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

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Presentation content

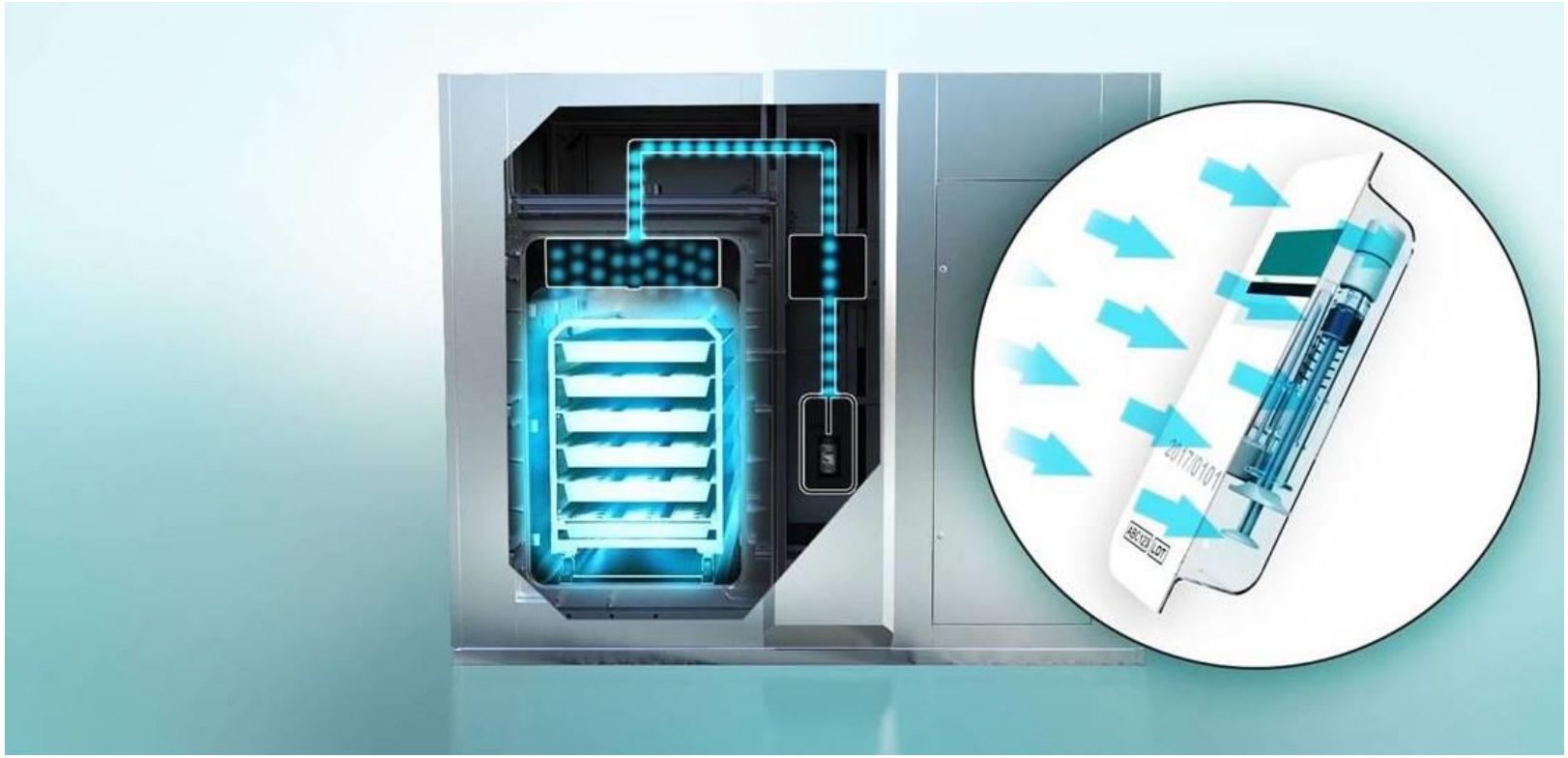
- Vaporized Hydrogen Peroxide (VHP)
- VHP low temperature surfaces sterilization process principle
- Applications
- **Cycle development and validation guidance**

