Medical Device Sterilization:

From Possibilities to Practice

September 21-23, 2022

Welcome

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Agenda

- Current state
- Minimum Sterilization Dose
- Maximum Acceptable Dose
- Loading Configurations – Dose Mapping
- Conclusion

A Practical Approach to Establishing a 2x Process for Radiation Sterilized Product

Abstract:

Changing radiation sterilization modalities *can be challenging with medical devices that have a narrow dose range****. Particularly, a change from Gamma to E-beam*** *can be challenging because the e-beam process* ***may increase dose uniformity ratio (DUR)*** *depending on the loading configuration used. Developing a process that allows for product to be sterilized more than once is not common for radiation due to the* ***material effects on sensitive polymers****. To optimize processing,* ***considerations must be made early in the product development and sterilization validation life cycle such as sterilization dose, maximum acceptable dose (MAD), and alternative dose mapping configurations.***

In practice, to achieve two times sterilization processing capability, the combined total maximum absorbed dose to product from the 1st and 2nd sterilization process should be below the established MAD of the product. ***Typically, a 2x process would consider doubling the max dose delivered to the product*** *from the 1x process (e.g a 1x dose range of 25 – 50 would have a max dose of 100 kGy and require an established MAD of 100 kGy).* ***For sensitive polymers, a MAD of 100 kGy may not be possible. The evaluation of alternate product configurations and lower sterilization dose may solve this problem.***

A dose ranging study to assess product performance impact of polytetrafluoroethylene (PTFE) across 30 – 90 kGy was conducted to evaluate if a product can be re-sterilized based on a current validated dose range of 25 – 50 kGy. The outcome showed that the traditional 25 – 50 kGy processing range did not allow for a 2x process, however lowering the sterilization dose to 20 kGy and increasing MAD to 65 kGy allowed for the opportunity for processing a 2nd time with an alternate loading configuration (low DUR).

A Practical Approach to Establishing a 2x Process for Radiation Sterilized Product

Current State

1) Product Development (min dose, max dose and dose mapping) is a project

» *Once the "project" is complete, resources, money and time are likely unavailable*

» *Is like a race - the most time and cost efficient, least risky, path is usually taken*

- *Leveraging*

2) A typical 25 – 50 kGy range will not accommodate a 2x process.

- *Is the minimum dose tied to the microbiological quality of the product?*
- *Is the maximum dose tied to the actual highest dose the product can withstand?*

Appropriate thought, effort and time must be given to the three components of the radiation sterilization validation during Product Development for a 2x process to be feasibly implemented

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Three main components of a radiation sterilization validation

