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Add the following:

▲Choline C 11 Injection

DEFINITION

Choline C 11 Injection is a sterile aqueous solution of choline chloride ($C_4{}^{11}CH_{14}NOCl$). It contains NLT 90% and NMT 110% of the labeled amount of [^{11}C] choline chloride expressed in MBq (or mCi)/mL at the time indicated in the labeling. It may contain buffering agents, preservatives, stabilizing agents, or sodium chloride. It may contain choline chloride carrier.

IDENTIFICATION

• **A. Radionuclidic Identity**

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

Acceptance criteria: The half-life of ^{11}C is 19.4–21.4 min.

• **B. Radiochemical Identity:** The retention time of choline C 11 from the radiochromatogram of the *Sample solution* is 90%–110% of the retention time of choline from the conductivity detector chromatogram of the *Standard solution* as determined in the *Radiochemical Purity* test.

ASSAY

• **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 radioactive concentration, in MBq (or mCi)/mL.

Acceptance criteria: 90%–110% at the time indicated on the label

PURITY

• **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 choline C 11 in the portion of Injection taken for 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 choline C 11, all decay corrected to the expiration time from the *Radionuclidic Impurities* test (Bq/mL) or (µCi/mL)

Acceptance criteria: At the time of expiration, NLT 99.5% of radionuclides in the Injection correspond to ^{11}C.

• **Radiochemical Purity**

Mobile phase: 6 mM methanesulfonic acid. Alternatively, *Mobile phase* can be generated electrolytically using an automatic eluant generator.

System suitability stock solution: 100 µg/mL each of USP Choline Chloride RS and 2-dimethylaminoethanol in 0.9% sodium chloride solution

System suitability solution: 10 µg/mL each of USP Choline Chloride RS and 2-dimethylaminoethanol from *System suitability stock solution* in 0.9% sodium chloride solution

Standard stock solution: 100 µg/mL of USP Choline Chloride RS and 1.5 mg/mL of 2-dimethylaminoethanol in 0.9% sodium chloride solution

Standard solution: 5 µg/mL of USP Choline Chloride RS and 75 µg/mL of 2-dimethylaminoethanol from *Standard stock solution* in 0.9% sodium chloride solution

Sample solution: Dilute a known volume of the Injection with an equal volume of water.

Chromatographic system

(See *Positron Emission Tomography Drugs for Compounding, Investigational, and Research Uses ⟨823⟩, Facilities and Equipment, System Suitability for QC Equipment*.)

Mode: LC

Detector: Conductivity with suppression and radiochemical detector in series

Columns

Guard: 4.0-mm × 5-cm; 7-µm packing L77

Analytical: 4.0-mm × 25-cm; 7-µm packing L77

Temperatures

Column: 30°

Conductivity detector: 30°

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 3.5 times the retention time of choline

System suitability

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

Suitability requirements: Use conductivity detector response for *System suitability*

Resolution: NLT 1.5 between 2-dimethylaminoethanol and choline, *System suitability solution*

Tailing factor: NMT 1.8 for choline, *Standard solution*

Relative standard deviation: NMT 1.0% for choline, *Standard solution*

Analysis

Sample: *Sample solution*

Measure the responses of all the peaks in the radiochromatogram.

Calculate the percentage of choline C 11 in the portion of Injection taken:

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

r_U = response of choline C 11 in the radiochromatogram

r_T = sum of the responses of all peaks in the radiochromatogram

Acceptance criteria: NLT 95% of the total radioactivity is due to choline C 11.

IMPURITIES

• **Radionuclidic Impurities**

(See *Radioactivity* ⟨821⟩.)

[Note—The Injection may be distributed or dispensed prior to completion of the test.]

Sample: A suitable volume of Injection, decayed for a suitable length of time to eliminate interference due to ^{11}C emissions

Analysis: Using a suitable gamma-ray spectrometer count an appropriate aliquot of the *Sample* 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 choline C 11, 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: From the radiochromatogram obtained in the *Radiochemical Purity* test, calculate the percentage of radiochemical impurities in the portion of Injection taken:

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

r_i = sum of areas of all the peaks other than choline C 11 in the radiochromatogram

r_T = sum of areas of all the peaks including the peak due to choline C 11 in the radio chromatogram

Acceptance criteria: NMT 5%

• **Limit of 2-Dimethylaminoethanol**

Mobile phase, System suitability stock solution, System suitability solution, Standard solution, and **Chromatographic system:** Proceed as directed in the *Radiochemical Purity* test.

