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Ammonia N 13 Injection

DEFINITION

Change to read:

▲Ammonia N 13 Injection is a sterile aqueous solution of [^{13}N] Ammonia ($^{13}NH_3$). It contains NLT 90% and NMT 110% of the labeled amount of [^{13}N] Ammonia ($^{13}NH_3$) expressed in MBq(mCi)/mL at the time indicated in the labeling. It may contain buffering agents, preservatives, stabilizing agents, or sodium chloride. It does not contain any added carrier.▲2S *(USP41)*

IDENTIFICATION

Change to read:

• **A. Radionuclidic Identity**

▲(See *Radioactivity ⟨821⟩, 5. Identification of Radionuclides, 5.1 Half-Life Determination*.) The half-life of ^{13}N is 9.5–10.5 min.▲2S *(USP41)*

Change to read:

• **B. Radiochemical Identity**

▲**Procedure:** After completing the *Analysis* in the *Radiochemical Purity* test, spray or stain the TLC strip with iodoplatinate TS. Allow the TLC strip to develop for 10 min. Place the developed TLC strip in an iodine chamber. The spot due to ammonium ion on the strip for the *Standard solution* appears as an orange-brown spot against a light maroon background.

Acceptance criteria: The R_F value of $^{13}NH_3$ in the *Sample solution* is 90%–110% of the R_F value of the ammonium ion as determined in the *Standard solution* in the test for *Radiochemical Purity*.▲2S *(USP41)*

ASSAY

Change to read:

• **Radioactive Concentration (Strength)**

(See *Radioactivity ⟨821⟩, 6. Assay of Radionuclides*.)

Analysis: Determine the radioactivity, in MBq (or mCi)/mL, of the Injection, using a suitable calibrated system.

Acceptance criteria: ▲90%–110% at the time indicated on the label▲2S *(USP41)*

PURITY

Change to read:

• **Radionuclidic Purity**

▲(See *Radioactivity ⟨821⟩, 5. Identification of Radionuclides, 5.2 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 ammonia N 13 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 ammonia N 13, 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 ^{13}N.▲2S *(USP41)*

Change to read:

• **Radiochemical Purity**

▲**Standard solution:** 100 mg/mL of USP Ammonium Chloride RS in water

Sample solution: A volume of Injection, appropriately diluted if necessary, to a concentration of 5–30 MBq (0.135–0.81 mCi)/mL or to a concentration suitable for the detector to be used

Chromatographic system

Mode: TLC

Detection: Radio-TLC scanner

Adsorbent: Cellulose diethylaminoethyl strips; 1.5-cm × 8-cm

Application volume: 0.5 µL

Developing solvent: Methanol and water (75:25)

Analysis

Samples: *Standard solution* and *Sample solution*

Apply the *Standard solution* and *Sample solution* independently as two adjacent spots on the TLC strip. Allow the spots to dry. Place the TLC strip in the developing chamber with *Developing solvent*. When the solvent front reaches about 1 cm from the top of the strip, remove the strip from the chamber and allow it to dry. Determine the radioactivity distribution by scanning the chromatogram with a suitable radiation detector. After completing the test for *Radiochemical Purity*, use the TLC radiochromatogram for the *Radiochemical Impurities* test. After completing the test for *Radiochemical Purity*, use the TLC strip for the *Radiochemical Identity* test.

Calculate the percentage of the labeled amount of $^{13}NH_3$ in the portion of Injection taken from the chromatogram of the *Sample solution*:

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

r_U = response of $^{13}NH_3$ from the *Sample solution*

r_T = sum of the responses of all peaks including $^{13}NH_3$ from the *Sample solution*

Acceptance criteria: NLT 95% of the total radioactivity is due to ammonia N 13.▲2S *(USP41)*

IMPURITIES

Add the following:

▲• **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: A suitable volume of Injection, decayed for a suitable length of time to eliminate interference due to ^{13}N 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 ammonia N 13, 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.▲2S *(USP41)*

Add the following:

▲• **Radiochemical Impurities**

Analysis: Calculate the percentage of radiochemical impurities in the portion of Injection taken from the TLC radiochromatogram of the *Sample solution*, as obtained in the *Radiochemical Purity* test.

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

r_i = sum of the responses all peaks excluding the response of $^{13}NH_3$ from the *Sample solution*

r_T = sum of the responses of all peaks including $^{13}NH_3$ from the *Sample solution*

Acceptance criteria: NMT 5%▲2S *(USP41)*

Delete the following:

▲• **Chemical Purity**

[Note—This article may be synthesized by different methods and processes and, therefore, contains 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.]

ALUMINUM (to be determined if Devarda's alloy is used to reduce ^{13}N nitrate/nitrite)

Standard solution: 2 µg/mL of aluminum prepared by dissolving 35.2 mg of aluminum potassium sulfate dodecahydrate in 1L of water

Blank standard solution Transfer 10mL of *Standard solution* to a 50mL volumetric flask. Add 3 drops of methyl orange TS and 2 drops of 6N ammonium hydroxide. Add 0.5N hydrochloric acid dropwise until the solution turns red. Add 1mL of edetate disodium TS. Add 5mL of eriochrome cyanine TS and 5mL of acetate buffer TS. Dilute with water to volume.

