# Morphine Sulfate Injection

## DEFINITION

Morphine Sulfate Injection is a sterile solution of Morphine Sulfate in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amount of morphine sulfate pentahydrate [$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$]. Injection intended for intramuscular or intravenous administration may contain sodium chloride as a tonicity-adjusting agent, and suitable antioxidants and antimicrobial agents. Injection intended for intrathecal or epidural use may contain sodium chloride as a tonicity-adjusting agent, but contains no other added substances.

## IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B. IDENTIFICATION TESTS—GENERAL,** *Sulfate* ⟨**191**⟩**:** It meets the requirements of the barium chloride test.

## ASSAY

- **PROCEDURE**

**Mobile phase:** Dissolve 0.73 g of sodium 1-heptanesulfonate in 720 mL of water, and add 280 mL of methanol and 10 mL of glacial acetic acid.

**System suitability solution:** 0.24 mg/mL of USP Morphine Sulfate RS and 0.15 mg/mL of phenol in *Mobile phase*

**Standard solution:** 0.24 mg/mL of USP Morphine Sulfate RS (on the anhydrous basis) in *Mobile phase*. [NOTE—Prepare a fresh solution daily.]

**Sample solution:** Nominally 0.24 mg/mL of morphine sulfate from the Injection in *Mobile phase*

**Chromatographic system**
(See *Chromatography* ⟨621⟩, *System Suitability*.)
**Mode:** LC
**Detector:** UV 284 nm
**Column:** 3.9-mm × 30-cm; packing L1
**Flow rate:** 1.5 mL/min
**Injection volume:** 25 µL

**System suitability**
**Samples:** *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for phenol and morphine are about 0.7 and 1.0, respectively.]
**Suitability requirements**
**Resolution:** NLT 2.0 between phenol and morphine sulfate, *System suitability solution*
**Tailing factor:** NMT 2.0 for the morphine sulfate peak, *System suitability solution*
**Relative standard deviation:** NMT 2.0%, *Standard solution*

**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of morphine sulfate pentahydrate [$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$] in each mL of the Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

$r_U$ = peak response from the *Sample solution*
$r_S$ = peak response from the *Standard solution*
$C_S$ = concentration of USP Morphine Sulfate RS in the *Standard solution* (mg/mL)
$C_U$ = nominal concentration of the *Sample solution* (mg/mL)
$M_{r1}$ = molecular weight of morphine sulfate pentahydrate, 758.83
$M_{r2}$ = molecular weight of anhydrous morphine sulfate, 668.77

**Acceptance criteria:** 90.0%–110.0%

## SPECIFIC TESTS

- **pH** ⟨**791**⟩**:** 2.5–6.5

***Change to read:***

- **BACTERIAL ENDOTOXINS TEST** ⟨**85**⟩**:** It contains NMT 17.0 USP Endotoxin Units/mg of morphine sulfate. ●If labeled for intrathecal use, it contains NMT 14.29 USP Endotoxin Units/mg of morphine sulfate.● (RB 1-Dec-2012)
- **PARTICULATE MATTER IN INJECTIONS** ⟨**788**⟩**:** Meets the requirements under small-volume injections
- **OTHER REQUIREMENTS:** It meets the requirements under *Injections* ⟨1⟩.

## ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light. Preserve Injection labeled "Preservative-free" in single-dose containers.

***Change to read:***

- **LABELING:** It meets the requirements for *Labeling* under *Injections* ⟨1⟩. Label it also to state that the Injection is not to be used if its color is darker than pale yellow, if it is discolored in any other way, or if it contains a precipitate. Injection containing no antioxidant or antimicrobial agents prominently bears on its label the words "Preservative-free", and includes, in its labeling, its routes of administration and the statement that it is not to be heat-sterilized. Injection containing antioxidant or antimicrobial agents includes in its labeling its routes of administration and the statement ●that it is not for intrathecal or epidural use.● (RB 1-Dec-2012)
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Endotoxin RS
  USP Morphine Sulfate RS