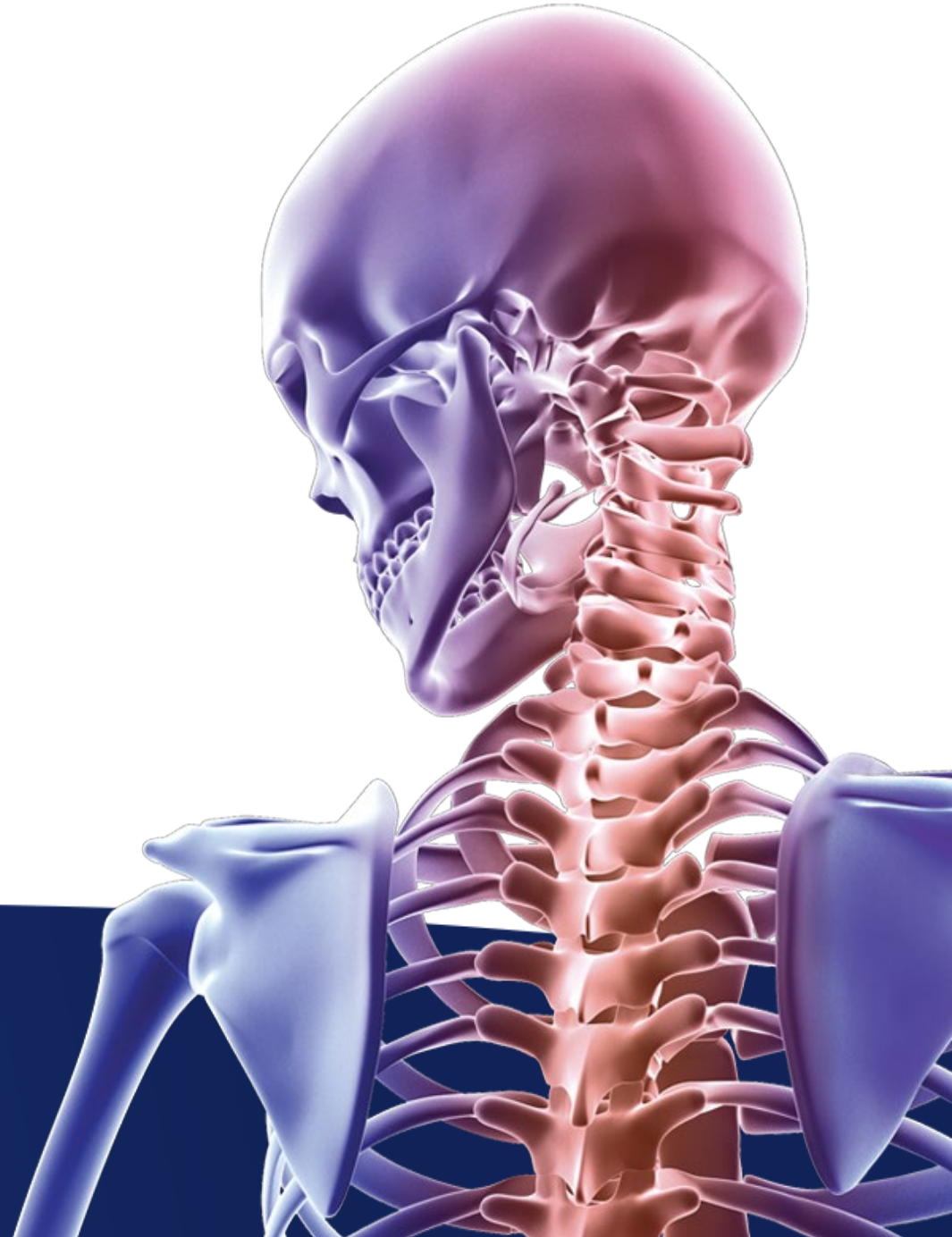

Resources

- Recognized Consensus Standards: Medical Devices (fda.gov)
- Sterilization for Medical Devices | FDA
- EN 556-1 Sterilization of Medical Devices - Requirements for Medical Devices to Be Designated "Sterile" - Part 1: Requirements for Terminally Sterilized Medical Devices

