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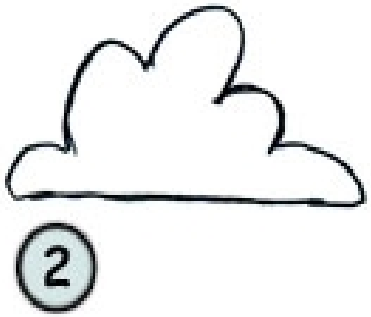
• Theory 1: Introduction to regulatory landscape of visual inspection

- USP 1, USP 788 and 1788, USP 790 and 1790
- PhEur e.g. 2.9.20
- JP e.g. 6.06
- Annex 1
- Similarities and differences in compendial methods
- 100% inspection and AQL testing
- Definitions and practical examples of inherent, intrinsic and extrinsic particles
- Examples of regulatory citations 483s

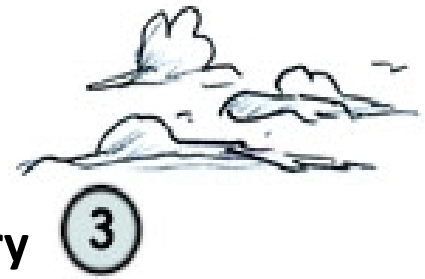
Mastering Automated Visual Inspection

Theory 1: Introduction to regulatory landscape of visual inspection

Technology

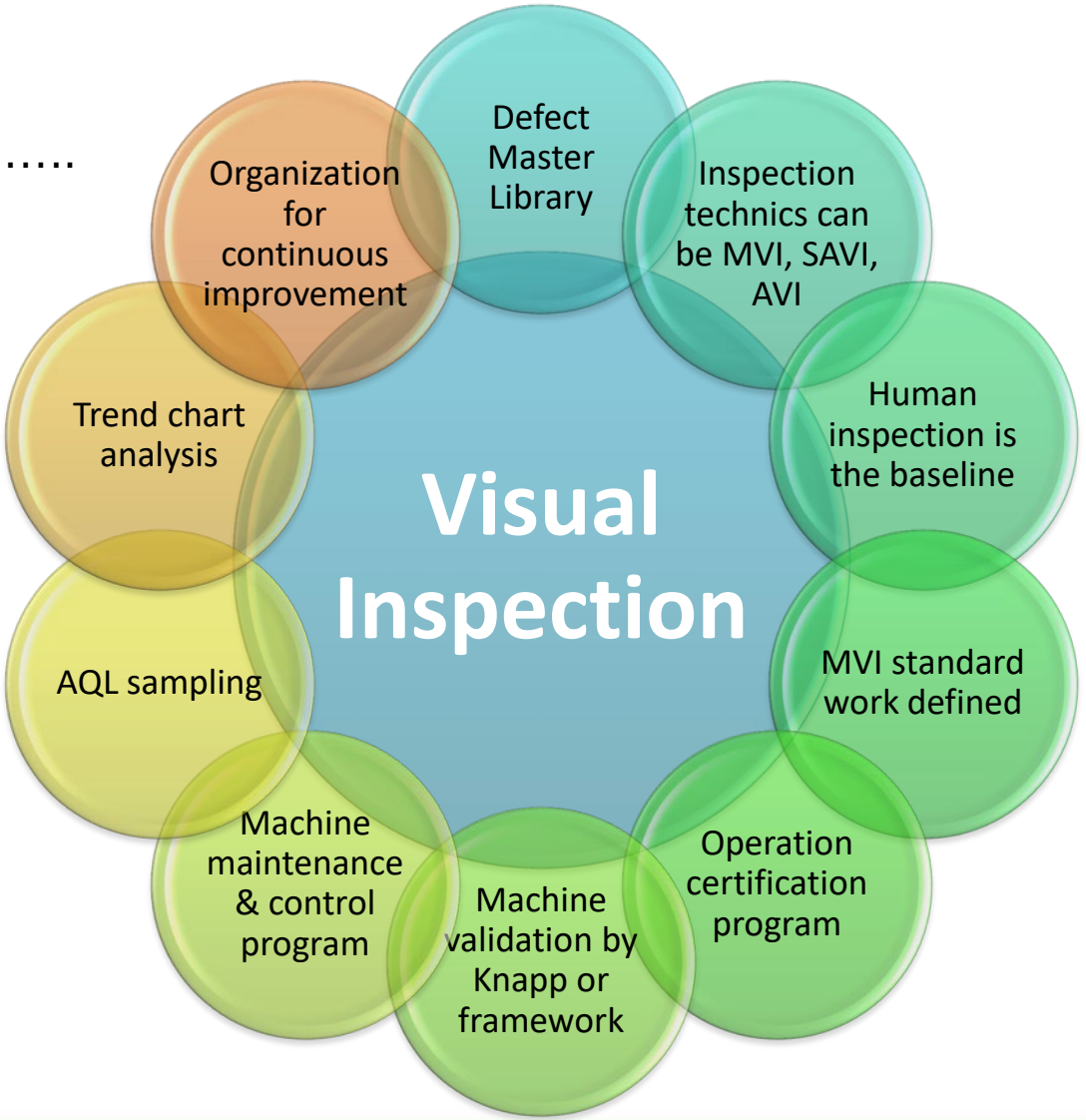


Quality / regulatory



Business

- 10 Golden rules for VI…..



- USP<1>
- USP<788> particle definition
- USP<790>and <1790>
- PhEur e.g. 2.9.20 vis
- JP e.g. 6.06
- Annex 1: new draft for comment dec 17
- Similarities and differences in compendial methods
- 100% inspection and AQL testing
- Definitions and practical examples of inherent, intrinsic and extrinsic particles

- USP<1790> Effective Aug. 2017

Adobe Acrobat Document

- New Annex 1 draft for comment dec 2017

Adobe Acrobat Document

- Example of FDA audit findings:

2015

« Quality oversight over visual inspection is deficient. For example,

a. AQL inspections are conducted by personnel that also perform the 100% visual inspection

b. From September 2013 to September 2015, QA oversight over the 100% visual inspection operations has occurred six times.”

- Example of FDA audit findings:

2015

« The ….. equipment are used to perform 100% visual inspection of lyophilized vials, including xxx on Line xxx. For example, 9.d.1. The light intensity of each unit is not verified during routine preventive maintenance and is not verified prior to use. 9.d.2 The functionality test used to determine the reject function of the equipment is required before and after 100% visual inspection. The functionality test results for each equipment is not clearly documented as to the test results. Only the line clearance results are documented. „

- Example of FDA audit findings:

2015

« There are no individual reject limits established for the critical defect categories of xxx particle and xxx

The defect category xxx which has an action limit of xxx includes vials that could have defects such as xxx The critical defect xxx does not have its own individual reject limit established.

The defect category of xxx is defined as xxx There is no reject limit established for this critical defect. A non-conformance is raised for each observed xxx defect.

Lots of finished drug products that fail the initial xxx automated visual inspection limit on the xxx system can then be re-inspected using the xxx semi-automated manual system. There are no established limits for hte number of times any single lot can be reinspected. Additionally, there are no tightened limits established for the re-inspection of lots of product that fail the initial xxx on the xxx inspection that are then re-inspected using the xxx semi-automated system.

