Strategies & Qualification methodologies for Visual Inspection

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Strategies & Qualification methodologies for Visual Inspection

1. Introduction: Defect categories & definitions
2. Qualification methodologies for automated inspection: Strategies and Mindsets
3. Quality Control testing of difficult to inspect products

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1. Defect categories & definitions

- Critical
  - may cause a lack of sterility, container integrity or cause serious (life threatening) harm to patients
  - e.g. cracks in the container
- Major
  - may alter the content or the function of the product or might possibly cause non-life threatening harm to patients
  - e.g. particles
- Minor
  - (Cosmetic) defects that are unlikely to affect patient health or product functionality
  - e.g. scratches

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Overview

URS	• User Requirements
RA EQ	• Risk Assessment for the equipment
DQ	• Design Qualification / Design review
FAT	• Factory Acceptance Testing, including inspection performance testing
SAT	• Site Acceptance Testing, including vision installation and acceptance testing

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Overview

IQ
- Installation Qualification: correct installation of GMP critical components, …

OQ
- Operational qualification: SOPs, mechanical runs, alarms, fail safe, user mgt, …

RA def.
- Risk Assessment for defects

PQ/PV
- Performance Qualification
- Process validation

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Risk Assessment for defects

- What is it used for?:
  - Recipe parameter development:
    - Which defect do we tune the machine for?
  - Input for qualification/validation:
    - Which defect do we qualify?
  - Deviations / CAPA's:
    - In case of deviations during qualification are they acceptable or not?
    - Do we have to implement extra control strategies?

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Risk Assessment for defects

- Based on:
  - the **severity** (classification) of the defect;
  - the **occurence**;
  - the **detectability**, this includes all control strategies: QC, AQL and (expected) inspection performance of the AI process
  - Example: 11. Back-up slide: Risk Assessment Defects

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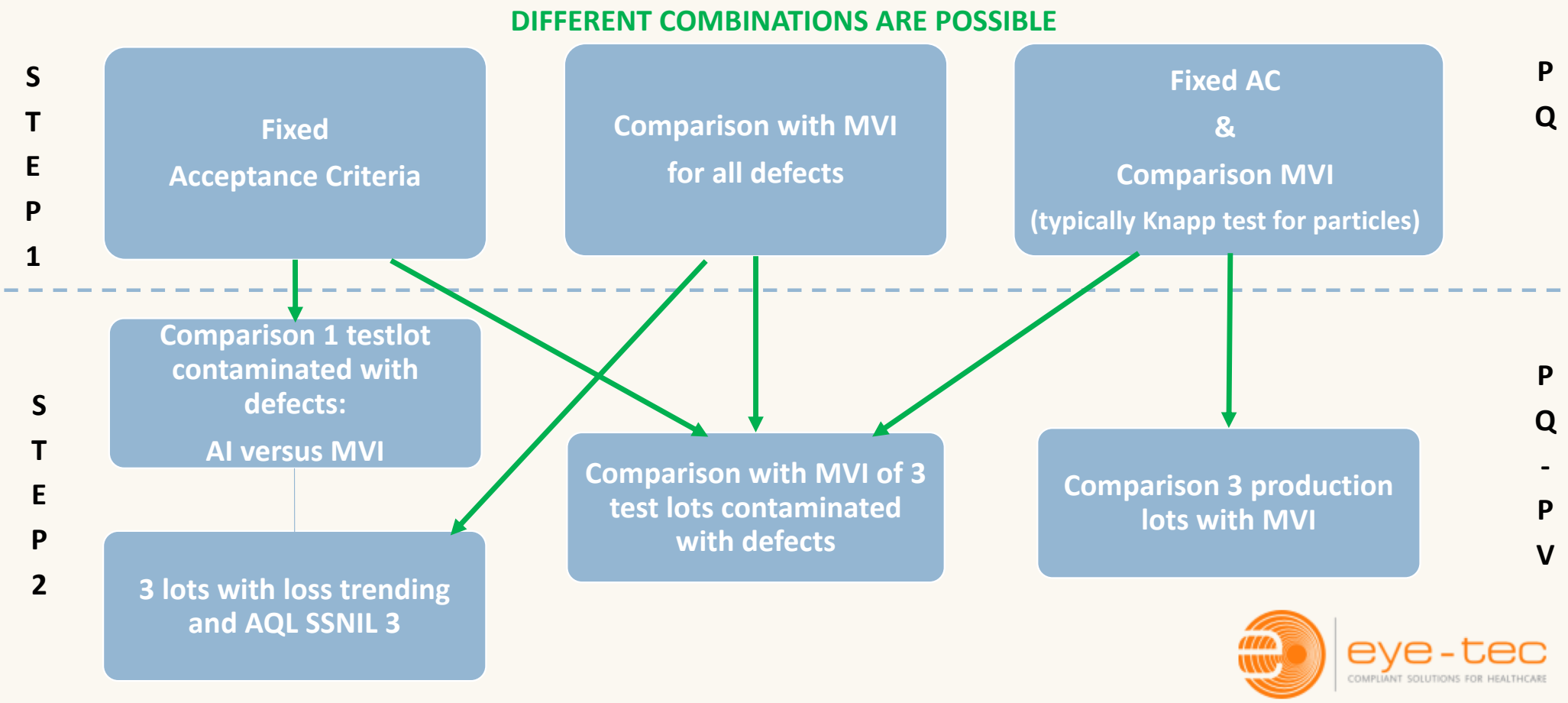
2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

