PHARMACOPOEIAL DISCUSSION GROUP

E-10 CELLULOSE, MICROCRYSTALLINE

REVISION 2

- Harmonised Attributes

Attribute	EP	JP	USP
Definition	+	+	+
Identification A (IR) B (wet chemistry) C (degree of polymerization)	 ± + +	 ± + +	 ± + +
Conductivity	+	+	+
pH	+	+	+
Loss on drying	+	+ (1)	+ (1)
Residue on ignition	+	+	+
Bulk density	-	+	+
Water-soluble substances	+	+	+
Ether-soluble substances	+	+	+

(1) JP and USP will retain, as local requirement, that the value can be within a percentage range, as specified within the labelling

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

- Non-harmonised attributes

Characters/Description, Microbial limits, Labelling, Containers and storage/Packaging and storage

- Local requirements

EP	JP	USP
Solubility	Definition (reference to labelling), Identification (2) – dispersion test, Heavy metals~~,~~ ~~Sulfated ash (on 2.0 g).~~	Particle-size distribution estimation by analytical sieving

Reagents and reference materials

KM
CW
14.0

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

Date: **Signatures:**

13-SEP-2017

European Pharmacopoeia

A. Okuda
for Fumi Yamamoto

Japanese Pharmacopoeia

United States Pharmacopeia

p.o. C. Viola

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E10 - 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—

[Note - Compliance is determined by meeting the requirements of *Identification* tests *A*, *B*, and *C*.]

A. Infrared Absorption

[Note—Disregard any peak between 800 and 825 cm^{-1} as well as those between 950 and 1000 cm^{-1}.]

Record the infrared absorption spectrum and compare with the Reference Spectrum or the spectrum obtained with the Reference Standard: the transmission minima correspond in position and relative size.

B: 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 Microcrystalline Cellulose on a watch glass, and disperse in 2 mL of iodinated zinc chloride solution: the substance takes on a violet-blue color.

C: Transfer 1.3 g of Microcrystalline 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

CW
H.O KPm

dissolved. Transfer an appropriate volume 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 2 marks on the viscosimeter, and record the flow time, t_1, in seconds. Calculate the kinematic viscosity, $(KV)_1$, of the Microcrystalline 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[1] 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 Microcrystalline 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 Microcrystalline Cellulose taken, and *%LOD* is the value obtained from the test for *Loss on drying.* The degree of polymerization is not greater than 350.

Conductivity—Shake about 5 g with 40 mL of water for 20 minutes, and centrifuge. Retain the supernatant liquid 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 per cm, measure the conductivity of the

supernatant solution after a stable reading is obtained, and measure the conductivity of the water used to prepare the test specimen. The conductivity of the supernatant solution does not exceed the conductivity of the water by more than 75 µS per cm.

pH : Shake about 5 g with 40 mL of water for 20 minutes, and centrifuge: between 5.0 and 7.5.

Loss on drying —Dry it at 105° for 3 hours: it loses not more than 7.0% of its weight.

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

Bulk density—Use a volume meter that has been fitted with a 10-mesh screen. The volume meter 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 inches) above the funnel through the volume meter, 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: the bulk density is within the labeled specification.

Water-soluble substances—Shake 5.0 g with about 80 mL of water for 10 minutes, filter with the aid of 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 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 12.5 mg (0.25%).

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 5.0 mg (0.05%).

4.0
CN FJW