BRIEFING

Powdered Cellulose, *NF 22* page 2847 and page 1307 of *PF* 29(4) [July–Aug. 2003]. The United States Pharmacopeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for the *Powdered Cellulose* monograph, as part of the process of international harmonization of monographs and general analytical methods of the European, Japanese, and United States pharmacopeias. The following monograph, which represents the **ADOPTION STAGE 6** document, is based on the corresponding monograph for *Powdered Cellulose* that was prepared by the U.S. Pharmacopoeia. This draft was based in part on comments from the European and Japanese Pharmacopoeias in response to the Provisional Harmonized Text Stage 5A and 5B drafts.

Pharmacopeial Discussion Group Sign-Off Document

Attributes	EP	JP	USP
Definition	+	+	+
Labeling	–	+	+
Identification A	+	+	+
Identification B	+	+	+
pH	+	+	+
Loss on drying	+	+	+
Residue on ignition	+	+	+
Water-soluble substances	+	+	+
Ether-soluble substances	+	+	+

Legend: + will adopt and implement; – will not stipulate.

Nonharmonized attributes: Identification C—Dispersion test (JP); Characters, Heavy metals, Microbial limits, Packaging and storage.

Specific local attributes: USP: Organic volatile impurities.

Reagents and reference materials: Each pharmacopeia will adapt the text to take account of local reference materials and reagent specifications.

Differences between the **ADOPTION STAGE 6** document and the current *NF* monograph include the following:

1. Definition—No change.
2. *Packaging and storage*— No change.

3. *Labeling*— No change.
4. *Identification* test *B*— This test is deleted. The former test *C* is now labeled as test *B*. The deleted test is considered a functionality-related test, which is not appropriate for Harmonization.
5. *Identification* test *C*— Now labeled as *Identification* test *B*. The lower limit for the degree of polymerization is deleted, as are requirements to be within the labeled specification.
6. *Microbial limits*— No change.
7. *pH*— No change.
8. *Loss on drying*— The limit is increased to 6.5% from 6.0% to conform to EP and JP standards. The drying time is increased from 2 hours to 3 hours.
9. *Residue on ignition*— The addition of sulfuric acid is allowed. The limit has not changed.
10. *Water-soluble substances*— No change.
11. *Ether-soluble substances*— No change.
12. *Heavy metals*— No change.
13. *Organic volatile impurities*— No change.

(EMC: J. Lane) RTS—41235-10

Change to read:

~~**Powdered Cellulose**~~

~~» Powdered Cellulose is purified, mechanically disintegrated cellulose prepared by processing alpha cellulose obtained as a pulp from fibrous plant materials.~~

~~**Packaging and storage—** Preserve in tight containers.~~

~~**Labeling—** The labeling indicates the nominal degree of polymerization value. Degree of polymerization compliance is determined using *Identification* test *C* .~~

~~**Identification—**~~

~~**A:** Prepare iodinated zinc chloride solution by dissolving 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 minutes. Place about 10 mg of Powdered Cellulose on watch glass, and disperse in 2 mL of iodinated zinc chloride solution: the substance takes on a violet-blue color.~~

B: Mix 30 g with 270 mL of water in a single-speed, high-speed (equal to or greater than 18,000 rpm) power blender that has a clover-shaped jar design for 5 minutes. The jar and blades meet the following specifications: the jar has an inside diameter of 7.0 cm at the bottom and 9.2 cm at the top, and an overall height of 21.9 cm; and the 4 blades are arranged so that 2 of the blades are pointed up and 2 are pointed down. Transfer 100 mL of the dispersion to a 100-mL graduated cylinder, and allow to stand for 1 hour: the Powdered Cellulose settles in the cylinder, and a supernatant liquid appears above the layer of the cellulose.

C: Transfer 0.25 g of Powdered Cellulose, accurately weighed to 0.1 mg, to a 125-mL conical flask. Proceed as directed for *Identification* test *B* under *Microcrystalline Cellulose* , beginning with "Add 25.0 mL of water." The degree of polymerization is between 440 and 2250 and is within the labeled specification.

Microbial limits ⟨61⟩ — The total aerobic microbial count does not exceed 1000 cfu per g, the total combined molds and yeasts count does not exceed 100 cfu per g, and it meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and for absence of *Escherichia coli* and *Salmonella* species.

pH ⟨791⟩ — Mix 10 g with 90 mL of water, and allow to stand with occasional stirring for 1 hour: the pH of the supernatant liquid is between 5.0 and 7.5 .

