MANUAL VISUAL INSPECTION FOR PARTICULATES IN SINGLE-USE SYSTEMS: METHOD DEVELOPMENT AND VALIDATION

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Single-use systems (SUS) are used not only in upstream and downstream processing of biopharmaceuticals, but also in critical applications such as final fill and finish, aseptic processing of vaccines, and cell and gene therapies. Typically, SUS are not rinsed prior to application. Especially for applications of SUS downstream of final filters, SUS cleanliness with respect to particulate matter is of high importance since particulates on the fluid-contacting surfaces could detach and directly end up in the final drug product.

Manufacturing of SUS occurs in a “clean-build” process within clean rooms. However, current SUS manufacturing technologies using cutting, welding and assembly processes often use manual labor and are not usually free of particulates. For the SUS supplier, an important part of the SUS manufacturing process is the final visual inspection of SUS for particulate matter and other defects. In addition, SUS end-users typically visually inspect SUS prior to implementation in biopharmaceutical processes.

Currently, most SUS manufacturers manually inspect components and assemblies for visible particle matter without a deep understanding of all the factors which may impact the probability of detection. Significant challenges arise in visual inspection due to the often large dimensions of assemblies, and due to challenges with translucent and turbid plastic materials. Visualization of particles on the interior fluid-contacting surfaces remains a significant challenge.

This presentation will show the results of the development and validation of a manual visual inspection method for loose particulates inside SUS. Carefully characterized test particles were seeded into single-use bag and tubing assemblies, and the probabilities of detection determined under controlled inspection conditions. The effect of particle size and particle type (black, clear, fiber), assembly type (bag, tubing), assembly size, lighting conditions and inspection timing were determined in designed experiments.

The particle size visible in an inspection of a small vial of final drug product is typically around 100 microns. However, we find that for the visual inspection of SUS under optimized conditions with well-trained inspectors, good detectability of black particles starts at around 500-1000 microns in size, whereas fibers are not reliably detected at 2000 microns in length.