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

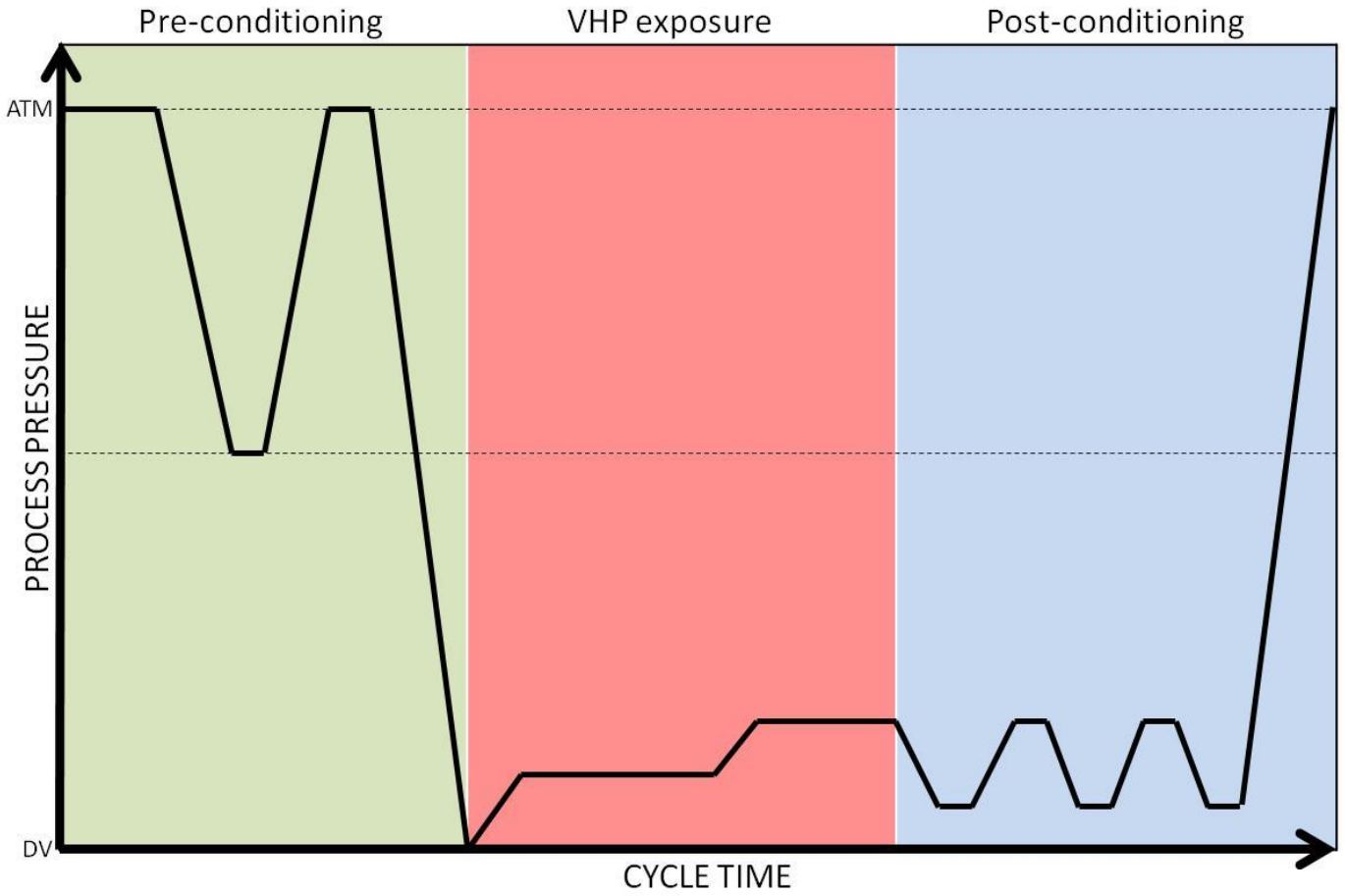
VHP low temperature surfaces sterilization process principle

VHP low temperature surfaces sterilization process principle



- Pre-conditioning
- Exposure
- Post-conditioning

Process graph



- 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 m^3
- 2…4 hours complete cycle time

Typical drug product applications

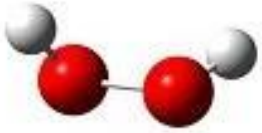
- Complex delivery devices, pre-filled syringes, vials
- E.g. protein-based drugs, hyaloronic acid, mixed substances, biologics, biosimilars
- Single-packaged in TYVEK or equivalent
- To claim entire packaged product sterility
- To simplify manufacturing and packaging process