1) Minimum Sterilization Dose – 25 KGy

» *The lower specification*

2) Maximum Acceptable Dose – 50 kGy

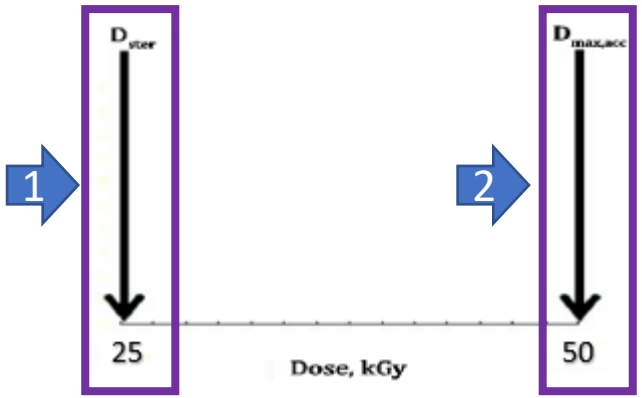
» *The upper specification*

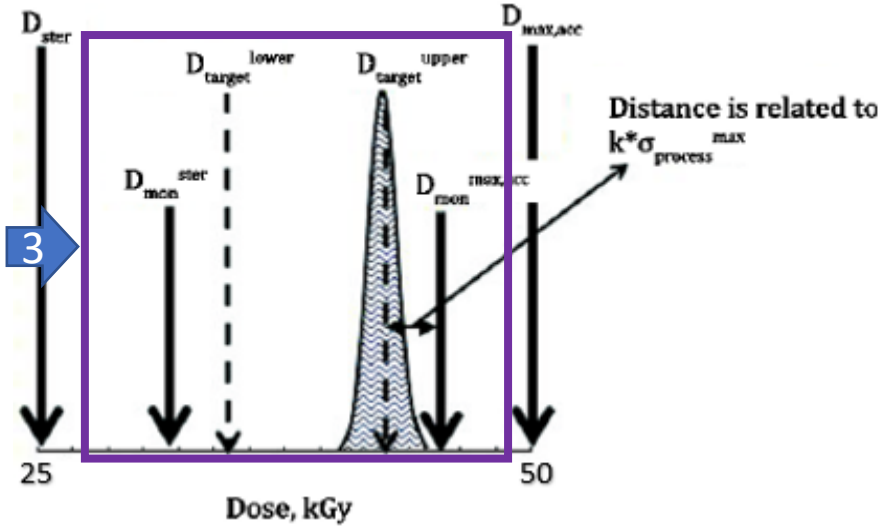
3) Dose Mapping

» *The process for staying within the specifications*

These should be considered synergistically

Affect the process, potentially, for the entire lifetime of the product





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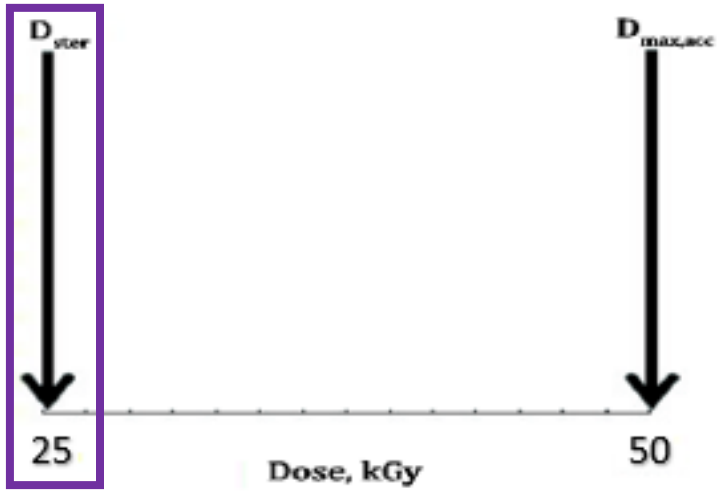
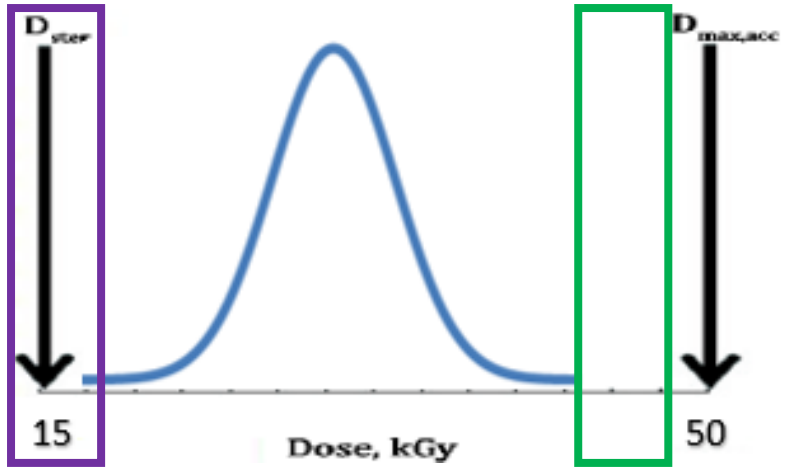
Lowering sterilization dose

1) Establish minimum dose based on the microbiological quality of the product

- *Method VDmax 25 kGy – 1000 cfu*
- *Method VDmax 20 kGy – 45 cfu*
- *Method VDmax 15 kGy – 1.5 cfu*
- *Historically, we've seen product with bioburden up to 1000x less than the limit.*





Evaluate product and process, use method that allows for setting the lowest feasible sterilization dose to allow for the widest possible acceptable dose range.

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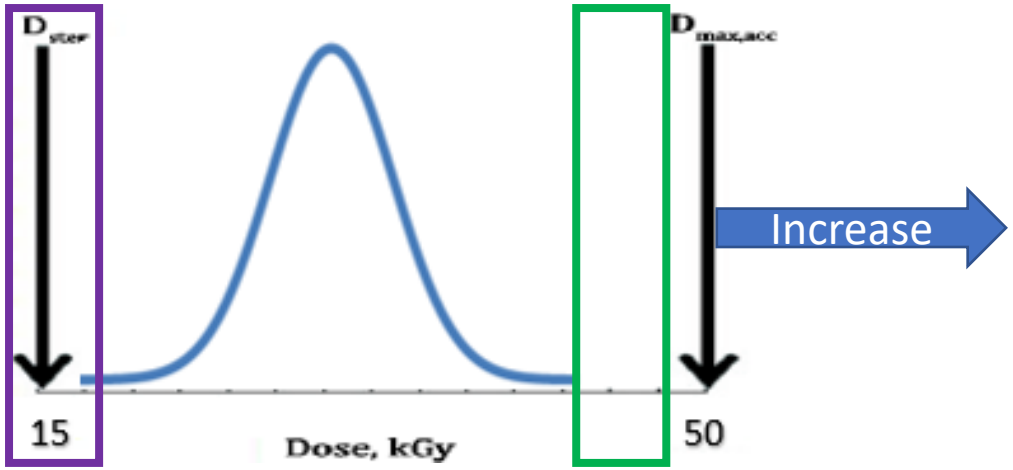
Increasing the Maximum Acceptable Dose

