Design, Control & Monitoring of SUS for Integrity Assurance, Volume 2

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the full BPSA SUS Integrity Assurance Committee

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AGENDA

- Why a new document on integrity of SUS?
- What will you find in this document?
- What did we learn and what are the next steps?

INTRODUCTION

- BPSA Tech Guide - 2017 - Volume 1
  - Principles
- Once upon a time in February 2021 …
- Why a Volume 2?
  - Case studies
  - Updates

THE SUS INTEGRITY ASSURANCE COMMITTEE

Patrick Evrard, Cytiva - *Board Sponsor and Committee Chair*

Committee Members

Emily Alkandry, Saint-Gobain
Sebastien Barry, Sanofi
Richard Bhella, Cytiva
Monica Cardona, Millipore Sigma
Joussef Chaaban, Cytiva
Katie Church, Watson Marlow
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Elke Roelandt, Pfizer
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BPSA Facilitator

Jeanette McCool

Authors Currently Out of the Committee

Michael Avraam (ChargePoint Technology)
Marc Hogreve, Sartorius*
Alain Vanhecke, Cytiva*

* sabbatical leave

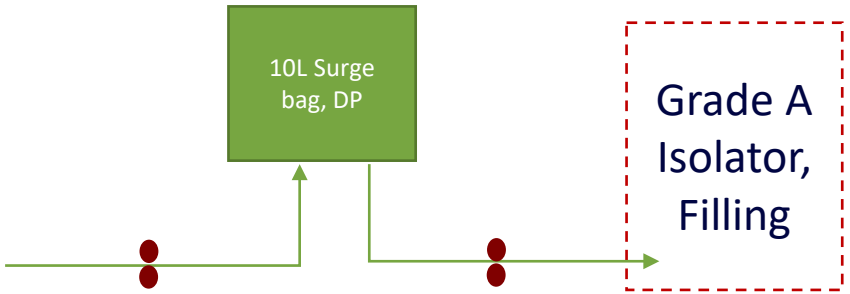
CONTENT

- Case study: design, qualification and validation of a SUS for a critical application using QbD principles
- Cases studies: integrity issues with various components
- Updates on integrity testing technologies
- Handling practices and training
- *Industry Interest Groups* initiatives and regulatory landscape
- Case studies: specific applications

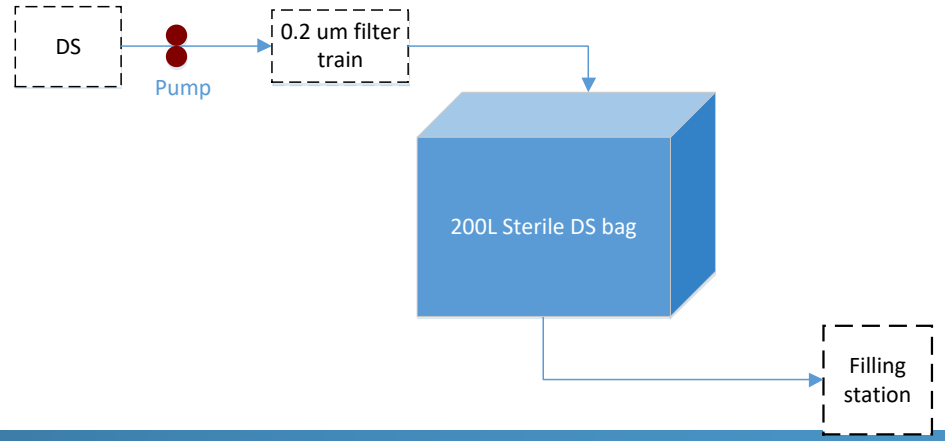
DESIGN, QUALIFICATION AND VALIDATION OF A SUS FOR A CRITICAL APPLICATION

Assessment of Criticality related to integrity

- Patient safety risk: Breach sterility



- Business risk: Massive product loss from leak



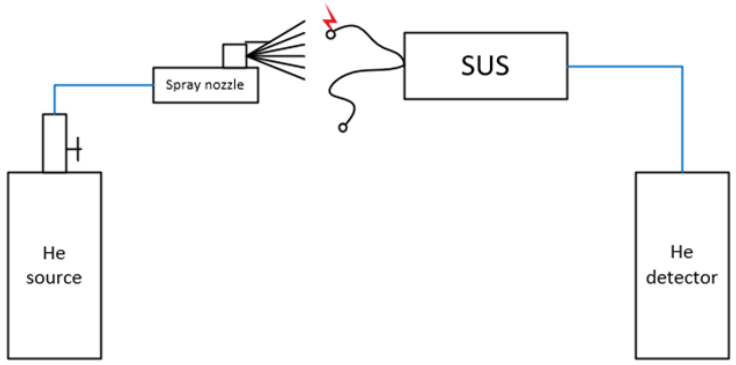
DESIGN, QUALIFICATION AND VALIDATION OF A SUS FOR A CRITICAL APPLICATION

- URS (BPSA/BPOG template), Design Review
  - Risk assessment matrix, e.g., connector type, bag film, agitation type, pump tubing …
  - End user and supplier communication
  - Sketch drawing (end user) → Eng. drawing (supplier), review
- Prototype, Design Verification, Qualification
  - Proof of concept, initial qualification test, and modification
  - End user and supplier interaction
  - Design lock-down
- Validation
  - Integrated functional test (IFT), wet runs and shakedown runs
  - Process monitoring and continuous improvement

