USP <825> Radiopharmaceutical: Preparation, Compounding, Dispensing, and Repackaging

About USP Chapter <825>

Radiopharmaceuticals are a subset of radioactive materials (RAMs) falling under the control of the U.S. Nuclear Regulatory Commission (NRC) or NRC-contracted agreement state agency.

USP Chapter <825> is intended to provide uniform minimum standards for the preparation, compounding, dispensing, and repackaging of sterile and non-sterile radiopharmaceuticals for humans and animals that occur as part of state-licensed activities (e.g., the practice of pharmacy and the practice of medicine).

Chapter <825> applies to all practice settings where radiopharmaceuticals are prepared, compounded, dispensed, or repackaged. Practice settings consisting of state-licensed nuclear pharmacies, federal nuclear pharmacy facilities, and other healthcare facilities, including, but not limited to nuclear medicine departments in hospitals and clinics, nuclear cardiology clinics (fixed site or mobile), and other specialty clinics.

Section 1.2: Sterile Radiopharmaceuticals

What does USP <825> say?

The most important factor for maintaining sterility is the avoidance of touch contamination.

- Wipe the vial septum with sterile 70% isopropyl alcohol (IPA) before initial needle puncture.
- If the vial shield top is then closed, the septum must be disinfected again with sterile 70% IPA before another needle puncture.
- Some vial shields are constructed so that the vial septum is recessed and difficult to access. One approach for disinfecting the vial septum in this type of vial shield is to use right-angle forceps to hold a sterile 70% IPA wipe and apply direct contact with the vial septum.
- Wipe the septum with sterile 70% IPA frequently whenever multiple punctures are occurring (e.g., removing several individual doses from a multiple-dose container).

Contec Product Solutions:

Critical Site® Sterile Wipes
SterileSorb™ Wipes
Contec® Sterile 70% Isopropanol

Section 2: Radiation Safety Concerns

What does USP <825> say?

- The handling of radiopharmaceuticals necessitates meeting the radiation regulatory agency requirements for worker safety. This involves licensing commitments to keep all exposure levels for the workers involved as low as reasonably achievable (ALARA) practices. Principles of radiation safety include time, distance, shielding, and contamination control.

2.4 Contamination Control

RAM contamination (e.g., spills, drips, sprays, volatility) is an important concern for radiation protection. Therefore, various techniques and materials may be used by handlers of radiopharmaceuticals to minimize radioactive contamination.

For example: Disposable absorbent pads are commonly used to contain such radioactive contamination, and when used in an ISO Class 5 PEC, the pads must be clean and low-lint.

Contec Product Solutions:

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tel: +1-864-503-8333

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Section 4: Personnel Qualifications, Training, and Hygiene

What does USP <825> say?

- Individuals entering a compounding area must be properly garbed and must maintain proper personal hygiene to minimize the risk of contamination to the environment and/or radiopharmaceuticals.

Section 4.1: Aseptic Qualifications

What does USP <825> say?

Personnel must prove competency, as applicable to their job functions, prior to performing radiopharmaceutical aseptic tasks that are beyond immediate use. These qualifications must be completed and documented initially, and then successfully repeated at intervals

Contec Healthcare representatives can provide training in the following:

- Garbing and Hand Hygiene
- PEC Cleaning and Disinfecting

USP Chapter <825> established two processes for Hand Hygiene: one for immediate use (patient area) and the other for Segregated Radiopharmaceutical Processing Area (SRPA).

Section 4.4: Hand Hygiene and Garbing for Immediate Use Preparations

Radiopharmaceuticals may be prepared and dispensed at immediate use, and the precautions related to personal hygiene must include the following:

- Hand hygiene: Wash hands and arms to the wrists with soap and water or use a suitable alcohol-based hand rub with a time based on institution policies to reduce bioburden on the hands.
- Garbing: Immediately after hand hygiene, don a clean coat/gown that has not been exposed to a patient or patient care area, and don either sterile gloves or non-sterile disposable gloves before disinfecting the gloves with sterile 70% IPA. [NOTE—A different lab coat must be worn to care for a patient than the coat/gown used for radiopharmaceutical preparation.]

