

Lactose Monohydrate

Portions of the monograph text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (↕) to specify this fact.

DEFINITION

Change to read:

■ Lactose Monohydrate is the monohydrate of *O*-β-D-galactopyranosyl-(1→4)-α-D-glucopyranose. ■^{1S} (USP35)
[NOTE—Lactose Monohydrate may be modified as to its physical characteristics. It may contain varying proportions of amorphous lactose.]

IDENTIFICATION

- **A. INFRARED ABSORPTION** (197K)
- ***B. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST** (201)
Diluent: Methanol and water (3:2)
Standard solution A: 0.5 mg/mL of USP Lactose Monohydrate RS in *Diluent*
Standard solution B: 0.5 mg/mL each of USP Dextrose RS, USP Lactose Monohydrate RS, USP Fructose RS, and USP 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)
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 *R_f* value to that from *Standard solution A*.

Delete the following:

- **C.**
Sample solution: 50 mg/mL of Lactose Monohydrate
Analysis: To 5 mL of the *Sample solution* add 3 mL of ammonium hydroxide, and heat in a water bath at 80° for 10 min.

Acceptance criteria: A red color develops. ■^{1S} (USP35)

IMPURITIES

Change to read:

- **RESIDUE ON IGNITION** (281)
Analysis: A sample ignited at a temperature of 600 ± 50° ■^{1S} (USP35)
Acceptance criteria: NMT 0.1%
- ***HEAVY METALS** (231)
Sample solution: 4 g in 20 mL of warm water. Add 1 mL of 0.1 N hydrochloric acid, and dilute with water to 25 mL.
Acceptance criteria: NMT 5 μg/g.

SPECIFIC TESTS

- **CLARITY AND COLOR OF SOLUTION**
Sample solution: 1 g in 10 mL of boiling water
Analysis: The *Sample solution* is clear and nearly colorless. Determine the absorbance of this solution at a wavelength of 400 nm.
Acceptance criteria: The absorbance divided by the path length, in cm, is NMT 0.04.
- ***MICROBIAL ENUMERATION TESTS** (61) and **TESTS FOR SPECIFIED MICROORGANISMS** (62): The total aerobic microbial count does not exceed 1 × 10² cfu/g, the total combined molds and yeasts count does not exceed 5 × 10¹ cfu/g, and it meets the requirements of the test for absence of *Escherichia coli*.
- **OPTICAL ROTATION, Specific Rotation** (781S)
Sample solution: Dissolve 10 g by heating in 80 mL of water to 50°. Allow to cool, and add 0.2 mL of 6 N ammonium hydroxide. Allow to stand for 30 min, and dilute with water to 100 mL.
Acceptance criteria: +54.4° to +55.9°, calculated on the anhydrous basis, determined at 20°

Change to read:

- **ACIDITY OR ALKALINITY**
Sample solution: Dissolve 6 g by heating in 25 mL of carbon dioxide-free water, cool, and add 0.3 mL of phenolphthalein TS.
Acceptance criteria: The solution is colorless, and NMT 0.4 mL of 0.1 N sodium hydroxide ■^{VS} ■^{1S} (USP35) is required to produce a ■ pink or ■^{1S} (USP35) red color.
- ***LOSS ON DRYING** (731)
Analysis: Dry a sample at 80° for 2 h.
Acceptance criteria
Monohydrate: NMT 0.5%
Monohydrate, modified: NMT 1.0%.
- **WATER DETERMINATION, Method I** (921)
Sample solution: Prepare a preparation containing Lactose Monohydrate in a mixture of methanol and formamide (2:1)
Acceptance criteria: 4.5%–5.5%
- **PROTEIN AND LIGHT-ABSORBING IMPURITIES** (See *Spectrophotometry and Light-Scattering* (851).)
Sample solution: 1% (w/v)
Analysis: Measure the light absorption of the *Sample solution* in the range of 210–300 nm.
Acceptance criteria: The absorbance divided by the path length, in cm, is NMT 0.25 in the range of 210–220 nm and is NMT 0.07 in the range of 270–300 nm.

ADDITIONAL REQUIREMENTS

- ***PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Where the labeling states the particle size distribution, it also indicates the *d*₁₀, *d*₅₀, and *d*₉₀ values

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and the range for each. For modified Lactose Monohydrate, also label it to indicate the method of modification.

- **USP REFERENCE STANDARDS** <11>
 - USP Dextrose RS
 - USP Fructose RS
 - USP Lactose Monohydrate RS
 - USP Sucrose RS_s