Product Transfer to Alternative Sterilization Methods: Gamma to X-ray

Medical Device Sterilization Workshop, September 22-24, 2021

Christiane Beerlage

Contents

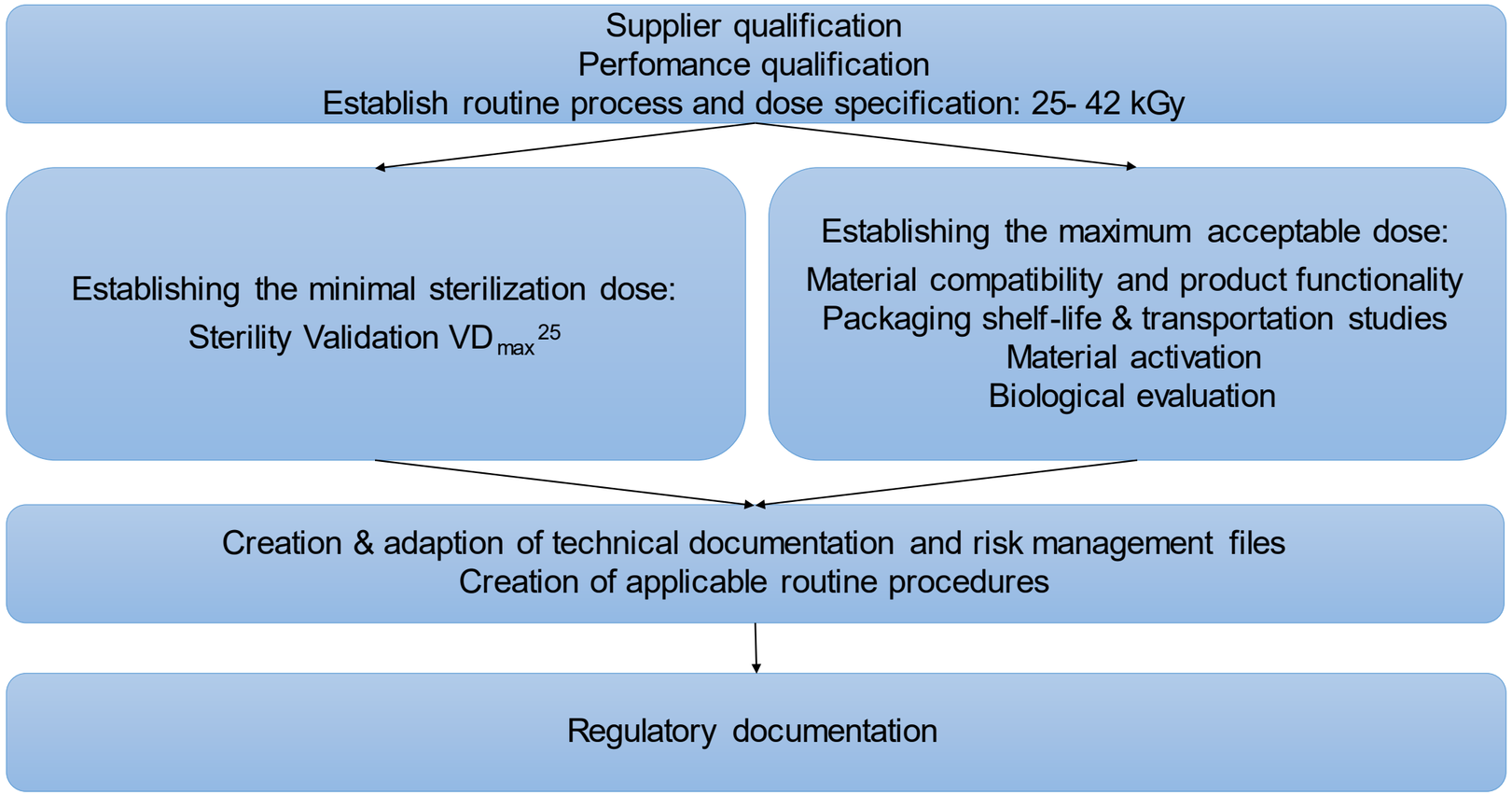
Initial Considerations - Physics

- X-ray closely related to Gamma
- Same Mode of Action: Photons
- Same Applicable Standards: ISO 11137 Series
- Higher Dose Rate
- Better Material Penetration
- Less Oxidative Stress on Polymers
- Material Compatibility Expected (AAMI TIR17)
  - “A material that formerly qualified at a low-dose rate (gamma) typically will require minimal qualification to demonstrate material compatibility at a higher dose rate…”