1) *Recommend dose ranging study*
   - *Expose different populations to range of ever increasing doses; 50 kGy, 60 kGy, 70 kGy, 80 kGy, 90 kGy, etc…*
   - *Requires adequate sample size at each dose point*
   - *Aging happens at the same rate regardless of how many units are included.*
   - *How much product would be saved with a 2x process?*
2) *Material Compatibility*
   - *TIR17*
   - *Not always indicative of how materials perform in specific applications within a product*
   - *Low compatibility with sterilization modality =/= product with that material will fail functional requirements*



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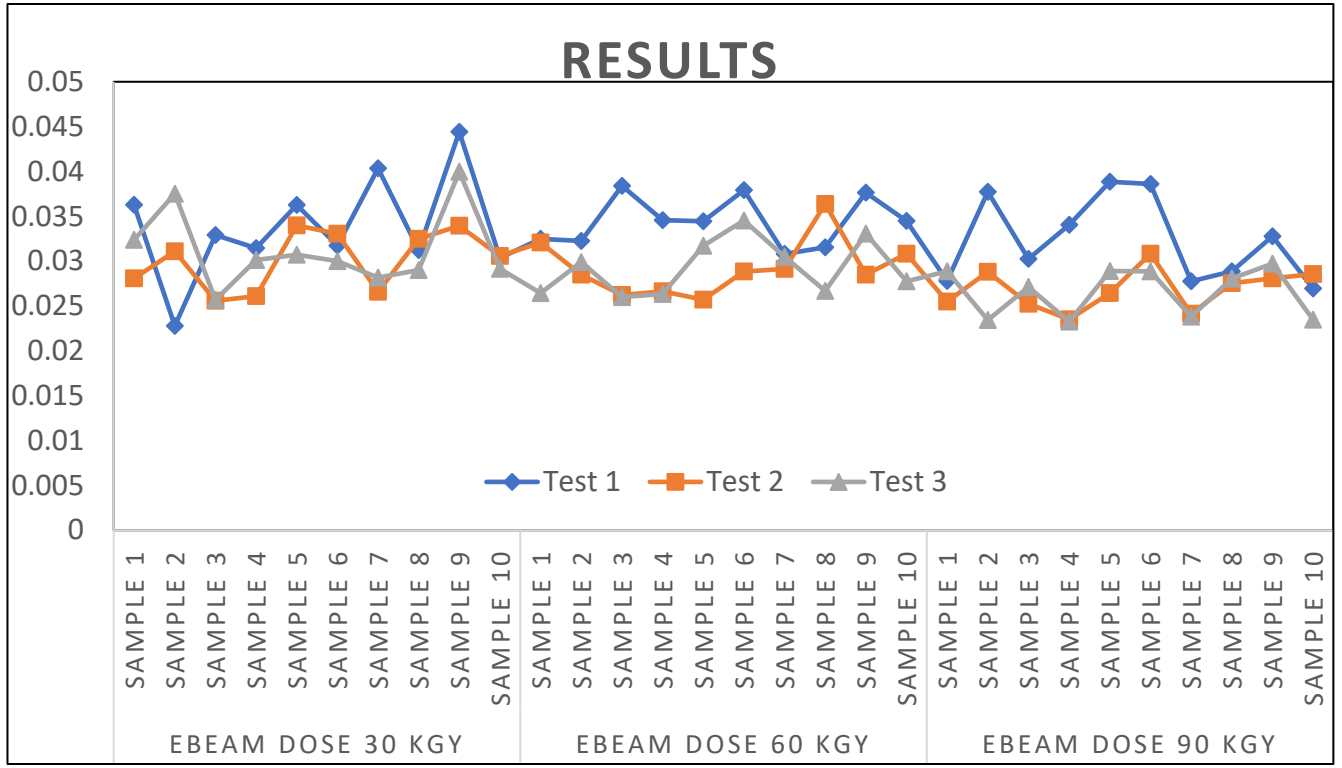
Material Compatibility

Dose ranging study to assess product performance impact of polytetrafluoroethylene (PTFE) across 30 – 90 kGy.

