



# Inspection Validation Methods

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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



# Inspection Standards



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# 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  $\geq$  70%) selected for inclusion.
- Typical Test Set Size
  - 500 to 1000 units



# 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



# Human Qualification

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





# 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:  $P = 0.7$  to  $1.0$
- Calculate Reject Zone Efficiency (RZE)
- Calculate Accept Zone Loss (AZL)



# RZE

$$RZE = RZR/RZN$$

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
<b>Never</b>	<b>5%</b>	<b>21%</b>	<b>8%</b>	<b>35%</b>
<b>Monthly</b>	<b>1%</b>	<b>5%</b>	<b>0%</b>	<b>8%</b>
<b>Quarterly</b>	<b>4%</b>	<b>0%</b>	<b>0%</b>	<b>8%</b>
<b>Semi-Annually</b>	<b>10%</b>	<b>11%</b>	<b>8%</b>	<b>16%</b>
<b>Annually</b>	<b>79%</b>	<b>63%</b>	<b>75%</b>	<b>69%</b>



# 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



# 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.



# 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

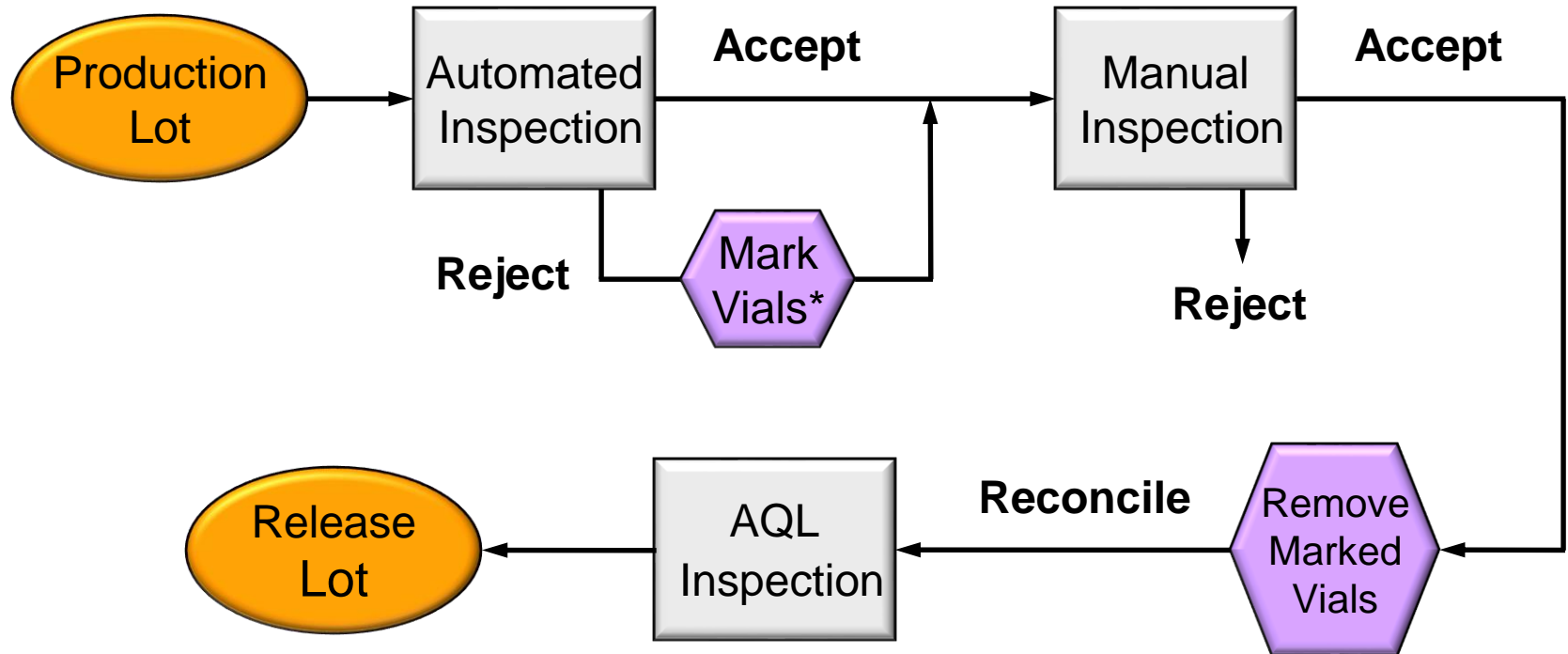


# Performance/Process Qualification

- 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



\* 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
<b>Never</b>	<b>1%</b>	<b>0%</b>	<b>0%</b>	<b>15%</b>
<b>Each Shift</b>	<b>1%</b>	<b>8%</b>	<b>13%</b>	<b>8%</b>
<b>Start of Lot</b>	<b>46%</b>	<b>42%</b>	<b>75%</b>	<b>38%</b>
<b>Start and End of Lot</b>	<b>8%</b>	<b>ND</b>	<b>ND</b>	<b>ND</b>
<b>Daily</b>	<b>15%</b>	<b>25%</b>	<b>19%</b>	<b>23%</b>
<b>Weekly</b>	<b>2%</b>	<b>0%</b>	<b>0%</b>	<b>8%</b>
<b>Monthly</b>	<b>2%</b>	<b>ND</b>	<b>ND</b>	<b>ND</b>
<b>Quarterly</b>	<b>1%</b>	<b>ND</b>	<b>ND</b>	<b>ND</b>
<b>Annually</b>	<b>19%</b>	<b>ND</b>	<b>ND</b>	<b>ND</b>

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

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Remember, everyone is an inspector!

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