Cycle Development and Validation Guidance for Vaporized Hydrogen Peroxide (VHP) Low Temperature Surfaces Terminal Sterilization Processes

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Presentation content

- Vaporized Hydrogen Peroxide (VHP)
- VHP low temperature surfaces sterilization process principle
- Applications
- Cycle development and validation guidance
Vaporized Hydrogen Peroxide (VHP)

- Low temperature dry vapour process (remains below dew point)
- Long established sterilant for full spectrum of biological contaminants
- Compatible with a wide variety of materials
- No penetration to product, no materials discoloration
- Breaks down to water vapour and oxygen
VHP low temperature surfaces sterilization process principle
VHP low temperature surfaces sterilization process principle

- Pre-conditioning
- Exposure
- Post-conditioning
• Typical process temperature +28...40 °C
• Typical cycle time 2...4 hours, depending on product, load config and materials
• Deep vacuum process (1...10 mbar level)
VHP Process limitations

• VHP is a surface sterilant.
• Wet surfaces will affect the process
• Load Temperature should be within reasonable limits (not directly from cold storage)
• Works well with Tyvek and plastics. No Cellulose, cotton or highly absorptive materials.
Applications
VHP Low Temperature Surfaces Terminal Sterilization

- In-house processing
- For temperature / radiation sensitive products
- Low Temperature VHP sterilization in vacuum (controlled environment!)
- Sterilized surfaces of device exterior and package interior (example: ophthalmic parenteral drug products)
- Typical production chamber sizes 0.5…10 m³
- 2…4 hours complete cycle time
Typical drug product applications

- Complex delivery devices, pre-filled syringes, vials
- E.g. protein-based drugs, hyaloronic acid, mixed substances, biologics, biosimilars
- Single-packaged in TYVEK or equivalent
- To claim entire packaged product sterility
- To simplify manufacturing and packaging process
VHP Low temperature sterilization applications

Taking packaging from the clean room to a more controlled and repeatable process
VHP distribution / penetration

• VHP vapor penetrates TYVEK layer
• Reaches dead legs
Application example – Mixing device
Application example - Vials
Typical single-packaged product
### Typical products by category

<table>
<thead>
<tr>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrapped Vials</td>
</tr>
<tr>
<td>Syringes, Hyaloronic acid based products</td>
</tr>
<tr>
<td>Syringes, Ophthalmic drug products</td>
</tr>
<tr>
<td>Wound Care Dispenser Devices</td>
</tr>
<tr>
<td>Pre-Injection Mixing Devices (combining components)</td>
</tr>
<tr>
<td>Packaged towel products</td>
</tr>
</tbody>
</table>
Cycle development and validation guidance
Step-by-step approach to implementing VHP low temperature surfaces sterilization process
Product feasibility testing

- Verify material compatibility with VHP (no color change etc.)
- Product integrity tests (plunger movement, deep vacuum level, no leaks to primary container => no contact to drug product)
- Use smaller amount of product samples
- Chemical indicators to show reaching inside blister/TYVEK® package
- Initial tests for reaching 10E6 kill (biological indicators)
- Verify package compliance (TYVEK® pass-through both ways)
Load Cycle Development

Cycle development tests using actual production unit and sample loads => Initial optimization and parameters to benefit the final validated cycle
Defined repeatable load quantities and loading patterns

• Defined load configurations for cycle repeatability and validation
Cycle Development and validation indicators

Chemical indicators show VHP coverage and presence in load and chamber

CYCLE DEVELOPMENT ONLY

Biological indicators prove sterilization efficacy (6-log CFU overkill of *Bacillus Stearothermophilus*

CYCLE DEVELOPMENT AND VALIDATION
Load mapping for cycle development

IV
Front of Chamber, Left Side

Rear of Chamber, Left Side

II

I

Front of Chamber, Right Side

Rear of Chamber, Right Side

- Biological Indicator
- Chemical Indicator
- RH Sensor
- Temperature Sensor
Challenging the packaged device

- Using actual product packages for cycle verification and challenge – place indicators inside and re-seal TYVEK for cycle
Challenging the packaged device

- Chemical indicator placed inside re-sealed packaged item
Challenging the packaged device

• Biological TYVEK-enveloped indicator placed inside re-sealed TYVEK-packaged item
Validation guidance


- For health care products but not limited to – applicable to be used as basis for validation for VHP low temperature surfaces sterilization process

- First two steps of feasibility testing and load cycle development testing well documented provide good basis for validation

- The surface sterilization process to be capable of delivering a Sterility Assurance Level (SAL) of $10^{-6}$ as it is defined in the annex of the standard

- Biological indicators used in validation cycles

RECENT DEVELOPMENTS

- **USP 1229.11 effective August 1, 2015 defines:**
  - VAPOR PHASE STERILIZATION
- - Includes VHP (H₂O₂), peracetic acid, formaldehyde and glutaraldehyde
- - VHP is a sterilant and can be validated as surface sterilization process
- - The need to prove environment control - temperature, humidity, concentration, vacuum level
- - The need to prove process consistency and repeatability
  - Need to prove 10E6 overkill by BI’s - establishing probability for process is recommended
  - Empty chamber / full load / half cycle / full cycle considerations
  - Product integrity and materials feasibility
Thank You!
Questions?

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