USP <789> Particulate Matter in Ophthalmic Solutions

AccuSizer® SPOS

The USP <789> Particulate matter in ophthalmic solutions test is used to quantify the count and size of subvisible particles in eye care products. The test calls for using a light obscuration particle counter and counting particles on a filter by microscopy. This application note describes the required tests and shows how the Entegris AccuSizer® A7000 SIS system is designed to meet, and exceed, all requirements in USP <789>.

Ophthalmic solutions should essentially be free of visible particles. Subvisible particles that are present in these solutions can be detected using two approaches. Stage 1: uses light obscuration (the AccuSizer) to count and size the particles. If the stage 1 test fails, then the sample must pass the microscopic procedure (Stage 2) that has its own set of limits. Sampling plans must be based on factors, such as product volume, historic count data, count variability between units, and size distribution of the particles present.

The system requirements for a light obscuration instrument used to comply with USP <789> are essentially the same as USP <788> and 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 ≥10 and 25 µm.

The AccuSizer A7000 SIS syringe injection sampler, manufactured by particle sizing systems is specifically designed for customers performing USP <789> and <788> particle testing.

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, unlike classical contamination monitoring systems which have 6 or 8 size classification channels. Each sensor is calibrated with ten particle size standards across the entire range and is validated for count efficiency at 15 µm.

The resolution is typically 5%, much better than the 10% required in USP <788>. The AccuSizer A7000 SIS sampler is capable of delivering extremely accurate volumetric sample aliquots for applications ranging from USP <789> testing to protein aggregation studies at much lower sample volume (~150 µL).

INTERPRETATION

The ophthalmic solution passes the USP <789> test if the average number of particles present in the units tested does not exceed the appropriate values listed in Table 1.

Diameter	≥10 µm	≥25 µm
Number of particles	50/mL	5/mL

Table 1. Count limits for USP <789>

EXPERIMENTAL

Two ophthalmic "red eye" solutions were purchased at a local pharmacy in Port Richey, FL, USA. One will be called the "Brand" and the other "Generic". Both bottles contained 30 mL of solution.

A test protocol was programmed into the A7000 to make three measurements of 5 mL for each sample. The first analysis was not used, and the second and third were reported at ≥10 and ≥25 µm. The results from the Brand and Generic sample analyses are shown in Figures 1 and 2. All easily pass the USP <789> limits.

Sample	Run Date/Time	Sample Volume (mL)	≥ 10 um (#/mL)	≥ 25 um (#/mL)
Brand Red Eye Rep. 2	02/23/2017 10:37	5.0	11	0
Sample	Run Date/Time	Sample Volume (mL)	≥ 10 um (#/mL)	≥ 25 um (#/mL)
Brand Red Eye Rep. 3	02/23/2017 10:38	5.0	10	0

Figure 1. Brand red eye results

Sample	Run Date/Time	Sample Volume (mL)	≥ 10 um (#/mL)	≥ 25 um (#/mL)
Generic Red Eye Rep. 2	02/23/2017 11:02	5.0	5	0
Sample	Run Date/Time	Sample Volume (mL)	≥ 10 um (#/mL)	≥ 25 um (#/mL)
Generic Red Eye Rep. 3	02/23/2017 11:03	5.0	8	0

Figure 2. Generic red eye results

The Brand sample was then spiked with 20 µL of a PSL standard from Micro Measurement Labs that had previously been used to check the calibration of the sensor at 10, 25 and 50 µm. This result shown in Figure 3 fails the USP <789> limits.

Sample	Run Date/Time	Sample Volume (mL)	≥ 10 um (#/mL)	≥ 25 um (#/mL)
Brand Spiked Rep. 2	02/23/2017 11:43	5.0	176	57

Figure 3. Brand spiked with PSL standard

CONCLUSIONS

The AccuSizer A7000 SIS Syringe Injection Sampler surpasses all requirements defined in USP <789> for ophthalmic solutions. The AccuSizer software platform is the most advanced package for performing these tests and will continue to support future requirements. This system can also be integrated with the Autosampler (Figure 4) for automated batch sampling of up to 60 samples/tray. Dual trays are also available.

Figure 4. Autosampler integrated with the AccuSizer A7000 SIS sampler

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