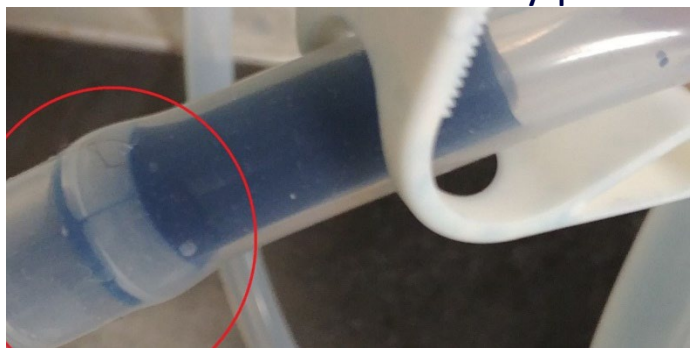
INTEGRITY ISSUES WITH VARIOUS COMPONENTS

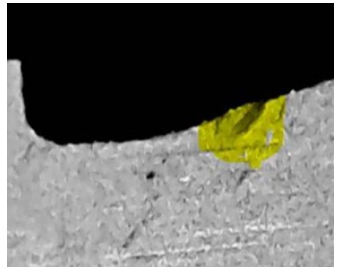
- Using integrity testing result as design verification
  - Integrity test allow detection of design defect during qualification and investigation
  - Examples : molding defects, connection robustness, closure

LLA[1] Screw cap issue using Helium spray mode



Mold defect detected by pressure decay





[1] LLA = Luer Lock Adapter

INTEGRITY ISSUES WITH VARIOUS COMPONENTS

- Other causes of integrity failure highlighted
  - Leak due to chemical resistance/MOC
  - Improper manipulation/training
  - Impact of elevated temperature
  - …

INTEGRITY TESTING TECHNOLOGIES - UPDATE

- "Leak testing" vs "Integrity testing" - MALL[1]
  - Correlation with barrier properties
- End-user experience with implementation of 100% integrity testing
- Updates on
  - Helium integrity testing technology
  - Pressure-based technologies

[1] MALL = Maximum Allowable Leak Limit

HANDLING PRACTICES - TRAINING

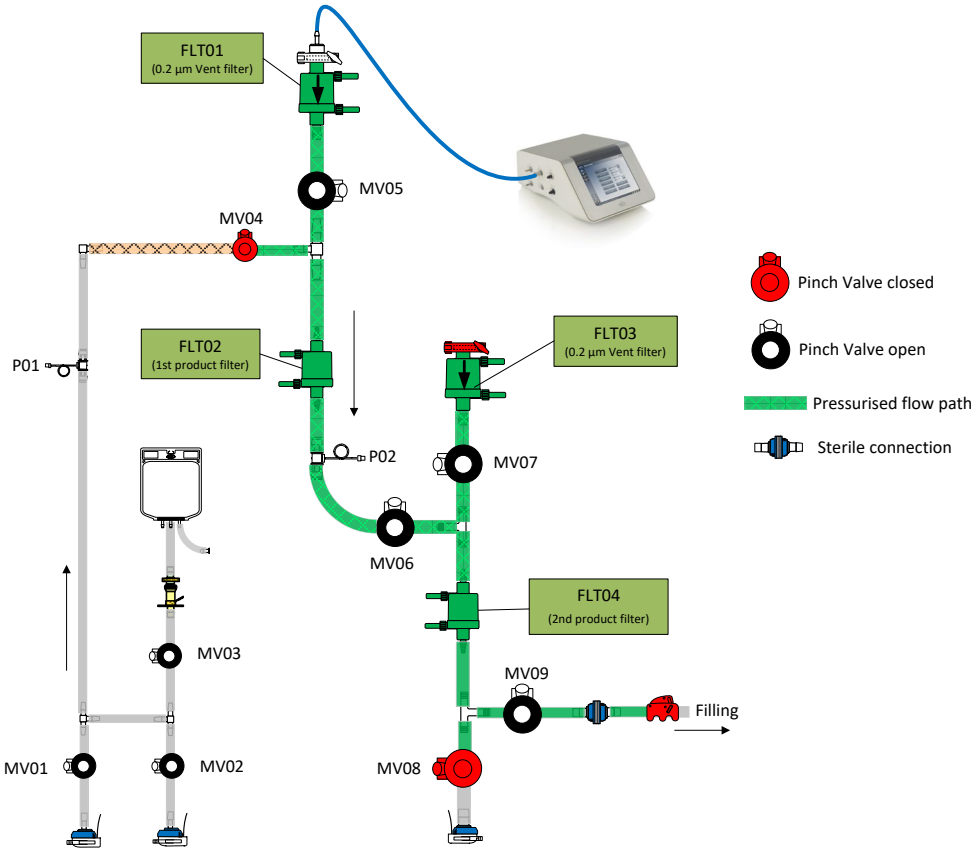
- Training - training - training
  - Underestimated by newcomers to the SU world
- List of typical tools supporting SUS integrity assurance
  - Full life-cycle: supplier and end-user

