NAMSA

Particulate Analysis

Particulate Matter consists of particles that will not dissolve in solution (other than gas bubbles), unintentionally present on the device or in the solution. Particulate can come from many sources in the processing. Limits for injectable solutions can be found in the appropriate pharmacopeia (EP, USP, JP, etc.). There are a few procedures for medical devices in other standards (examples are in the reference section), but traditionally, the majority of devices do not have specific procedures for testing or proposed limits. In 2010, a new standard was released, AAMI/TIR 42, Evaluation of Particulates Associated with Vascular Medical Devices.

The purpose of the testing is to determine the quantity and size of particles on the device or in the solution. With the addition of TIR 42, the importance not only of the size of the particulates is a focus, but also the shape, identification and quantity.

Testing is performed in injections, parenteral infusions, and medical devices. Since there is no one test method for testing parenteral products or medical devices, NAMSA prepares a test specification for every sample tested. This may be set up in advance of the sample arriving. When performing particulate analysis consider how manufacturing, sterilization, shipping and distribution, packaging, shelf storage and use with other devices effects the particulate levels of the device.

Methods

For injectable (parenteral) products, testing is performed according to USP procedures unless otherwise specified. For devices, the solution is analyzed for particulate matter according to USP procedures unless otherwise specified. If a special procedure, ISO, EP, JP, particulate test is needed, please inquire.

There are two methods to analyze particulate matter according to USP <788> Injections and <789> Ophthalmic Solutions, the Light Obscuration Method and the Microscopic Method. The USP states that the Light obscuration method is to be preferably applied. If limits are not met or the product cannot be tested using this method (examples: solution is colored, too viscous and cannot be diluted, etc.), the microscopic method may be used or test using both methods to reach a conclusion about the number of particles in the solution.

Light Obscuration Method: This method analyzes the device rinse solution or injectable product using a light obscuration particulate analyzer. Four (4), 5 ml portions of the extract are analyzed by the instrument; the data from the first count is discarded. The second through fourth count is averaged and then compensated for the entire extract (or reported in particles per ml). The advantage to this method is that it is a quick easy method to count particulate and it can count high amounts of particulate in the solution. A minimum of 25 mL of solution is required to perform this method.

Microscopic Method: This method filters the device rinse solution or injectable product through a 0.8 µm grey gridded filter. The filter is then counted microscopically at 100x to determine the number of particles. This method counts particles in the entire test solution. The disadvantages are that if there are too many particles, they cannot be counted or only a partial count is performed. The test is more labor intensive, and therefore has a longer turn around time and is more expensive than light obscuration.

The data from the Microscopic Method tends to be lower, so the pharmacopeia makes up for the difference by having lower limits for the microscopic method. Both methods count particles greater than 10 µm and greater than 25 µm (and greater than 50 µm for USP <789 Ophthalmic Solutions). Note that other sizes may be counted upon request.

Since procedures for testing devices are not covered in the USP, it is up to the sponsor to determine the method of testing and the procedure to remove the particulate from the device. Some procedures include: flushing, filling, covering, sonicating, rinsing, etc.).

Identification

The identity of the particulates and potential source of matter may be an important consideration when investigating or characterizing particulate matter on a medical device. It might be important to consider the identity, source, and potential toxicity of each type of particulate as well as the sizes, shapes, and quantities of particulates. It is not expected that all particles need to be identified, but efforts at identification should be undertaken when appropriate, e.g., when particulate levels have exceeded limits, and as necessary to better derive the source of particles.

References

United States Pharmacopeia, General Chapter <788> Particulate Matter in Injections

United States Pharmacopeia, General Chapter <789>, Particulate Matter in Ophthalmic Solutions

European Pharmacopeia, Section 2.9.19 Particulate Contamination: Sub-Visible Particles

ISO 14708-1, Implants for surgery - Active implantable medical devices - Part 1: General requirements for safety, marking and for information to be provided by the manufacturer", Section 14.2

EN 45502-01, Active Implantable Medical Devices - Part 1: General requirements for safety, marking and information to be provided by the manufacturer, Section 14.2

EN 45502-2-1, Active Implantable Medical Devices - Part 2-1 Particular requirements for active implantable medical devices intended to treat bradyarrhythmia (cardiac pacemakers), Section 14.2

AAMI/TIR 42, Evaluation of Particulates Associated with Vascular Medical Devices

ISO 15798 Ophthalmic implants – Ophthalmic viscosurgical devices

ISO 16671 Ophthalmic implants – irrigating solutions for ophthalmic surgery

ISO 8536-4 Infusion equipment for medical use – Part 4: Infusion sets for single use, gravity feed

ISO 1135-4 Transfusion equipment for medical use- Part 4: Transfusion sets for single use

Particle free containers: www.epscientific.com/product/overview-cep.aspx

VWR TraceClean Environmental Sample Containers: www.vwrsp.com/literature/products/pdf/92526.pdf

MDDI, October 2006, Sample Size Selection Using a Margin of Error Approach, http://www.devicelink.com/mddi/archive/06/10/002.html.

National Institute of Standards and Technology, Selecting Sample Sizes, http://www.itl.nist.gov/div898/handbook/ppc/section3/ppc333.htm.

NAMSA

USA Coporate Headquarters

6750 Wales Rd
Northwood, Ohio 43619
T 866.666.9455 (Toll Free)
F 419.662.4802
www.namsa.com