- Example of FDA audit findings:

2015

« lot xxx exceeding the Acceptable Quality Limit (AQL) for Particulates after being inspected in the xxx automated inspection system. A total of (21) vials were found containing particles and the allowabel number of Major defets is xxx The lot was reinspected using the xxx semi automated inspection system and operators, over a period of xxx The reinspection resulted in an additional xxx vials found with particles. THe initial inspection performed by the xxx found xxx particles defects. The particles were identified as endofenous (aluminum phosphate) and some as xxx which could not be identified after a detailed mutli-department investigation. The investigation indicates that this is the first occurrence of this particle at the site and that it is confirmed to pose no risk to human health. The investigation is deficient for the following:

There is a lack of assurance that the xxx automated visual inspection system can detect all particles. The investigation indicates that there were xxx vials classified as 'no apparent defect' which could have included vials with particles as reason for the discrepant number in vials found with particles between the initial inspection and the reinspection.

There was no tightened 100% inspection performed for this lot even though the initial AQL failed for a Major defect. This lot was inspected at the same reject limit for particulates as the initial inspection.

There is a lack of assurance that the xxx automated and the xxx semi automated visual inspection systems are comparable in their detectino of particles in product. The xxx is used to perform the reinspection of lots that have initially failed inspections on the xxx.”

- Example of FDA audit findings:

2015

« batch ….exceeding the upped control limit for critical defects due to …..glass particles observed during …..inspection. No AQL failures were observed during the initial AQL inspection; however, the investigation indicates the primary root cause was misalignment of the transport belt in the ….

No tightened AQL inspection or re-inspection was performed on the portion of the lot accepted and released …... Particles size was not determined to facilitate assessment of the reliability of detection during visual inspection

- Example of FDA audit findings:

2016

« Qualification of visual inspectors and validation and verification of the ….inspection system are not based on well-characterized test sets.

No written procedure has been established to ensure test sets for visual inspection include particles in the visible size range similar to production rejects other than a …..micron glass particle.

No record documenting the creation of test sets used for qualification of visual inspectors was provided, for examples; the particulate inspection qualification set used to re-qualify an inspector on…..

- Example of FDA audit findings:

2017

« …. Input to and output from the computer or related system of formulas or other records or data were not

adequately checked for accuracy. Specifically: the validations of the xxx vials inspection machines xxx

and xxx as corrective actions to previous 2015 FDA-483

….. There is no documentation of Process Qualification study of the xxx machines capabilities to detect vials heel crack defects.”

- Example of FDA audit findings:

2014

« There is lack of assurance that all lots that are visually inspected by the xxxx automated inspection system are inspected and removed (called) to acceptable reject levels in that:

-There are no individual reject rates for the critical xxxx major xxxx, and minor xxxx defect categories for 100% Automated Inspection conducted by the xxxx automated visual Inspection system for the xxxx finished drug products.

-All categories of defects are totalled and areject rate (xxx is established for an individual lot of finished drug product which can contain up to xxxx syringes for the xxxx products. There have been approximately xxxx released to date.

Syringes that may have been rejected at unacceptable rates for the critical, major and minor defects as listed above, during the 100% automated xxxx inspection are not investigated for assignable cause. Deviations are not raised until a total of xxx x of the lot has a cumulative reject rate.

The 100% manual inspection, that are conducted when a finished lot fails an (AQL) inspection, have no reject Rates established for the individual defect categories of critical major and minor"

- Example of FDA audit findings:

2013

« The firm failed to track and trend the result of the QA Auditor referee visual inspection for xx as an indicator of process control or product quality.

There is no tracking or trending of the number of xx vials initially rejected as “Particulate Fiber” and “Particulate Other” that are subsequently determined to be acceptable by the QA Auditor referee visual inspection and are returned to the batch. “

- Example of FDA audit findings:

2011

« test the vial body and the ……test the bottom of the vial. The xx ……visual inspection process for liquid vials allows vials that were initially rejected for ……to be re-inspected and …….tested by. There are no data to support subjecting the vials to ……testing does not affect product and or vial quality.

Additionally, vials that are initially rejected for …..are re-inspected and could possibly be accepted as an …..vial upon the ….and ultimately rejected/accepted on…...

There is no documentation to support the monitoring of discrepant results for vials that may have been initially rejected and subsequently accepted on the …….