Iron Dextran Injection

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 2 Expert Committee has revised the Iron Dextran Injection monograph. The purpose of this revision is to remove the test for *Acute Toxicity.*

The Iron Dextran Injection Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact V. Durga Prasad, Senior Scientist II (91-40-4448-8723 or durgaprasad.v@usp.org).

Revision Bulletin
Official: October 5, 2023

Iron Dextran Injection

DEFINITION

Iron Dextran Injection is a sterile, colloidal solution of ferric hydroxide in complex with partially hydrolyzed Dextran of low molecular weight, in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of iron. It may contain NMT 0.5% of phenol as a preservative.

IDENTIFICATION

● **A.** To 1 mL of Injection on a watch glass add 2 drops of ammonium hydroxide. No precipitate is formed. Add 2 mL of hydrochloric acid, and add 2 mL of ammonium hydroxide. A brown precipitate is formed.

ASSAY

● **Procedure for Iron**

Solution A: Transfer 2.64 g of calcium chloride dihydrate to a 1000-mL volumetric flask. Add 500 mL of water, and swirl to dissolve. Add 5.0 mL of hydrochloric acid, and dilute with *water* to volume.

Standard stock solution: 50 µg/mL of iron prepared as follows. Transfer 350 mg of ferrous ammonium sulfate hexahydrate to a 1000-mL volumetric flask. Add water to dissolve, dilute with water to volume, and mix.

Standard solutions: 1.0, 2.0, 3.0, 4.0, and 5.0 µg/mL of iron from *Standard stock solution* prepared as follows. To separate 100-mL volumetric flasks transfer 2.0, 4.0, 6.0, 8.0, and 10.0 mL, respectively, of *Standard stock solution*. Dilute the contents in each flask with *Solution A* to volume, and mix.

Sample stock solution: Nominally equivalent to 0.5 mg/mL of iron prepared as follows. Using a "to contain" pipet, transfer a volume of Injection, nominally equivalent to 100 mg of iron, to a 200-mL volumetric flask. Dilute with *Solution A* to volume, and mix.

Sample solution: Nominally equivalent to 4 µg/mL of iron in *Solution A* from *Sample stock solution* prepared as follows. Transfer 2.0 mL of *Sample stock solution* to a 250-mL volumetric flask, and dilute with *Solution A* to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption

Analytical wavelength: Iron emission line of 248.3 nm

Lamp: Iron hollow-cathode

Flame: Air–acetylene

Blank: *Solution A*

Analysis

Samples: *Standard solutions* and *Sample solution*

Plot the absorbance of each of the *Standard solutions* versus concentration, in µg/mL, of iron, and draw the straight line best fitting the five plotted points. From the graph so obtained, determine the concentration of iron, in µg/mL, in the *Sample solution*, C_A.

Calculate the percentage of the labeled amount of iron in the portion of Injection taken:

$$\text{Result} = (C_A / C_T) \times 100$$

C_A = concentration of iron in the *Sample solution*, determined from the standard calibration graph (µg/mL)

C_T = nominal concentration of the *Sample solution* (µg/mL)

Acceptance criteria: 95.0%–105.0%

OTHER COMPONENTS

- **Antimicrobial Agents—Content, *Phenol* ⟨341⟩:** NMT 0.5%

IMPURITIES

- **Content of Chloride**

Sample: Using a "to contain" pipet, transfer 10.0 mL of Injection to a 150-mL beaker, rinsing the pipet into the beaker with several small portions of water. Add 50 mL of water and 2 mL of nitric acid.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis: Titrate with *Titrant* determining the endpoint potentiometrically using silver–glass electrodes. Each mL of *Titrant* consumed is equivalent to 3.545 mg of chloride (Cl).

Acceptance criteria

For products labeled to contain 50 mg/mL of iron: 0.48%–0.68%

For products labeled to contain 75 or 100 mg/mL of iron: 0.8%–1.1%

- **Nonvolatile Residue**

Sample solution: Using a "to contain" pipet, transfer 1.0 mL of Injection onto 3–5 g of sand spread in a shallow layer in a stainless steel dish, the dish and sand having been previously dried and weighed. Rinse the pipet, with several small portions of water, onto the sand.

Analysis: Evaporate the *Sample solution* on a steam bath to dryness, continue the drying in an oven at 105° for 15 h, and weigh.

Acceptance criteria

For products labeled to contain 50 mg/mL of iron: 28.0%–32.0%

For products labeled to contain 75 mg/mL of iron: 35.0%–40.0%

For products labeled to contain 100 mg/mL of iron: 37.0%–43.0%

SPECIFIC TESTS

- **pH ⟨791⟩:** 4.5–7.0
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.50 USP Endotoxin Units/mg of iron

Delete the following:

▲● **Acute Toxicity**▲ (RB 5-Oct-2023)

- **Absorption from Injection Site**

Analysis: Prepare a site over the semitendinosus muscle of one leg of each of two rabbits by clipping the fur and disinfecting the exposed skin. Inject each site with a dose of 0.4 mL/kg of body weight in the following manner. Place the needle in the distal end of the semitendinosus muscle at an angle such as to ensure that the full length of the needle is used, then pass it through the sartorius and vastus medialis muscles. House the rabbits separately. Seven days after the injection, sacrifice the rabbits, and dissect the treated legs to examine the muscles.

Acceptance criteria: No heavy black deposit of unabsorbed iron compounds is observed, and the tissue is only lightly colored.

- **Other Requirements:** Meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I or Type II glass.

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Not Applicable

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