IDENTIFICATION

• **A. Infrared Absorption** ⟨**197K**⟩**:** Do not dry specimens.

ASSAY

• **Phthalyl Content**

Sample solution: Transfer 1 g to a conical flask, dissolve in 50 mL of a mixture of alcohol and acetone (3:2), and add phenolphthalein TS.

Analysis: Titrate the *Sample solution* with 0.1 N sodium hydroxide VS. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩).

Calculate the percentage of phthalyl on the acid-free basis:

$$\text{Result} = \{[(1.491 \times A/W) - (1.795 \times B)]/(100 - B)\} \times 100$$

A = volume of 0.1 N sodium hydroxide consumed, corrected for the blank (mL)
W = weight of Cellacefate taken, calculated on the anhydrous basis (g)
B = percentage of acid found in the test for *Limit of Free Acid*

Acceptance criteria: 30.0%–36.0% of phthalyl ($C_8H_5O_3$) on the anhydrous, acid-free basis

• **Content of Acetyl**

Sample solution: Transfer 100 mg to a glass-stoppered flask, and add 25.0 mL of 0.1 N sodium hydroxide VS. Connect the flask to a reflux condenser, and reflux for 30 min. Cool, and add phenolphthalein TS.

Analysis: Titrate the *Sample solution* with 0.1 N hydrochloric acid VS. Perform a blank determination (see *Titrimetry* ⟨541⟩).

Calculate the free and combined acids as acetyl:

$$\text{Result} = 0.4305 \times (A/W)$$

A = volume of 0.1 N sodium hydroxide consumed, corrected for the blank (mL)
W = weight of Cellacefate taken, calculated on the anhydrous basis (g)

Calculate the percentage of acetyl on the acid-free basis:

$$\text{Result} = \{[(P - 0.5182 \times B)/(100 - B)] - (0.5772 \times C)\} \times 100$$

P = free and combined acids, as acetyl
B = percentage of acid found in the test for *Limit of Free Acid*
C = percentage of phthalyl found in the test for *Phthalyl Content*

Acceptance criteria: 21.5%–26.0% of acetyl (C_2H_3O) on the anhydrous, acid-free basis

IMPURITIES

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

• **•Heavy Metals,** *Method II* ⟨**231**⟩**:** NMT 10 µg/g•

• **Limit of Free Acid**

Sample solution: Transfer 3.0 g to a glass-stoppered flask, add 100 mL of dilute methanol (1 in 2), insert the stopper in the flask, and shake for 2 h. Filter, and wash the flask and the filter with two 10-mL portions of the methanol solution, adding the washings to the filtrate.

Analysis: Titrate the combined filtrate and washings from the *Sample solution* with 0.1 N sodium hydroxide VS to a phenolphthalein endpoint. Perform a blank determination on 120 mL of the dilute methanol (1 in 2) (see *Titrimetry* ⟨541⟩).

Calculate the percentage of free acid, B:

$$\text{Result} = 0.8306 \times A/W$$

A = volume of 0.1 N sodium hydroxide consumed, corrected for the blank (mL)
W = weight of Cellacefate taken, calculated on the anhydrous basis (g)

Acceptance criteria: NMT 3.0%, calculated as phthalic acid

SPECIFIC TESTS

• **Water Determination,** *Method I* ⟨**921**⟩

Sample: 0.5 g

Analysis: Dissolve the *Sample* in a mixture of dehydrated alcohol and methylene chloride (3:2) instead of methanol as the solvent.

Acceptance criteria: NMT 5.0%

• **Viscosity—Capillary Viscometer Methods** ⟨**911**⟩

Sample: 15 g, calculated on the anhydrous basis

Analysis: Dissolve the *Sample* in 85 g of a mixture of 249 parts of anhydrous acetone and 1 part of water, by weight.

Acceptance criteria: The apparent viscosity (see *Viscosity—Capillary Viscometer Methods* ⟨911⟩, *Method I*) is between 45 and 90 centipoises, determined at 25 ± 0.2°.

ADDITIONAL REQUIREMENTS

• **•Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨**11**⟩

USP Cellacefate RS•

Microcrystalline Cellulose

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

• **A. Procedure**

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.

• **B. Procedure**

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 two marks on the viscometer, and record the flow time, t_1, in s.

Calculate the kinematic viscosity, $(KV)_1$, of the Microcrystalline Cellulose taken:

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

t_1 = flow time (s)
k_1 = viscometer constant (see *Viscosity—Capillary Viscometer 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 the 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:

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

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

Acceptance criteria: The degree of polymerization is not greater than 350.

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Heavy Metals,** *Method II* **⟨231⟩:** NMT 10 ppm

SPECIFIC TESTS

- **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 1000 cfu/g, and the total combined molds and yeasts count does not exceed 100 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
- **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 7.0% of its weight, or some other lower percentage, or is within a percentage range, as specified in the labeling.
- **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.
- **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.
- **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

- **Packaging and Storage:** Preserve in tight containers.
- **Labeling:** The labeling indicates the nominal loss on drying, bulk density, and degree of polymerization values. Degree of polymerization compliance is determined using *Identification* test *B*. 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.

Microcrystalline Cellulose and Carboxymethylcellulose Sodium

DEFINITION

Microcrystalline Cellulose and Carboxymethylcellulose Sodium is a colloid-forming, attrited mixture of Microcrystalline Cellulose and Carboxymethylcellulose Sodium. It contains NLT 75.0% and NMT 125.0% of the labeled amount of carboxymethylcellulose sodium, calculated on the dried basis. The viscosity of its aqueous dispersion of percent by weight stated on the label is NLT 60.0% and NMT 140.0% of that stated on the label in centipoises.

IDENTIFICATION

- **A.**
  Sample: 6 g
  Analysis: Mix the *Sample* with 300 mL of water in a blender at 18,000 rpm for 5 min.
  Acceptance criteria: A white, opaque dispersion is produced that does not settle on standing.
- **B.**
  Sample: The dispersion obtained in *Identification* test *A*
  Analysis: Add several drops of the *Sample* to a solution of aluminum chloride (100 mg/mL).
  Acceptance criteria: Each drop forms a white, opaque globule that does not disperse on standing.