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Sodium Fluoride F 18 Injection

Change to read:

DEFINITION

Sodium Fluoride F 18 Injection is a sterile, aqueous solution of fluoride F 18. It contains NLT 90% and NMT 110% of the labeled amount of ▲sodium▲ (USP 1-Dec-2023) fluoride F 18 expressed in MBq (mCi)/mL at the time indicated on the label. It may contain buffering agents, preservatives, stabilizing agents, or sodium chloride. It does not contain any added carrier.

IDENTIFICATION

• **A. Radionuclidic Identity**

(See *Radioactivity ⟨821⟩, Identification of Radionuclides, Half-Life Determination*.)

Acceptance criteria: The half-life of fluoride F 18 is 105–115 min.

Change to read:

• **B. Radiochemical Identity**

Procedure: After completing the *Analysis* in the test for *Radiochemical Purity*, confirm that the 0.9% sodium chloride rinse of the anion exchange cartridge contains most of the applied radioactivity. The identity of ▲sodium▲ (USP 1-Dec-2023) fluoride F 18 is confirmed by its presence in the 0.9% sodium chloride rinse of the anion exchange cartridge.

Acceptance criteria: The following criteria must be met in order for radiochemical identity to meet specification:

- The amount of applied radioactivity recovered in the 0.9% sodium chloride rinse of the anion exchange cartridge (i.e., *Radiochemical Purity*) must be NLT 95%.
- The half-life (as determined by the *Radionuclidic Identity* test) must fall within 105–115 min.

ASSAY

Change to read:

• **Radioactive Concentration (Strength)**

(See *Radioactivity ⟨821⟩, Assay of Radionuclides*.)

Analysis: Using a dose calibrator or other suitable instrument for radiation measurements, measure the quantity of radioactivity in a known volume of the Injection. Determine the radioactivity in MBq (or mCi)/mL of the Injection by using a suitable calibrated system.

Acceptance criteria: ▲90%–110%▲ (USP 1-Dec-2023) at the time indicated on the label

PURITY

• **Chemical Purity:** This article may be synthesized by different methods and processes, and therefore may contain different impurities. The presence of unlabeled ingredients, reagents, and by-products specific to the process must be controlled, and their potential for physiological or pharmacological effects must be considered.

Change to read:

• **Radiochemical Purity**

Sample solution: A volume of Injection, containing between 5 and 40 mCi, diluted with water to 3 mL.

Solid phase extraction using anion and cation exchange cartridges: Set up the system as follows. Attach a cation exchange cartridge (preconditioned with a 5 mL rinse of water) to the top port of a 3-way stopcock. An anion exchange cartridge (preconditioned with a 20 mL rinse of 0.9% sodium chloride solution followed by a 5 mL rinse of water) is attached to the bottom port of the 3-way stopcock. Attach a syringe needle or similar device to the bottom of the anion exchange cartridge for eluant delivery to a collection vial. A syringe containing 5 mL of 0.9% sodium chloride solution is attached to the side port of the 3-way stopcock. The apparatus is kept in a vertical position using a ring stand. Position the 3-way stopcock to where the top port is open. A 20-mL collection vial is used to collect the sample eluant that

passes through the cartridges and the 0.9% sodium chloride rinse of the anion exchange cartridge (see *Figure 1*).

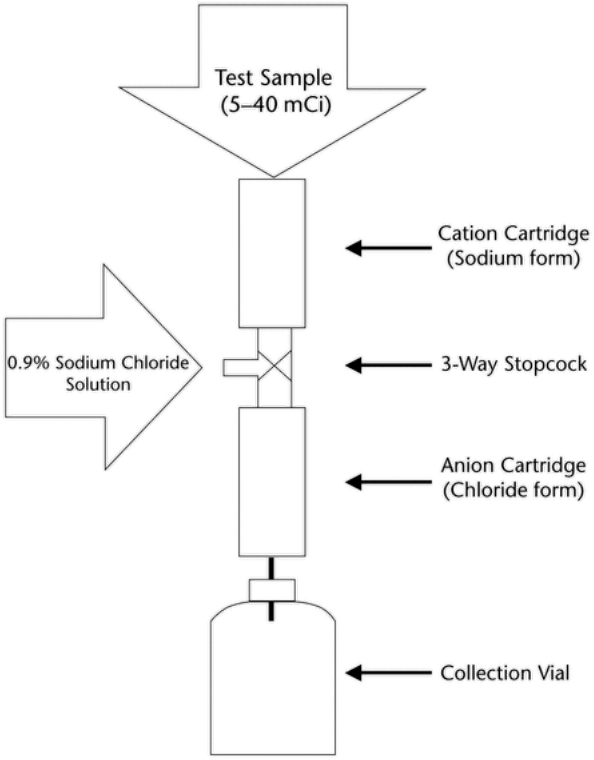

Figure 1. Solid phase ion exchange extraction system.

