Inspection Validation Methods

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October 2021

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Agenda

- Requirements / Specifications

- Installation Qualification

- Human Baseline Performance

- Test Set Composition

- Operational Qualification

- Performance / Process Qualification

- Routine Performance Verification

Validation vs. Qualification

- Equipment must be validated
  - IQ/OQ/PQ

- Human inspectors are trained and qualified
  - NOT validated

Human Performance Baseline

- Establish human inspection performance with defect test set.

- Can use to make direct comparison to compendial inspection method.
  - USP and EP

Test Set Composition

- Defects to include in Test Set
  - Multiple examples of anticipated defects
  - Weighted toward critical defects
  - Defect examples are qualified by multiple inspection by qualified inspectors. Reject zone defects (with POD ≥ 70%) selected for inclusion.

- Typical Test Set Size
  - 500 to 1000 units

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Test Set Composition

- Production Defects vs. Standards
  - "Real" defects necessary to validate production performance
  - Standard spheres useful to establish baseline, compare methods and settings and monitor routine performance

- Defect rate in test set
  - For human studies, 10% or less is preferred to avoid Hawthorne Effect (positive reinforcement)
  - Not relevant for machine studies

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Human Qualification

- Inspector Selection
  - Visual Acuity (near-vision)
  - Color Perception
- Initial Training
  - Defect Examples
- Initial Qualification
- Periodic Requalification

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Knapp Method

- Multiple inspections of test set to determine reject probabilities of individual units

- Sort results into the following ranges:
  - Accept Zone: P = 0.0 to 0.3
  - Gray Zone: P = 0.3 to 0.7
  - Reject Zone: P = 0.7 to1.0

- Calculate Reject Zone Efficiency (RZE)

- Calculate Accept Zone Loss (AZL)

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$$RZE = RZR/RZN$$

Where:

RZR = Reject Zone Rejects, the number of vials rejected in the Reject Zone

RZN = Reject Zone Number, the total number of vials in the Reject Zone

Knapp Method

- Calculate comparable terms for the Gray and Accept Zones.

- Accept Zone Loss (AZL) is a measure of the false reject rate.

- The RZE for an alternative method should be the same or better than the reference method.

- Gray Zone vials may be "sacrificed" to achieve higher RZE.

Knapp Method

- Remember, as originally published, this method was designed to assess inspection for particles only.

- To apply the method to the full range of visible defects normally addressed, it is necessary to categorize defects by risk and determine an RZE for each risk category.

- As published, defect test sets have a ~30% defect rate. This is very high and likely to bias the results. A defect rate of 10% or less is recommended.

How often are inspectors requalified?

	2014	2008	2003	1996
Never	**5%**	21%	8%	35%
Monthly	**1%**	5%	0%	8%
Quarterly	**4%**	0%	0%	8%
Semi-Annually	**10%**	11%	8%	16%
Annually	**79%**	63%	75%	69%

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Equipment Validation (Manual and Semi-Auto Inspection)

- Equipment Specifications
- Installation Qualification (IQ)
  - Utilities
- Operational Qualification (OQ)
  - Light Intensity
  - Inspection Rate (Semi-Auto)
  - Rotation (Semi-Auto)
  - Rejection (Semi-Auto)
- Process Qualification (PQ)
  - Operator Training and Qualification

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Specification / Requirements

- User Requirements and Specifications (URS)
  - Good validation starts with clear documentation of the performance expectations for the new equipment.

Factory Acceptance Test (FAT)

- Equipment performance should be confirmed before acceptance for shipment.
  - Check against URS
  - Inspection performance should be tested with samples defects.
  - The false reject rate should also be determined.

Installation Qualification (IQ)

- Installation Qualification (IQ) should document receipt and installation of equipment
  - Model and serial number
  - Features / operating ranges
  - Version numbers of software / firmware
  - Verify utility connection(s)
  - Calibration
  - Spare parts
  - Change parts

Operational Qualification (OQ)

- Operational Qualification (OQ) should document proper function of equipment component systems
  - Emergency stop(s)
  - Eject system(s)
  - Man/Machine Interface (MMI)
    - Reports
  - Other features?
    - e.g., lamp failure detection
  - Establish appropriate operating ranges

Operational Qualification (OQ)

– Detection probability for each defect type

- Compare with human baseline
- Establish reference for routine continuous performance verification.

