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Insulin Injection

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-insulin-injection-20190401

DEFINITION

Insulin Injection is an isotonic, sterile solution of Insulin. Its potency, based on the sum of the insulin and desamido insulin components, is NLT 95.0% and NMT 105.0% of the potency stated on the label, expressed in USP Insulin Units/mL.

IDENTIFICATION

Change to read:

• **A.** The retention time of the insulin ▲pork ▲ (RB 1-May-2019) peak of *Sample solution A* or *Sample solution B* corresponds to that ▲▲ (RB 1-May-2019) of the *Identification solution*, as obtained in the *Assay* ▲and no other significant peaks are observed.▲ (RB 1-May-2019) [NOTE—It may be necessary to inject a mixture of *Sample solution* and *Identification solution*.]

ASSAY

Change to read:

• **PROCEDURE**

Solution A: Dissolve 28.4 g of anhydrous sodium sulfate in 1000 mL of water. Pipet 2.7 mL of phosphoric acid into the solution, and adjust with ethanolamine to a pH of 2.3, if necessary.

Mobile phase: Acetonitrile and *Solution A* (26:74). [NOTE—The acetonitrile is warmed to NLT 20° to avoid precipitation.]

System suitability solution: 1.5 mg/mL of ▲▲ (RB 1-May-2019) insulin pork in 0.01 N hydrochloric acid. ▲▲ (RB 1-May-2019) Allow to stand at room temperature for NLT 3 days to obtain a solution containing NLT 5% of A-21 desamido insulin. [NOTE—The *Identification solution*, *Standard solution*, and *Sample solutions* may be stored at room temperature for up to 12 h or in a refrigerator for up to 48 h.]

Identification solution: 0.6 mg/mL of ▲▲ (RB 1-May-2019) USP Insulin Pork RS in 0.01 N hydrochloric acid

Standard solution: 1.5 mg/mL of ▲▲ (RB 1-May-2019) USP Insulin Pork RS in 0.01 N hydrochloric acid. ▲▲ (RB 1-May-2019)

Sample solution A (for Injection labeled as containing 40 USP Insulin Units/mL)**:** Add 2.5 µL of 9.6 N hydrochloric acid for each milliliter of an accurately measured volume of Injection. Allow the suspension, if present, to clarify, and mix.

Sample solution B (for Injection labeled as containing 100 USP Insulin Units/mL)**:** Add 2.5 µL of 9.6 N hydrochloric acid for each milliliter of an accurately measured volume of Injection. Allow the suspension, if present, to clarify, and mix. [NOTE—Pooling several package units may be necessary to obtain sufficient volume of the sample.] Pipet 2 mL of this solution into a 5-mL volumetric flask, dilute with 0.01 N hydrochloric acid to volume, and mix.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 15-cm; packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between insulin and A-21 desamido insulin, *System suitability solution*

Tailing factor: NMT 1.8 for the insulin peak, *System suitability solution*

Relative standard deviation: NMT 1.6%, *Standard solution*

Analysis

Samples: *Identification solution*, *Standard solution*, and either *Sample solution A* or *Sample solution B*

Measure the peak responses for insulin and A-21 desamido insulin using the chromatogram of the *Identification solution* to identify the insulin peaks.

▲▲ (RB 1-May-2019) Calculate the potency, in USP Insulin Units/mL, in the portion of Injection taken:

$$\text{Result} = (\Sigma r_U / \Sigma r_S) \times C_S \times D$$

r_U = sum of the peak responses of insulin and A-21 desamido insulin from the *Sample solution*

r_S = sum of the peak responses of insulin and A-21 desamido insulin from the *Standard solution*

C_S = concentration of ▲▲ (RB 1-May-2019) USP Insulin Pork RS in the *Standard solution* (USP Insulin Units/mL)

D = dilution factor used to prepare the *Sample solution*

▲▲ (RB 1-May-2019)

Acceptance criteria: 95.0%–105.0% of the potency stated on the label, expressed in USP Insulin Units/mL

OTHER COMPONENTS

Change to read:

• **Zinc Determination ⟨591⟩:** 10–40 µg for every 100 USP Insulin Units ▲▲ (RB 1-May-2019)

PRODUCT-RELATED SUBSTANCES AND IMPURITIES

• **Physicochemical Analytical Procedures for Insulins ⟨121.1⟩,** *Limit of High Molecular Weight Proteins*: Proceed as directed in the chapter, except for the *Sample solution*. It meets the requirements.

Sample solution: Quantitatively add 4 µL of 6 N hydrochloric acid to each milliliter of an accurately measured volume of Injection, and mix.

Acceptance criteria: NMT 2.0%

SPECIFIC TESTS

• **pH ⟨791⟩:** 7.0–7.8

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 80 USP Endotoxin Units per 100 USP Insulin Units

• **Sterility Tests ⟨71⟩,** *Test for Sterility of the Product to Be Examined, Membrane Filtration*: Meets the requirements

• **Injections and Implanted Drug Products ⟨1⟩:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in the unopened, multiple-dose container provided by the manufacturer. Do not repackage. Store in a refrigerator, protect from sunlight, and avoid freezing.

Change to read:

• **Labeling:** Label it ▲▲ (RB 1-May-2019) as porcine ▲▲ (RB 1-May-2019) . If the Insulin Injection is made from insulin that is purified, label it as such. Label it to state that it is to be stored in a refrigerator and that freezing is to be avoided. The label states the potency in USP Insulin Units/mL.

Change to read:

• **USP Reference Standards ⟨11⟩**

▲▲ (RB 1-May-2019)

USP Insulin Pork RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
INSULIN INJECTION	Jennifer Tong Sun Senior Scientist II	BIO2 Biologics Monographs 2 - Proteins

Chromatographic Database Information: Chromatographic Database

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