Microcrystalline Cellulose

Add the following:

▲Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (•◆•) to specify this fact.▲ NF 1-Dec-2019

Cellulose [9004-34-6].

DEFINITION

Microcrystalline Cellulose is purified, partially depolymerized cellulose prepared by treating alpha cellulose, obtained as a pulp from fibrous plant material, with mineral acids.

IDENTIFICATION

Add the following:

▲[NOTE—Compliance is determined by meeting the requirements of *Identification A*, *B*, and *C*.]▲ NF 1-Dec-2019

Add the following:

▲• **A. INFRARED ABSORPTION** ⟨197K⟩ or ⟨197A⟩**:** [NOTE—Disregard any peak between 800 and 825 cm^{-1} as well as those between 950 and 1000 cm^{-1}.]▲ NF 1-Dec-2019

Change to read:

▲• **B.**▲ NF 1-Dec-2019

Iodinated zinc chloride solution: Dissolve 20 g of zinc chloride and 6.5 g of potassium iodide in 10.5 mL of water. Add 0.5 g of iodine, and shake for 15 min.

Sample: 10 mg

Analysis: Place the *Sample* on a watch glass, and disperse in 2 mL of *Iodinated zinc chloride solution*.

Acceptance criteria: The substance takes on a violet-blue color.

Change to read:

▲• **C.**▲ NF 1-Dec-2019

Sample: 1.3 g of Microcrystalline Cellulose, accurately weighed to 0.1 mg

Analysis: Transfer the *Sample* to a 125-mL conical flask. Add 25.0 mL of water and 25.0 mL of 1.0 M cupriethylenediamine hydroxide solution. Immediately purge the solution with nitrogen, insert the stopper, and shake on a wrist-action shaker, or other suitable mechanical shaker, until completely dissolved. Transfer an appropriate volume of the sample solution to a calibrated number 150 Cannon-Fenske, or equivalent, viscometer. Allow the solution to equilibrate at 25 ± 0.1° for NLT 5 min. Time the flow between the 2 marks on the viscometer, and record the flow time, t_1, in seconds. Calculate the kinematic viscosity, $(KV)_1$, of Microcrystalline Cellulose taken:

$$\text{Result} = t_1 \times k_1$$

t_1 = flow time (s)
k_1 = viscometer constant (see *Viscosity—Capillary Methods* ⟨911⟩)

Obtain the flow time, t_2, for 0.5 M cupriethylenediamine hydroxide solutions using a number 100 Cannon-Fenske, or equivalent, viscometer. Calculate the kinematic viscosity, $(KV)_2$, of the solvent:

$$\text{Result} = t_2 \times k_2$$

t_2 = flow time for 0.5 M cupriethylenediamine hydroxide solutions (s)
k_2 = viscometer constant

Determine the relative viscosity, η_{rel}, of the Microcrystalline Cellulose specimen taken:

$$\text{Result} = (KV)_1/(KV)_2$$

$(KV)_1$ = kinematic viscosity of Microcrystalline Cellulose taken
$(KV)_2$ = kinematic viscosity of the solvent

Determine the intrinsic viscosity, $[\eta]_c$, by interpolation, using the *Intrinsic Viscosity Table* in the *Reference Tables* section.

Calculate the degree of polymerization, *P*:

$$\text{Result} = [(95) \times [\eta]_c/\{W_S \times [(100 - \%\text{LOD})/100]\}$$

$[\eta]_c$ = intrinsic viscosity
W_S = weight of Microcrystalline Cellulose taken (g)
%LOD = value obtained from the test for *Loss on Drying*

Acceptance criteria: The degree of polymerization is NMT 350.

IMPURITIES

INORGANIC IMPURITIES

• **Residue on Ignition** ⟨281⟩**:** NMT 0.1%

SPECIFIC TESTS

• **MICROBIAL ENUMERATION TESTS** ⟨61⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** The total aerobic microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g. It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and for the absence of *Escherichia coli* and *Salmonella species*.