Analysis

Sample: *Sample solution*

Withdraw the 3-mL *Sample solution* into a syringe and attach the syringe to the top of the cation exchange cartridge. Slowly push the *Sample solution* in the syringe onto the cartridges at a dropwise flow rate. Remove the 3-mL syringe and replace it with a second syringe filled with 3 mL of water. Slowly rinse the cartridges with the 3 mL of water at a dropwise flow rate. Move the position of the 3-way stopcock to where the top port is closed and the side port is open. Slowly rinse the anion exchange cartridge with the 5 mL of 0.9% sodium chloride that is in the 5 mL syringe attached to the side port of the 3-way stopcock at a dropwise flow rate. The *Sample solution* eluant, the water rinse of the cartridges, and the 0.9% sodium chloride rinse of the anion exchange cartridge are collected together in the 20-mL collection vial. Both cartridges and the 20-mL collection vial are removed from the apparatus. Both ends of the cation and anion exchange cartridges are capped and then placed into a dose calibrator to measure the amount of radioactivity bound to each cartridge. The 20-mL collection vial is placed into a dose calibrator to measure the amount of radioactivity that was eluted off the anion exchange cartridge.

Calculate the percentage of the total radioactivity due to ▲sodium▲ (USP 1-Dec-2023) fluoride F 18 in the portion of Injection taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = radioactivity (mCi or MBq) measured in the 20-mL collection vial

r_T = sum of radioactivity (mCi or MBq) measured on the cation exchange cartridge, anion exchange cartridge, and in the 20-mL collection vial

Acceptance criteria: NLT 95% of the total radioactivity is due to ▲sodium▲ (USP 1-Dec-2023) fluoride F 18.

• **Radionuclidic Purity**

(See *Radioactivity ⟨821⟩, Identification of Radionuclides, Gamma-Ray Spectrometry*.)

[Note—This may be a periodic quality indicator test. The Injection may be distributed and dispensed prior to completion of this test.]

Analysis: Determine the purity of fluoride F 18 in the portion of Injection taken in the *Radionuclidic Impurities* test:

$$\text{Result} = [1 - (C_i/C_T)] \times 100$$

C_i = sum of the concentrations of all longer-lived radionuclides, decay corrected to the expiration time from the *Radionuclidic Impurities* test (Bq/mL or µCi/mL)

C_T = sum of the concentrations of all long-lived radionuclides and fluoride F 18, all decay corrected to the expiration time from the *Radionuclidic Impurities* test, (Bq/mL or mCi/mL)

Acceptance criteria: At the time of expiration, NLT 99.5% of radionuclides in the Injection correspond to fluoride F 18.

IMPURITIES

Change to read:

• **Radionuclidic Impurities**

[Note—This may be a periodic quality indicator test. The Injection may be distributed or dispensed prior to completion of the test.]

Sample ▲solution▲ (USP 1-Dec-2023) **:** A suitable volume of Injection, decayed for a suitable length of time to eliminate interference due to fluoride F 18 emissions.

Analysis: Using a suitable gamma-ray spectrometer, count an appropriate aliquot of the *Sample solution* for a period of time sufficient to collect a gamma spectrum. The resultant gamma spectrum should be analyzed for the presence of identifiable photopeaks, which are characteristic of radionuclidic impurities.

Determine the concentration of radionuclidic impurities in Bq (or µCi)/mL, decay corrected to the expiration time of the Injection:

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

C_i = sum of the concentrations of all longer-lived radionuclides, decay corrected to the expiration time (Bq/mL or µCi/mL)

C_T = sum of the concentrations of all long-lived radionuclides and fluoride F 18, all decay corrected to the expiration time (Bq/mL or µCi/mL)

Acceptance criteria: Total radionuclidic impurities are NMT 0.5% of the radioactivity of the Injection (see the *Assay*), decay corrected to the time of expiration.

• **Radiochemical Impurities**

Analysis

Calculate the radiochemical impurities in the portion of Injection taken from the solid phase ion exchange cartridge chromatography analysis as obtained in the *Radiochemical Purity* test:

$$\text{Result} = (r_i/r_T) \times 100$$

r_i = sum of radioactivity (mCi or MBq) measured on the cation and anion exchange cartridges

r_T = sum of radioactivity (mCi or MBq) measured on the cation and anion exchange cartridges, and in the 20-mL collection vial

Acceptance criteria: NMT 5%

SPECIFIC TESTS

• **Appearance:** Clear, colorless solution, free from visible particulates.

• **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements

• **pH**

Sample: A suitable volume of Injection

Analysis: Apply the *Sample* to pH indicator paper, short-range

Acceptance criteria: 4.5–8.0

Change to read:

• **Sterility Tests ⟨71⟩:** Meets the requirements. ▲The Injection may be distributed or dispensed prior to completion of the test, which must be started within 30 h after completion of production.▲ (USP 1-Dec-2023)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers that are adequately shielded. Store at controlled room temperature.

Change to read:

• **Labeling:** The label indicates the time and date of calibration, the radioactivity concentration of fluoride F 18 expressed in MBq (mCi)/mL at the time of calibration; the expiration time and date, and the name and quantity of any added preservative or stabilizer. Calculate the correct dosage from the date and time of calibration. The labeling indicates that in making dosage calculations, a correction is to be made for radioactive decay. The radioactive half-life of fluoride F 18 is ▲109.7 min.▲ (USP 1-Dec-2023) The label also indicates the following:

[**Caution—**Radioactive material. Do not use if cloudy or if it contains visible particulate matter.]

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

Topic/Question	Contact	Expert Committee
SODIUM FLUORIDE F 18 INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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