Section 4.5: Hand Hygiene and Garbing for Buffer Areas and Segregated Radiopharmaceutical Processing Area (SRPA)

Radiopharmaceuticals may be prepared and dispensed at immediate use, and the precautions related to personal hygiene must include the following:

In situations involving repackaging, dispensing, preparation, preparation with minor deviations, or compounding of sterile radiopharmaceuticals in an ISO Class 5 PEC, the following precautions related to personal hygiene are to be followed:

1. Before entering the SRPA or buffer area, personnel must remove outer garments (e.g., bandanas, coats, hats, jackets, sweaters, vests); all cosmetics; all hand, wrist, and other exposed jewelry including piercings that could interfere with the effectiveness of the garbing (e.g., the fit of gloves, cuffs of sleeves, and eye protection). Nail products (e.g., artificial nails, polish, extenders) are prohibited. Natural nails must be kept neat and trimmed. Remove earbuds and headphones. Radiation dosimetry devices are allowed, as required by the RAM license.
2. Do not bring electronic devices that are not necessary for compounding or other required tasks.
3. Immediately before entering the SRPA or buffer area, remove visible debris from underneath fingernails under warm running water using a disposable nail cleaner. Personnel must wash hands and arms up the elbows with soap and water for at least 30 seconds and then dry hands using low-lint towels. Alternatively, hand washing may be performed after donning shoe covers, head/hair covers, and face mask, as described below.

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4. Personnel must don the following garb—shoe covers, head/hair/facial hair covers, face mask—in an order that eliminates the greatest risk of contamination, as defined in facility SOPs.
5. If not already performed, remove visible debris from underneath fingernails under warm running water using a disposable nail cleaner. Personnel must then wash hands and arms up to the elbows with soap and water for at least 30 seconds and then dry hands using low-linting towels. Electronic hand dryers are not permitted.
6. Personnel must then perform hand antisepsis cleansing using a suitable alcohol-based hand rub.
7. Personnel must then don a low-linting gown with sleeves that fit snugly around the wrists and enclosed at the neck. Disposable gowns are preferred. If reusable gowns are used, a clean gown must be donned daily.
8. Personnel must then aseptically don sterile, powder-free gloves. Gloves must completely and snugly cover the ends of the gown cuffs so that skin on the wrists and upper hands is completely enveloped.
9. Because gloves may not remain sterile due to touching or handling potentially non-sterile materials, personnel must periodically apply sterile 70% IPA to gloves while balancing the risk of radioactivity contamination. (new requirement)
10. Personnel must also routinely inspect the gloves that they are wearing for holes, punctures, radioactivity contamination, or tears. If a defect, radioactivity contamination, or malfunction is detected, personnel must immediately remove the gloves, repeat antiseptic hand cleansing using an alcohol-based hand rub, and don new sterile gloves.
11. Direct personnel touch contamination is the most common source of microorganisms, so personnel must avoid touch contamination of container septa, needles, syringe and needle hubs, and other critical sites.
12. When personnel exit the buffer area or SRPA, shoe covers, head/hair covers, face masks, and gloves must be properly disposed of and new ones donned for each reentry into the buffer area or SRPA. Gowns may be re-used within the same shift if the gown is maintained in a classified area or in (or immediately outside of) the SRPA that minimizes contamination (e.g., away from sinks).

Contec Product Solutions:

Contec® CritiGear™ Sterile Nitrile Gloves
Contec® Healthcare Low-Lint Hand Drying Wipes
Amplitude™ EcoCloth™ Wipes
Contec® CritiGear™ Cleanroom Frocks

Section 5.4: Placement and Movement of Materials

What does Chapter <825> say?

All items must be wiped with low-lint wipes and an appropriate disinfectant by personnel wearing gloves before they are brought into the clean side of ante-room(s), pass-through(s), into an SRPA or an ISO 5 PEC. However, constraints that would lead to excessive radiation exposure to radiation for workers and thereby be contradictory to following ALARA safety principles (e.g., the wiping of unshielded sources of radioactive material) might preclude this from occurring.