THANK YOU

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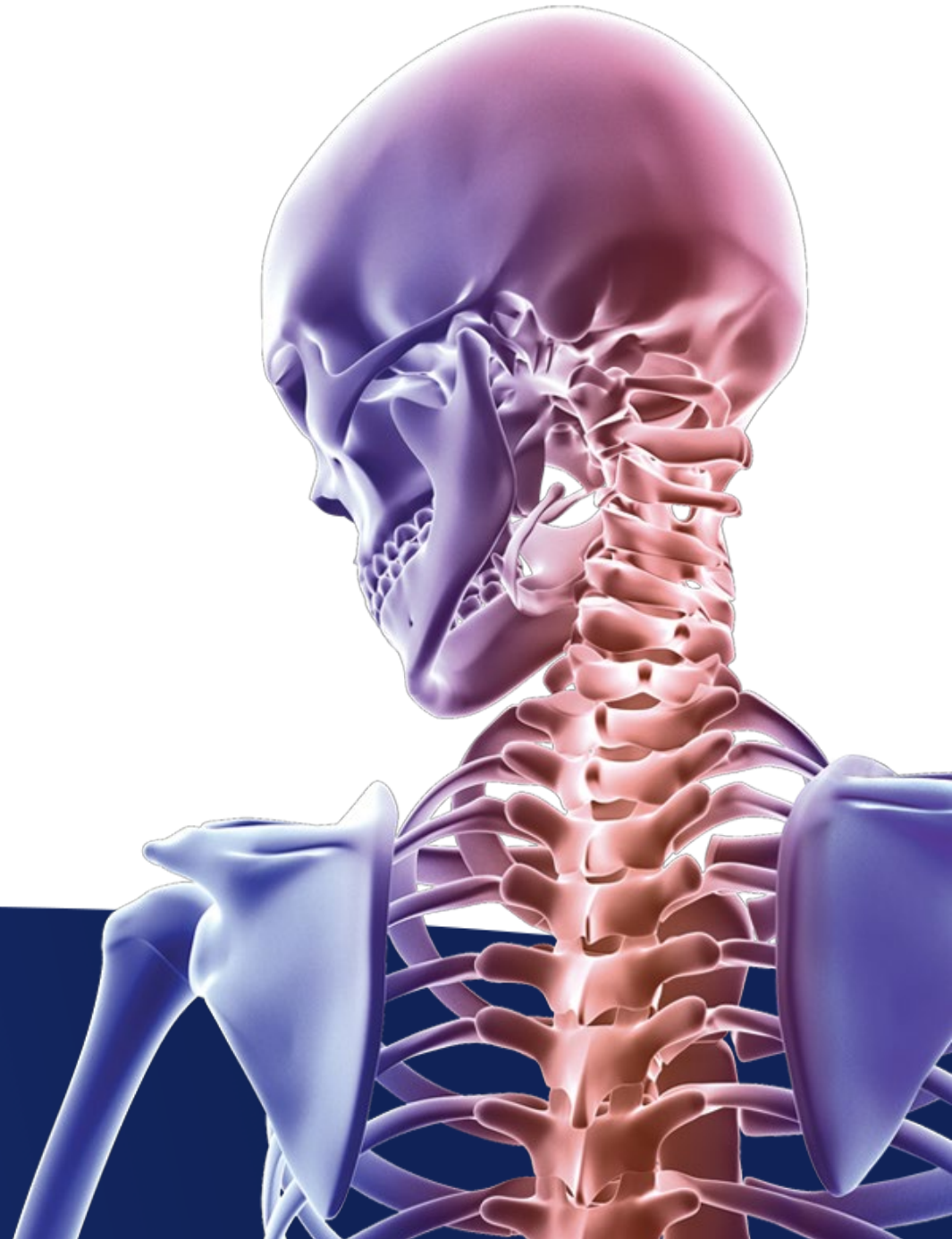
at OMTECexpo.com



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