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USP 23

NF 18

THE UNITED STATES PHARMACOPEIA

THE NATIONAL FORMULARY

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UNITED STATES PHARMACOPEIAL CONVENTION, INC.

Continuous Revision of the USP and the NF

The need for continuously refining specifications and updating standards is a natural consequence of the introduction of new drugs and the accelerated growth of knowledge in the pharmaceutical sciences.

In order to keep the *United States Pharmacopeia* and the *National Formulary* abreast of these developments and to maintain the official standards accordingly, the main volume is revised regularly by *Supplements*. *Interim Revision Announcements* are issued between *Supplements* as necessary.

Interim Revision Announcements pertaining to this volume of *USP* and *NF* are published in the journal, *Pharmacopeial Forum*. Reprints of *Interim Revision Announcements* are available on order. A single copy of each *Interim Revision Announcement* is available without charge for each subscription to *USP-NF*. Each request should be sent to USPC at the address shown below. Corrections and revisions included in *Interim Revision Announcements* are incorporated in the next regular *Supplement*.

Supplements* to *USP 23–NF 18 are issued serially as necessary, with the *Index* in the latest *Supplement* being fully cumulative with respect to all *Supplements* issued previously. Thus, in order to keep the compendia up to date, the user needs to keep all of the *Supplements*. Cumulation of the *Supplements* into a new main volume will occur whenever the amount of text in the *Supplements* becomes unwieldy for the user, or the logistics of publication so dictate. The publication cycle of main volumes may therefore vary from the five-year interval characteristic of new main volumes published since 1950.

Electronic publication of the USP-NF first occurred in November 1992. The complete text of USP is available in a fully searchable electronic format for ease of use. It allows the user to conduct searches that would not have been cost effective or possible with the printed format, and provides fully integrated up-to-date text as it is updated with each *Supplement*.

Inquiries, Comments, and Suggestions

for revisions in the *USP* or *NF* text should be addressed to the Drug Standards Division:

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USP-NF Continuous Revision Process

Requests/comments submitted

⬇

DSD Subcommittee reviews requests/comments

⬇

Publish in *Pharmacopeial Forum* for public review
(*In-process Revision* or *Pharmacopeial Previews*)

⬇

Subcommittee approves

⬇

DSD Executive Committee approves

⬇

Executive Committee of Revision approves

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or for use by either jet or syringe injection, whichever is applicable. Label the Vaccine in single-dose containers, if such containers are not light-resistant, to state that it should be protected from sunlight. Label it also to state that constituted Vaccine should be discarded if not used within 8 hours.

Rubidium Chloride Rb 82 Injection

» Rubidium Chloride Rb 82 Injection is a sterile solution, suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{82}Rb expressed in megabecquerels (or in millicuries) per mL at the time indicated in the labeling. It is obtained by elution from a strontium 82–rubidium 82 generator system. ^{82}Rb, with a half-life of 76 seconds, is a short-lived positron-emitting radionuclide formed by the radioactive decay of the parent nuclide ^{82}Sr. Strontium Sr 82 with a half-life of 25.5 days is produced by the proton irradiation of rubidium or spallation of molybdenum. The chemical form of the Injection is $^{82}RbCl$. [NOTE—Elute with additive-free Sodium Chloride Injection only. Discard the first 50 mL of the eluate each day the generator is eluted.]

Packaging, storage, and labeling—Requirements for packaging, storage, and labeling do not apply; Rubidium Chloride Rb 82 Injection is obtained by elution from the generator and is administered by direct infusion.

USP Reference standards ⟨11⟩—*USP Endotoxin RS*.

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

Radionuclide identification (see *Radioactivity* ⟨821⟩)—[NOTE—Perform this test quickly, because of the rapid decay of the ^{82}Rb.] The gamma-ray spectrum of eluted ^{82}Rb exhibits photopeaks at 511 and 777 keV.

pH ⟨791⟩: between 4.0 and 8.0.

Radionuclidic purity—Using a suitable counting assembly (see *Selection of a Counting Assembly* under *Radioactivity* ⟨821⟩), determine the radioactivity of each radionuclidic impurity, in kBq per MBq (or μCi per mCi), of Rb 82 in the generator eluate by use of a calibrated system as directed under *Radioactivity* ⟨821⟩. [NOTE—For the following tests, use the generator eluate containing ^{82}Rb that has been allowed to decay for 1 hour after the end of elution.]