Contec Product Solutions:

PeridoxRTU® Sporicidal Disinfectant and Cleaner
Contec® Sterile 70% Isopropanol
Amplitude™ EcoCloth™ Wipes
Sanotex® Environmental Surface Wipes

Section 7: Cleaning and Disinfecting

What does Chapter <825> say?

Surfaces must be cleaned before being disinfected unless an Environmental Protection Agency (EPA)-registered (or equivalent) one-step disinfectant cleaner is used to accomplish both the cleaning and disinfection in one step. After cleaning and disinfecting or the application of a one-step disinfectant cleaner in a PEC, apply sterile 70% IPA to remove any residue.

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Cleaning and disinfecting surfaces should occur at the minimum frequencies specified in [Table 5] or if activities are not performed daily, cleaning and disinfecting must be completed before initiating activities.

The act of reducing or removing radioactivity (radioactive decontamination) from an object or surface must be balanced with the risk of spreading radioactive contamination. At times the best approach may be to shield the area until the radiation exposure levels are lower. The PEC should be checked for radioactive contamination before cleaning and disinfecting to prevent spreading radioactive contamination in the PEC.

Cleaning must be performed in the direction of most to least clean areas.

The manufacturer's direction or published data for the minimum contact time must be followed for the cleaning, disinfecting, and sporicidal agents used. When sterile 70% IPA is used, it must be allowed to dry.

Table 5 – Minimum Cleaning Frequency for Cleaning and Disinfecting in Classified Areas and within the Perimeter of the SRPA

Site	Cleaning	Disinfecting*	Apply Sporicidal
PEC(s) and equipment inside the PEC(s)	Prior to performing sterile processing of radiopharmaceuticals on each day that activities are carried out, the walls, bars, torso shield and any exposed surface of equipment inside the PEC must be cleaned to the extent possible as specified by the equipment manufacturer or the assessment of a qualified individual (e.g., microbiologist or industrial hygienist). Radioactive contamination may be shielded with appropriate temporary material, providing the material is covered with low-linting absorbent pads or has equivalent low shedding properties.	Following cleaning on each day that activities are carried out, exposed surfaces of the equipment should be disinfected to the extent possible as specified by the equipment manufacturer or the assessment of a qualified individual (e.g., microbiologist or industrial hygienist). When used, remove low-linting absorbent pads and survey the PEC for radioactive contamination prior to disinfecting. Replace with new pads after disinfecting or as required after spills.	Monthly
Surfaces of sink(s)	Daily	Daily	Monthly
Hot-cells (all interior surfaces, dependent on design, equipment, and shielding present)	Daily	Daily	Monthly
Work surface(s) outside the PEC	Daily	Daily	Monthly
Ceiling(s)	Monthly	Monthly	Monthly
Wall(s), door(s), door frame(s), & other fixtures	Monthly	Monthly	Monthly
Floors	Daily	Daily	Monthly
Storage shelving and storage bins	Monthly	Monthly	Monthly

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**Many disinfectants registered with the EPA are one-step cleaning and disinfecting agents, which means that the disinfectant has been formulated to be effective in the presence of light to moderate soiling without a separate cleaning step. Cleaning and disinfecting must be balanced with the risk of spreading radiation contamination. The best approach may be to shield the area until the radiation exposure levels are lower.*

Contec Product Solutions:

PeridoxRTU® Sporicidal Disinfectant and Cleaner
Contec® Sterile 70% Isopropanol
PROSAT® Sterile™ PS-911EB
Contec® MicroCinch™ Mop
Amplitude™ EcoCloth™ Wipes

Section 7.1: Cleaning, Disinfecting and Sporicidal Agents

What does Chapter <825> say?

Only the 70% IPA used in the ISO Class 5 PEC must be sterile.

Table 6 – Purpose of Cleaning, Disinfectant and Sporicidal Agents

Type of Agent	Purpose
Cleaning Agent	An agent for the removal of residues (e.g., dirt, debris, microbes, and residual drugs or chemicals) from surfaces.
Disinfecting Agent	A chemical or physical agent used on inanimate surfaces and objects to destroy fungi, viruses, and bacteria.
Sporicidal Agent	A chemical or physical agent that destroys bacterial and fungal spores when used in sufficient concentration for specified contact time. It is expected to kill all vegetative microorganisms.