Initial Considerations - Business

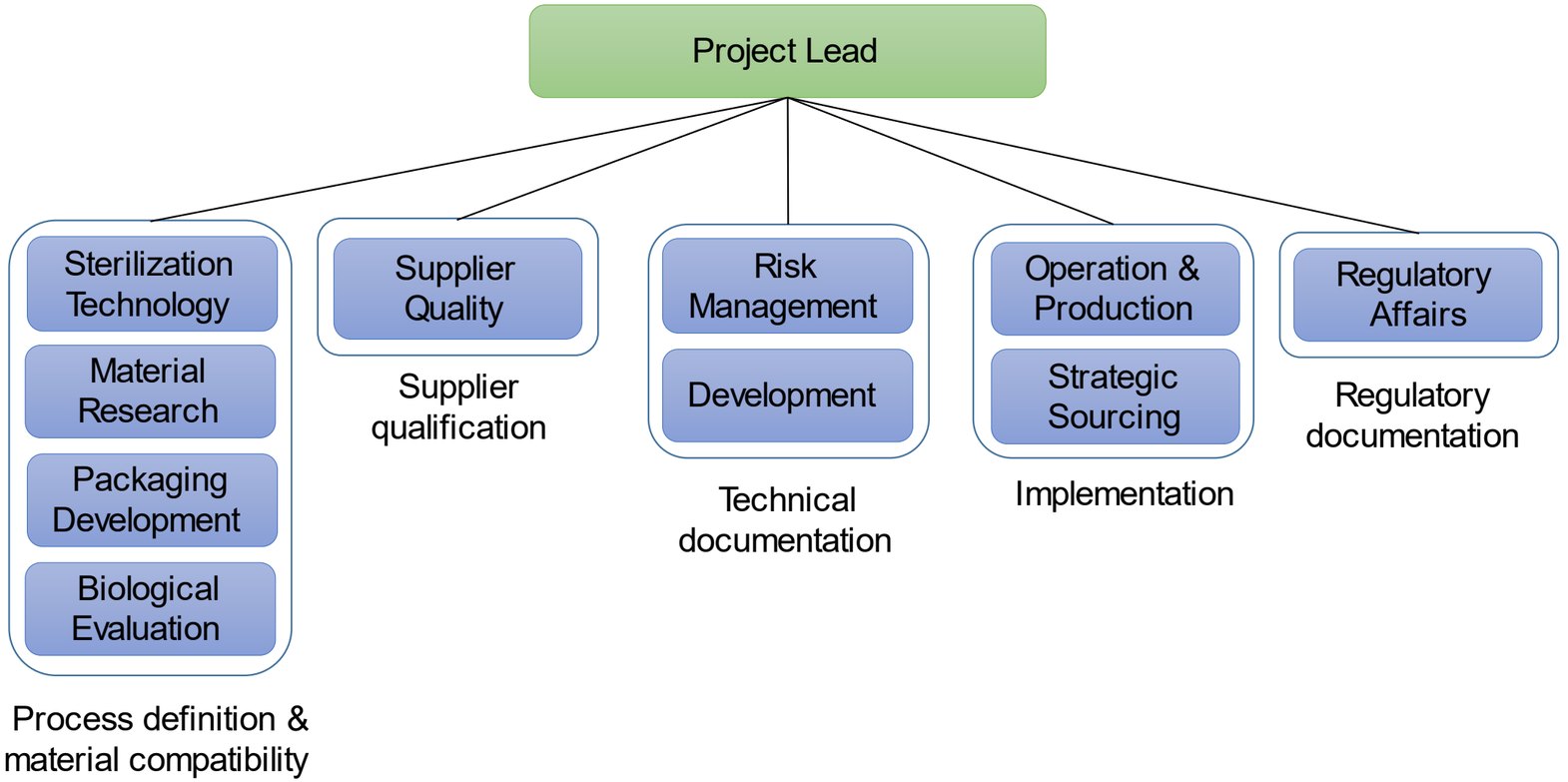
- Business Continuity
  - Back-up for Gamma Sterilizers
  - Additional Sterilization Method
- Supply Chain
  - Contract Sterilizer Capabilities & Capacities
  - Price Stability (Cobalt-60 vs. Electricity)
- Mangement Decision
  - Considerable validation effort needed → New Sterilization Method
  - Dedication of Ressources
  - Costs for implementation

Project Organization - Tasks



Source: Reprinted with permission from Beerlage C, Wiese B, Kausch AR, Arsenijevic M. Change in Radiation Sterilization Process from Gamma Ray to X-ray. *Biomed Instrum Technol.* 2021;55(s3):78–84.