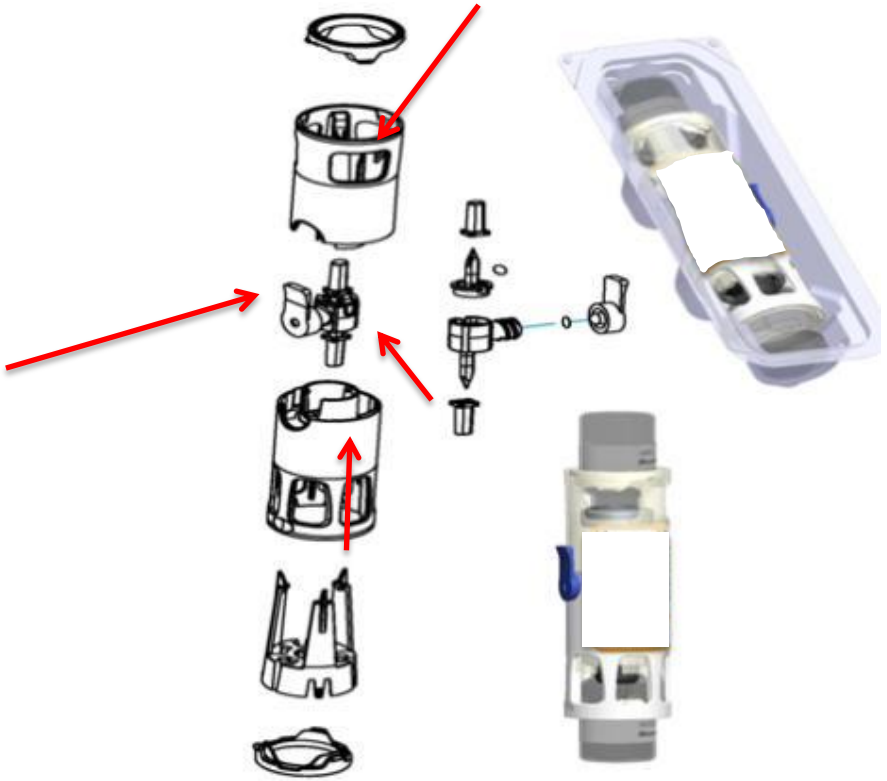
VHP Low temperature sterilization applications

