

Procedure Guideline for the Use of Radiopharmaceuticals 4.0*

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I. PURPOSE

This guideline was developed by the SNM to describe important factors common to most nuclear medicine procedures. It is intended to guide nuclear medicine practitioners in establishing policies and procedures for the use of radiopharmaceuticals in clinical practice. This guideline is intended to be concordant with the regulations of the Nuclear Regulatory Commission and other state and federal government agencies.

II. BACKGROUND INFORMATION AND DEFINITIONS

A. Radiopharmaceuticals

Radiopharmaceuticals (also known as radioactive drugs) are drugs that contain radionuclides that emit radiation. The distribution of the radiopharmaceutical within the body is determined by the physicochemical properties of the drug, the stability of the radiolabel, the purity of the radiopharmaceutical preparation, the pathophysiologic state of the patient, and the presence or absence of interfering drugs. Dynamic and static images of the distribution of the radiopharmaceutical within the body can be obtained using a γ -camera or another suitable instrument appropriate for the radiopharmaceutical being imaged—for example, positron-emitting radiopharmaceuticals. After administration of the radiopharmaceutical, radioactivity in specified sites of accumulation or in biologic samples can be measured for non-imaging procedures. High-dose, nonpenetrating radiation in localized sites of accumulation of the radiopharmaceutical can be useful for therapeutic procedures.

B. Physiologic and Pharmacologic Interventions

Physiologic and pharmacologic interventions increase the sensitivity or specificity of a nuclear medicine procedure by affecting the distribution and pharmacokinetics of

the administered agents through an alteration in organ physiology.

III. PROCEDURES

A. Clinical Use of Radiopharmaceuticals

1. All radiopharmaceuticals dispensed and administered must be pursuant to an order (e.g., prescription) by an authorized physician. The order should specify the procedure desired, the drugs to be used, the amounts to be administered, the route of administration, and, if applicable, the rate of infusion. Alternately, the order may specify a standard procedure with the other required information, that is, standing orders, specified in a routinely updated and physician-approved procedure manual located within the nuclear medicine facility.
2. Prescribing physicians are ultimately responsible for the safety, quality, and correctness of all radiopharmaceuticals prepared and dispensed for administration under their direction.
3. Nuclear pharmacists are ultimately responsible for the safety, quality, and correctness of radiopharmaceuticals prepared and dispensed under their supervision.
4. The preparation, quality control, dispensing, and administration to patients of radiopharmaceuticals and adjunctive drugs may be delegated to qualified personnel, in accordance with applicable state and local laws.
5. There must be a signed and dated written directive for each patient for ¹²⁵I- or ¹³¹I-sodium iodide in quantities of 1.1 MBq (30 μ Ci) or more and for all therapeutic radiopharmaceuticals.
6. The identity of the radiopharmaceutical and patient and the route of administration must be verified before administration. Syringes and outer shields or containers must be labeled for verification of contents.
7. Female patients who are postmenarcheal and premenopausal should be asked about pregnancy, lactation, and breast feeding before administration. Pregnancy testing in females of childbearing capability

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should be performed before administration of any radiopharmaceutical that could potentially result in a dose to an embryo or fetus of 50 mSv (5 rem) or more (e.g., ^{131}I therapy).

8. The quantity of each radiopharmaceutical dose must be determined before administration to patients and must be consistent with that ordered by the physician or as stipulated in the applicable standing orders in the nuclear medicine procedure manual. The quantity of radioactivity dispensed should be within 10% of the prescribed dose or dose range, and the actual quantity administered should be within 20% unless otherwise directed by the authorized physician and recorded in the patient's medical record.
9. Radiopharmaceuticals should not be used beyond the expiration date or time recommended by the manufacturer unless quality control testing demonstrates that the product still meets the specifications of the United States Pharmacopeial Convention (USP) at the time of use.
10. Any discrepancies must be resolved before administration.

B. Elution of Generators and on-Site Preparation of Kits

1. Each time a generator is to be eluted, the generator to be eluted and the volume of eluate to be used should be selected on the basis of the calibration and elution history of the generator. The quantity of radioactivity eluted and the concentration of parent nuclide breakthrough must be measured and recorded for each elution performed. The extent of breakthrough must be verified to be below the regulatory limit. The final volume of the eluate, the identity of the person performing the elution, and the date and time of elution should be recorded. Radiation safety procedures and aseptic technique must be used throughout the elution process.
2. Radiopharmaceuticals should be prepared according to the instructions of the manufacturer. The prescribing physician or nuclear pharmacist may deviate from the instructions on the package insert, but in such instances, the physician or pharmacist responsible for preparing the radiopharmaceutical is responsible for ensuring that it meets USP specifications.
3. Aseptic procedures must be followed whenever parenteral or ophthalmic radiopharmaceutical preparations or their components are handled.
4. A comprehensive radiopharmaceutical quality control program should be developed and implemented. The scope of the program should be compatible with the type of practice and the availability of equipment and personnel. The parameters to monitor in a radiopharmaceutical quality control program include chemical purity, radiochemical purity, radionuclidic purity, biologic purity (sterility and apyrogenicity), and pharmaceutical purity (e.g., pH, particle size, and absence of foreign particulate matter).