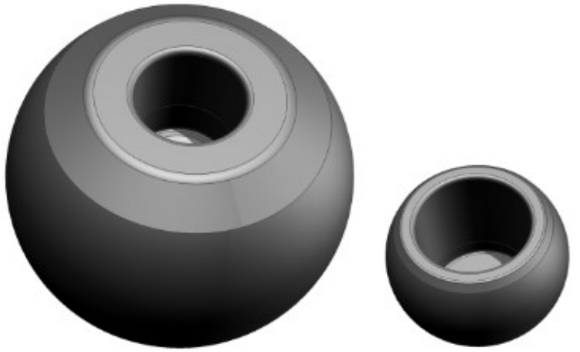
Project Organization - Team



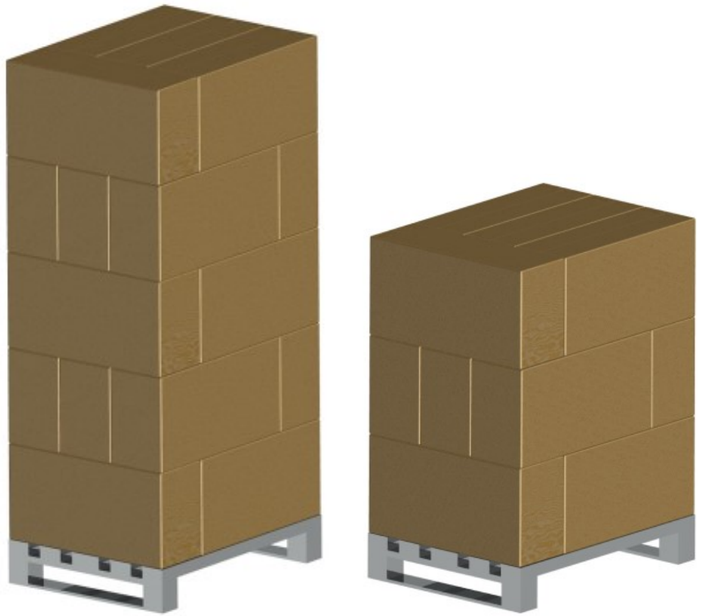
Source: Reprinted with permission from Beerlage C, Wiese B, Kausch AR, Arsenijevic M. Change in Radiation Sterilization Process from Gamma Ray to X-ray. *Biomed Instrum Technol.* 2021;55(s3):78–84.

Product Scope

- Pilot Study:
  - Limited Product / Material Complexity
  - Limited Packaging Complexity
  - Limited Sterilization Container Complexity
  - Benefit for Process Efficiency



Dummy products



Pallet configuration

Supplier Qualification

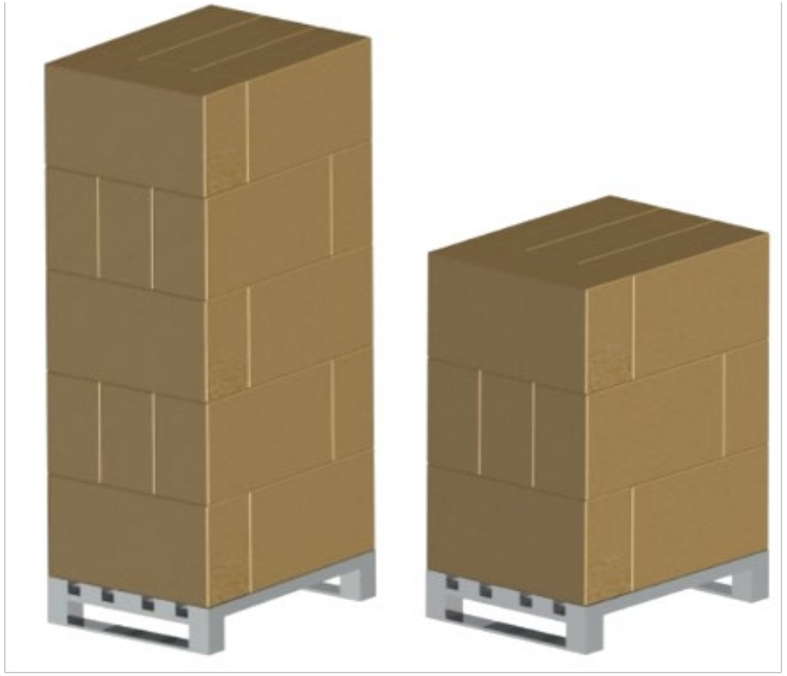
- General GMP / ISO 13485 Certification
- General ISO 11137 Certificate / Compliance Audit
- IQ/OQ of X-ray Machine
- Specific Production Flow
- X-ray Process Audit
- Contractural Aspects

