# Ethylene Oxide and Radiation Sterilisation

# Method Selection and Critical Success Factors

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# Main Sterilization Technologies

## Ethylene Oxide (55%)

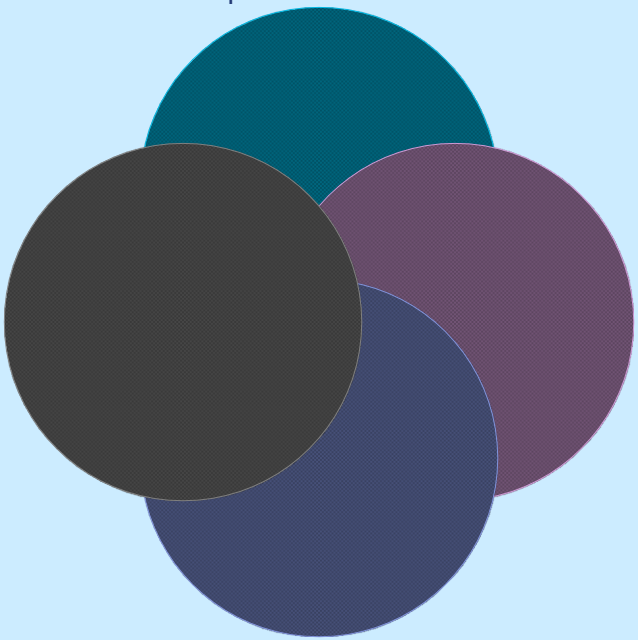
- Surface sterilant
- Typically 100%
- Sterilize under vacuum
- Process variables include
  - ✓ Temperature
  - ✓ RH
  - ✓ Time
  - ✓ Pressure
  - ✓ EO concentration
- Preconditioning / Aeration

## 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
  - ✓ $VD_{max}^{15\ /\ 25}$ 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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