Sterigenics®
A Sotera Health company

Annual Requalification Review

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CONFIDENTIAL

Presenter: Russell Gonsiorowski

- Experience
  - Biology (B.S.) from Iowa State University / Technical Advisor
  - 19+ years – Microbiological Testing, Sterilization, Validation, and Process Development
- Expertise
  - EO Sterilization: cycle development, contract sterilization, product adoption, parametric release, sterility assurance
- Personal
  - I enjoy craft beer, local sports, and live music

Agenda

- ANSI/AAMI/ISO 11135
  - Requirements
  - Guidance
- Annual Revalidation Review
  - Equipment
  - Product
  - Process
  - Process history
  - Regulatory change
- Output of Requalification Review
- Assessment of Change
- Assessment of Equivalence
- Summary

Requalification – ANSI/AAMI/ISO 11135

Section 12 – Maintaining Process Effectiveness

12.3 Requalification

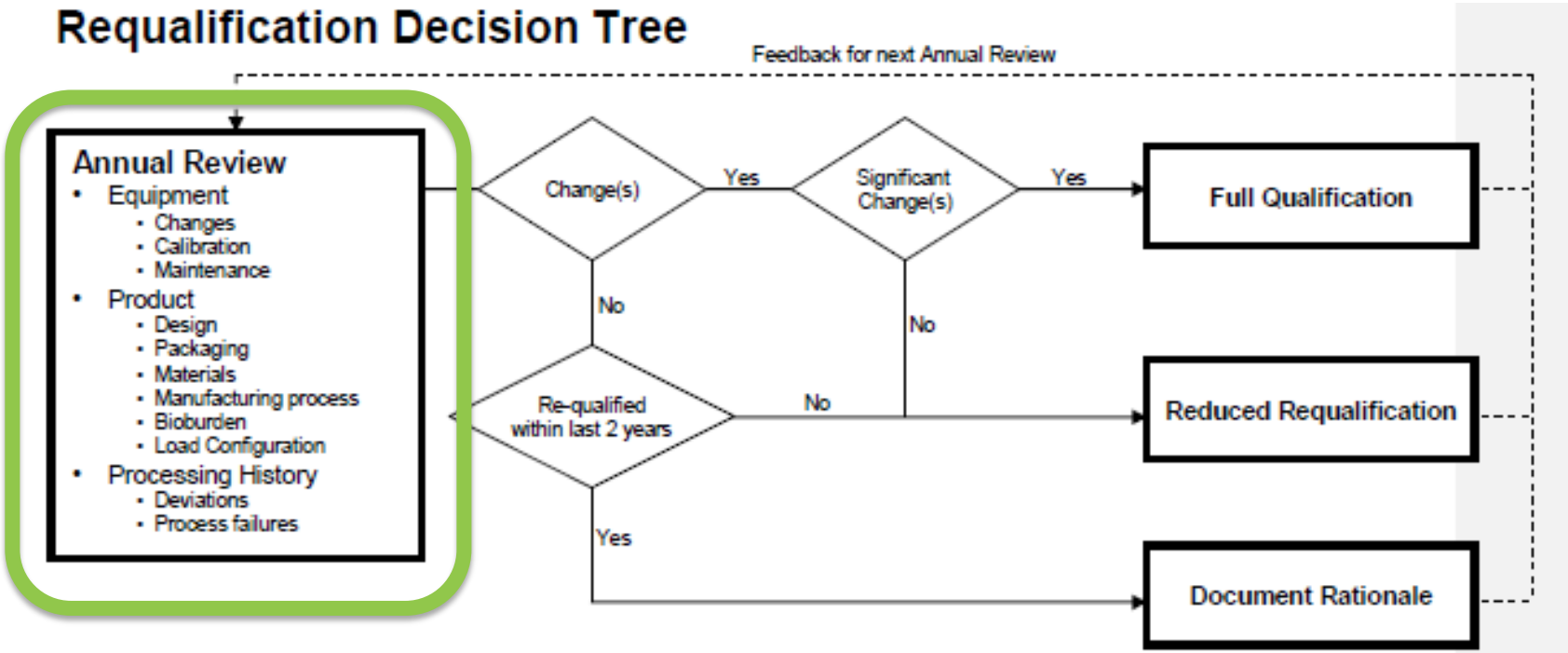
12.3.1 **IQ, OQ, PQ and subsequent requalification(s) shall be reviewed annually** to determine the extent of requalification that is necessary. This shall include an assessment of the need to reconfirm the product SAL through microbiological studies. The outcome of this review, including the rationale for decisions reached, shall be documented.

12.3.2 Requalification of a sterilization process carried out with specified equipment shall be performed at defined intervals against specified acceptance criteria and in accordance with documented procedures. These intervals shall be justified.

The simplest route to compliance

- Have a documented procedure that requires an annual review of validation (IQ, OQ, PQ)
- Use the Requalification Decision Tree detailed in D.12.3.2

D.12.3.2 Requalification



Note – Where more than one configuration is validated, this should be reflected in any requalification activity

Requalification – Equipment Review

Changes to Equipment

- Have there been any changes?
- Have changes been requalified and documented correctly?