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

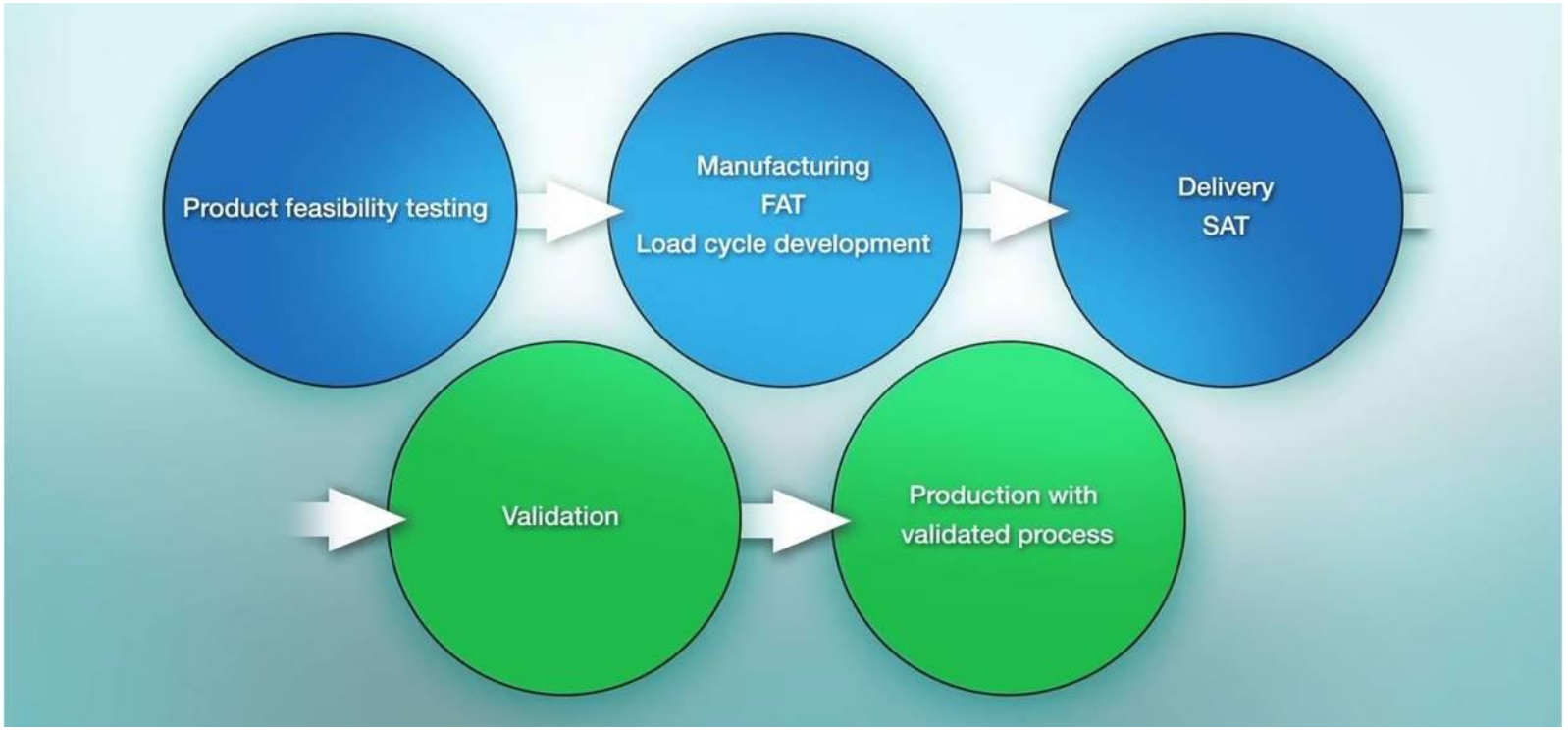
Application example - Vials

Typical single-packaged product

Typical products by category
Wrapped Vials
Syringes, Hyaloronic acid based products
Syringes, Ophthalmic drug products
Wound Care Dispenser Devices
Pre-Injection Mixing Devices (combining components)
Packaged towel products

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
- Intial tests for reaching 10E6 kill (biological indicators)
- Verify package compliance (TYVEK® pass-through both ways)

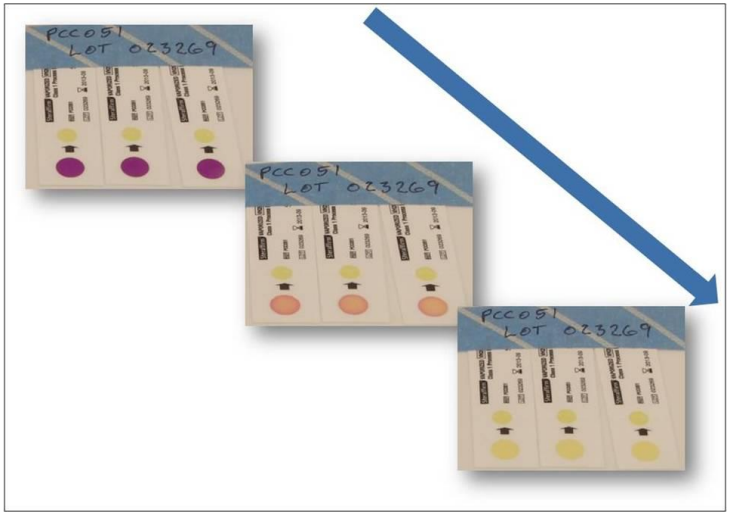
Load Cycle Development

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

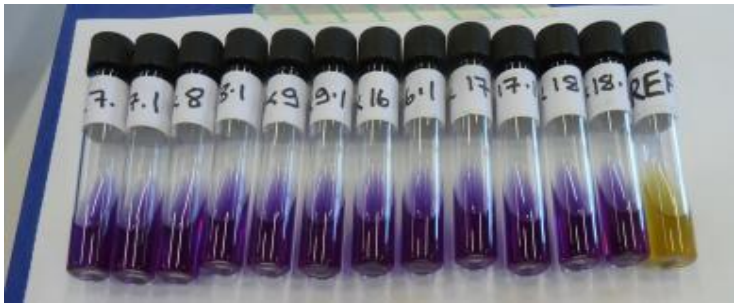
- Defined load configurations for cycle repeatability and validation

