SOP: Visual Inspection Training of Manufactured Drug Product for Particulate and Cosmetic/Functional Defects.

Approvals:

Preparer: Dr. Sengyong Lee — Date: 11JUL17
Reviewer: Dr. Matt Marshall — Date: 01SEP17

1. **Purpose:**
   1.1. Each final container of all parenteral drug preparations must be inspected to the fullest extent possible for the presence of observable foreign and particulate matter and other cosmetic defects.
2. **Scope and Applicability:**
   2.1. Final visual inspection is performed manually by human operators.
   2.2. Prior to being qualified as an inspector, each inspector must be successfully trained and qualified per this procedure.
3. **Summary of Method:**
   3.1. Test Sets
      3.1.1. Different test sets needed for each drug product category.
      3.1.2. Test sets can be made up of production rejects or created manually with characterized particulate material.
      3.1.3. **Qualify an inspector using a test set that is representative of the product to be inspected.**
         3.1.3.1. Inspectors are qualified if their detection of rejects is ≥ 70% detection of known rejects and ≤ 30% of blanks (false reject) in any given test set. The inspector must meet this requirement three (3) times before being considered a qualified manual visual inspector.
   3.2. Inspector Re-Qualification Schedule:
      3.2.1. Visual inspectors are re-qualified annually.
      3.2.2. If inspection performance declines, re-qualification may be required in shorter time-frames.
      3.2.3. Annual eye sight exams at optometrist for visual acuity with 20/20 vision or 20/20 corrected. If eyesight is corrected with eye glasses or contact lenses, then those must be worn during the product inspection process.
4. **References:**
   4.1. USP <1>, Injections and Implanted Drug Products (Parenterals) – Product Quality Tests
   4.2. USP <790> Visible Particulates in Injections
   4.3. USP <1790> Visual Inspection of Injections
5. **Definitions:**
   5.1. **Essentially Free**: When injectable drug products are inspected and as described in USP <790>, no more than the specified number of units may be observed without magnification to contain visible particulates.
   5.2. **Particulate Matter**: Extraneous mobile undissolved particles, other than gas bubbles, unintentionally present in solutions. Examples of such particulates may include, but are not limited to, fibers, glass, metal, elastomeric materials, and precipitates.
   5.3. **100% Inspection**: Complete inspection of the container-closure system and its contents.

SOP: Visual Inspection Training of Manufactured Drug Product for Particulate and Cosmetic/Functional Defects.

6. Precautions:

6.1. None

7. Responsibilities:

7.1 It is the responsibility of the management to ensure that visual inspectors are qualified per this SOP.

7.2 It is the responsibility of the Quality Assurance (QA) to perform investigations of inspectors who do not meet requalification requirements.

8. Equipment and Materials:

8.1. Test Set (See Section 9.1)

8.2. Sticky dot labels.

8.3. Containers for sorting defects and passed vials.

9. Procedure: The inspection process is designed to ensure that 100% of every container of every lot of parenteral preparations is "essentially free" from visible particulates.

9.1. Test Sets

9.1.1. Different test sets needed for each drug product category.

9.1.1.1.Clear liquids,
9.1.1.2.Colored liquids,
9.1.1.3.Lyophilized,
9.1.1.4.Suspensions,
9.1.1.5.Powders,
9.1.1.6.etc.

9.1.2. Test sets can be made up of production rejects or created manually with characterized particulate material. Test sets are made up of blank vials, seeded (contaminated) vials, and other non-conforming vials (container/closure defects).

9.1.2.1.The percentage of reject vials should be between 10% and 30% of the entire test set.

9.1.2.2.Test sets are labeled so as to keep the identity of the rejects unknown to the trainee.

9.1.3. Units that are no longer usable in a test set due to breakage, particle no longer detectable, cake breakage, etc. will be replaced.

9.1.4. Seeded vials: each seeded vial contains a single particle not smaller than the limits of human detection, ≥ 100uM for particles and ≥ 500uM for fibers. Particle material used to seed the vials are representative of the contaminants encountered in the production process, glass, polyethylene, dark particles, fibers, etc.

9.1.5. Non-conforming container/closure defect vials:

9.1.5.1.Under-crimped cap so that it is fitted around the vial but the cap can still be "spun" around the neck of the vial.

9.1.5.2.Over-crimped cap so that the cap is visibly "crushed" against the neck of the vial.

9.1.5.3.Small but visible scratch in the vial.

9.1.5.4.Small but visible smudge on the outside of the cap or stopper.

SOP: Visual Inspection Training of Manufactured Drug Product for Particulate and Cosmetic/Functional Defects.

9.1.6. **Qualify an inspector using a test set that is representative of the product to be inspected.** For example, if the product to be inspected is lyophilized, qualify the inspector using the lyophilized test set.

9.1.6.1. Inspectors are qualified if their detection of rejects is ≥ 70% detection of known rejects and ≤ 30% of blanks (false reject) in any given test set. The inspector must meet this requirement three (3) times before being considered a qualified manual visual inspector.

9.1.6.2. The trainee is trained on the operation of the manual inspection booth.

9.1.6.3. The trainee is shown the rejects within the test set to be trained upon. Each of the rejects is described as the trainee inspects the rejects within the test set. A blank is also given for inspection as well.

9.1.6.4. Ensure that operators spend appropriate time (5+ seconds against each colored background) with each product container during the visual inspection process.

9.1.6.5. The reject vials are then mixed in with the rest of the test set and the trainee inspects each vial while being observed by the trainer. The trainee inspects all of the vials and notes the defect code for the reject vials while maintaining separation of the rejects and the blanks.

9.1.6.6. Upon completion the trainer compares the trainee's determinations to the actual defects/blanks. ≥ 70% detection of known rejects and ≤ 30% of blanks (false reject) is required to pass. The trainee repeats the inspection process until successfully passing three (3) times.

9.1.6.7. The Trainer documents each trainee inspection on the Visual Inspector Qualification Form.

10. Inspector Re-Qualification Schedule:

10.1. Visual inspectors are re-qualified annually.

10.2. If inspection performance declines, re-qualification may be required in shorter time-frames.

10.2.1. Common causes of declined performance that may lead to a need for re-qualification include fatigue, demonstration of an improper reject rate during operations, etc. and/or causing excessive product investigations.

10.3. Annual eye sight exams at optometrist for visual acuity with 20/20 vision or 20/20 corrected. If eyesight is corrected with eye glasses or contact lenses, then those must be worn during the product inspection process.

History

Revision Number	***Effective Date***	***Preparer***	***Description of Change***
0	11JUL17	Sengyong Lee	Initial release