Seeing is Believing: Mastering Design, Qualification and Life Cycle Management of Visual Inspection Test Sets

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PDA TRAINING

1.3. Design of test sets

General considerations - lifecycle approach

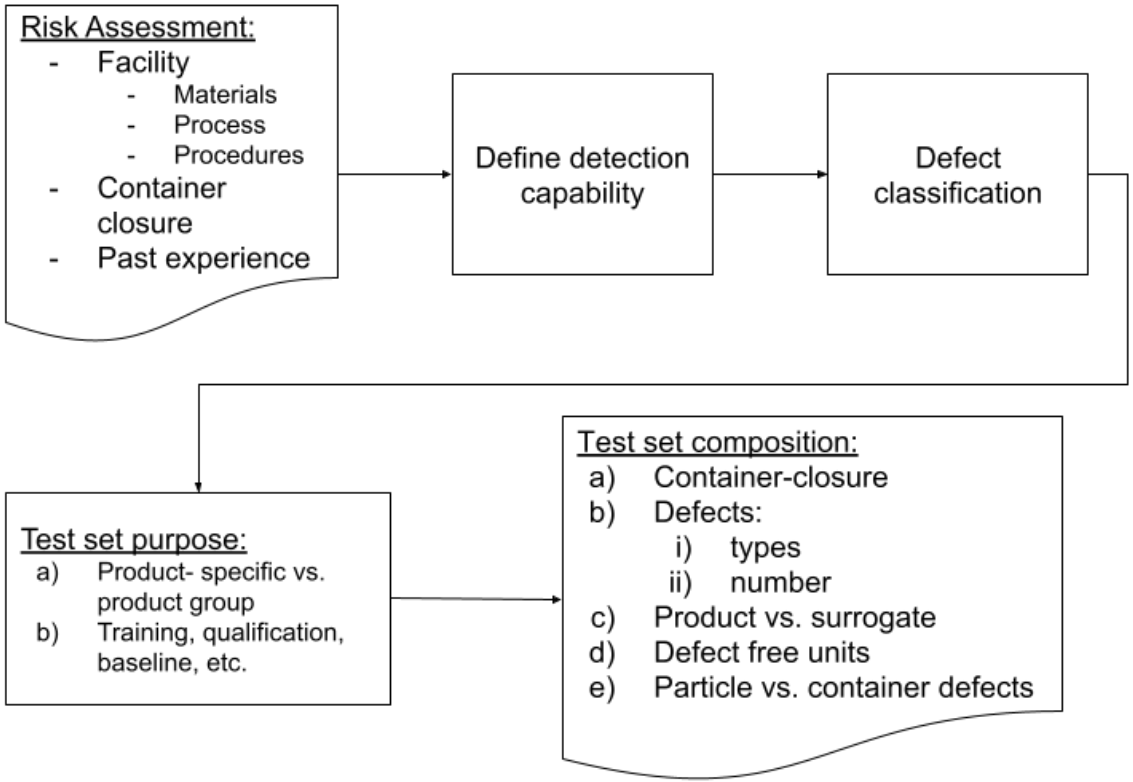
- Qualification of methods
- Training and qualification of personnel

General considerations - lifecycle approach (cont.)

- Quality should be **built-in**
- Incoming component control - specifications, acc. crit
  - Ready-to-use (RTU) components
  - Single-use systems (SUS) and consumable cleanroom materials
- Fill & finish process and components
- 100% VI
- Sampling and testing

General considerations - lifecycle approach (cont.)

- Stability and retention sample inspection
- Customer complaints
- Trending - action limits
- Investigative procedures
- Categorization and identification of particles
- Facility-specific libraries



Risk assessment

- Potential sources of particle ingress
- Potential sources of container defects
- Facility assessment
  - materials (product contact materials and non-product contact materials)
  - manufacturing process
  - procedures
- Container closure
- Past experience (trending) vs. new facility

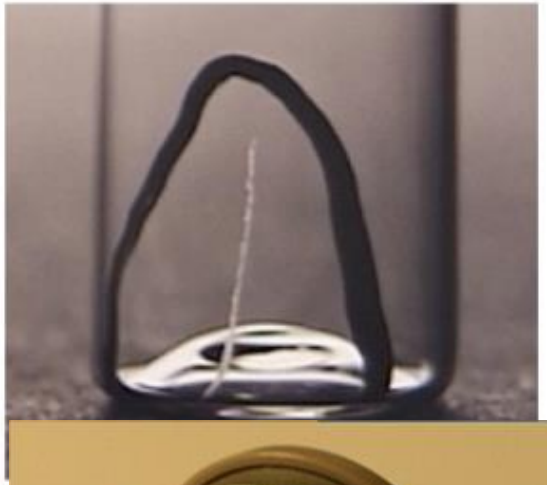
Risk assessment (cont.)