Analytical standard solution Transfer 10mL of *Standard solution* to a 50mL volumetric flask. Add 3 drops of methyl orange TS and 2 drops of 6N ammonium hydroxide. Add 0.5N hydrochloric acid dropwise until the solution turns red. Add 25mL of sodium thioglycolate TS. Add 5mL of eriochrome cyanine TS and 5mL of acetate buffer TS. Dilute with water to volume.

Sample solution: Use the Injection

Blank sample solution: Transfer 1mL of Injection to a 50mL volumetric flask. Add 3 drops of methyl orange TS and 2 drops of 6N ammonium hydroxide. Add 0.5N hydrochloric acid dropwise until the solution turns red. Add 1mL of edetate disodium TS. Add 5mL of eriochrome cyanine TS and 5mL of acetate buffer TS. Dilute with water to volume.

Analytical sample solution: Transfer 1mL of Injection to a 50mL volumetric flask. Add 3 drops of methyl orange TS and 2 drops of 6N ammonium hydroxide. Add 0.5N hydrochloric acid dropwise until the solution turns red. Add 25mL of sodium thioglycolate TS. Add 5mL of eriochrome cyanine TS and 5mL of acetate buffer TS. Dilute with water to volume.

Instrumental Conditions:

Mode: Vis

Analytical wavelength: 535 nm

Analysis:

Samples: *Blank Standard solution,Analytical standard solution, Blank sample solution* and *Analytical sample solution*

Procedure: Measure the absorbance of the *Samples* immediately. Calculate the amount of aluminum in µg/mL in the portion of the Injection taken:

$$\text{Result} = [(A_u - A_{ub})/A_s - A_{sb})] \times C_s \times (V_s/V_u)]$$

A_u = absorbance of *Analytical sample solution*

A_{ub} = absorbance of *Blank sample solution*

A_s = absorbance of *Analytical standard solution*

A_{sb} = absorbance of *Blank standard solution*

C_s = concentration of aluminum in *Standard solution*, µg/mL

V_s = volume of Standard solution in *Analytical standard solution*

V_u = volume of Injection in *Analytical sample solution*

Acceptance criteria: NMT 10 µg/mL ▲2S *(USP41)*

Add the following:

▲• **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 solution: 3.1 mg/mL of ethanol prepared as follows. Transfer 2 mL of USP Alcohol Determination±Alcohol RS to a 10 mL volumetric flask. Dilute with water to volume.

Sample solution: Use the Injection.

Chromatographic system

Mode: GC

Detector: Flame ionization

Column: 0.25-mm × 30-m fused-silica; coated with a 0.5-µm film of phase G16

Temperatures

Injection port: 250°

Detector: 300°

Column: See *Table 1*.

[Note—Depending on the syringe wash solvent, an additional ramp at 10°/min to bring the column to 240° with no hold time may be used before returning the column oven to initial conditions.]

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	0.5
40	40	110	1

Carrier gas: Hydrogen

Flow rate: 1.3 mL/min

Injection volume: 1 µL

Injection type: Split ratio, 15:1

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The response for ethanol in the *Sample solution* is NMT the response of ethanol in the *Standard solution* (3.1 mg/mL of ethanol).▲2S *(USP41)*

SPECIFIC TESTS

Change to read:

• **pH**

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

Acceptance criteria: 4.5–7.5▲2S *(USP41)*

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:**▲ Meets the requirements▲2S *(USP41)*

Add the following:

▲• **Sterility Tests ⟨71⟩**

[Note—The Injection may be distributed or dispensed prior to completion of the test, the latter test being started within 36 h of final manufacture.]

Sample: Use 0.1–0.3 mL of Injection

Acceptance criteria: Meets the requirements▲2S *(USP41)*

Add the following:

▲• **Appearance:** Clear, colorless solution, free of foreign particulates▲2S *(USP41)*

Delete the following:

▲• **Specific Activity:** No carrier added ▲2S *(USP41)*

Delete the following:

▲• **Other Requirements:** It meets the requirements under *Injections ⟨1⟩*, except that the Injection may be distributed or dispensed before completion of the test for *Sterility Tests ⟨71⟩*, the latter test being started within 24 h of final manufacture, and except that it is not subject to the recommendation in *Volume in Container*. ▲2S *(USP41)*

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers that are adequately shielded. ▲Store at controlled room temperature.▲2S *(USP41)*

Change to read:

• **Labeling:** ▲The label indicates the time and date of calibration; the concentration of ^{13}N as ammonia 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 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 ^{13}N is 9.96 min. The label also indicates the following: [**Caution—**Radioactive Material. Do not use if cloudy or if it contains visible particulate matter.]▲2S *(USP41)*

Change to read:

• **USP Reference Standards** ⟨11⟩

▲ USP Alcohol Determination±Alcohol RS▲2S *(USP41)*

USP Ammonium Chloride RS

▲▲ (CN 1-May-2018)

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

Topic/Question	Contact	Expert Committee
AMMONIA N 13 INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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