Loss on drying ⟨731⟩ — Dry it at 105° for 2 hours: it loses not more than 6.0% of its weight.

Residue on ignition ⟨281⟩ **:** not more than 0.3%, calculated on the dried basis, the addition of sulfuric acid being omitted from the procedure.

Water-soluble substances— Mix 6.0 g with 90 mL of recently boiled and cooled water, and allow to stand with occasional stirring for 10 minutes. Filter, with the aid of vacuum, discard the first 10 mL of the filtrate, and pass the filtrate through the same filter a second time, if necessary, to obtain a clear filtrate. Evaporate a 15.0-mL portion of the filtrate in a tared evaporating dish to dryness without charring, dry at 105° for 1 hour, cool in a desiccator, and weigh: the difference between the weight of the residue and the weight obtained from a blank determination does not exceed 15.0 mg (1.5%).

Ether-soluble substances— Place 10.0 g in a chromatography 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 minutes, cool in a desiccator, and weigh: the difference between the weight of the residue and the weight obtained from a blank determination does not exceed 15.0 mg (0.15%).

Heavy metals, *Method II* ⟨231⟩ **:** 0.001%.

Organic volatile impurities, *Method IV* ⟨467⟩ **:** meets the requirements.

Auxiliary Information—*Staff Liaison* : Justin Lane, B.S., Scientific Associate
Expert Committee : (EMC) Excipients: Monograph Content
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Add the following:

■ **Powdered Cellulose**

» Powdered Cellulose is purified, mechanically disintegrated cellulose prepared by processing alpha cellulose obtained as a pulp from fibrous plant materials.

Packaging and storage— Preserve in tight containers.

Labeling— The labeling indicates the nominal degree of polymerization value. Degree of polymerization compliance is determined using *Identification* test *B*.

Identification—

A: Prepare iodinated zinc chloride solution by dissolving 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 minutes. Place about 10 mg of Powdered Cellulose on a watch glass, and disperse in 2 mL of iodinated zinc chloride solution: the substance takes on a violet-blue color.

B: Transfer 0.25 g of Powdered Cellulose, accurately weighed to 0.1 mg, 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 7.0 mL of the solution to a calibrated number 150 Cannon-Fenske, or equivalent, viscosimeter. Allow the solution to equilibrate at 25 ± 0.1° for not less than 5 minutes. Time the flow between the two marks on the viscosimeter, and record the flow time, t_1, in seconds. Calculate the kinematic viscosity, $(KV)_1$, of the Powdered Cellulose taken by the formula:

$$t_1 (k_1),$$

in which k_1 is the viscosimeter constant (see *Viscosity* ⟨911⟩). Obtain the flow time, t_2, for a 0.5 M cupriethylenediamine hydroxide solution using a number 100 Cannon-Fenske, or equivalent, viscosimeter. Calculate the kinematic viscosity, $(KV)_2$, of the solvent by the formula:

$$t_2 (k_2),$$

in which k_2 is the viscosimeter constant. Determine the relative viscosity, η_{rel}, of the Powdered Cellulose specimen taken by the formula:

$$(KV)_1 / (KV)_2.$$

Determine the intrinsic viscosity, $[\eta]c$, by interpolation, using the *Intrinsic Viscosity Table* in the *Reference Tables* section. Calculate the degree of polymerization, *P*, by the formula:

$$(95)[\eta]c / W_S [(100 - \%LOD)/100],$$

in which W_S is the weight, in g, of the Powdered Cellulose taken; and %*LOD* is the value obtained from the test for *Loss on drying.* The degree of polymerization is greater than 440.

Microbial limits ⟨61⟩ **—** The total aerobic microbial count does not exceed 1000 cfu per g, the total combined molds and yeasts count does not exceed 100 cfu per g, and it meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and for absence of *Escherichia coli* and *Salmonella* species.

pH ⟨791⟩ **—** Mix 10 g with 90 mL of water, and allow to stand with occasional stirring for 1 hour: the pH of the supernatant is between 5.0 and 7.5.

Loss on drying ⟨731⟩ **—** Dry it at 105° for 3 hours: it loses not more than 6.5% of its weight.

Residue on ignition ⟨281⟩ **:** not more than 0.3%, calculated on the dried basis.

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