Per TIR17, PTFE has a "poor" single use rating and a "not likely" rating for re-sterilization



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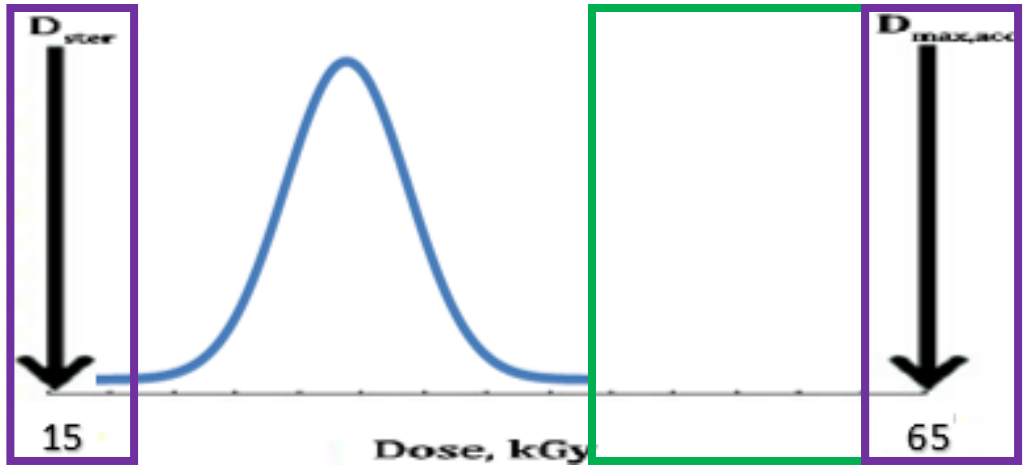
Potential for 2x Processing

1) *Lower minimum dose + Higher Maximum Dose = Wider acceptance range*

2) *Wider acceptance range expands possible combinations, allowing for greater flexibility on how the 1st processing can be done, and still allow for 2x*



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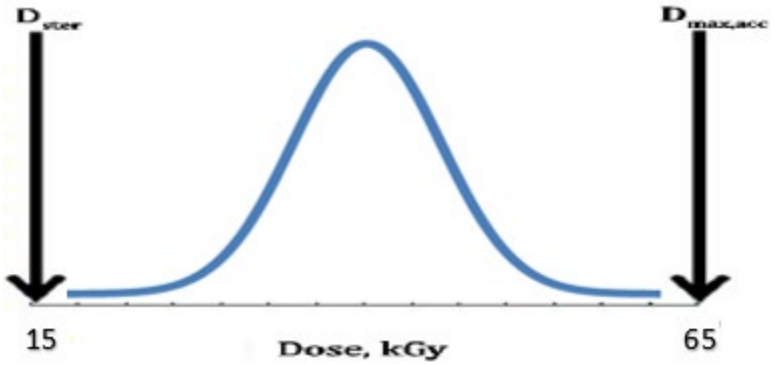
Dose Mapping – New Range 15 – 65 kGy

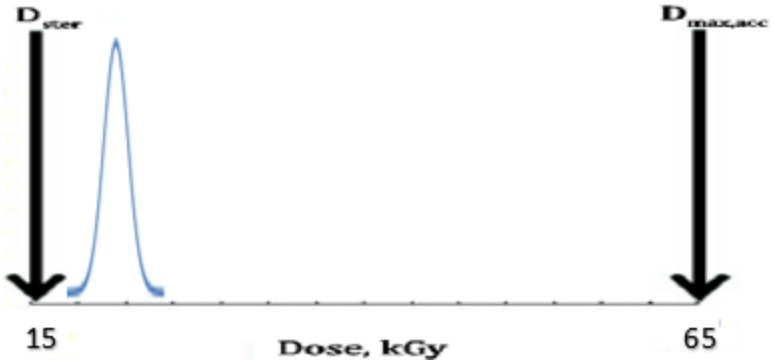
1) Routine Processing

- *Configuration focused on volume efficiency*
- *Higher Dose Uniformity Ratio (DUR) – Less uniform dose distribution*



2) Dose Audit

- *Configuration focused on dose uniformity*
- *Lower DUR – More uniform dose distribution*



