The proposed wording of the section "Visible Particulates in Injections" is as follows:

> This test is intended to be applied to product that has been 100% inspected as part of the manufacturing process; it is not sufficient for batch release testing alone, and a complete program for the control and monitoring of particulate matter remains an essential prerequisite. This includes dry sterile solids for injection when reconstituted as directed in the labeling. Other methods that have been demonstrated to achieve the same or better sensitivity for visible particulates may be used as an alternative to the one described below. Injections shall be clear and free from visible particulates when examined without magnification (except for optical correction as may be required to establish normal vision) against a black background and against a white background with illumination that at the inspection point has an intensity between 2000 and 3750 lux. This may be achieved through the use of two 15-W fluorescent lamps (e.g. F15/T8). The use of a high-frequency ballast to reduce flicker from the fluorescent lamps is recommended. Higher illumination intensity is recommended for examination of product in containers other than those made from clear glass. Before performing the inspection, remove any adherent labels from the container and wash and dry the outside. The unit to be inspected shall be gently swirled, ensuring that no air bubbles are produced, and inspected for approximately 5 s against each of the backgrounds. The presence of any particles should be recorded. For batch-release purposes, sample and inspect the batch using ANSI/ASQ Z1.4 (2008)[2] General Inspection Level II single sampling plans for normal inspection, AQL 0.65. Not more than the specified number of units contains visible particulates. For product in distribution, sample and inspect 60 units. Not more than one unit contains visible particulates.

PERSONNEL

Personnel responsible for detection of visible particulate matter must be thoroughly trained for this important quality evaluation. Training is not an easy task because of a variety of reasons: vision capabilities, concentration, sample standards of particulate types, inspection environment, and qualifications of the trainer(s).

The following sections will discuss current practices, procedures, issues and trends with respect to personnel training and qualification, inspection of different products, and establishment of inspection criteria and limits.

Training/Qualification of Inspectors

All inspectors should be trained and evaluated based on objective standards. Examples of acceptable and defective containers are very useful for training inspectors especially for defect types such as minor blemishes on a glass vial, which are very subjective. Regular inspectors as well as production representative or Quality Assurance personnel performing the inspection of statistical samples to verify inspection effectiveness should be trained in the same manner. Qualification of inspectors should be conducted at the same speed at which regular inspections will be carried out.

The human inspector determines the quality and success of the manual inspection process. Since the inspection process is subjective in nature, the main limitation of the process lies with restriction in the vision, attitude, and training of the individual inspector.

As a minimum standard, personnel assigned as inspectors should have good vision, corrected, if necessary, to acceptable standards. Inspectors should not be color-blind. Visual acuity should be tested at least on an annual basis.

Since the number and size of particles in parenteral solutions have become important characteristics to evaluate, it has been assumed that particles larger than 40 or 50 μm are detectable by the unaided eye. Thus, in complying with the USP requirements that any container showing visible evidence of particulate matter be rejected, it must be assumed that the average inspector will pass those solutions containing particles with a size > 40 μm. This, of course, presents some discomfort for those who believe that particulate matter, especially in the size range of 10 to 40 μm, is clinically hazardous.

[2] Two other inspection standards are MIL-STD-105E and ISO 2859-1 (1999).