Cycle Development and validation indicators



Chemical indicators show VHP coverage and presence in load and chamber

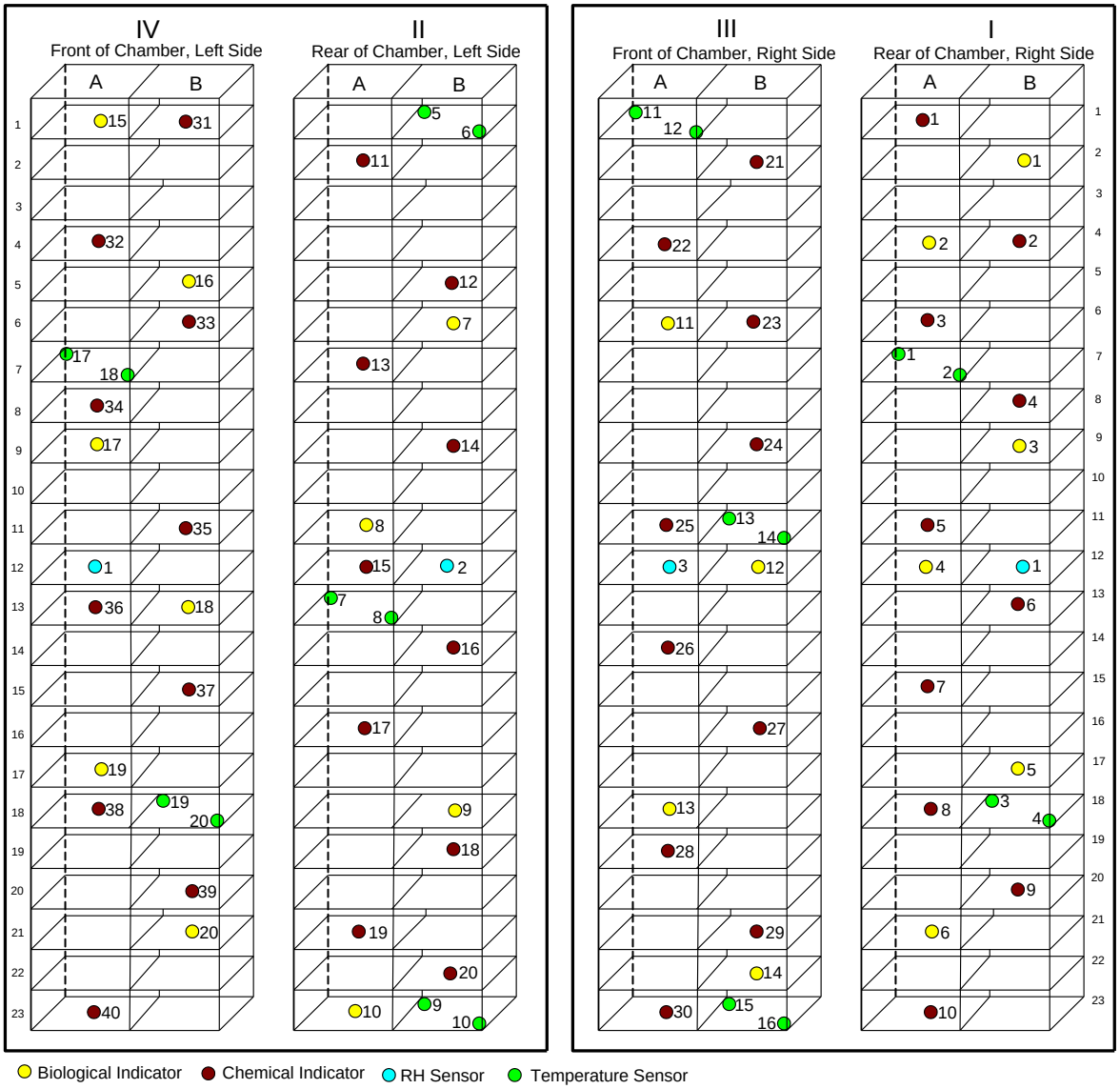
