Ethylene Oxide and Radiation Sterilisation

Method Selection and Critical Success Factors

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Main Sterilization Technologies

Ethylene Oxide (55%)

- Surface sterilant
- Typically 100%
- Sterilize under vacuum
- Process variables include
  - Temperature
  - RH
  - Time
  - Pressure
  - EO concentration
- Preconditioning / Aeration

Irradiation (45%)

- Penetrative sterilant
- Gamma
  - Cobalt 60
  - Alpha particles
  - High penetration
- Electron Beam
  - Accelerated electrons
  - Beta particles
  - Processing speed dependant on power (Kwatts)
  - Penetration dependant on energy / particle speed (MeV)
Criteria to Consider

Validation
- Initial validation
- Cross Plant / Cross Line
- Requalification / Maintenance

Product / Materials
- Material Compatibility
- Packaging
- Electronic Components

Operations / Logistics
- Speed to market
- Processing Cost
- Turnaround Time
- Product Release
- Processing Risks
- Capacity Management
- Residuals

Health, Safety & Environmental
Initial Validation

Ethylene Oxide

- Set out in ISO11135
- Typically takes 8-12 weeks
- Protocol needs to take into consideration
  - Load configuration
  - Placement of internal BI’s
  - EO residuals
  - Product functionality
  - Number of samples
- Changes to product / load configuration

Irradiation

- Set out ISO11137
  - $V_{D_{\text{max}}}^{15/25}$ most common
    - Small # of samples required
  - Methods 1 & 2
    - Larger # of samples required
- Detail on Bioburden
- Typically can be carried out in 3-4 weeks
  - Test of sterility incubation time of 14 days
- Ebeam needs to factor in scatter
Cross Line / Plant Requirements

Ethylene Oxide

• Within same plant need to evaluate process equivalence and may be able to justify reduced validation activity.
  ✓ Capacity
  ✓ Load Configuration
  ✓ Equipment Capability

• With different plant, equivalence often difficult to establish and therefore requires full validation.

Irradiation

• Gamma → Gamma
  ✓ Dosimetric Only

• Gamma → Ebeam
  ✓ Dosimetric
  ✓ Microbiological

• Ebeam → Ebeam (Similar Operating Mode)
  ✓ Dosimetric Only

• Ebeam → Ebeam (Different Operating Mode)
  ✓ Dosimetric
  ✓ Microbiological
Maintenance / Requalification

Ethylene Oxide

- Generally re-qualified every 1-2 years
- Review of
  - Process history
  - Product / packaging changes
  - Equipment changes

Irradiation

- Quarterly dose audits
- Control of routine Bioburden
- Product / packaging changes quicker to qualify
- Changes in orientation
New Product Speed to Market

Ethylene Oxide

- Long validation lead time
- Complex validation
- Extra validation activity to accommodate scale up.

Irradiation

- Quicker validation
- Smaller # of samples for validation
- Product for clinical trials
- Scalable from product development
Processing Cost

Ethylene Oxide

- By Chamber (e.g. 10 Pallets)
- Cycle price dictated by cycle length
- Expensive for small volume loads
- Extra costs may include
  - Extra aeration
  - BI’s
  - Other testing
- Factor in WIP cost due to longer lead times

Irradiation

- By pallet / Carrier / tote or box
  - Easier to manage unit costs
  - Optimize batch size to reduce dosimetry
- Processing cost dictated by density of product
- Factor in lower WIP due to faster lead times
Processing Time

Ethylene Oxide

- Typically 7-10 days
  - Processing: 20-48 hours
  - BI testing: 2 – 7 days
  - Aeration: 0-5 days
  - Some products may require post sterilization processing

- Parametric Release may shorten turnaround time by elimination of BI’s

- Long turnaround times result in increased WIP

Irradiation

- Typically 2-3 days
  - No BI’s to test
  - No Aeration requirements
  - Minimal requirement for post sterilisation processing

- Can be as quick as < 24 hours

- Ebeam
  - Tote or box to box so can be even quicker than gamma

- Quick turnaround time result in less WIP
Product Release

Ethylene Oxide

- Up to 7 days
- Review of Batch record
  - Cycle parameters within specification
  - BI results
  - Aeration Complete
- Parametric release an option for quicker release

