date and time of calibration; the expiration date and time; the lot or batch number; the name and quantity of any added preservative or stabilizer; an indication on the labeling that states, "Do not use if cloudy or if it contains particulate matter;" and the statement "Caution—Radioactive Material." The labeling indicates that in making dosage calculations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{11}C is 20 minutes.

USP Reference standards ⟨11⟩—
USP Endotoxin RS

Radionuclide identification ⟨821⟩—Its gamma-ray spectrum is identical to that of a specimen of ^{11}C in that it exhibits a positron annihilation peak at 0.511 MeV and possibly a sum peak of 1.022 MeV, dependent upon geometr y and detector efficiency.

Bacterial endotoxins ⟨85⟩—It contains not more than 175/*V* USP Endotoxin Unit per mL, in which *V* is the maximum recommended total dose, in mL, at the expiration date or time.

pH ⟨791⟩: between 4.5 and 8.5.

Radionuclidic purity ⟨821⟩—A multichannel analyzer is used to count all radioactivity from 40 to 2,500 keV to determine the absence of radiation, other than at 0.511 MeV and 1.022 MeV, over a period of 4 hours. Determine the half-life by a suitable detector system.

Chemical purity—

Mobile phase—Add 14 mL of 0.5 N sulfuric acid to 500 mL of water in a 1000-mL volumetric flask. Add 100 mL of acetonitrile, dilute with water to volume, and mix. Filter and degas. Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Reference solution—Dissolve an accurately weighed quantity of sodium acetate in water to obtain a solution having a known concentration of about 1 mg per mL. Quantitatively dilute a portion of this solution with *Mobile phase* to obtain a solution having a known concentration of about 20 µg per mL.

Test solution—Prepare a solution by quantitatively diluting an accurately measured volume of Injection, equivalent to about 1 mCi of radioactivity with 10 parts of *Mobile phase*, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 210-nm detector and a 7.8-mm × 10-cm column that contains packing L9. The flow rate is about 1 mL per minute. Chromatograph the *Reference solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 minutes for acetate and 1.0 minute for carbonate; the resolution, *R,* between acetate and carbonate is not less than 1.4; the column efficiency is not less than 85 theoretical plates; and the relative standard deviation for replicate injections is not more than 10%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Reference solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the acetate peaks. Calculate the concentration, in µg per mL, of sodium acetate in the Injection by the formula:

$$C(r_U / r_S)$$

in which *C* is the concentration, in g per mL, of sodium acetate in the *Reference solution*; and r_U and r_S are the acetate peak responses obtained from the *Test solution* and the *Reference solution*, respectively.

Radiochemical purity—

Mobile phase and *Reference solution*—Proceed as directed under *Chemical purity*.

Chromatographic system—Proceed as directed under *Chemical purity* except that the liquid chromatograph is also equipped with a suitable collimated radiation detector (see *Radioactivity* ⟨821⟩).

Procedure—Inject about 30 µL of the Injection into the chromatograph, record the chromatogram, and measure the areas for the major peaks. The radioactivity under the acetate C 11 peak is not less than 95% of the total area of all peaks observed, and its retention time is within ±10% of that obtained for the *Reference solution*, similarly chromatographed.

Other requirements—It meets the requirements under *Injections* ⟨1⟩, except that the Injection may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the day following final manufacture, and except that it is not subject to the recommendation of *Volume in Container*.

Assay for radioactivity ⟨821⟩—Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity in MBq (mCi) per mL, of the Injection by use of a calibrated system.

Urea C 13

» Urea C 13 contains not less than 99.0 per cent and not more than 100.5 per cent of $^{13}CH_4N_2O$.

Packaging and storage—Preserve in well-closed containers at room temperature.

USP Reference standards ⟨11⟩—
USP Urea C 13 RS

Limit of biuret—

Standard solution—Dissolve an accurately weighed quantity of biuret in water, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.033 mg per mL.

Test solution—Transfer 100.0 mg of Urea C 13 to a test tube, and dissolve in 3 mL of water.

Procedure—To the *Test solution* and to 3 mL of the *Standard solution* add 3 mL of sodium hydroxide solution (10 in 100) and about 3 drops of copper sulfate solution (0.5 in 100), mix, and allow to stand for 5 minutes. Any reddish violet color in the *Test solution* is not more intense than that obtained from the *Standard solution:* not more than 0.1% of biuret is found.

Isotopic purity—

Test solution—Prepare a solution in methanol containing about 12 mg of Urea C 13 per mL.

Chromatographic system (see *Chromatography* ⟨621⟩ and *Mass Spectrometry* ⟨736⟩)—The gas chromatograph is connected to a mass spectrometer, and is equipped with a 0.25-mm × 15-m capillary column coated with a 0.1- µm film of phase G47. The injection port is maintained at a temperature of 250 °, the detector is maintained at a temperature of 200 °, and the transfer line to the mass spectrometer is maintained at a temperature of 265°. Helium is used as the carrier gas. The mass spectrometer is operated in a single-ion response mode. The electron energy is 70 eV.

