USP <788> Particulate Matter in Injections

AccuSizer® single particle optical sizing (SPOS)

OVERVIEW

The USP <788> Particulate Matter in Injections test is used to quantify the count and size of subvisible particles in parenteral drugs. The test calls for using a light obscuration particle counter and counting particles on a filter by microscopy. The Entegris AccuSizer® Syringe Injection System (SIS) is designed to meet and exceed all requirements in USP <788>.

Parenteral drugs administered by injection to patients should be essentially free of visible particles. Subvisible particles in parenteral drugs are detected using a light obscuration particle counter, microscopic inspection on a filter, or both. The system requirements for a light obscuration instrument used to comply with USP <788> include:

Technique: Light obscuration sensor with suitable sample feeding device.

Sensor: The concentration range should be greater than the concentration of the particles to be counted. The dynamic range must include the smallest size particle to be measured. The sensor must be calibrated for size at several points, verified for count efficiency, and tested for resolution.

Sampler: The sample volume accuracy must be within 5% of the appropriate sample volume for the test.

Reporting: Particle concentration greater than 10 and 25 µm.

The AccuSizer A2000 SIS (Figure 1) is specifically designed for customers performing USP <788> particle testing.

Figure 1. AccuSizer SIS system

The standard sensor used for USP <788> testing is the LE400 that measures from 0.5 – 400 µm at concentrations up to 10,000 particles/mL. This is a high resolution particle sizing sensor with a patented optical design. The sensor is coupled to the AccuSizer high resolution counter that contains over 512 size channels. Each sensor is calibrated with ten particle size standards across the entire range, and is validated for count efficiency at 15 µm.

The sensor resolution is typically less than 5%, much better than the 10% required in USP <788>. An example sensor resolution report from the automated software test is shown in Table 1.

Table 1. Sensor resolution report result

Sample	Nominal diameter	Nominal standard deviation	Low channel	Median channel	High channel	Sensor resolution
Sensor resolution test	10.000 µm	0.090 µm	9.728 µm	9.817 µm	9.996 µm	1.5 %

The AccuSizer A2000 SIS sampler is capable of delivering extremely accurate volumetric sample aliquots for applications ranging from USP <788> testing to protein aggregation studies at much lower sample volume (less than 150 µL).

The AccuSizer A2000 SIS is both a particle counter and a high resolution particle sizing instrument. It is the first fully automated single-particle sizer to provide high resolution particle size distributions without any assumptions concerning the shape of the distribution. The raw data reported by the instrument are particle counts versus size. Using simple statistics, the software can convert these data points into a host of other useful weighted distributions (i.e., volume, area, number, volume/surface, etc.) and provide accurate statistical information that is traceable to the raw data.

The AccuSizer is available with CFR 21 Part 11 compliant software that is very flexible and is designed to work with USP <788>. It contains an unlimited number of user defined recipes for experimental parameters with simple dialog boxes that define the types of samples and the size pass fail criteria. The users can use the standard USP <788> or their own internal tests for examining their samples. This flexibility is a very valuable tool when working on internal standards that meet or exceed the USP criteria.

The measurement protocol dialogs boxes are shown in Figures 2 and 3.

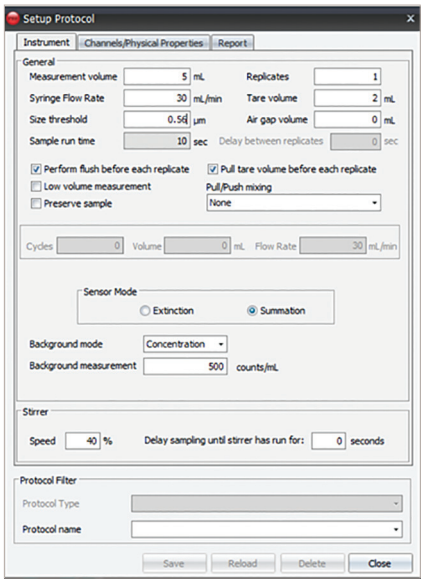

Figure 2. Setup protocol, instrument settings

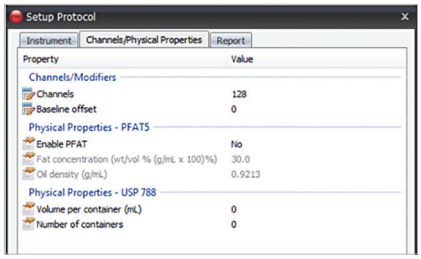

Figure 3. Setup protocol, channels/physical properties settings

When configured properly including entering the volume and number of containers the system can fully automate USP <788> testing and provide a complete report, including a pass or fail based on the appropriate criteria (Tables 2 and 3).

Table 2. USP <788> pass/fail criteria

	>10 microns	>25 microns
Small volume injections	6000	600 per container
Large volume injections	25	3 per mL

Table 3. USP <788> report

Sample	Run date/time	Containers (#)	Container volume (#)	Sample volume (mL)	≥10 µm (#)	≥10 µm (#/cont.)	≥25 µm (#)	≥25 µm (#/cont.)
SVIT3 Rep.2	14:01 02/13/2019	10	25.0	5.0	56	280	2	10
SVIT3 Rep.3	14:02 02/13/2019	10	25.0	5.0	49	245	2	10
SVIT3 Rep.4	14:03 02/13/2019	10	25.0	5.0	55	275	3	15
				Mean	53.3	266.6	2.3	11.6

Test criteria	Result
(Mean #/container ≥10 µm) ≤6000/container and (Mean #/container ≥25 µm) ≤600/container (Pass)	Pass

AUTOMATION

USP <788> testing can be fully automated using the AccuSizer Autosampler, Figure 4. Load the samples into the tray, program the system with the desired protocols and let the system process the entire tray automatically.

Figure 4. AccuSizer Autosampler

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