Minimizing Particulate Contamination in Single-Use Systems for Biopharmaceutical and Pharmaceutical Industries

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INTRODUCTION

- Particulate contamination from single-use systems (SUS) for pharma/biopharma production can potentially impose negative risks for yield, purity, and patient health[1].
- Effective particulate contamination monitoring and control are important to minimize the risks.
- Pharmaceutical products need to meet USP <788> and USP <790> criteria to get FDA approval for patient use.
- Entegris' Liquid Particle Counting (LPC) systems can measure particle count with size down to 0.5 µm.
- Entegris' Aramus fluoropolymer SUS is much cleaner than other SUS with different materials.
- Entegris is positioned uniquely to provide both SUS with minimal particulate contamination and instruments to monitor particulate level in SUS.

WHY PARTICULATES MATTER

Process performance – **yield**

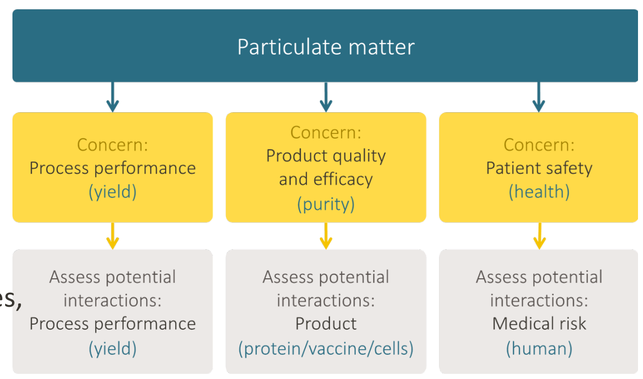
Product quality and efficacy – **purity**

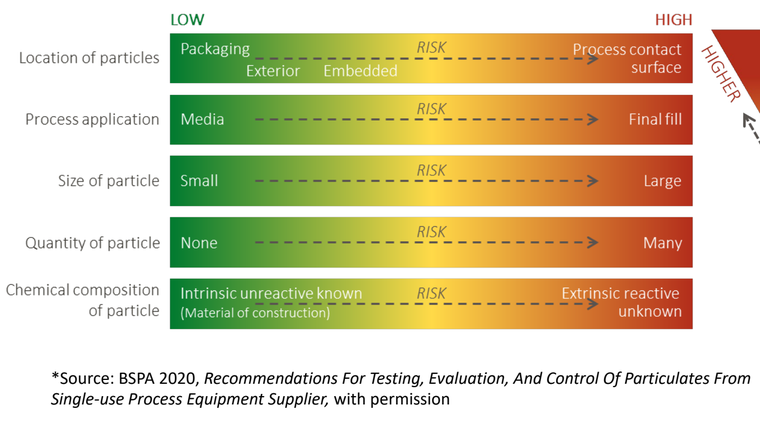
Patient safety – **health**

Harm = Impact of particulate matter

Particulate Matter = Extraneous particles, foreign particles

Risk of Harm = Probability of occurrence × Detectability × Severity of harm





*Source: BSPA 2020, *Recommendations For Testing, Evaluation, And Control Of Particulates From Single-use Process Equipment Supplier,* with permission

HOW TO MINIMIZE PARTICULATE CONTAMINATION

Quality by Design

- High-quality raw material with better particulate control
- Operator training for quality work
- In-process and lot release quality control (QC)
- ISO 9001 and ISO 13485 certification for quality management systems