Calibration

Review of IQ status

- Control and monitoring equipment calibrated?

Review of OQ Status

- Has periodic requalification of equipment been performed?

Maintenance

- Preventative maintenance complete?
- Equipment appropriately requalified after maintenance interventions?
- Maintenance activities properly documented?

Requalification – Product Review

Design

- Have there been significant changes and are they documented?*
- Have new products been adopted into validation?

Packaging

- Have there been significant changes and are they documented?*
  - Instructions for use, Breathable area, Packaging materials

Materials

- Have there been significant changes and are they documented?*

Maintenance

- Have there been significant changes in the manufacturing process that could impact product characteristics?*
  - i.e. Bioburden, EO residues, SAL

Bioburden

- Have bioburden tests been performed in accordance with ISO11737-1?
- Are bioburden data consistent with original validation?

Load Configuration

- Have there been significant changes in the load configuration?*

*Has rationale been recorded for adopted changes?

Requalification – Processing History

Process Design Changes

Have there been any significant changes in the sterilization process design?

Process Deviations

Biological Indicator failures

Process Failures

Non-Conformance failures

Parametric Release

Capability assessment key parameters

Other Process History

- Number of processes
- Capability assessment
- Ethylene Oxide residues

Requalification – Processing History

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Parametric Release

Capability assessment key parameters

Other Process History

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Process Design Changes

Have there been any significant changes in the sterilization process design?

- Any change to parameters / specifications for :
  - Preconditioning?
    - Time, temperature, RH, other..
  - Sterilizer phase? – (Check value change)
    - Evacuation /injection set points or rates
    - Temperature
    - Steam additions
    - Dwell phase times and set points
    - Other..
  - Aeration phase?
    - Time, temperature, other

Any changes should be detailed, assessed for their impact on Product safety/SAL and documented

Requalification – Processing History

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Have there been any BI positives in routine processes since previous review/ validation?

Some considerations for review:

- Were potential causes of failure reviewed at the time?
- Are failures indicative of marginal process that could impact Product SAL?
- Are failures indicative of External Process Challenge Device that provides a too severe challenge and is unrepresentative of IPCD?
- What are laboratory ‘false positive’ levels?

Requalification – Processing History

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Some factors to be considered

- How many NC's?
  - Were they all 'closed out' and documented appropriately?
- Were root causes established?
- Any associated CAPA's?
  - Have they been closed out?
  - Effectiveness verification?
- Any trends evident?
- If equipment was the cause:
  - Was equipment repaired effectively?
  - Was equipment re-qualified (if necessary) prior to release back to production?

Requalification – Processing History

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Parametric Release

Capability assessment key parameters

Other Process History

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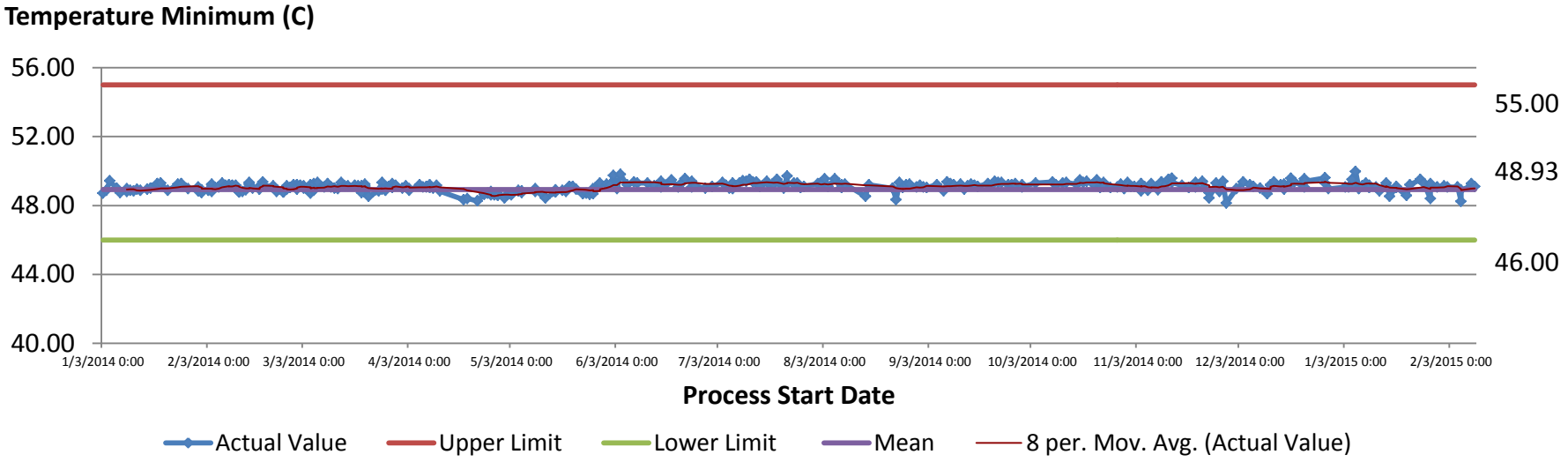
Review/Trend Capability data for key parameters (i.e.)

