BRIEFING

Carboxymethylcellulose Calcium, NF 22 page 2841 and page 1252 of PF 28(4) [July–Aug. 2002]. The United States Pharmacopeia is the coordinating pharmacopeia for the international harmonization of compendial standards for this article. The revisions presented in this proposal, which represents the ADOPTION STAGE 6 draft, reflect the Committee of Revision’s results in this harmonization effort and have been accepted by the members of the Pharmacopeial Discussion Group.

Pharmacopeial Discussion Group Sign-Off Document

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

Nonharmonized attributes: Characters, Heavy metals, Packaging and storage

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

Proposed changes from the current NF monograph include the following:

1. Definition— No change.
2. Packaging— No change.
3. Identification— No change.
4. Alkalinity— No change.
5. Loss on drying— No change.
6. Residue on ignition— Default ignition temperatures are employed.
7. Heavy metals— No change.
8. Limit of chloride— No change.
9. **Limit of sulfate**—The limit has been modified to 1.0% from 0.96%.
10. **Silicate**—Deleted, based on comments that this test is unnecessary since silicate is not added to the article of commerce.
11. **Starch**—Deleted, based on comments that this test is unnecessary since starch is not added to the article of commerce.
12. **Organic volatile impurities**—Deleted, based on information that no organic solvents are used in the manufacture of the article of commerce.

(EMC: J. Lane) RTS—40769-6

**Change to read:**

**Carboxymethylcellulose Calcium**

Cellulose, carboxymethyl ether, calcium salt.

Cellulose-carboxymethyl ether-calcium salt [ 9050-04-8 ].

Carboxymethylcellulose Calcium is the calcium salt of a polycarboxymethyl ether of cellulose.

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

**Identification**—

**A:** Shake thoroughly 0.1 g with 10 mL of water, followed by 2 mL of 1 N sodium hydroxide, allow to stand for 10 minutes, and use 1 mL of this solution as the test solution, retaining the remainder of it for **Identification** tests **B** and **C**. To 1 mL of the test solution add water to make 5 mL, then to 1 drop of the resulting solution add 0.5 mL of chromotropic acid TS, and heat in a water bath for 10 minutes: a red-purple color develops.

**B:** Shake 5 mL of the test solution obtained in **Identification** test **A** with 10 mL of acetone: a white, flocculent precipitate is formed.

**C:** Shake 5 mL of the test solution obtained in **Identification** test **A** with 1 mL of ferric chloride TS: a brown, flocculent precipitate is formed.

**D:** Ignite 1 g to ash, dissolve the residue in 10 mL of water and 5 mL of 6 N acetic acid, and filter, if necessary. Boil the filtrate, cool, and neutralize with 6 N ammonium hydroxide: the solution responds to the tests for Calcium (191).

**Alkalinity**—Shake thoroughly 1.0 g with 50 mL of freshly boiled and cooled water, and add 2 drops of phenolphthalein TS: no red color develops.

**Loss on drying** (731)—Dry it at 105° for 4 hours: it loses not more than 10.0% of its weight.

**Residue on ignition** (281): between 10.0% and 20.0%, about 0.5 g, previously dried, being used for the test, and an ignition temperature of 450° to 550° being used.

**Chloride** (221)—Shake thoroughly 0.80 g with 50 mL of water, dissolve in 10 mL of 1 N sodium hydroxide, add water to make 100 mL, and use 20 mL of this solution as the test solution, retaining the remainder of it for the test for **Sulfate**. Heat 20 mL of the test solution with 10 mL of 2 N nitric acid in a water bath until a flocculent precipitate is formed, cool, centrifuge, and remove the supernatant liquid. Wash the
precipitate with three 10-mL portions of water by centrifuging each time, combine the supernatant liquid and the washings, add water to make 100 mL, and mix: a 25-mL portion of this solution shows no more chloride than is contained in 0.20 mL of 0.020 N hydrochloric acid (0.36%).

Silicate—Weigh accurately about 1 g, ignite in a platinum dish, add 20 mL of 3 N hydrochloric acid, cover with a watch-glass, and boil gently for 30 minutes. Remove the watch-glass, and evaporate in a water bath, with the aid of a current of air, to dryness. Continue heating for 1 hour, add 10 mL of hot water, stir well, and filter through quantitative filter paper. Wash the residue with hot water, dry it together with the filter paper after no turbidity is produced on the addition of silver nitrate TS to the last washing, then ignite to constant weight: not more than 1.5% of residue is obtained.

