4206 Determination of Particulate Matter for Pharmaceutical Packaging Materials and Containers

The test for particulate matter is applied to determine the size and number of particulate matter in drug packaging materials. It is applied to determine the size and number of particulate matter in rubber closures for injections, plastic containers for injections, plastic components for injections (inner caps and interfaces), plunger stopper for prefilled syringes and pen-injectors, sub-assembled prefilled syringes, cartridge systems for prefilled pen-injectors, metal components for pharmaceutical packaging (inhalation canisters, aerosols and soft tubes), etc.

This test consists of light obscuration and microscopic test. If the test result using light obscuration test dose not comply with the requirements or this test is not applicable for the sample, microscopic test should be followed to reach a conclusion on conformance to requirements.

Test environment, measurement principles of light obscuration and microscopic test, test apparatus and instrument calibration are the same as those in general chapter 0903 Test for Particulate Matter in Injections.

Method 1 Light obscuration particle count test

(1) Rubber closures for injections: Take several rubber closures (with a total surface area of approximately 100cm^2) to be tested, put them in a conical flask with a volume of 250mL, place a volume of particle-free water(the ratio of the volume of particle-free water to the total surface area of rubber closures is 1:1), cover the conical flask use aluminum foil (or other suitable sealing material) and place it in an oscillator(horizontal circular rotation, oscillation diameter 12mm±1mm, oscillation frequency 300 rpm±10 rpm) for 20s, carefully remove the aluminum foil (or other suitable sealing material), pour a portion of specimen to wash the bottleneck and sample container, transfer the specimen in the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots, each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

(2) Plastic containers for injections: Non-BFS plastic bottles and bags for injection: Take a number of samples to be tested, place the marked amount of particle-free water into the test sample. Fill, seal and sterile according to the product process, and wash the outside walls of the test sample being examined with water; BFS plastic bottles and plastic ampoules for injection: Take a number of samples filled with particle-free water to be tested, wash the outside walls of the test sample being examined with water, mix the contents by inverting the container 20 times and carefully open the container immediately, pour a portion of specimen to wash the bottleneck and sample container, transfer the specimen in the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots , each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

Note: If applicable, the finished product can be directly tested.

（3）Plastic components for injections (inner caps and interfaces): Take 5 plastic

components being examined into a conical flask with a volume of 250ml or other appropriate test containers, add 250ml of particle-free water into the test containers for particle inspection, cover the conical flask use aluminum foil (or other suitable sealing material) and place it in an oscillator(horizontal circular rotation, oscillation diameter 12mm±1mm, oscillation frequency 300 rpm±10 rpm) for 20s, carefully remove the aluminum foil (or other suitable sealing material), pour a portion of specimen to wash the bottleneck and sample container, transfer the specimen in the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots , each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

（4）Plunger stopper for prefilled syringes and pen-injectors: Take several plunger stopper for prefilled syringes and pen-injectors(with a total surface area of approximately 50cm^2) to be tested, put them into a conical flask with a volume of 250ml, place a volume of particle-free water(the ratio of the volume of particle-free water to the total surface area of rubber closures is 1:1), cover the conical flask use aluminum foil (or other suitable sealing material) and place it in an oscillator(horizontal circular rotation, oscillation diameter 12mm±1mm, oscillation frequency 300 rpm ±10 rpm), shake for 20s, carefully remove the aluminum foil (or other suitable sealing material), pour a portion of specimen to wash the bottleneck and sample container, transfer the specimen in the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots, each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

（5）Sub-assembled prefilled syringes: Take several sub-assembled prefilled syringes to be tested, filling the sample with the marked amount of particle-free water, mix the contents by inverting the container 20 times, shake the contents during inverting to suspend the particles. Remove the tip cap/needle shield of the syringes, press the plunger stopper with rod to transfer the contents of syringes into the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots, each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