• **CONDUCTIVITY**

Sample: 5 g

Analysis: Shake the *Sample* with 40 mL of water for 20 min, and centrifuge. Retain the supernatant for use in the *pH* test. Using an appropriate conductivity meter that has been standardized with a potassium chloride conductivity calibration standard having a conductivity of 100 µS/cm, measure the conductivity of the supernatant after a stable reading is obtained, and measure the conductivity of the water used to prepare the test specimen.

Acceptance criteria: The conductivity of the supernatant does not exceed the conductivity of the water by more than 75 µS/cm.

• **PH** ⟨791⟩**:** 5.0–7.5 in the supernatant obtained in the *Conductivity* test

Change to read:

• **LOSS ON DRYING** ⟨731⟩

Analysis: Dry a sample at 105° for 3 h.

Acceptance criteria: NMT 7.0%▲•◆• NF 1-Dec-2019 or some other lower percentage, or is within a percentage range, as specified in the labeling▲◆▲ NF 1-Dec-2019

• **BULK DENSITY**

Analysis: Use a volumeter that has been fitted with a 10-mesh screen. The volumeter is freestanding of the brass or stainless steel cup, which is calibrated to a capacity of

25.0 ± 0.05 mL and has an inside diameter of 30.0 ± 2.0 mm. Weigh the empty cup, position it under the chute, and slowly pour the powder from a height of 5.1 cm (2 in) above the funnel through the volumeter, at a rate suitable to prevent clogging, until the cup overflows. [NOTE—If excessive clogging of the screen occurs, remove the screen.] Level the excess powder, and weigh the filled cup. Calculate the bulk density by dividing the weight of the powder in the cup by the volume of the cup.

Acceptance criteria: The bulk density is within the labeled specification.

Change to read:

- ▲◆▲ NF 1-Dec-2019**PARTICLE SIZE DISTRIBUTION**

[NOTE—In cases where there are no functionality-related concerns regarding the particle size distribution of the article, this test may be omitted.]

Where the labeling states the particle size distribution, determine the particle size distribution as directed in *Particle Size Distribution Estimation by Analytical Sieving* ⟨786⟩, or by a suitable validated procedure.▲◆▲ NF 1-Dec-2019

- **WATER-SOLUBLE SUBSTANCES**

Sample: 5.0 g

Analysis: Shake the *Sample* with 80 mL of water for 10 min, and pass with the aid of a vacuum through filter paper (Whatman No. 42 or equivalent) into a vacuum flask. Transfer the filtrate to a tared beaker, evaporate to dryness without charring, dry at 105° for 1 h, cool in a desiccator, and weigh.

Acceptance criteria: The difference between the weight of the residue and the weight obtained from a blank determination does not exceed 12.5 mg (0.25%).

- **ETHER-SOLUBLE SUBSTANCES**

Sample: 10.0 g

Analysis: Place the *Sample* in a chromatographic column having an internal diameter of about 20 mm, and pass 50 mL of peroxide-free ether through the column. Evaporate the eluate to dryness in a previously dried and tared evaporating dish with the aid of a current of air in a fume hood. After all the ether has evaporated, dry the residue at 105° for 30 min, cool in a desiccator, and weigh.

Acceptance criteria: The difference between the weight of the residue and the weight obtained from a blank determination does not exceed 5.0 mg (0.05%).

ADDITIONAL REQUIREMENTS

Change to read:

- ▲◆▲ NF 1-Dec-2019**PACKAGING AND STORAGE:** Preserve in tight containers.▲◆▲ NF 1-Dec-2019

Change to read:

- ▲◆▲ NF 1-Dec-2019**LABELING:** The labeling indicates the nominal loss on drying, bulk density, and degree of polymerization values. Degree of polymerization compliance is determined using *Identification* ▲*C.*▲ NF 1-Dec-2019 Where the particle size distribution is stated in the labeling, proceed as directed in the test for *Particle Size Distribution*. The labeling indicates with which technique the particle size distribution was determined if a technique other than analytical sieving was used; and the labeling indicates the d_{10}, d_{50}, and d_{90} values and the range for each.▲◆▲ NF 1-Dec-2019

Add the following:

▲• **USP REFERENCE STANDARDS** ⟨11⟩

USP Microcrystalline Cellulose RS
▲ NF 1-Dec-2019