PERFORMANCE QUALIFICATION / PROCESS VALIDATION



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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Knapp test

- a method which has been developed to evaluate the inspection efficiency of an inspection process/system (semi-automatic or automatic) with a reference inspection method (in most cases manual visual inspection)

- Basics:
  - All containers which are rejected ≥ 70% by manual visual inspection are considered defects
  - Acceptance criteria:
    - The overall inspection efficiency for these defects of automatic visual inspection has to be equal or greater than the inspection efficiency of manual inspection for these defects

- Initially developed for particles. Is and can be used for other defects.

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Performance qualification / Process Validation – recommendations

- Regulatory expectation: compare every defect category to Manual Visual Inspection (gold standard)
- Use bracketing approach during PQ/PV for defining which lots should be inspected, based on:
  - Container type (e.g 2 ml vial)
  - Fill level / strength, e.g. lowest and highest fill level
  - Product type (suspension, solution, freeze dry, …)

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets
TEST SETS

- What should be in?:
  - All defects which can be inspected by AI
  - Existing products: based on hystorical data / defect library
  - New products: based on upstream processes or hystorical data of similar products
- Composition: based on hystorical data and criticality
- Assembly:
  - OPTION 1: Real production defects
  - OPTION 2: Artificially and characterized defects
  - For test sets which are compared with MVI:
    - Use invisble ink to mark (UV)
    - Not more than 10 % defects
- Use a logbook for each test set

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2. Qualification Methodologies for Automated Visual Inspection: Strategies and Mindsets

Control strategies

- Routine operation:
  - Functional test set: clear defects, use to check functionality of machine
  - Reject trending & control limits: for automated inspection, overall reject, per reject station, per camera station and/or area of inspection (e.g. side wall)
  - AQL sampling (ANSI/ASQ Z1.4, ISO2859-1):
    - Critical 0.01 – 0.1
    - Major 0.1 – 0.65
    - Minor 1.0 – 4.0
- Requalification / Revalidation
  - Periodic review of production data, change controls, CAPA's
  - Every 3 to 5 years product specific?

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3. Quality Control testing of difficult to inspect products

Introduction

Visual Inspection may have limited adequacy to detect visible particulate matter, due to

- Product characteristics (non-transparent)
- Container characteristics

Guidance Documents

- PDA TR79 Particulate Matter Control in Difficult to Inspect Parenterals
- USP <1790> Visual Inspection of Injections
- USP <1> Injections

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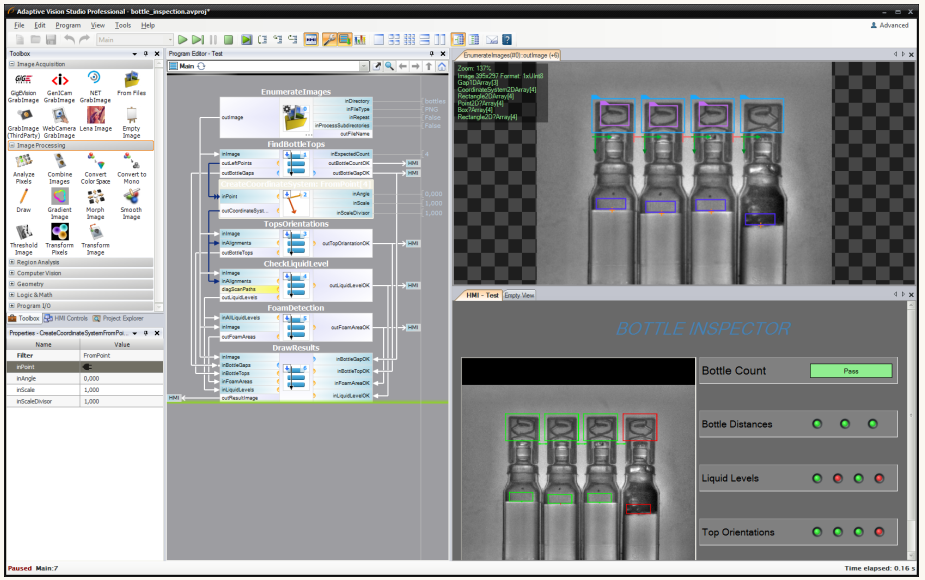
3. USP <1790>

