# Aramus™ Single-Use Bag Particle Testing

*Particle count testing to assure surface cleanliness*

Cleanliness of parts or enclosures is important to avoid the presence of particulate contamination that can be detrimental to quality or performance. An accepted approach to determine cleanliness is the use of liquid particle counters to quantify size and count of particles in water after exposure to the part of interest. This application note explains the use of the Entegris AccuSizer™ (formerly known as Particle Sizing System AccuSizer) liquid particle counter to qualify the cleanliness of the Entegris Aramus single use 2D bag assemblies.

## INTRODUCTION

Single-use systems (SUS) or single-use technologies (SUT) are becoming more common and widely-accepted in bioprocessing, including downstream steps such as mixing, filling operations, and storage. As use increases in SUS/SUT components, so does the concern for purity levels in these components including the level of particulate contamination. No compendial or regulatory guidance has been written specifically addressing particulate levels in SUS/SUT components. Recently The Bio-Process Systems Alliance (BPSA) issued a useful document on this topic, *"The 2014 Particulates Guide: Recommendations for Testing, Evaluation and Control of Particulates from Single-Use Process Equipment"*.[1] The BPSA document addresses a range of relevant topics including:

- Why are particulates an issue with SUT?
- Why particles in SUT may be a contamination risk to:
  - the active ingredient and/or formulated product.
  - the biological cells which produce the product.
  - the patient who is treated with the product.
- How to control particulates during the manufacture of SUT?
- How to control particulates during the use of SUT?
- How to address situations when particulates are found in or attributed to SUT?

Under the topic of Liquid Measurement Methods the BPSA document states "Liquid measuring methods for free particles in SUT have evolved from those methods used for final formulation, e.g., USP <788>[2], because of the absence of a standard or another methodology for more appropriate assessment of the level of particles within the SUT."

## USP 788

Parenteral drugs administered by injection to patients should essentially be free of visible particles. USP test 788, Particulate Matter in Injections, dictates how to quantify subvisible particles present in injectable drugs and sets acceptable particle concentration limits. Subvisible particles in parenteral drugs are detected using a light obscuration particle counter, microscopic inspection on a filter, or both. The majority of all USP 788 tests are performed using an optical liquid particle counter such as the AccuSizer (Figure 1). The particle limits for large volume drugs (>100 mL) are less than 25 particles/mL >10 µm and less than 3 particles/mL >25 µm.

*Figure 1. The AccuSizer SIS system*

## ACCUSIZER SYSTEM

The AccuSizer A7000 SIS system available from Entegris is the most advanced instrument available for USP <788> testing. It meets or exceeds all requirements in USP <788> by providing size and count data at the required 10 and 25 µm and easily passes all system standardization tests described in USP <1788>.[3] The LE400 sensor measures from 0.5 – 400 µm, calculates results in up to 1024 size channels, and is operated by the AccuSizer software that automates both operation and reporting per USP 788.

## ARAMUS SINGLE-USE BAGS

The Aramus single-use 2D bags are made of a high-grade, gamma-stable fluoropolymer, providing higher purity, greater compatibility, and increased safety for critical process fluids and final products. With a new single-layer technology that contains no curing agents, antioxidants, plasticizers, or adhesives, the number of potential contaminants is greatly reduced. These assemblies offer the widest operating temperature range, making them more durable in frozen applications (to -85°C [-121°F] or lower) without negatively affecting the film. The configuration of Aramus bags is shown in Figure 2.

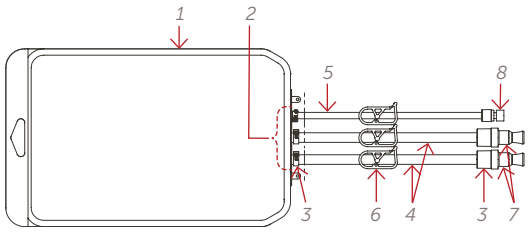


*Figure 2. Aramus bag configuration*

| Item | Description |
|---|---|
| 1 | Aramus fluoropolymer film with slot for hanging |
| 2 | Fluoropolymer "boat" fitment with three hose barb ports |
| 3 | Tubing connection (BarbLock® or Oetiker StepLess® clamp) |
| 4 | Tubing ¼" ID x ⅜" OD (platinum cured silicone or C-Flex® 374) |
| 5 | Tubing ⅛" ID x ¼" OD (platinum cured silicone or C-Flex 374) |
| 6 | Pinch clamps |
| 7 | CPC MPC male/female with plugs |
| 8 | Luer male/female with plugs |

### Particle Testing Procedure

The basic approach used to determine the particulate contamination level on a part or within an enclosure is to expose the part to clean water, add energy to remove particles from the device, and then measure the water using a liquid particle counter. The standard method for enclosure testing is "sloshing or swirling." In the case of testing Aramus bags, the bags are filled with clean water, placed on a 3D rocker (Figure 3) and agitated for a set amount of time.

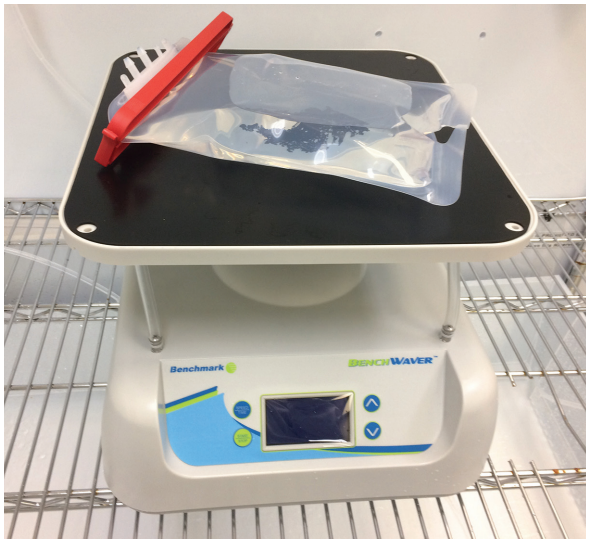


*Figure 3. Aramus bag on 3D rocker*

The procedure used is shown below:

1. Connect bag to test-system plumbing.
2. Flush process line with ultrapure water through a 0.45 µm filter, bypassing the single-use bag.
3. Pump ultrapure water through a 0.45 µm filter into the single-use bag.
4. Agitate the bag using the 3D rocker for two minutes.
5. Pull two 50 mL samples from the effluent stream to be subjected to USP <788> testing.
6. Repeat with next sample.

## RESULTS

The measurement noted in step 5 is made by the AccuSizer liquid particle counter. The Aramus single-use bags pass the USP 788 specifications of less than 25 particles/mL >10 µm and less than three particles/mL >25 µm. Multiple measurements are made on each sample to assure statistical accuracy and the average result is recorded.

## CONCLUSIONS

Entegris now owns both the ability to manufacture materials and components such as the Aramus single use bags along with the analysis technology and experience available through its acquisition of Particle Sizing Systems. This unique combination assures a complete microcontamination solution and a Pure Advantage to our customers.

## REFERENCES


[1] *The 2014 Particulates Guide: Recommendations for Testing, Evaluation and Control of Particulates from Single-Use Process Equipment*, available at: http://bpsalliance.org/technical-guides/

[2] USP 788, *Particulate Matter in Injections*, available at: http://www.usp.org/

[3] USP 1788, *Methods for the Determination of Particulate Matter in Injections and Ophthalmic Solutions*


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Entegris

Corporate Headquarters
129 Concord Road
Billerica, MA 01821
USA

Customer Service
Tel +1 952 556 4181
Fax +1 952 556 8022
Toll Free 800 394 4083