BRIEFING

Corn Starch, page 882 of *PF* 28(3) [May–June 2002]. The United States Pharmacopeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for the *Corn Starch* 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 *Starch* that was prepared by the United States Pharmacopeia. The USP draft was based in part on comments from the Japanese Pharmacopoeia and the European Pharmacopoeia in response to the Provisional Harmonized Text Stage 5A and 5B drafts prepared by USP. The current *NF* monograph for *Starch* will be proposed for deletion, to be replaced by new monographs for *Corn Starch, Potato Starch,* and *Wheat Starch.*

Pharmacopeial Discussion Group Sign-Off Document

Attributes	EP	JP	USP
Definition	+	+	+
Identification A	+	+	+
Identification B	+	+	+
Identification C	+	+	+
pH	+	+	+
Loss on drying	+	+	+
Residue on ignition	+	+	+
Limit of iron	+	+	+
Limit of oxidizing substances	+	+	+
Sulfur dioxide determination	+	+	+

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

Nonharmonized attributes: Characters, Microbial contamination, Storage, Labeling.

Specific local attributes: Foreign matter (EP).

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

Differences between the International Harmonization Adoption Stage 6 document for Corn Starch and the current *NF* Starch monograph include the following:

1. Definition— Changed to include only Corn Starch, as to conform to the individual monograph for Corn Starch.
2. *Identification* test *C*— The test is modified to use 1 mL of mucilage, instead of 10 mL, and a new, less concentrated test solution is added.
3. *Packaging*— No change.
4. *Labeling*— A requirement that the label indicate where it is intended for use in preparing Absorbable Dusting Powder is added to ensure that microbial limits are met.
5. *Botanical characteristics*— This test has been modified and moved to the *Identification* section.
6. *Identification*— A microscopic test is added that is similar to the *Botanical characteristics* section. The other two tests are modified slightly for clarification.
7. *Microbial limits*— The revised limit for the total combined molds and yeasts count in the test is based on comments received. The addition of the requirements for Absorbable Dusting Powder are based on specific microbial requirements for Absorbable Dusting Powder.
8. *pH*— The lower limit is expanded in order to conform with EP standards.
9. *Loss on drying*— The revised test conditions reportedly correspond to ISO 1666 and are preferred by users of starches because of reduced testing time.
10. *Residue on ignition*— The standard for this test is increased from 0.5% to 0.6% in order to conform with EP standards.
11. *Limit of iron*— The test procedure is changed in order to conform to EP standards.
12. *Limit of oxidizing substances*— No change.
13. *Limit of sulfur dioxide*— The change in the standard reflects the corresponding limits proposed by the EC food laws.
14. *Organic volatile impurities*— This test is deleted, as it is not necessary.

(EMC: J. Lane) RTS—40773-4

Add the following:

▲ **Corn Starch**

» Corn Starch consists of the starch granules separated from the mature grain of corn [*Zea mays* Linné (Fam. Gramineae)].

Packaging ~~and storage~~ — Preserve in well-closed containers.

Labeling— Where Corn Starch is intended for use in preparing Absorbable Dusting Powder, it is so labeled and the label states that it must be subjected to further processing during the preparation of Absorbable Dusting Powder.

Identification—

A: Under a microscope, using not less than 20× magnification and using a mixture of glycerin and water (1:1) as a mounting agent, it appears as either angular polyhedral granules of irregular sizes with diameters ranging from about 2 µm to about 23 µm or as rounded or spheroidal granules of irregular sizes with diameters ranging from about 25 µm to about 35 µm. The central hilum consists of a distinct

cavity or two- to five-rayed cleft, and there are no concentric striations. Between crossed nicol prisms, the starch granules show a distinct black cross intersecting at the hilum.

B: Suspend 1 g of it in 50 mL of water, boil for 1 minute, and cool: a thin, cloudy mucilage is formed.

~~**C:** To 10 mL of the mucilage obtained in *Identification* test *B,* add 0.04 mL of iodine and potassium iodide TS: an orange-red to dark blue color is produced, which disappears on heating.~~

C: To 1 mL of the mucilage obtained in *Identification* test *B,* add 0.05 mL of *Iodine solution:* an orange-red to dark blue color is produced, which disappears on heating.

Iodine solution— Dissolve 12.7 g of iodine and 20 g of potassium iodide in water, and dilute with water to 1000.0 mL. To 10.0 mL of this solution, add 0.6 g of potassium iodide, and dilute with water to 100.0 mL. Prepare immediately before use.

Microbial limits ⟨61⟩ **—** The total aerobic microbial count does not exceed ~~1000~~ 10^3 per g, the total combined molds and yeasts count does not exceed ~~100~~ 10^2 per g, and it meets the requirements of the test for the absence of *Escherichia coli.* Where it is intended for use in preparing Absorbable Dusting Powder, it also meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

pH ⟨791⟩ **—** Prepare a slurry by weighing 5.0 g of Corn Starch, transferring to a suitable nonmetallic container, and adding 25.0 mL of freshly boiled and cooled water. Agitate continuously at a moderate rate for 1 minute. Stop the agitation, and allow to stand for 15 minutes. Determine the pH to the nearest 0.1 unit: the pH, determined potentiometrically, is between 4.0 and 7.0.

Loss on drying ⟨731⟩ **—** Dry about 1 g, accurately weighed, at 130° for 90 minutes: it loses not more than 15.0% of its weight.

Residue on ignition ⟨281⟩ **:** not more than 0.6%, determined on a 1.0-g test specimen. Ignition temperature 600 ± 50°.