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Validation Criteria

- 100% validate automated inspection equipment.
- Validation Criteria:
  - Equivalent to manual: 51%
  - Better than manual: 28%
  - Other, Not compared to manual: 21%

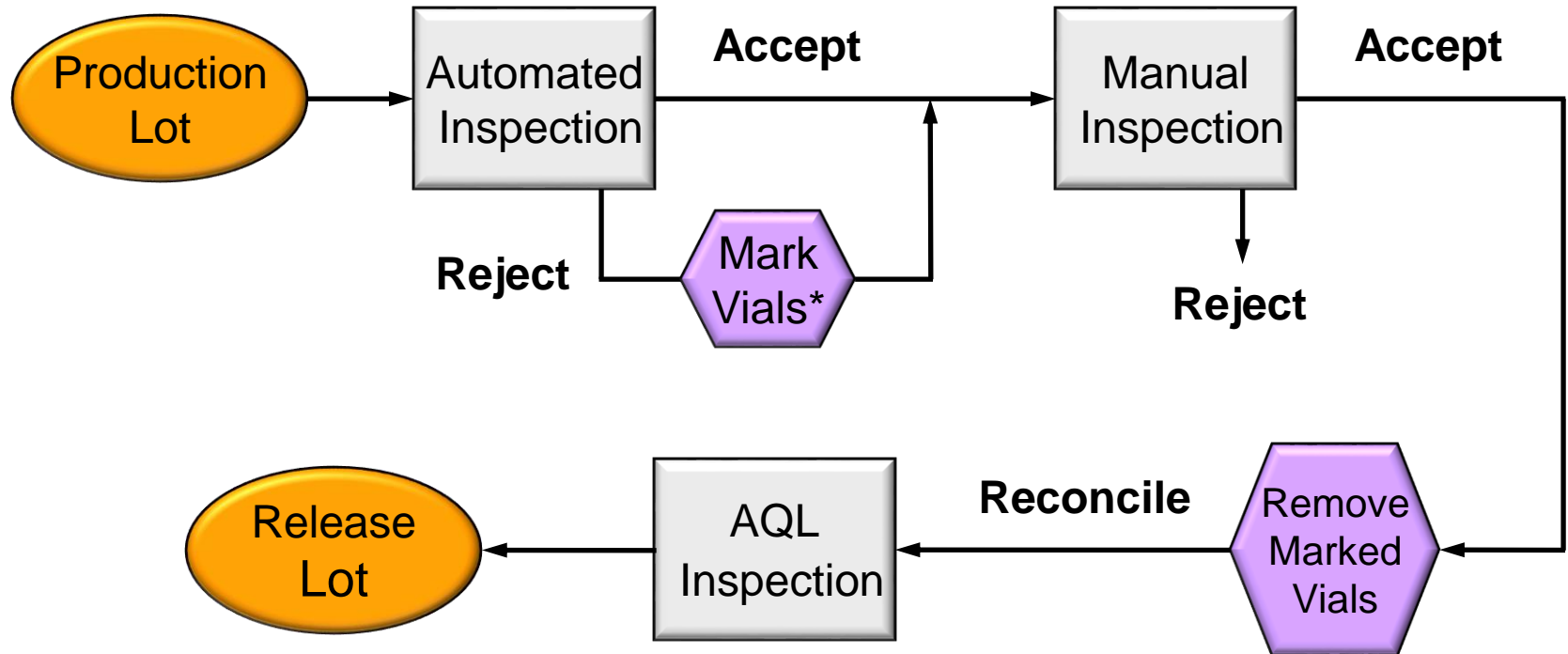From 2014 PDA Survey of Visual Inspection Practices

Performance/Process Qualification

- Performance / Process Qualification (PQ) confirms expected performance with full production lots
  - Method 1
    - Inspect three production lots by both manual and automated methods
    - Compare defect detection rates
    - Determine false reject rate
  - Method 2
    - Inspect three production lots by automated method and use a tightened sampling plan to assess performance
    - Determine false reject rate

PQ Method 1

Production Lot → Automated Inspection

Automated Inspection — **Accept** → Manual Inspection

Automated Inspection — **Reject** → Mark Vials* → (back to Manual Inspection path)

Manual Inspection — **Accept** → Remove Marked Vials

Manual Inspection — **Reject**

Remove Marked Vials — **Reconcile** → AQL Inspection → Release Lot

* Vials marked with UV ink; not visible during Manual Inspection

Routine Performance Verification

- Typically run before each batch

- Small test set to challenge each sensor/camera station

- Gross examples to assure rejection, Go/No Go test

- Does not challenge sensitivity, but rather camera alignment, functionality and proper operation of reject system.

How frequently do you challenge or retest automated inspection equipment?

	2014	2008	2003	1996
Never	**1%**	0%	0%	15%
Each Shift	**1%**	8%	13%	8%
Start of Lot	**46%**	42%	75%	38%
Start and End of Lot	**8%**	ND	ND	ND
Daily	**15%**	25%	19%	23%
Weekly	**2%**	0%	0%	8%
Monthly	**2%**	ND	ND	ND
Quarterly	**1%**	ND	ND	ND
Annually	**19%**	ND	ND	ND

ND = No Data, question not asked in survey from this year

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Remember, everyone is an inspector!

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