PHARMACOPEIAL DISCUSSION GROUP

CORRECTION 1

E24-LACTOSE, MONOHYDRATE

(Correction to Rev. 2 signed on June 5, 2008)

	Harmonized attributes		
	EP	JP	USP
Definition	+	+	+
Clarity and color of solution	+(1)	+	+
Identification IR	+	+	+
Identification (TLC)	+(2)	-	+
Specific optical rotation	+	+	+
Acidity or alkalinity	+	+	+
Water	+	+	+
Residue on ignition	+	+	+
Loss on drying	-	+	+
Protein and light-absorbing impurities	+	+	+
Microbial limits (TAMC, *E. coli*)	+	+	+
Microbial limits (TYMC)	–	+	+

(1) In EP, reference suspension I is used to evaluate the opalescence of the solution in the test for clarity and colour of solution. Each pharmacopeia has similar but minor difference in the acceptance criteria.

(2) In EP, the identification test by TLC is included in the second series of identification.

Legend + will adopt and implement; – will not stipulate

Non-harmonized attributes

Characters/Description, Packaging and storage, Labeling

Local requirements

EP	JP	USP
Identification (water), Second identification (TLC, colour reaction, water); FRC (Particle-size distribution, Bulk and tapped density)	The definition section also covers granulated lactose, It also states: "It is a disaccharide obtained from milk, consist of one unit of glucose and one unit of galactose." The test for water is restricted to granulated forms (4.0-5.5%);	The definition section includes the following: "NOTE—Lactose Monohydrate may be modified as to its physical characteristics. It may contain varying proportions of amorphous lactose."

	Heavy metals; Microbial limits: *Salmonella*	

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

European Pharmacopoeia

Signature: Date

2/10/19

Japanese Pharmacopoeia

Signature: Date

Oct. 2nd, 2019

United States Pharmacopeia

Signature: Date

02-OCT-2019

Analysis Samples:

Standard solution A, *Standard solution B*, and *Sample solution*

Allow the spots to dry, and develop the plate in a paper-lined chromatographic chamber equilibrated with *Developing solvent system* for about 1 h prior to use. Allow the chromatogram to develop until the solvent front has moved about three-quarters of the length of the plate. Remove the plate from the chamber, dry in a current of warm air, and redevelop the plate in fresh *Developing solvent system*. Remove the plate from the chamber, mark the solvent front, and dry the plate in a current of warm air. Spray the plate evenly with *Spray reagent*. Heat the plate at 130° for 10 min.

System suitability:

The test is not valid unless the chromatogram of *Standard solution B* shows four clearly discernible spots, disregarding any spots at the origin.

Acceptance criteria:

The principal spot from the *Sample solution* corresponds in appearance and *RF* value to that from *Standard solution A*

Specific optical rotation-

Dissolve 10 g by heating in 80 mL of water to 50 degrees. Allow to cool, and add 0.2 mL of 6 N ammonium hydroxide. Allow to stand for 30 minutes, and dilute with water to 100 mL: the specific rotation, calculated on the anhydrous basis, determined at 20 degrees, is between +54.4 degrees and +55.9 degrees.

Acidity or alkalinity-

Dissolve 6 g by heating in 25 mL of carbon dioxide-free water, cool, and add 0.3 mL of a solution of phenolphthalein (1 g in 100 mL of alcohol): the solution is colorless, and not more than 0.4 mL of 0.1 N sodium hydroxide is required to produce a change to a pink or red color .

H.O

LACTOSE MONOHYDRATE

Correction 1 to Rev. 2, Stage 3B

Definition

Lactose Monohydrate is the monohydrate of O-β-D-galactopyranosyl-(1→4)-α-D-glucopyranose.

Clarity and color of solution- A solution of 1 g in 10 mL of boiling water is clear and nearly colorless. Determine the absorbance of this solution at a wavelength of 400 nm. The absorbance divided by the path length in centimeters is not more than 0.04.

Identification-

A. Infrared Absorption.
Record the infrared absorption spectrum of lactose monohydrate and compare with the Reference Spectrum or the spectrum obtained with the Reference Standard: the transmission minima correspond in position and relative size.

B. Thin-layer chromatography

Diluent: Methanol and water (3:2)

Standard solution A: 0.5 mg/mL of Lactose Monohydrate RS in *Diluent*

Standard solution B: 0.5 mg/mL each of Dextrose RS, Lactose Monohydrate RS, Fructose RS, and Sucrose RS in *Diluent*

Sample solution: 0.5 mg/mL of Lactose Monohydrate in *Diluent*

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 2 µL

Developing solvent system: Ethylene dichloride, glacial acetic acid, methanol, and water (10:5:3:2)

Spray reagent: 5 mg/mL of thymol in a mixture of alcohol and sulfuric acid (19:1)

H.D

Water, Karl Fischer - between 4.5% and 5.5%, determined on a preparation containing lactose monohydrate in a mixture of methanol and formamide (2:1).

Residue on ignition- not more than 0.1%. Ignition temperature is 600 ± 50°

Protein and light-absorbing impurities - Measure the light absorption of a 1% (w/v) solution in the range of 210 to 300 nm. The absorbance divided by the path length in centimeters is not more than 0.25 in the range of 210 to 220 nm and is not more than 0.07 in the range of 270 to 300 nm.

Loss on Drying – Dry a sample at 80° for 2 h. Not more than 0.5%

Microbial Limits (internationally harmonized methods) -
The total aerobic microbial count is NMT 10^2 cfu/g and the total combined molds and yeasts count is NMT 50 cfu/g. It meets the requirements of the test for absence of *Escherichia coli*.

H.O
Ces
ICM