Procedure—Inject about 1 µL of the *Test solution* into the gas chromatograph, record the total ion chromatogram, and combine all of the mass spectra scans across the entire major peak. Record the peak intensities at mass-to-charge ratios of 60, 61, 62, and 63. Calculate the per centage of carbon that is C 13 in the portion of Urea C 13 taken by the formula:

$$100[(I_{61} + I_{63})/(I_{60} + I_{61} + I_{63})]$$

in which I_{60}, I_{61}, and I_{63} are the relative peak intensities at mass-to-charge ratios of 60, 61, and 63, respectively: not less than 99% is found. Calculate the per centage of oxygen that is O 18 in the portion of Urea C 13 taken by the formula:

$$100[(I_{62} + I_{63})/(I_{60} + I_{61} + I_{62} + I_{63})]$$

in which I_{62} is the relative peak intensity at a mass-to-charge ratio of 62, and the other terms are as defined above: not more than 15% is found.

Other requirements—It meets the requirements for *Identification* tests *A* and *B*, *Melting range*, *Residue on ignition*, *Alcohol-insoluble matter*, *Chloride*, *Sulfate*, and *Heavy metals* under *Urea*.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, methanol, and water (89:10:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Biuret stock solution—Transfer about 15 mg of biuret, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. T ransfer 1.0 mL of this solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

System suitability preparation—Transfer about 25 mg of urea, accurately weighed, to a 10-mL volumetric flask. Pipet 1.0 mL of *Biuret stock solution* into the flask, dilute with *Mobile phase* to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Urea C 13 RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessar y, with *Mobile phase* to obtain a solution having a known concentration of about 2 mg per mL.

Assay preparation—Transfer about 100 mg of Urea C 13, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 200-nm detector and a 4.6-mm × 25-cm column that contains 5- µm packing L8. The flow rate is about 0.8 mL per minute. Chromatograph the *System suitability preparation* and the *Standard preparation,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between urea and biuret is not less than 1.5; and the relative standard deviation for replicate injections is not more than 1%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $^{13}CH_4N_2O$ in the portion of Urea C 13 taken by the formula:

$$(M_U / M_S)50C(r_U / r_S)$$

in which M_U and M_S are the molecular weights of Urea C 13 and USP Urea C 13 RS, respectively; C is the concentration, in mg per mL, of USP Urea C 13 RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Urea C 13 for Oral Solution

» Urea C 13 for Oral Solution is a dr y powder prepared from Urea C 13. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of urea C 13 ($^{13}CH_4N_2O$). It contains no preser vatives.

Packaging and storage—Preserve in sterile, well-closed containers.

Labeling—Label it to indicate that the solution is to be discarded if particulate matter is visible after reconstitution. [NOTE—It is to be reconstituted with *Sterile Purified Water*.]

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**The total aerobic microbial count does not exceed 1000 cfu per g, the total combined molds and yeasts count does not exceed 100 cfu per g, and it meets the requirements for the absence of *Salmonella* species and *Escherichia coli*.

Completeness of solution ⟨641⟩: meets the requirements, a solution in carbon dioxide-free water containing 100 mg per mL being used.

Other requirements—It meets the requirements for *Identification* tests *A* and *B* under *Urea* and for the *Assay* under *Urea C 13*, and for packaged solids under *Uniformity of Dosage Units* ⟨905⟩.

Urea C 14 Capsules

» Urea C 14 Capsules contain $^{14}CH_4N_2O$ in which a portion of the molecules are labeled with radioactive ^{14}C to provide 0.04 MBq (or 1 µCi) of radioactivity per capsule. It contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of ^{14}C expressed as MBq (or µCi).

Packaging and storage—Preserve in tight containers, and store at controlled room temperature.

Expiration date—The expiration date is not later than two years from the date of manufacture.

Labeling—Label it to include the following: the amount of ^{14}C, expressed in MBq (or µCi) per Capsule at the time of calibration; the expiration date; the total radioactivity per container; and the statement, "Caution—Radioactive material."

Radionuclide identification ⟨821⟩**—**A solution of 1 or more Capsules in 1 N hydrochloric acid when tested using a liquid scintillation counter produces beta emission having a 49 keV mean and a 156 keV max.

Dissolution ⟨711⟩**—**

Medium: simulated gastric fluid TS; 500 mL.

Apparatus 1: 50 rpm.

Time: 10 minutes.

Procedure—Determine the background levels of ^{14}C with a 1-mL portion of the solution under test using a liquid scintillation counter.

Tolerances: not less than 80% *(Q)* of the labeled amount of ^{14}C is dissolved in 10 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Radionuclidic purity ⟨821⟩**—**Determine the radionuclidic purity of a solution of 1 or more Capsules in water using a liquid scintillation counter: not less than 99.9% of the radioactivity is present as C 14.

Radiochemical purity—

Adsorbent: 0.25-mm layer of chromatographic cellulose.

Test solution—Open 2 Capsules and place them in a suitable container, add 8 mL of methanol, and mix.

Reference solution: 40 mg of urea per mL, in water.

Application volume: 20 µL of the *Test solution* and 4 µL of the *Reference solution*.

Developing solvent system: n-butanol saturated with water.

Procedure—Proceed as directed for *Thin-Layer Chromatography* under *Chromatography* ⟨621⟩. Locate the spots on the plate by spraying with Ehrlich's reagent. Determine the radioactivity distribution with a suitable radiation detector (see *Radioactivity* ⟨821⟩), and obtain the R_F value: the R_F value of the principal spot from the *Test solution* corresponds to that obtained from the *Reference solution*, and the radioactivity of the ^{14}C band is not less than 90% of the total radioactivity.

Assay for radioactivity ⟨821⟩**—**Prepare a solution of 1 or more Capsules in 1 N hydrochloric acid. Using a liquid scintillation counter, determine the radioactivity, in MBq (or mCi) per mL by use of a calibrated system.