C. Positron-Emitting Radiopharmaceuticals

Radiopharmaceuticals used in PET require specialized personnel, facilities, and equipment, primarily because of the relatively short physical half-lives of the radionuclides, their energetic photon emissions, and the chemical syntheses necessary for their preparation. Preparation of all PET radiopharmaceuticals must comply with USP chapter 823 (Radiopharmaceuticals for PET: Compounding) or the manufacturing requirements of the Food and Drug Administration. Nuclear medicine practitioners involved in PET should consult with qualified chemists, pharmacists, physicists, and technologists in establishing and operating a PET program.

D. Record Keeping

1. Records on the receipt, use, administration, and disposal of all radiopharmaceuticals should be kept in compliance with license conditions and medical record and radiation control regulations.
2. Records on the receipt of packages containing radioactive material should include the identity of contents and the results of inspection for physical damage, measurement of the radiation dose-rate emanating from the package, and testing for removable contamination, as required by the regulatory agency. Records on the receipt of radioactive material should be maintained and stored in accordance with local state and federal regulations. Such records should include the identity of the radiopharmaceutical, its source, the amount of activity received, and the results of radiation surveys and contamination testing. Any discrepancies must be reported to the manufacturer or the regulatory agency.
3. For all radiopharmaceuticals prepared on-site, records should include the date and time of preparation; the quantity, volume, and concentration of radioactivity used; reagent lot numbers; quality control data; the expiration time; waste disposal information; and the name or initials of the individual responsible for the preparation.
4. For all radiopharmaceuticals, the identity of the radiopharmaceutical, the amount of radioactivity administered, the identity of the patient and of individual performing the administration; the route of administration; and the date and time of use must be recorded.
5. Records on testing of the radionuclide dose calibrator for constancy, accuracy, linearity, and geometric variation must be maintained.
6. All radioactive material must be disposed of in accordance with institutional, state, and federal regulations. Policies and procedures should be developed to ensure that radioactive material does not enter the normal waste stream of the institution, except in exempt quantities or in exempt forms (e.g., patient excreta).

E. Adverse Reactions/Product Problems

Adverse reactions associated with administration of radiopharmaceuticals should be investigated and documented.

Serious adverse reactions and problems with products should be reported to the appropriate individuals and entities.

F. Medical Events Involving Radiopharmaceuticals

Policies and procedures should be developed that ensure that the correct patient receives the correct drug at the correct time, in the correct dose, and by the correct route of administration. Medical events have been defined by federal and state regulatory agencies and accreditation bodies (e.g., Joint Commission) and include a requirement for timely reporting. When reporting of such events is required, the report should be made to the appropriate agency within the time frame specified.

G. Special Considerations for Labeled Blood Products

Although the misadministration of any radiopharmaceutical is serious, special precautions are needed to prevent the misadministration of radiopharmaceuticals containing blood products, that is, ^{99m}Tc -red blood cells and ^{111}In - and ^{99m}Tc -leukocytes. Procedures that involve the removal of blood for radiolabeling and subsequent reinjection have potential for misadministration to the wrong patient. The handling and administration of blood products must be subjected to special safeguards and procedures, the goal of which is to eliminate any possibility of administration to the wrong patient, contamination of the blood by environmental substances, and contamination of workers during radiolabeling procedures.

H. Drug Interactions and Altered Distribution Patterns

1. The in vivo distribution of radiopharmaceuticals can be altered by concurrent medications and prior diagnostic tests (including contrast agent and previous radiopharmaceuticals). The nuclear medicine practitioner should be familiar with documented drug interactions and consider this information when planning the nuclear medicine procedure and when identifying altered distribution patterns on patient studies.
2. Problems with the formulation of radiopharmaceuticals can result in altered distribution patterns. Quality control programs should identify such problems before patient administration. The possibility of a formulation-related cause of an altered distribution pattern should be considered in the evaluation of any unexplained image findings.

IV. ISSUES REQUIRING FURTHER CLARIFICATION

All compounded sterile preparations should be prepared in accordance with USP chapter 797 (Pharmaceutical Compounding: Sterile Preparations) and in accordance with the state board of pharmacy and other state and local requirements.

V. CONCISE BIBLIOGRAPHY

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VI. DISCLAIMER

The SNM has written and approved this Procedure Guideline as an educational tool designed to promote the cost-effective use of high-quality nuclear medicine procedures in medical practice or in the conduct of research and to assist practitioners in providing appropriate care for patients. The Procedure Guideline should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The guidelines are neither inflexible rules nor requirements of practice and are not intended nor should they be used to establish a legal standard of care. For these reasons, the SNM cautions against the use of this Procedure Guideline in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment about the propriety of any specific procedure or course of action must be made by the physician when considering the circumstances presented. Therefore, an approach that differs from the Procedure Guideline is not necessarily below the standard of care. A conscientious practitioner may responsibly adopt a course of action different from that set forth in the Procedure Guideline when, in his or her reasonable judgment, that course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge

or technology subsequent to publication of the Procedure Guideline.

All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of this Procedure Guideline is to assist practitioners in achieving this objective.

Advances in medicine occur at a rapid rate. The date of a Procedure Guideline should always be considered in determining its current applicability.

VII. APPROVAL

This Procedure Guideline was approved by the Board of Directors of the SNM on June 1, 2007.