Use combination of these to create 2x process

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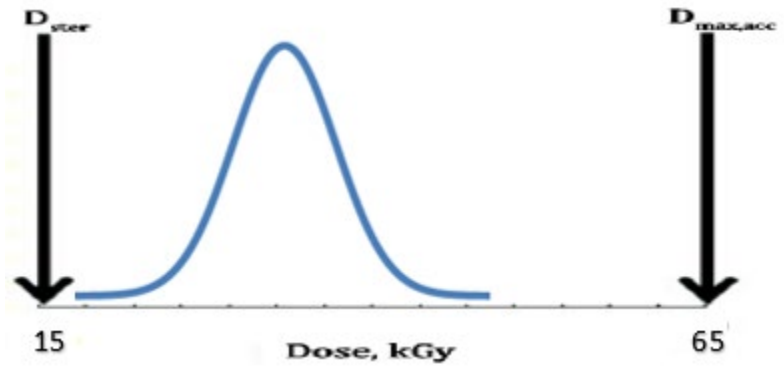
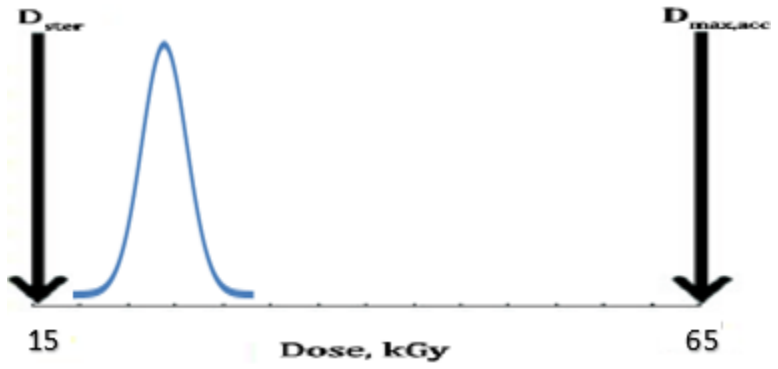
Dose Mapping – New Range 15 – 65 kGy

1) *Configuration focused on volume efficiency*



2) *Configuration focused on dose uniformity*



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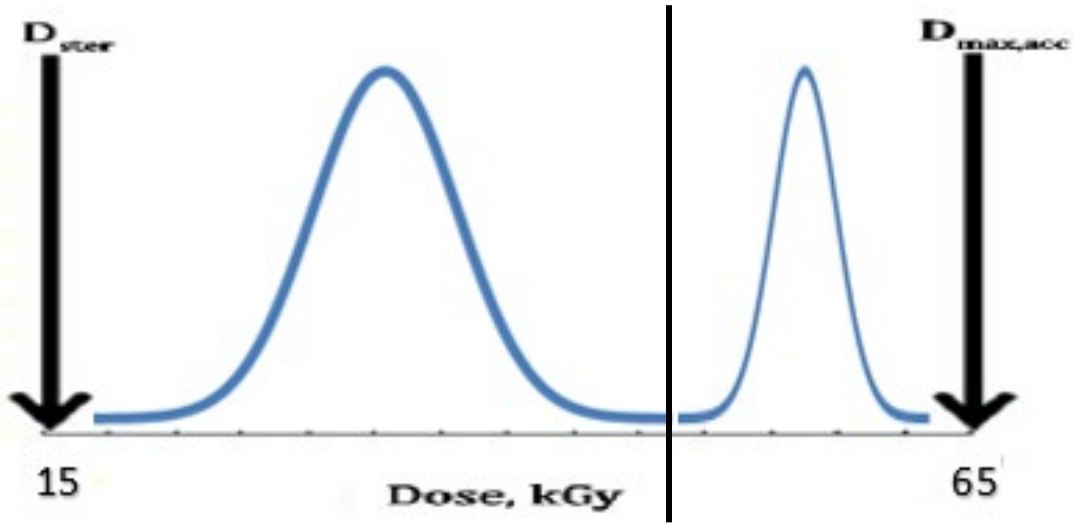
Dose Mapping – New Range 15 – 65 kGy

2x Process



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References:

ISO11137-1:2006/Amd 1:2013/Amd 2:2018 - Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

ISO11137-2:2013/Amd 1:2022 - Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose

ISO11137-3:2017 - Sterilization of health care products—Radiation—Part 3: Guidance on dosimetric aspects of development, validation and routine

TIR17: 2017 - Compatibility Of Materials Subject To Sterilization

Questions?

Input your questions for speakers at any time via the Q&A function at the bottom of your screen: