

**BRIEFING**

**Cellacefate**, *NF* 22 page 2845 and page 1253 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 Pharmacopoeial Discussion Group.

**Pharmacopoeial Discussion Group Sign-Off Document**

<b>Attributes</b>	<b>EP</b>	<b>JP</b>	<b>USP</b>
Definition	+	+	+
Packaging and storage	+	+	+
Identification	+	+	+
Viscosity	+	+	+
Water	+	+	+
Residue on ignition	+	+	+
Limit of free acid	+	+	+
Phthalyl content	+	+	+
Content of acetyl	+	+	+

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

**Nonharmonized attributes:** Characters, Heavy metals, Organic volatile impurities.

**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. *USP Reference standards*— No change.
4. *Identification*— Test *B* is deleted, because it is not needed, as the polymeric character of Cellacefate can be identified by the viscosity determination.
5. *Viscosity*— No change.
6. *Water*— No change.
7. *Residue on ignition*— No change.
8. *Heavy metals*— No change.

9. *Limit of free acid*— No change.
10. *Organic volatile impurities*— No change.
11. *Phthalyl content*— The strength of sodium hydroxide is corrected to be constant throughout the test.
12. *Content of acetyl*— No change.

(EMC: J. Lane )      RTS—40875-2

### **Change to read:**

#### **Cellacefate**

~~Cellulose, acetate, 1,2-benzenedicarboxylate.~~

~~Cellulose acetate phthalate [ 9004-38-0 ].~~

~~» Cellacefate is a reaction product of phthalic anhydride and a partial acetate ester of cellulose. It contains not less than 21.5 percent and not more than 26.0 percent of acetyl ( $C_2H_3O$ ) groups and not less than 30.0 percent and not more than 36.0 percent of phthalyl(  $\theta$ -carboxy benzoyl,  $C_8H_5O_3$  ) groups, calculated on the anhydrous, acid-free basis.~~

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

~~**USP Reference standards** <11>— *USP Cellulose Acetate Phthalate RS.*~~

#### ~~**Identification**—~~

~~**A:** *Infrared Absorption* <197K>— Do not dry specimens.~~

~~**B:** Dissolve about 150 mg in 1 mL of acetone, and pour onto a clear glass plate in an area of good airflow: a glossy, clear film is deposited as the acetone evaporates.~~

~~**Viscosity** <911>— Dissolve 15 g, calculated on the anhydrous basis, in 85 g of a mixture of 249 parts of anhydrous acetone and 1 part of water, by weight: the apparent viscosity (see *Procedure for Methylcellulose* under *Viscosity* <911>) is between 45 and 90 centipoises, determined at  $25 \pm 0.2^\circ$ .~~

~~**Water, Method I** <921>: not more than 5.0%, a mixture of dehydrated alcohol and methylene chloride (3:2) being used instead of methanol as the solvent.~~

~~**Residue on ignition** <281>: not more than 0.1%.~~

~~**Heavy metals, Method II** <231>: 0.001%.~~

~~**Limit of free acid**— Transfer 3.0 g, accurately weighed, to a glass stoppered flask, add 100 mL of dilute methanol (1 in 2), insert the stopper in the flask, and shake for 2 hours. Filter, and wash the flask and the filter with two 10 mL portions of the methanol solution, adding the washings to the filtrate. Titrate the combined filtrate and washings 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). Calculate the percentage of free acid,  $B$ , by the formula:~~

$$0.8306 A / W \text{ ,}$$

~~in which  $A$  is the volume, in mL, of 0.1 N sodium hydroxide consumed, corrected for the blank, and  $W$  is the weight, in g, of the Cellacefate, calculated on the anhydrous basis. Not more than 3.0%, calculated as phthalic acid, is found.~~

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

~~**Phthalyl content**—Transfer about 1 g, accurately weighed, to a conical flask, dissolve in 50 mL of a mixture of alcohol and acetone (3:2), add phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS. Perform a blank determination, and make any necessary correction. Calculate the percentage of phthalyl, on the acid-free basis, by the formula:~~

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

~~in which  $A$  is the volume, in mL, of 0.1 N sodium hydroxide consumed after correction for the blank,  $W$  is the weight, in g, of Cellacefate taken, calculated on the anhydrous basis, and  $B$  is the percentage of acid found in the test for [Limit of free acid](#) .~~

~~**Content of acetyl**—Transfer about 500 mg, accurately weighed, to a glass stoppered flask, and add 50 mL of water and 50.0 mL of 0.5 N sodium hydroxide VS. Connect the flask to a reflux condenser, and reflux for 60 minutes. Cool, add 5 drops of phenolphthalein TS, and titrate with 0.5 N hydrochloric acid VS. Perform a blank determination. Calculate the free and combined acids, as acetyl, taken by the formula:~~

$$2.152( A / W ) \text{ ,}$$

~~in which  $A$  is the volume, in mL, of 0.5 N sodium hydroxide consumed after correction for the blank, and  $W$  is the weight, in g, of Cellacefate taken, on the anhydrous basis. Calculate the percentage of acetyl, on the acid-free basis, taken by the formula:~~

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

~~in which  $P$  is the free and combined acids, as acetyl,  $B$  is the percentage of acid found in the test for [Free acid](#) , and  $C$  is the percentage of phthalyl found in the test for [Phthalyl content](#) .~~

~~**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~~

**Add the following:****▲ Cellacefate**

Cellulose, acetate, 1,2-benzenedicarboxylate.  
Cellulose acetate phthalate [9004-38-0].

» Cellacefate is a reaction product of phthalic anhydride and a partial acetate ester of cellulose. It contains not less than 21.5 percent and not more than 26.0 percent of acetyl ( $C_2H_3O$ ) groups and not less than 30.0 percent and not more than 36.0 percent of phthalyl(*o*-carboxybenzoyl) ( $C_8H_5O_3$ ) groups, calculated on the anhydrous, acid-free basis.

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

**USP Reference standards** <11> — *USP Cellulose Acetate Phthalate RS*.

**Identification, Infrared absorption** <197K> — Do not dry specimens.

**Viscosity** <911> — Dissolve 15 g, calculated on the anhydrous basis, in 85 g of a mixture of 249 parts of anhydrous acetone and 1 part of water, by weight: the apparent viscosity (see *Procedure for Methylcellulose* under *Viscosity* <911> ) is between 45 and 90 centipoises, determined at  $25 \pm 0.2^\circ$ .

**Water, Method I** <921> : not more than 5.0%, a mixture of dehydrated alcohol and methylene chloride (3:2) being used instead of methanol as the solvent.

**Residue on ignition** <281> : not more than 0.1%. ~~Ignition temperature  $600 \pm 50^\circ$ .~~

**Heavy metals, Method II** <231> : 0.001%.

**Limit of free acid**— Transfer 3.0 g, accurately weighed, to a glass-stoppered flask, add 100 mL of dilute methanol (1 in 2), insert the stopper in the flask, and shake for 2 hours. Filter, and wash the flask and the filter with two 10-mL portions of the methanol solution, adding the washings to the filtrate. Titrate the combined filtrate and washings 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). Calculate the percentage of free acid, *B*, by the formula:

$$0.8306A / W,$$

in which *A* is the volume, in mL, of 0.1 N sodium hydroxide consumed, corrected for the blank; and *W* is the weight, in g, of the Cellacefate, calculated on the anhydrous basis. Not more than 3.0%, calculated as phthalic acid, is found.

**Organic volatile impurities, Method IV** <467> : meets the requirements.

**Phthalyl content**— Transfer about 1 g, accurately weighed, to a conical flask, dissolve in 50 mL of a mixture of alcohol and acetone (3:2), add phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS. Perform a blank determination, and make any necessary correction. Calculate the percentage of phthalyl, on the acid-free basis, by the formula:

$$100[(1.491A / W) - 1.795B] / (100 - B),$$

in which  $A$  is the volume, in mL, of 0.1 N sodium hydroxide consumed after correction for the blank;  $W$  is the weight, in g, of Cellacefate taken, calculated on the anhydrous basis; and  $B$  is the percentage of acid found in the test for *Limit of free acid*.

**Content of acetyl**— Transfer about 100 mg, accurately weighed, 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 minutes. Cool, add 5 drops of phenolphthalein TS, and titrate with 0.1 N hydrochloric acid VS. Perform a blank determination. Calculate the free and combined acids, as acetyl, taken by the formula:

$$0.4305 (A/W),$$

in which  $A$  is the volume, in mL, of 0.1 N sodium hydroxide consumed after correction for the blank; and  $W$  is the weight, in g, of Cellacefate taken, on the anhydrous basis. Calculate the percentage of acetyl, on the acid-free basis, taken by the formula:

$$[100(P - 0.5182B)/(100 - B)] - 0.5772C,$$

in which  $P$  is the free and combined acids, as acetyl;  $B$  is the percentage of acid found in the test for *Limit of free acid*; and  $C$  is the percentage of phthalyl found in the test for *Phthalyl content*. ▲ NF23

**Auxiliary Information**—*Staff Liaison* : [Catherine Sheehan, Senior Scientific Associate](#)

*Expert Committee* : (EMC) Excipients: Monograph Content

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