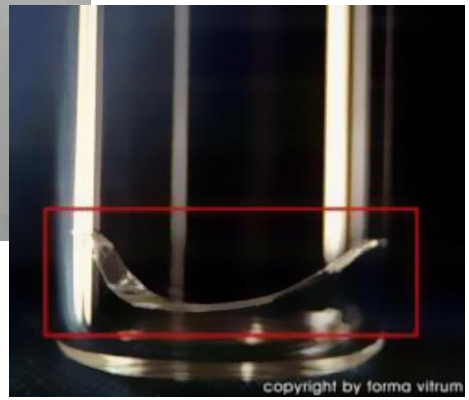
- Particle ingress:
  - Identify the typical visible particulates that could contaminate the injectable product
  - type (composition)
  - size ranges

Define mitigation strategies and prevention (monitoring, continuous improvement measures)

Risk assessment (cont.)

- Determine risks for each type of defect:
  - probability of occurrence
  - severity (potential safety impact)
  - detectability





Risk assessment (cont.)

Clinical risks - relevant considerations:

- related to sterility
- related to clinical administration

Risk assessment (cont.)

- Sources, monitoring, continuous improvement measures (mitigation strategies and prevention)

- Visual descriptions (e.g. photographs)

Defect Categorization

- Defect categories
  - Critical
  - Major
  - Minor
- Particle Categories:
  - Inherent
  - Intrinsic
  - Extrinsic
- Regional differences

Relevant guidelines

- EP 2.9.20/ USP <790>/ JP 6.06
- USP <771> Ophthalmic Products
- All applicable GMP guidelines
- US FDA Inspection of Injectable Products for Visible Particulates: Guidance for Industry

Non-mandatory guidance

- **USP <1790> Visual Inspection of Injections**
- EP 5.17.2. Recommendations on testing of particulate contamination: visible particles

Threshold studies

- Test set composition
- Method (study conditions)
- Assessment criteria

Test set composition - overview

- Knapp methodology
- Product or surrogate?
- Exact presentation or bracketing?
- Good (80-90%) and defective units (10-20%)
- Defects - which defects to include?
- Blinded (labelling - UV, QR codes, randomized numbers)

Test set design - A. Primary packaging

- Ideally, the exact product presentation should be used *(highly recommended for commercial products)*
- PP bracketing approach may be justified *(e.g. clinical development)*, provided that certain conditions are met:
  - product groups - vial, syringe, liquid, lyo, etc.
  - risk assessment - e.g. review impact, define worst case

Bracketing strategies

- Risk assessment to consider appropriate bracketing:
  - Justifications - consider influence on detectability
  - Supportive data?

- Factors:
  - Product attributes (color, viscosity, clarity/ opalescence, foaming)
  - Primary packaging
  - Product type (lyo vs. liquid, vial vs. syringe)

Test set design - B. Defects

Type of defects to include:

- informed by the RA
- previously detected/ common in the facility?
- What does atypical mean?

Test set design - B. Defects

- Expectations to particle defects - typical process-related
  - Metal
  - Glass
  - Plastic (what types?)
  - Fibers (what types?)
- Relevance - defects are context-dependent - consider the process and the facility (RA; e.g. vial vs. BFS)

Test set design - B. Defects

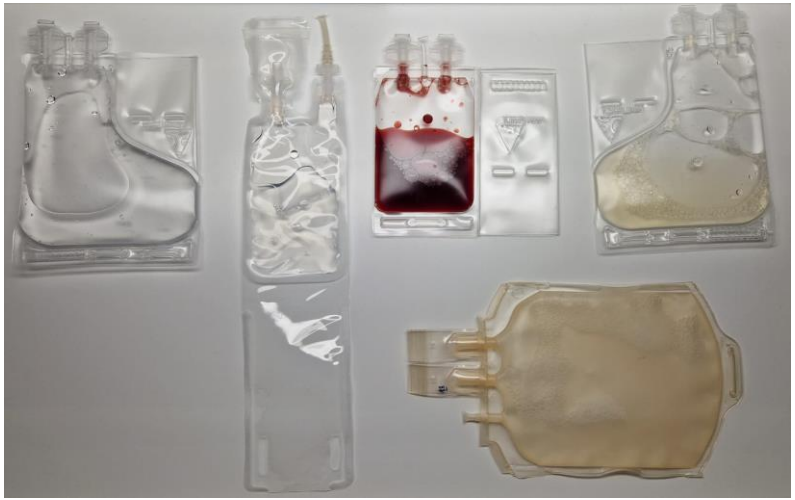
- Container defects - typical process-related
- For an extensive catalogue of glass defects – refer to PDA TR-43 (Revised 2023) - see separately
- But also:
  - Container closure defects
  - Assembly defects
  - Bag defects etc.

Test set design - B. Defects

- Life cycle management:
  - Shelf life
  - Replacement units
  - Update – e.g. generic kits, bracketing strategies

Test set design - B. Product vs. Surrogate

- Important considerations:
  - Product stability
  - Personnel safety



- Product attributes:
  - Color
  - Turbidity
  - Viscosity

  Surrogate modifications may impact test set shelf-life!

Quality investigations

Important assessment criteria used in quality assessments:

- Frequency of occurrence
- Typical vs. atypical

Typical vs. Atypical

- What is atypical?
  - Intrinsic - examples
  - Extrinsic - examples
  - Inherent - examples
- Specific considerations:
  - ATMPs - cell clumps (qualified?)
  - Biologics - proteinaceous particles (qualified?)

Generic test sets

- What circumstances justify the use of generic test sets?
- Bracketing approaches
- Phase appropriate approach

GROUP EXERCISE

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