Sulfate (221)—Heat 10 mL of the test solution obtained in the test for Chloride with 1 mL of hydrochloric acid in a water bath until a flocculent precipitate is formed, cool, centrifuge, and remove the supernatant liquid. Wash the precipitate with three 10-mL portions of water by centrifuging each time, combine the supernatant liquid and the washings, add water to make 100 mL, and mix: a 25-mL portion of this solution shows no more sulfate than is contained in 0.20 mL of 0.020 N sulfuric acid (0.96%).

Heavy metals (231)—Determine as directed in the test for Heavy metals under Methylcellulose, except to use only 1 g of Carboxymethylcellulose Calcium. The limit is 0.002%.

Starch—Heat 0.10 g with 10 mL of water, cool, and add 2 drops of iodine TS: no blue color develops.

Organic volatile impurities, Method IV (467): meets the requirements.

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

▲ Carboxymethylcellulose Calcium

Cellulose, carboxymethyl ether, calcium salt.
Cellulose carboxymethyl ether calcium salt [9050-04-8].

» Carboxymethylcellulose Calcium is the calcium salt of a polycarboxymethyl ether of cellulose.

Packaging and storage — Preserve in tight containers.

Identification—

A: Shake thoroughly 0.1 g with 10 mL of water, followed by 2 mL of 1 N sodium hydroxide, allow to stand for 10 minutes, and use 1 mL of this solution as the test solution, retaining the remainder of it for Identification tests B and C. To 1 mL of the test solution add water to make 5 mL, then to 1 drop of the resulting solution add 0.5 mL of chromotropic acid TS, and heat in a water bath for 10 minutes: a red-purple color develops.

B: Shake 5 mL of the test solution obtained in Identification test A with 10 mL of acetone: a white flocculent precipitate is formed.

C: Shake 5 mL of the test solution obtained in Identification test A with 1 mL of ferric chloride TS: a brown, flocculent precipitate is formed.

D: Ignite 1 g to ash, dissolve the residue in 10 mL of water and 5 mL of 6 N acetic acid, and filter, if necessary. Boil the filtrate, cool, and neutralize with 6 N ammonium hydroxide: the solution responds to the tests for Calcium (191).

Alkalinity—Shake thoroughly 1.0 g with 50 mL of freshly boiled and cooled water, and add 2 drops of phenolphthalein TS: no red color develops.

Loss on drying (731) — Dry it at 105º for 4 hours: it loses not more than 10.0% of its weight.

Residue on ignition (281): between 10.0% and 20.0%, about 1.0 g, previously dried, being used for the test. and an ignition temperature of 450º to 550º being used.

Heavy metals (231) — Determine as directed in the test for Heavy metals under Methylcellulose, except to use only 1 g of Carboxymethylcellulose Calcium. The limit is 0.002%.

Limit of chloride (221) — Shake thoroughly 0.80 g with 50 mL of water, dissolve in 10 mL of 1 N sodium hydroxide, add water to make 100 mL, and use 20 mL of this solution as the test solution, retaining the remainder of it for the test for Limit of sulfate. Heat 20 mL of the test solution with 10 mL of 2 N nitric acid in a water bath until a flocculent precipitate is formed, cool, centrifuge, and remove the supernatant. Wash the precipitate with three 10-mL portions of water by centrifuging each time, combine the supernatant and the washings, add water to make 100 mL, and mix: a 25-mL portion of this solution shows no more chloride than is contained in 0.20 mL of 0.020 N hydrochloric acid (0.36%).

Limit of sulfate (221) — Heat 10 mL of the test solution obtained in test for Limit of chloride with 1 mL of hydrochloric acid in a water bath until a flocculent precipitate is formed, cool, centrifuge, and remove the supernatant. Wash the precipitate with three 10-mL portions of
water by centrifuging each time, combine the supernatant and the washings, add water to make 100 mL, and mix: a 25-mL portion of this solution shows no more sulfate than is contained in 0.21 mL of 0.020 N sulfuric acid (1.0%). ▲ NF23

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