“ Supplemental testing is required when the nature of the product or container limits visual inspection of the contents…”

- *3.1. 100% Inspection*



Different particulate matter types:

- Extrinsic
- Intrinsic
- Inherent
  - Typical aspect of the (biological) product
  - Emulsions / Suspensions

- 5.1.1. EXTRINSIC, INTRINSIC, OR INHERENT PARTICLES

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3. USP <1790>

Section	DIP type	Sampling	Method
5.2.1.	Lyophilised product	ANSI/AQS Z1.4 S-3 and S-4	Reconstitution after 100% inspection of cake
5.2.2.	Powder product	ANSI/AQS Z1.4 S-3 and S-4	Reconstitution after 100% inspection of powder
5.2.3.	Amber Containers	N/A (100%)	Increased light intensity Directional lighting from behind (transfer to clear container)
5.2.4.	Translucent Plastic Containers	N/A (100%)	Increased light intensity Directional lighting from behind
5.2.5.	Large Volume Containers	N/A (100%)	Increased inspection time Increased light intensity Directional lighting from behind
5.2.6.	Combination Products	N/A (100%)	Inspection prior assembly Second inspection post assembly if needed

3. PDA Technical Report No. 79

PDA Survey on DIP (3.1)

- All companies do 100% inspection
- Only half of companies perform supplemental destructive testing
- Only 1/3 apply AQL limits <0,1% for DIP
- Sampling plans based on
  - ISO 2859
  - ANSI/ASQ Z1.4
  - Fixed sample sizes

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3. PDA Technical Report No. 79

Supplemental (Destructive) Acceptance Sampling and Testing (4.4)

- Only required under USP <790>; not in other pharmacopoeia
- *In addition to* AQL sampling
- Inspection of contents that is
  - Constituted (dried)
  - Withdrawn (transferred to another container)
- Filtration / Sieving / Panning

3. PDA Technical Report No. 79

Inspection Approaches for DIP Products / Containers / Devices (5.0)

- Non-destructive (100% inspection with modifications) (5.1)
  - Increased light intensity
  - Increased inspection dwell time
  - Illumination variations
  - Magnification
  - Mechanical fixtures
  - And other

3. PDA Technical Report No. 79

Inspection Approaches for DIP Products / Containers / Devices (5.0)

- Destructive (supplemental, based on sampling plan) (5.2)

	Description	Product	Remarks / Process
Method 1	Reconstitution	Lyo & powder	Diluent purity (filtered) MVI for clear solutions
Method 2	Filtration	Reconstituted p. liquids	USP <788-2> 0,8 micron Bigger pore size • Only visible particles inspection • Viscous product • Inherent particles to pass Adapted membrane materials for spectroscopic analysis

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3. PDA Technical Report No. 79

- Destructive (supplemental, based on sampling plan) (5.2) - continued

	Description	Product	Remarks / Process
Method 3	Clarification	Emulsion Suspension Solid excipient	Solvent, acid or base (filtered) MVI for clear solutions or filtration
Method 4	Transfer / Diluent	Coloured solution Opaque container	Transfer to clear container / dillution ! : exclusion by needle ! : generation of stopper particles MVI for clear solutions or filtration
Method 5	Sieve / Mesh	Suspensions (known part size)	Microscopy of retain material 5 – 30 micron sieve (+ part size data)
Method 6	Panning	Suspensions (broad distr)	Transfer to clean petri dish + microscopy

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3. PDA Technical Report No. 79

- Destructive (supplemental, based on sampling plan) (5.2) - continued

	Description	Product	Remarks / Process
Method 7	Rinse / Flush + filtration	Implantable devices Empty containers Infusion tubing	Rinsing Filtration and microscopic evaluation

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END

Thank you for listening

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Back-up slide: Risk Assessment Defects

CQA	Defect	Defect category	SEVERITY	OCCURENCE	Current control strategy	DETECTION	RPN	Proposed control strategy
Product identity / safety	No wrong product in correct ampoule	C	10	1	No strategy in inspection is used to detect this defect	10	100	
	No wrong ampoule (different size)	C	10	3	AQL sampling	1	30	
	No wrong color ring (with same size)	C	10	1	**OPTION 1** Visual inspection when feeding ampoules at infeed, traying ampoules at outfeed. AQL sampling	7	70	
		C	10	1	**OPTION 2** 100 % automatic inspection of color ring and rejection if number of rings or ring color is wrong. AQL sampling	1	10	
Extractable volume	Too low or too high filling volume according to PPS specifications	C	5	5	No inspection control strategy is used to control this requirement. SPC (IPC) is used in the filling department to control this.	10	250	
	Too low or too high filling volume (outside ± 20% in height, not volume)	C	7	5	100 % automatic inspection of filling volume AQL sampling	1	35	
	No empty containers	M	5	7	100 % automatic inspection of filling volume AQL sampling	1	35	

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