Limit of iron— Shake 1.5 g of Corn Starch with 15 mL of 2 N hydrochloric acid, and filter. Transfer 10 mL of the filtrate to a test tube, add 2 mL of citric acid solution (2 in 10), 0.1 mL of thioglycolic acid, and mix. Add 10 N ammonium hydroxide until the solution is distinctly alkaline to litmus, dilute with water to 20 mL, and mix *(Test Solution).* Prepare a *Standard Iron Solution* containing the equivalent of 10 µg of iron per mL as directed under *Iron* ⟨241⟩ . Immediately before use, quantitatively dilute an accurately measured volume of this solution with water to obtain a *Diluted Standard Iron Solution* containing the equivalent of 1 µg of iron per mL. Prepare the *Standard Solution* by transferring 10 mL of the *Diluted Standard Iron Solution* to a test tube and proceeding in the same manner as directed for the preparation of the *Test Solution,* beginning with "add 2 mL of citric acid solution (2 in 10)." After 5 minutes, any pink color in the *Test Solution* is not more intense than that in the *Standard Solution,* corresponding to a limit of 10 µg of iron per g.

Limit of oxidizing substances— Transfer 4.0 g to a glass-stoppered, 125-mL conical flask, and add 50.0 mL of water. Insert the stopper, and swirl for 5 minutes. Transfer to a glass-stoppered, 50-mL centrifuge tube, and centrifuge to clarify. Transfer 30.0 mL of the clear supernatant to a glass-stoppered, 125-mL conical flask. Add 1 mL of glacial acetic acid and 0.5 g to 1.0 g of potassium iodide. Insert the stopper, swirl, and allow to stand for 25 to 30 minutes in the dark. Add 1 mL of starch TS, and titrate with 0.002 N sodium thiosulfate VS to the disappearance of the starch-iodine color. Perform a blank determination, and make any necessary correction. Each mL of 0.002 N sodium thiosulfate is equivalent to 34 µg of oxidant, calculated as hydrogen peroxide. Not more than 1.4 mL of 0.002 N sodium thiosulfate is required (20 µg per g, calculated as H_2O_2).

Limit of sulfur dioxide— Not more than 50 µg per g.

Reagents—

Carbon dioxide— Use carbon dioxide, with a flow regulator that will maintain a flow of 100 ± 10 mL per minute.

Bromophenol blue indicator solution— Dissolve 100 mg of bromophenol blue in 100 mL of dilute alcohol (1 in 5), and filter if necessary.

Hydrogen peroxide solution— Dilute 30% hydrogen peroxide with water to obtain a 3% solution. Just before use, add 3 drops of *Bromophenol blue indicator solution,* and neutralize to a violet-blue endpoint with 0.01 N sodium hydroxide. Do not exceed the endpoint.

Apparatus— In this test, the sulfur dioxide is released from the test specimen in a boiling acid medium and is removed by a stream of carbon dioxide. The separated gas is collected in a dilute hydrogen peroxide solution where the sulfur dioxide is oxidized to sulfuric acid and titrated with standard alkali. The apparatus consists essentially of a 500-mL three-neck, round-bottom, boiling flask, a separatory funnel having a capacity of 100 mL or greater, a gas inlet tube of sufficient length to permit introduction of the carbon dioxide within 2.5 cm of the bottom of the boiling flask, a reflux condenser having a jacket length of 200 mm, and a delivery tube connecting the upper end of the reflux condenser to the bottom of a receiving test tube. Apply a thin film of stopcock grease to the sealing surfaces of all of the joints except the joint between the separatory funnel and the boiling flask, and clamp the joints to ensure tightness.

Procedure— Add 150 mL of water to the boiling flask. Close the stopcock of the separatory funnel, and begin the flow of carbon dioxide at a rate of 100 ± 5 mL per minute through the *Apparatus.* Start the condenser coolant flow. Add 10 mL of *Hydrogen peroxide solution* to a receiving test tube. After 15 minutes, without interrupting the flow of carbon dioxide, remove the separatory funnel from the boiling flask, and transfer 25.0 g of test specimen into the boiling flask with the aid of 100 mL of water. Apply stopcock grease to the outer joint of the separatory funnel, and replace the separatory funnel in the boiling flask. Close the stopcock of the separatory funnel, and add 80 mL of 2 N hydrochloric acid to the separatory funnel. Open the stopcock of the separatory funnel to permit the hydrochloric acid solution to flow into the boiling flask, guarding against the escape of sulfur dioxide into the separatory funnel by closing the stopcock before the last few mL of hydrochloric acid drain out. ~~Position the *Apparatus* in a water bath, and~~ Boil the mixture for 1 hour. Remove the receiving test tube, and transfer its contents to a 200-mL wide-necked, conical flask. Rinse the receiving test tube with a small portion of water, add the rinsing to the 200-mL conical flask, and mix. Heat on a water bath for 15 minutes, and allow to cool. Add 0.1 mL of *Bromophenol blue indicator solution,* and titrate the contents with 0.1 N sodium hydroxide VS until the color changes from yellow to violet-blue, with the color change lasting for at least 20 seconds. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Calculate the content, in µg per g, of sulfur dioxide in the test specimen taken by the formula:

$$1000(32.03)VN/W,$$

in which 32.03 is the milliequivalent weight of sulfur dioxide; V is the volume, in mL, of titrant consumed; N is the normality of the titrant; and W is the weight, in g, of test specimen taken.

~~**Organic volatile impurities,** *Method IV* ⟨467⟩ **:** meets the requirements.~~ ▲ *NF23*

Auxiliary Information—*Staff Liaison* : Catherine Sheehan, Senior Scientific Associate
Expert Committee : (EMC) Excipients: Monograph Content
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Phone Number : 1-301-816-8262