Clean Manufacturing Environment

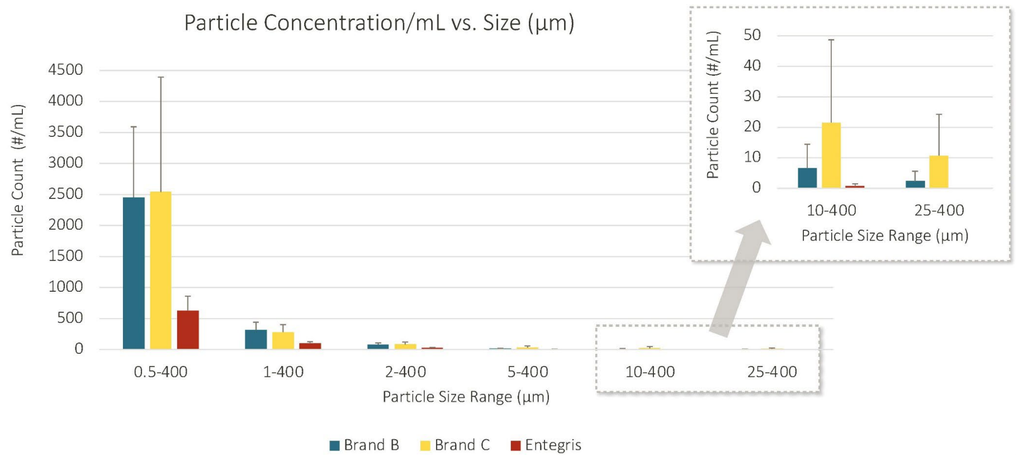
ISO 5 and ISO 7 clean room

Quality Control Testing

AccuSizer SPOS Systems, Entegris

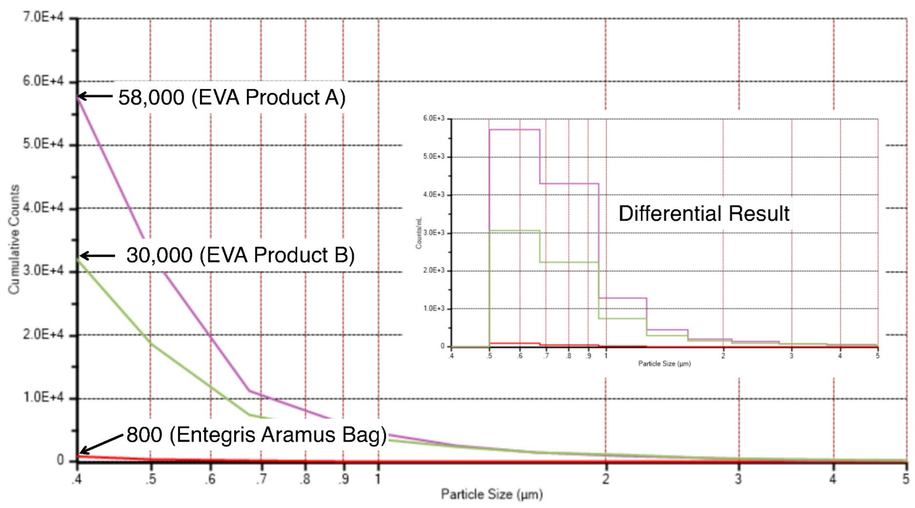
Nicomp Nano DLS/ZLS Systems, Entegris

ARAMUS SUS PARTICULATE TESTING & BENCHMARKING



- Aramus SUS passes USP <788> - Particulate matter in injections
- PE bag of Brand B and Brand C higher counts with large standard deviation, some fails USP <788> (inset)

Aramus Fluoropolymer Bag vs. EVA Bag



- Entegris Aramus bag has the lowest cumulative particulate counts with particulates/mL ≥ 0.5 µm
- Entegris Aramus SUS is 72X cleaner than EVA Product A, 38X cleaner than EVA Product B

CONCLUSION

- Entegris Life Sciences can leverage semiconductor purity and yield to biopharma/pharma manufacturing
- Entegris SUS products are manufactured in the cleanest environment
- Entegris' liquid particle counter AccuSizer SPOS system offers particulate monitoring down to 0.5 µm
- Aramus single-use systems has the lowest particulate counts comparing to market offerings of PE and EVA bags, especially down to 0.5 µm particle size

FUTURE WORK

- In-line monitoring of particulate size for LNP production
- Profiling of particulate contamination in SUS assembly together with different tubings and connectors
- Subvisible particulate contamination's impact on purity, yield and potency of loaded viral vector
- Subvisible particulate contamination's impact on purity, yield and potency of loaded lipid nanoparticle