CYCLE DEVELOPMENT ONLY



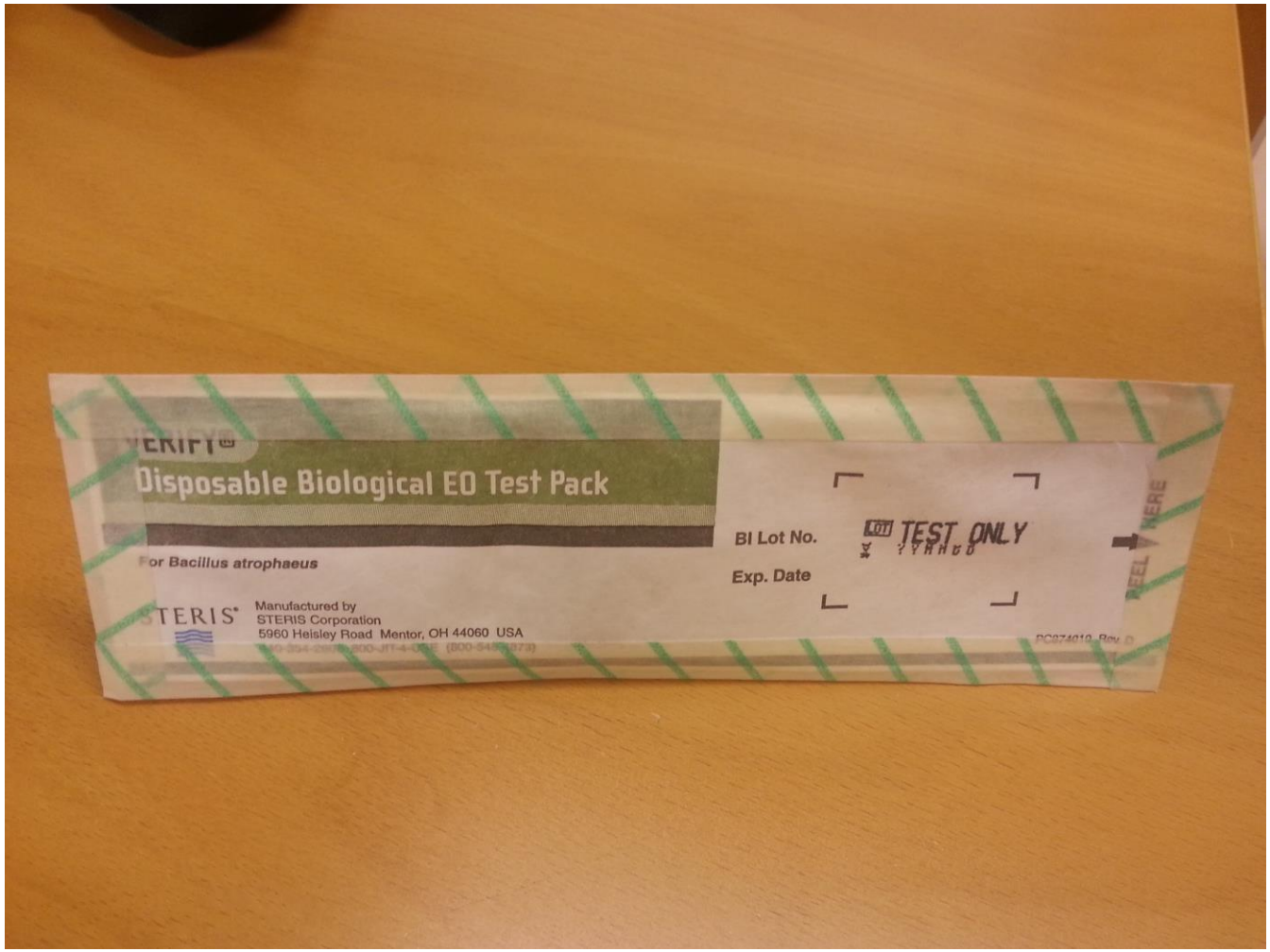
Biological indicators prove sterilization efficacy (6-log CFU overkill of *Bacillus Stearothermophilus*