Test Plan - Process Validation

- Extended Dose Mapping
  - Minimum and Maximum Product & Pallet Size
  - Typical PQ Grid & additional strategically located dosimeters
  - Dose Uniformity Ratio (DUR)
  - Acceptance Criteria: 25 – 42 kGy

Results	
Sterilization Dose	25 – 42 kGy
Dose Uniformity Ratio	1.28 (vs. Gamma: 1.64)
Temperature	45 °C (vs. 56 °C Gamma)

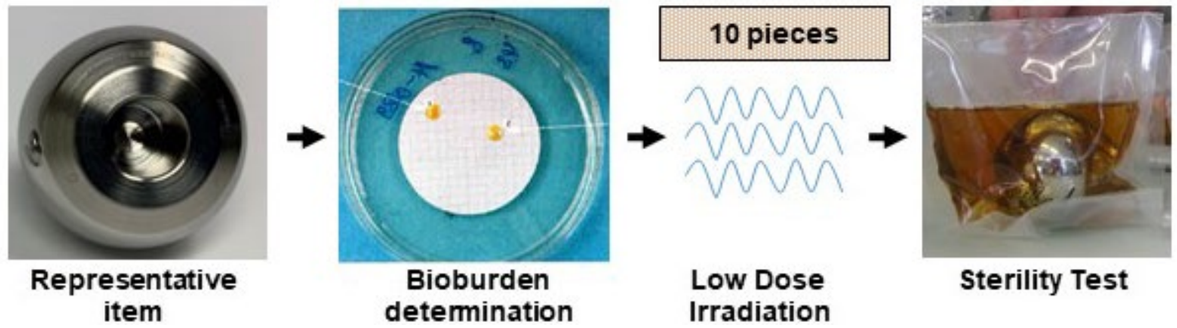
Max- & Min-load Dummy



Max- & Min-load pallet

Test Plan – Establishing the minimal sterilizaton dose

- Method VD_{max}
  - Same Minimum Sterilization Dose as Gamma: 25 kGy
  - Same Tables of ISO 11137-2 and ANSI/AAMI/ISO TIR 13004 apply
  - Dose substantiation: Passed
  - Process Maintenance / Dose Audit has to be X-ray



Test Plan – Material Compatibility

- Implant Material:
  - All Metal CoCrMo alloys
  - Stable in Gamma and X-ray → No Tests

- Packaging Material:
  - Polymer Pouch, Double Blister, Cardbord Box
  - Stresses: Irradiation, Thermal, Ozone → Performance & Shelf Life Tests

Test Plan – Biological Evaluation

- Interaction of Packaging Material with Product: Leachables, «Sticky Bag»
- Radio-Activation of Material by X-ray

Biocompatibility and Material Interaction	
Interaction Study	Chemical Characterization in Progress
Radioactivation Study	Slight induction (< 20 Bq/kg) of Co-60, Cr-51 and Mo-99 (Conforms to Swiss Law 814.501)

Regulatory Considerations

- Sterilization Modality Change ≠ Sterilization Method Change?
- European Notified Body Expectation
  - Gamma to X-ray is a Sterilization Method Change = Major Change
  - Submisson of Full Data Set Expected
  - MDR Submission Trigger
- FDA Expectation
- Consequences for Test, Time and Budget Planning
  - Advantages of a Limited Pilot Project

Summary

- Promising Test Results
- Good Technical Feasibility of the Sterilization
- European Regulation is Conservative → Sterilization Method Change
- Consider Testing of Product Materials and Packaging
- Biocompatibility and Radio-Activation Testing
- High Project Complexity
- Expect Long Timeline and Significant Costs

Acknowledgement

THANKS FOR YOUR VALUED ATTENTION

- Thank you to my colleagues at Zimmer Biomet, Winterthur
  - Björn Wiese
  - Annemie Rehor Kausch
  - Milorad Arsenijevic
  - Thomas Trachsler

ZIMMER BIOMET

Moving You Forward.™