Sample solution: Use the Injection.

System suitability

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

Suitability requirements: Use the conductivity detector response for both *System suitability* and *Analysis*.

Resolution: NLT 1.5 between 2-dimethylaminoethanol and choline, *System suitability solution*

Tailing factor: NMT 1.8 for 2-dimethylaminoethanol, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The conductivity detector response of 2-dimethylaminoethanol in the *Sample solution* is NMT that of the *Standard solution*.

• **Limit of Ethanol**

[Note—Perform this test if ethanol is known to be present in the article. This may be a periodic quality indicator test. The Injection may be distributed and dispensed prior to completion of this test.]

Standard stock solution: 5 mg/mL of ethanol prepared as follows. Transfer 0.3 mL of USP Alcohol Determination±Alcohol RS to a 10-mL volumetric flask. Dilute with water to volume.

Standard solution: Transfer 1 mL of *Standard stock solution* and 4 mL of water to a suitable flask to obtain 5 mL.

Sample solution: Transfer 1 mL of the Injection and 4 mL of water to suitable flask to obtain 5 mL.

Chromatographic system (See *Positron Emission Tomography Drugs for Compounding, Investigational, and Research Uses ⟨823⟩, Facilities and Equipment, System Suitability for QC Equipment*.)

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused-silica; coated with a 1-µm film of phase G16

Temperatures

Injection port: 250°

Detector: 300°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	0	0	2.5
50	15	80	0
80	80	225	2

Carrier gas: Helium

Flow rate: 5 mL/min

Injection volume: 0.5 µL

Injection type: Split, Split ratio 10:1

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2%

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The response for ethanol from the *Sample solution* is NMT the response of ethanol in the *Standard solution*.

SPECIFIC TESTS

• **Specific Activity**

From the conductivity detector chromatogram obtained in the *Radiochemical Purity* test, calculate the concentration of choline (C_U) in the portion of the Injection taken:

$$C_U = (r_U/r_S) \times C_S$$

r_U = conductivity detector response of choline in the *Sample solution*

r_S = conductivity detector response of choline in the *Standard solution*

C_S = concentration of USP Choline Chloride RS in the *Standard solution* (µg/mL)

[Note—mCi/µmol is the same as Ci/mmol.]

Calculate the specific activity in MBq (mCi)/µmol:

$$\text{Result} = (A \times B)/C_U$$

A = radioactive concentration determined at the end of synthesis (mCi/mL)

B = molecular weight of choline, 139.62 (µg/µmol)

C_U = concentration of choline in the *Sample solution* calculated in the previous equation (µg/mL)

Acceptance criteria: NLT 55,500 MBq (1500 mCi)/µmol

• **pH**

Analysis: Place a suitable volume of the Injection on pH indicator paper, short-range.

Acceptance criteria: 4.5–7.5

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

• **Sterility Tests ⟨71⟩**

[Note—The Injection may be distributed or dispensed prior to completion of the test, the latter test being started within 30 h of final manufacture.]

Sample: Use 0.1–0.3 mL of Injection

Acceptance criteria: Meets the requirements

• **Appearance:** Clear, colorless solution, free of foreign particulates

ADDITIONAL REQUIREMENTS

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

• **Labeling:** The label indicates the time and date of calibration; the concentration of choline C 11 expressed in MBq (mCi)/mL, at the time of calibration; the expiration time and date; the name and quantity of any added preservative or stabilizer. Calculate the correct dosage from date and time of calibration. The labeling indicates that in making dosage calculations, correction is to be made for radioactive decay. The radioactive half-life of ^{11}C is 20.4 min. The label also indicates the following:

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

• **USP Reference Standards ⟨11⟩**

USP Alcohol Determination±Alcohol RS

USP Choline Chloride RS▲ (USP 1-Dec-2021)

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

Topic/Question	Contact	Expert Committee
CHOLINE C 11 INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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