（6）Cartridge systems for prefilled pen-injectors: Take several cartridge systems for prefilled pen-injectors to be tested, filling the sample with the marked amount of particle-free water. If the cartridge is sterile, fill one end of the cartridge with clean disc or plunger, then fill the other end with clean disc or plunger after filling. If the cartridge is pre-plungered and sterile, fill the cartridge with clean disc. If the cartridge is pre-capped and sterile, fill the cartridge with clean plunger. Mix the contents by inverting the container 20 times, shake the contents during inverting to suspend the particles. Open the cartridge systems with a proper approach to reduce the risk of cross-contamination, transfer the contents of syringes into the sample container, degas by allowing to stand for 15 minutes or an appropriate time, swirl gently by hand to disperse evenly, withdraw a minimum of three aliquots, each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

(7) Metal components for pharmaceutical packaging (inhalation canisters, aerosols and soft tubes): Take several samples to be tested, clean the outer surfaces of the samples using a jet of particle-free water, fill each sample with the marked amount of particle-free water, swirl gently by hand to disperse evenly. For small-volume containers, e.g. less than 25ml in volume, the contents of sufficient units are combined in a cleaned container to obtain three test contents. For samples with a capacity of > 25ml, test at least 3 individual units. Eliminate gas bubbles by appropriate measures such as allowing to stand for 15 min or an appropriate time or sonicating. Withdraw a minimum of three aliquots, each not less than 5ml in volume, record the data, discard the data from the first portion of each specimen, calculate the average of consecutive counts.

Method 2 Microscopic test particle count test

（1）Rubber closures for injections:

a. Place a number of rubber closures being examined (with a total surface area of approximately 100cm^2) into a conical flask with a volume of 250ml, place a volume of particle-free water(the ratio of the volume of particle-free water to the total surface area of rubber closures is 1:1) , cover the conical flask use aluminum foil (or other suitable sealing material) and place it in an oscillator(horizontal circular rotation, oscillation diameter 12mm±1mm, oscillation frequency 300 rpm ±10 rpm), shake for 20s, carefully remove the aluminum foil (or other suitable sealing material), specimen test solution for further testing.

b. Transfer 25ml of specimen to the pretreated filter gently along the inner walls of the filter, filter under gentle suction (transfer in batches when the volume of the specimen is greater than the filter). Release the vacuum and wash the inner walls of the filter with 25 mL of water for particle-free water, remove the washing by suction, release the vacuum and remove the membrane with the forceps. Place the membrane on a Petri slide, using a very thin layer of glycerine, if necessary, to hold the membrane flat and in its place. Allow the membrane to dry and place the covered slide on the micrometer stage of the microscope. Examine the membrane under 100× or other suitable magnification with the incident light at a suitable angle and adjust the microscope to see the grid clearly. Count the number of particles, repeat the entire operation twice, calculate the average of two determined data.

（2）Plastic containers for injections: Prepare specimen as directed under procedure （2）in light obscuration particle count test, proceed as directed for procedure（1）b.

Note: If applicable, the finished product can be directly tested.

（3）Plastic components for injections (inner cap and interfaces): Prepare specimen as directed under procedure（3）in light obscuration particle count test, proceed as directed for procedure（1）b.

（4）Plunger stopper for prefilled syringes and pen-injectors: Prepare specimen as directed under procedure（4）in light obscuration particle count test, proceed as directed for procedure（1）b.

（5）Sub-assembled prefilled syringes: Prepare specimen as directed under procedure（5）in light obscuration particle count test, proceed as directed for procedure

（1）b.

（6）Cartridge systems for prefilled pen-injectors: Prepare specimen as directed under procedure（6）in light obscuration particle count test, proceed as directed for procedure（1）b.

（7）Metal components for pharmaceutical packaging (inhalation canisters, aerosols and soft tubes): Prepare specimen as directed under procedure（7）in light obscuration particle count test, proceed as directed for procedure（1）b.

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