PARTICULATE CONTAMINATION IN SINGLE USE SYSTEMS: MEASUREMENT CHALLENGES

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In conventional biopharmaceutical processes using stainless steel components, the pharmaceutical manufacturer is responsible for process cleanliness. However for single use systems, the pharmaceutical manufacturer “outsources” process cleanliness to the manufacturer of the single use systems, since no rinsing or cleaning occurs prior to implementation. Especially critical applications such as final fill and finish or aseptic processes demand a high degree of cleanliness with respect to particulate contamination. Although single use component assembly occurs in carefully controlled cleanroom environments, risks arise for particulate contamination from incoming components, cutting and welding operations, and human activity during manually intensive assembly processes.

While visual inspection may detect “visible” (> 100 microns) particles, the probability of detecting particles on fluid contacting surfaces within single use components remains low due to the difficulty of seeing through translucent or turbid plastics. Extraction (flushing, washing) of fluid contact surfaces allows collection of particles for quantitative microscopic analysis. While most single use manufacturers claim compliance with the USP 788 particles standard, USP 788 applies only to sub-visible particles in final injectable drug products, and does not describe particle extraction and counting methods for single use systems.

This presentation addresses the scientific and technical challenges found in the development of reliable methods for particulates contamination measurement in single use systems. Automated microscopy measurement of particles collected on filter membranes, or counting of particles dispersed in liquid are imperfect but widely accepted methods. The main challenge resides in development of robust extraction methods, especially for complex single use components. The highly developed “technical cleanliness” standards (ISO 16232) for automotive components provide some guidance. Studies comparing rinsing methods with agitation methods, and studies comparing different extraction fluids (solvents vs. aqueous media) highlight the challenges in the development of methods for measuring particulate contamination in single use systems.