CYCLE DEVELOPMENT AND VALIDATION

Load mapping for cycle development

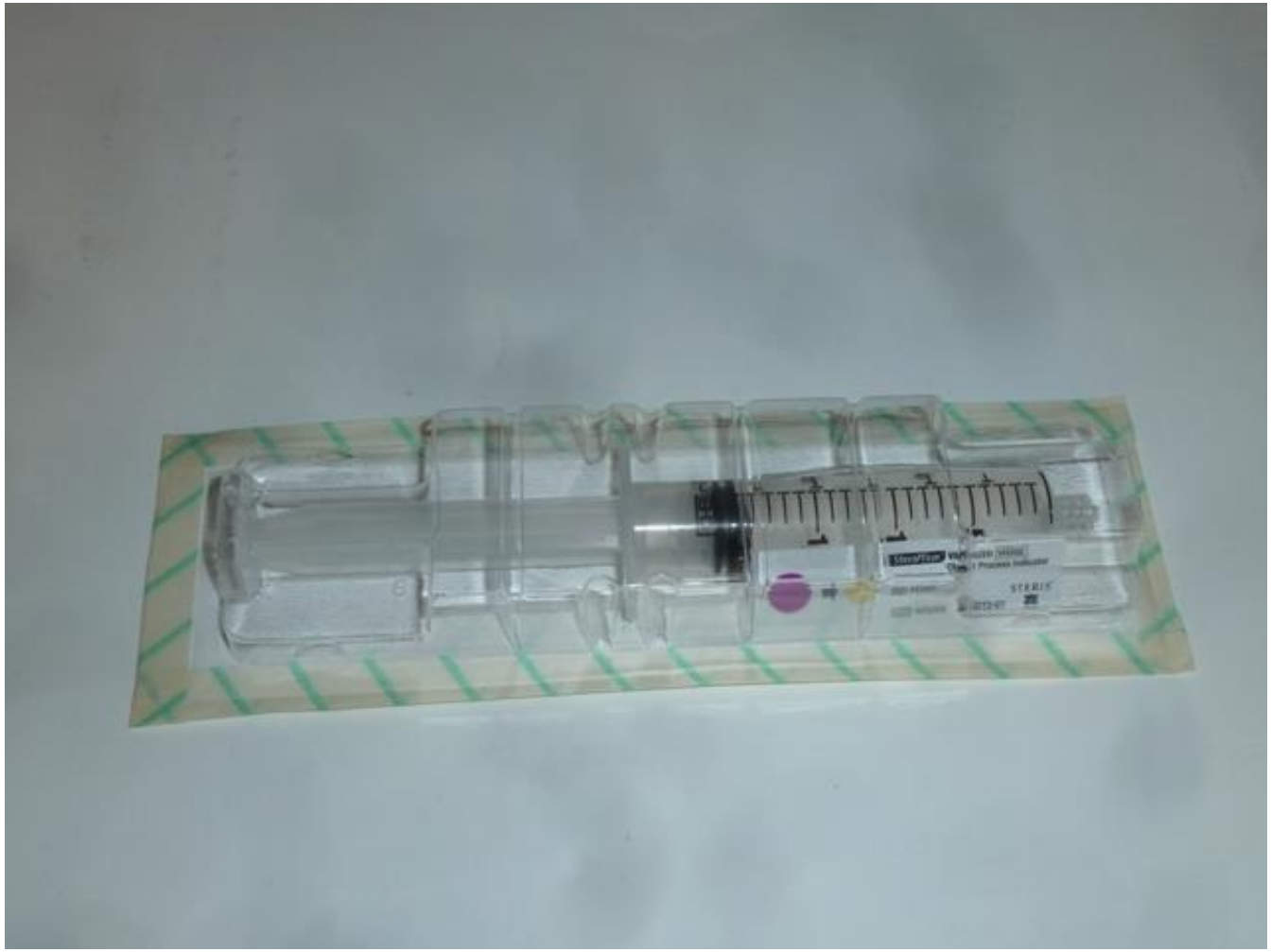


Challenging the packaged device



- 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

- ISO 14937:2009 – ”Sterilization of health care products – general requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices”
- 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
- Sterility Assurance Level (SAL) ISO TS Technical Specification 11139:2006

RECENT DEVELOPMENTS

- **USP 1229.11 effective August 1, 2015 defines: VAPOR PHASE STERILIZATION**
- - Includes VHP (H_2O_2), 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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