Chapter 13

Radiopharmaceuticals as Compounded Sterile Preparations

George H. Hinkle

Introduction

Except for a few unit-dose radiopharmaceuticals obtained from manufacturers in ready-to-inject forms, sterile injectable radiopharmaceuticals are compounded as defined by USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations. This chapter specifies that sterile compounding pertains to all preadministration manipulations (preparation, storage, and transport) of compounded sterile preparations (CSPs) and to radiopharmaceuticals and nonradioactive drugs dispensed by nuclear pharmacies.[1] Application of practice standards described in USP Chapter <797> will help ensure the aseptic processing of radiopharmaceuticals and other parenteral medications dispensed from nuclear pharmacies. The majority of hospitals and clinics in which radiopharmaceuticals are used for diagnostic and therapeutic procedures outsource the compounding of these radioactive drugs to commercial nuclear pharmacies. In 2004, The Joint Commission and other accrediting bodies expanded the focus on the safe use of drugs to include radiopharmaceuticals. As part of the responsibilities assumed by accredited institutions to meet medication management standards, the department of pharmacy must take steps to properly manage the use of radiopharmaceuticals. In addition to assessment of facilities, equipment, personnel, training, and regulatory compliance, the overall review of a commercial nuclear pharmacy providing unit-dose radiopharmaceuticals to the institution must include compliance with USP Chapter <797> standards.[2] Achieving the goals of USP Chapter <797>, while maintaining good radiation safety practices, provides additional challenges involving the design/layout of the nuclear pharmacy, use of required radiation shielding devices and instruments for the measurement of radioactivity, and observation of mandated radiation safety practices seemingly contradictory to sterile compounding procedures.

Microbial Risk Levels for Radiopharmaceuticals as CSPs

When compounding using only sterile ingredients/components, procedures are followed to maintain sterility during the process to ensure final product sterility. Compounding with

ingredients/components not known to be sterile requires achievement of a sterile product at the end of the process. The majority of radiopharmaceutical preparations involve the manipulation of sterile ingredients/components in closed, sterile containers obtained from reputable manufacturers. Because most radionuclides used to prepare radiopharmaceuticals have short half-lives (decay quickly), radiopharmaceuticals are short-lived CSPs. Patient administration and expiration times typically are within a few hours of compounding requiring routine preparation throughout the day. The radiopharmaceutical manufacturers supply the multiple-dose vials (kits) containing all of the nonradioactive ingredients that are used to prepare the final product by the addition of the short half-life radionuclide to the sterile, closed container (usually a 10-mL glass vial). This practice, applicable to radiopharmaceutical CSPs compounded according to manufacturer's directions found in the package insert and conforming to quality assurance requirements including expiration time, procedures, and maintenance of environmental controls, is considered low-risk compounding. The majority of radiopharmaceutical preparation in nuclear pharmacies, such as the routine preparation of technetium-99m radiopharmaceutical kits according to the manufacturer's directions, exemplifies low-risk compounding activity. These preparations must be completed by qualified personnel in an International Organization for Standardization (ISO) Class 5 laminar airflow workbench (LAFW) located in an ISO Class 8 buffer area and must meet other restrictions if dispensed as single dosages including volume (≤15 mL) and expiration times (≤18 hours). See Chapter 25, Table 25-1, for details on ISO Classes.

Sterile, radioactive drugs—which are supplied by manufacturers and contain radionuclides produced in a cyclotron facility that contains preservatives with stated expiration times of 72 hours or less—also meet low-risk level compounding guidelines. This does not include the preparation of positron emission tomography (PET) drugs, which is detailed in USP Chapter <823> Radiopharmaceuticals for Positron Emission Tomography—Compounding.[2]

The molybdenum-99/technetium-99m radionuclide generator system providing sterile, pyrogen-free technetium-99m for radiopharmaceutical compounding must be eluted according to the manufacturer's instructions and applicable regulations. This elution (removal of the technetium-99m radionuclide from the generator system) must be completed in an ISO Class 8 environment. Proper storage of the generator between elutions includes the use of the manufacturer-provided elution needle protective cover containing preservatives for maintenance of sterility throughout the 2-week shelf life of the generator.

Adjunctive medications or interventional agents used for their pharmacologic effects to enhance or improve the diagnostic quality of the nuclear medicine study are often compounded in and dispensed from nuclear pharmacies. Similar to the radiopharmaceutical compounding using manufacturer's sterile kits, the preparation of interventional agents from commercially available products is categorized as low-risk compounding activity.

Radiolabeling blood cells (white blood cells, red blood cells, and platelets) for diagnostic imaging are also often compounded in and dispensed from nuclear pharmacies. Handling blood products introduces a biohazard to the work associated with this particular procedure. Radiolabeling blood cells with radionuclides is categorized as a medium-risk activity in USP Chapter <797> and must be isolated from other sterile compounding functions within the nuclear pharmacy. Guidelines for handling blood products should be established to prevent cross-contamination of other products and to protect nuclear pharmacy personnel from potential infectious organisms in infected blood.

Few radiopharmaceuticals involve direct administration to the patient from the manufacturer's supplied vial or delivery system. For example, the short half-life radionuclide, rubidium-82, is delivered directly into the venous system from the commercially available radionuclide generator system. In the case where no preparation or withdrawal into a syringe for delivery to the patient is involved, this is termed *immediate-use compounding* and is exempted from environmental requirements used for other radiopharmaceutical CSPs. Aseptic technique should be observed when administering radiopharmaceuticals for immediate use. **Table 13-1** contains representative radiophar-