Contec Product Solutions:

PeridoxRTU® Sporicidal Disinfectant and Cleaner
PREempt™ RTU Disinfectant Solution
Contec® Sterile 70% Isopropanol

Section 7.2: Cleaning Supplies

What does Chapter <825> say?

All cleaning supplies (e.g., wipes and mop heads), except for tool handles and holders, must be low-linting and should be disposable. If disposable cleaning supplies are used, they must be discarded after each cleaning activity. Reusable cleaning tools must be made of cleanable materials (e.g., no wooden handles) and must be cleaned and disinfected before and after each use.

Reusable cleaning tools must be dedicated for use in the classified areas or SRPAs and must not be removed from these areas except for disposal. They must be discarded after an appropriate amount of time, to be determined based on the condition of the tools.

Cleaning supplies and solutions used in the classified areas and SRPAs should be monitored for radioactive contamination after use and prior to disposal, as per facility SOPs. Dispose of cleaning supplies used in the classified areas and SRPAs in a manner that minimizes the potential for dispersing particulates into the air.

Contec Product Solutions:

Contec® MicroCinch™ Mop
Klean Max™ Wall Washing System
Amplitude™ EcoCloth™ Wipes

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Section 7.3: Cleaning and Disinfecting the PEC

What does Chapter <825> say?

Clean and disinfect the PEC at the minimum frequencies specified in Table 5. If the PEC contains a removable work tray, all sides of the work tray and the area underneath the work tray must be cleaned and disinfected at least monthly.

Process:

1. Survey all surfaces of the PEC for radioactive contamination and follow facility SOPs to decontaminate, if necessary.
2. Remove, if necessary, any particles, debris, or residue with an appropriate solution (e.g., Sterile Water for Injection or Sterile Water for Irrigation) using sterile, low-linting wipes.
3. Apply a cleaning agent followed by a disinfecting agent or apply an EPA-registered (or equivalent) one-step disinfectant cleaner and ensure that the contact time specified per manufacturer instructions is achieved.
4. Apply Sterile 70% IPA.
5. Allow the surfaces to dry completely before beginning activities.
6. The PEC must be wiped with a sporicidal agent at least monthly.

Contec Product Solutions:

PeridoxRTU® Sporicidal Disinfectant and Cleaner
SterileSorb™ Wipes
EasyReach™ Cleaning Tool
Contec® Sterile 70% Isopropanol

Section 7.4: Disinfecting Supplies for Classified Areas and SRPAs

What does Chapter <825> say?

Before items are introduced into a classified area or SRPA, they must be wiped with a sporicidal agent, EPA-registered (or equivalent) one-step disinfectant cleaner, or sterile 70% IPA using low-linting wipers. The agent used for disinfecting the packaging must be compatible with the packaging and must not render the product label unreadable.

Any item to be transferred into the PEC from the classified area or SRPA must be disinfected with a sterile disinfectant (e.g., sterile 70% IPA).

Contec Product Solutions:

PeridoxRTU® Sporicidal Disinfectant and Cleaner
Amplitude™ EcoCloth™ Wipes
Contec® Sterile 70% Isopropanol
PROSAT® *Sterile*™ PS-911EB

Section 7.5: Disinfecting Critical Sites

What does Chapter <825> say?

Critical sites (e.g., vial stoppers) must be wiped with sterile 70% IPA. The critical site must be wiped ensuring that both chemical and mechanical actions are used to remove contaminants. The sterile 70% IPA must be allowed to dry before piercing critical sites.

Contec Product Solutions:

Contec® Critical Site™ Sterile Wipes

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Section 7.6: Cleaning and Disinfecting Items from Patient Care Area

What does Chapter <825> say?

Radiation shielding and equipment used in the classified area/SRPA or PEC that is exposed to patient care areas during the process of administration must be cleaned and disinfected before returning to any classified area.

Contec Product Solutions:

- PeridoxRTU® Sporicidal Disinfectant and Cleaner
- Sanotex® Environmental Surface Wipes
- Contec® Sterile 70% Isopropanol
- PROSAT® *Sterile*™ PS-911EB or Healthcare equivalent

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