Minimum temperature during gas dwell over prior 12 months:

Cycle #: xx; GAS DWELL (EO) Phase; Chamber 2; Somercotes, UK



Whole Data Set	Mean	Max	Min	STDEV	CSA_SP	CSA_Max	CSA_Min	CSA_ID
Temperature Minimum (C)	49.1	50.0	48.1	0.3	49.0	55.0	46.0	16806

Other parameters to consider

- Minimum product temperature prior to process, RH during Steam Dwell,
- EO concentration during Gas Dwell exposure

Requalification – Processing History

Process Design Changes

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Non-Conformance failures

Parametric Release

Capability assessment key parameters

Other Process History

- Number of processes
- Capability assessment
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Other Processing History

- Number of processes
  - How many processes ran?
  - In which chambers? (i.e. were all validated chambers used?)
- Capability assessment
  - Assess capability for key parameter?
- EO residues
  - Have residue tests been performed?
  - Any relevance in ‘spot’ test to ensure product compliance after validated aeration conditions

Requalification Review, if Not Already Done

- ISO 11135 was updated in July 2014 and contains:
  - Changes to Requirements and a significant amount of new guidance
  - As of July 2017; this is now the only applicable Standard
- During your current Requalification Review process:
  - It is appropriate to assess the existing validation vs the changes in requirements in ISO 11135:2014
- Keep records of the review and detail either:
  - Any actions to be taken or;
  - A rationale to justify no actions are needed

Let‘s discuss some scenarios and see how you would approach your Requalifcation

Requalification – Output of Review

Scenario 1

✔	Some changes, but not significant
✔	Good processing history
✔	Previous validation 1 year ago

Review Output = NO NEED FOR REQUALIFICATION

- Document the decision and any rationale used to reach this decision
- Might consider residue tests to confirm compliance to ISO 10993/7

Requalification – Output of Review

Scenario 2

✓ Some changes, but not significant	✓ Good processing history	✓ Validation or last requalification 1 year ago

Or:

✓ No changes	✓ Good processing history	✓ Validation or last requalification 2 years ago

Review Output = REDUCED REQUALIFICATION

- Document the decision and any rationale used to reach this decision
- Typically, 1x Half Cycle with T/RH monitoring

Requalification – Output of Review

Scenario 3

✔ Some changes, and significant	✔ Good processing history

Or:

✔ No changes	✔ Poor processing history*

*i.e. regular BI failure

Review Output = FULL REQUALIFICATION

- Document the decision and any rationale used to reach this decision
- Typically, 3 or 4x Half Cycle with T/RH monitoring
- 1-3 Full Cycle processes

Assessment of Equivalence

- Process Equivalence
  - Process equivalence can be established through analysis of process data in combination with a microbiological evaluation.
  - The process data should demonstrate that the candidate equipment is performing within an acceptable range of control (i.e., validated process parameters can be reliably delivered to the product).
  - The microbiological evaluation will demonstrate that the required SAL is achieved.

Assessment of Equivalence

- Product
  - The review for product equivalence can be conducted within each product family or processing category. The following aspects of product evaluation should be addressed.
  - Determination of adverse effects to product (Does it still work as intended? Are the EO Residuals effected?)
  - Determination of product design effects (Obstacles to temp, humidity, or EO penetration?)
  - Determination of product material and characteristics effects (Is the bioburden affected?)
  - Determination of sterile barrier system effects (Obstacles to EO, heat, or humidity penetration?)
  - Determination of load configuration effects (Change in density or configuration?)

Assessment of Change

- Requirements and Guidance for Product Adoption are discussed in ANSI/AAMI/ISO 11135:2014 and AAMI TIR 28:2016
  - Changes to manufacturing operations, product, sterilization equipment, and/or the sterilization process shall be assessed for their effect on the effectiveness of the sterilization process.
  - The appropriateness of the internal and/or external PCD in relation to the bioburden of the product shall be reconfirmed as a result of change.
  - The load configuration shall be re-evaluated following a change for its appropriateness, and the results of this evaluation shall be documented.
  - The magnitude of the change shall be considered in determining the extent to which process definition, IQ, OQ, or PQ is undertaken.
  - The outcome of the assessment, including the rationale for decisions reached, shall be documented.

Requalification – Summary

- Have procedure that defines:
  - How validated product list is maintained
  - How Product families, Master products PCD's are established
  - How products might be adopted on to validated product list
  - Annual validation review process
  - Changes/circumstances that define need for requalification
- Perform review annually
  - Document outcome of review and rationale to make decisions
- Perform a requalification run at least every 2 years

Questions?

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Thanks for Listening