INDUSTRY INTEREST GROUPS & REGULATORY

- Updates from
  - BPSA - Reliability report(s)
  - ASTM - 3 standards
  - ASME-BPE - mapping of leak test methods
  - PDA (TR 86) - Pharmaceutical package integrity testing
  - BioPhorum - SUS Bag Assembly Leakage and defect toolkit
  - Learnings from setting up ASTM standards
  - Revision of EU GMP Annex 1

SPECIFIC APPLICATIONS
High pressure applications

- Risk for leaks
  - **Upstream of the filters** associated to high pressure applied (eg in-situ PUPSIT)
  - **Downstream of the filters** due to SUS handling or pressure being applied during filtration
- Pressure decay test at max pressure supported by supplier - sensitivity of 30 to 10 µm NDOS depending on
  - Applied pressure
  - Size and type of tubing
- Design recommendations
  - Avoid complex design - limit number of components and junctions
  - Test junctions with integrity/leak test



SPECIFIC APPLICATIONS
Handling Powders

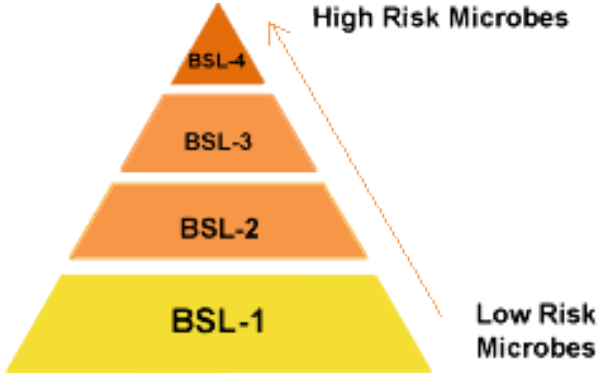
Powders create different challenges than liquids

- Non-Toxic powders have less risk for operator exposure issues but open handling will allow airborne particulate that causes several known risks
- Toxic powders (small percentage in bio processing) requires greater consideration of operator protection along with the same risks associated with airborne particulate

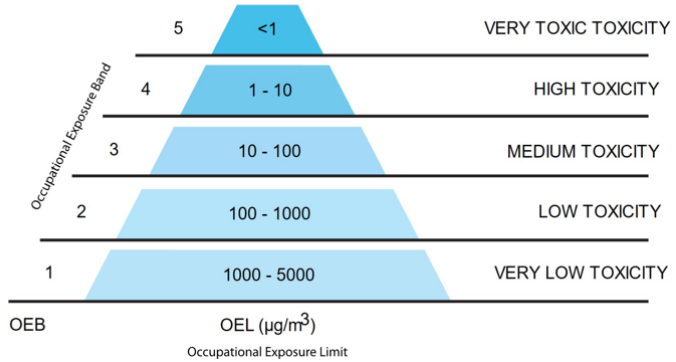
SPECIFIC APPLICATIONS
Handling Powders

Containment for powders (developing a CCS)

- Closed powder handling using single use technology solves many issues
- Contained powder handling mitigates risks of airborne particulates and operator exposure risks



Risk analysis for powders to develop a CCS



REVIEW FEEDBACKS

"Approved !!"
BPSA Director

"The paper looks great"
BPSA Director

"Please share my thanks to the author of this great example. Well explained with visuals to support.
BPSA former Director

"Summarizing the regulatory guidelines is very helpful to Industry"
BPSA former Director

"Helpful to see this in writing ..."
BPSA former Director

"Excellent document, which I believe will be very valuable to users and suppliers alike"
BSPA former chair

"Great point"
BPSA former Director

"The paper is excellent"
BPSA Director

LEARNINGS AND KEY TAKE-HOME MESSAGES

- "One size fits all" is neither feasible nor desirable
- Many examples included in this new technical guide are exemplary of the most demanding applications
- Eat the dinosaur in slices
  - Volume 2 is a 49-pages document - Sections can be read fully separately
- Switching from high-level principles to practical illustrations generated a lot of comments and some warm debates … outside of the committee
  - Shows the value of such illustrations …

NEXT STEPS - THANKS

- Webinar after summer
- Next directions to be discussed end of the year

- Special thanks to
  - Jeff Carter, Cytiva
  - Rachelle Morrow, Qosina
  - Kirsten Strahlendorf, Sanofi
  - Kevin Ott, BPSA
  - BPSA Board of Directors

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