Irradiation

- 1-2 days
- Dosimeters
- Certificate of Processing
- Quality review and approval
Processing Risk

**Ethylene Oxide**
- Batch Process – 1-32 pallets
- Multiple parameters to be controlled and monitored
- Multiple sterilization capability recommended
- Only option is to reprocess or scrap

**Irradiation**
- Gamma
  - ✓ Pallet / Carrier / tote
- Ebeam,
  - ✓ Tote / box to box
  - ✓ Product orientation
  - ✓ Incremental dose
- Dose is cumulative
- Dose augmentation
- Load presentation
  - ✓ Critical for Ebeam
Capacity Management

Ethylene Oxide
- Lengthy process to add capacity
  - Equipment lead time
  - Commissioning
  - PQ
- Typically 12 – 18 months
- High capital cost

Irradiation
- Quicker lead time to increase capacity

  - Gamma
    - Increase cobalt source
    - Run on extra shifts

  - Ebeam
    - Increase power → Speed up conveyor
    - Run extra shifts
Residuals

Ethylene Oxide

• EO & ECH levels on product must meet limits set out in ISO10993-7.
• Can result in increased processing time to get limits below required limits.
• Influenced by
  ✓ Aeration temperature
  ✓ Materials
  ✓ Product design
  ✓ Layers of packaging

Irradiation

• No known residual issues with irradiation of medical devices.
• Irradiation does not have high enough energy to impart radioactivity.
Product / Material Compatibility

Ethylene Oxide

- Product design
  - Tortuous pathway
  - Dead legs
  - Coatings
- Most materials compatible
- May be issue where product is temperature / RH sensitive
- EO / ECH residuals

Irradiation

- Cross linkage
- Discolouration
- Reduced with Ebeam
  - Shorter exposure
  - Incremental dose
  - Reduced oxidization effects
- Additives to reduce impact of irradiation
Packaging

Ethylene Oxide

• Porous to EO
• May need post sterilization activity of product is RH sensitive
• Packaging validation needs to take pressure changes into consideration.
• Ideally need to minimize layers to facilitate EO penetration

Irradiation

• Can use non-permeable materials
  ✓ Foil pouches
  ✓ No pressure change implications
  ✓ No temperature / RH restrictions
  ✓ Potential for cheaper packaging
• Reduced need for post processing packaging
• Most materials suitable for Ebeam
• Unsuitable materials for Gamma
  ✗ Standard polypropylene – Brittle
  ✗ UPVC – Discolouration / Brittle
Electrical Components

**Ethylene Oxide**
- Increased risk of source of ignition
- Cycle can be designed outside flammable zone
- May result in longer cycle leading to higher processing costs

**Irradiation**
- Devices incorporating passive components may tolerate irradiation
- Some electronic components susceptible to irradiation
- Damage is gradual rather than sudden
Health & Safety / Environmental

Ethylene Oxide

- Hazardous Gas
- Occupational exposure
- Facility design
  - Atex
  - Fail Safe
- Emission Control

Irradiation

- Radiological shielding
- Occupational exposure
- Production of small amount of Ozone
- Transportation & control of Cobalt
- Ebeam can be quickly shut down

- Does not impart radioactivity
- No known residuals
Conclusions

• Irradiation offers significant advantages over Ethylene Oxide

• There are limitations with irradiation, but there are strategies to minimise these.

• Electron Beam offers the advantages of Gamma but with fewer of the limitations.
Questions to Ask Yourself

- Am I using the most suitable sterilization method for my product?
  - Was it selected based on availability at the time?
  - Are there other materials that would be irradiation compatible?
  - Has anything changed to make my product capable of using an alternative sterilization method?

- Can I change to a different sterilization method?
  - Is my product compatible?
  - What are the regulatory requirements?
  - How long will it take?
  - Will it be worth the while – Financially and operationally?

- Am I considering the sterilization method early enough in the product design phase?
Thank-you for listening.

Any questions?

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