Sr 82 and Rb 83—Obtain a gamma-ray spectrum of the hour-old eluate, and measure the activities of the radionuclidic impurities directly from the spectrum. Sr 82 exhibits photopeaks at 511 and 777 keV and decays with a radioactive half-life of 25.5 days. Rb 83 exhibits a photopeak at 530 keV and decays with a radioactive half-life of 86.2 days. The activity levels of Sr 82 and Rb 83 are not more than 0.02 kBq per MBq (0.02 μCi per mCi) and not more than 0.05 kBq per MBq (0.05 μCi per mCi) of Rb 82 at the end of elution, respectively.

Sr 85—Obtain a gamma spectrum of the hour-old eluate, and, using the same system and geometry, obtain a gamma spectrum of a pure Rb 82 specimen (generator eluate containing ^{82}Rb taken within 10 minutes of elution). Sr 85 exhibits a major photopeak at 514 keV and decays with a radioactive half-life of 64.8 days. Sr 85 may be determined by subtraction of the 511 and 777 keV peaks in the pure Rb 82, from the 511-514 keV and 777 keV peaks in the hour-old eluate. The activity level of Sr 85 is not

Other gamma-ray emitters—The total of other gamma-ray emitting radionuclidic impurities does not exceed 0.005 kBq per MBq (0.005 μCi per mCi) of Rb 82 at the end of elution.

Chemical purity—

Electrolyte solution—Transfer 107 g of ammonium chloride, 25 g of gelatin, and 42 mL of hydrochloric acid to a 500-mL volumetric flask. Add about 450 mL of water, and sonicate until a clear solution is obtained. Dilute with water to volume, and mix.

Tin stock standard solution—Dissolve 100 mg of metallic tin (Sn), accurately weighed, in 10 mL of dilute hydrochloric acid (1 in 2), and dilute with water to 100 mL.

Tin standard solution A—Transfer 0.5 mL of *Tin stock standard solution* to a 50-mL volumetric flask and dilute with 0.1 *N* hydrochloric acid to volume.

Tin standard solution B—Transfer 1.0 mL of *Tin standard solution A* to a 50-mL volumetric flask. Add 10.0 mL of 0.9% sodium chloride solution, dilute with *Electrolyte solution* to volume, and mix.

Test solution—Obtain a 50-mL eluate from the generator, and allow to stand for at least 1 hour to allow for the complete decay of ^{82}Rb. Transfer 10.0 mL of the eluate to a 50-mL volumetric flask, dilute with the *Electrolyte solution* to volume, and mix.

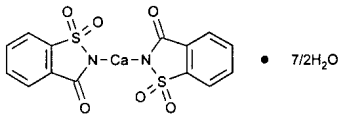
Procedure—Transfer a portion of the *Test solution* to a polarographic cell, and deaerate by bubbling nitrogen through the solution for 5 minutes. Insert the dropping mercury electrode of a suitable polarograph, and obtain the differential pulse polarogram from −0.15 to −0.75 volts, at a current range of 0.5 μA, using a saturated calomel electrode as the reference electrode and a platinum wire as the auxiliary electrode (see *Polarography* ⟨801⟩). Similarly, transfer a portion of the *Tin standard solution B* to a polarographic cell and obtain the polarogram. A peak at −0.52 volts indicates the presence of tin. The peak height of the *Test solution* is not greater than that of the *Tin standard solution B* (1 μg per mL).

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 of final manufacture, and except that it is not subject to the recommendation for *Volume in Container* under *Injections* ⟨1⟩.

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

Saccharin—*see* Saccharin NF

Saccharin Calcium



$C_{14}H_8CaN_2O_6S_2 \cdot 3½H_2O$ 467.49

1,2-Benzisothiazol-3(2*H*)-one, 1,1-dioxide, calcium salt, hydrate (2:7).

1,2-Benzisothiazolin-3-one 1,1-dioxide calcium salt hydrate (2:7) [*6381-91-5*].

Anhydrous 404.44 [*6485-34-3*].

» Saccharin Calcium contains not less than 98.0 percent and not more than 101.0 percent of $C_{14}H_8CaN_2O_6S_2$, calculated on the anhydrous basis.