SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

September 5, 2014

Jane A. Axelrad, Esq.
Associate Director for Policy
Center for Drug Evaluation and Research
Food and Drug Administration
White Oak Office Building 51
10903 New Hampshire Ave.
Silver Spring, Maryland 20993

Dear Ms. Axelrad:

RE: Radiopharmaceutical Compounding

Thank you for meeting with the Society of Nuclear Medicine and Molecular Imaging (SNMMI) on legislative and regulatory issues impacting the field of nuclear medicine and molecular imaging. The SNMMI would like to follow up with our recommendations for radiopharmaceutical compounding. SNMMI's more than 18,000 members set the standard for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals, meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice.

Our members recognize that radiopharmaceuticals and compounded positron emission tomography (PET) drugs are exempted from the "Safe Harbors" found in Section 503A of the Federal Food, Drug and Cosmetic Act related to pharmacy compounding. The existing public guidance defining FDA's enforcement policy regarding compounding radiopharmaceutical and PET drugs consists of the *"Nuclear Pharmacy Guideline Criteria for Determining When to Register as a Drug Establishment"* published by FDA in 1997, originally developed in May 1984. This guidance treats the conventional pharmacy practices conducted in nuclear pharmacies consistently with Section 503A of the Federal Food, Drug and Cosmetic Act related to pharmacy compounding. Accordingly, there is no additional statutory, regulatory authority, or systematic code to allow the traditional pharmacy practices described in Section 503A of the Federal Food, Drug and Cosmetic Act related to pharmacy compounding that are performed in nuclear pharmacies.

As such, SNMMI offers the following recommendations for radiopharmaceutical compounding:

- **Interstate Delivery**
  Radiopharmaceuticals are drugs prepared from FDA approved ingredients pursuant to a physician's prescription or order. Radionuclides, a common active ingredient in all radiopharmaceuticals, possess a short radioactive half-life; therefore a radiopharmaceutical preparation exhibits a very short beyond-use-date (hours) and is prepared for a small number of patients. Nearly all radiopharmaceuticals are prepared in commercial radiopharmacies operating as licensed pharmacies. Due to the specialized nature of radiopharmaceutical preparation, most radiopharmacies are located within, or adjacent to metropolitan areas. Radiopharmaceuticals are delivered to healthcare facilities within a small geographic radius,

owing to the very short beyond use date. Delivery of radiopharmaceutical preparations cross state lines when dictated by population distribution and geography, where they are administered to an individually identified patient.

SNMMI does not support assigning an arbitrary percentage to limit the amount of interstate delivery as such a requirement would not improve patient safety. Interstate delivery is necessary due to the aforementioned issues identified:

1) A small quantity of radiopharmaceuticals are prepared
2) Radiopharmaceuticals possess a short radioactive half-life and must be delivered from the site of preparation
3) Radiopharmaceuticals possess very short beyond-use-dates (hours)
4) Preparations of radiopharmaceuticals are for an individually identified patient pursuant to a physician's prescription.

- **Copies of Approved Products**
  SNMMI supports the prohibition of making a compounded radiopharmaceutical preparation that is essentially a copy of a commercially available (FDA-approved) radiopharmaceutical product. SNMMI recommends that a compounded radiopharmaceutical preparation that appears on the drug shortage list established under FDC Act Section 506E or that is the same as a FDA approved product but was withdrawn from the market by the manufacturer for reasons unrelated to safety or efficacy, should not be defined as "essentially a copy of a commercially available radiopharmaceutical product."

- **Licensed Nuclear Pharmacy**
  SNMMI recommends that a radiopharmaceutical is compounded by, or under the supervision of a licensed pharmacist in a state-licensed pharmacy that also holds a radioactive materials license issued by the Nuclear Regulatory Commission (NRC) or by a State pursuant to an agreement with the NRC. Additionally, SNMMI suggests that a physician who is authorized to compound drugs under State law should also be recognized as an Authorized User on a radioactive materials license issued by the NRC or an Agreement State.

- **Valid Prescription or Order**
  SNMMI recommends that a radiopharmaceutical is compounded and dispensed based on a valid prescription order that identifies an individual patient, and that is received from a licensed practitioner authorized by state law to prescribe drugs.

- **USP Compounding Chapters**
  SNMMI supports radiopharmaceutical compounding in accordance with the chapters on pharmacy compounding in the United States Pharmacopoeia (USP).

- **Bulk Drug Substances**
  SNMMI recommends that bulk drug substances (including radioisotopes) used in the compounding of the radiopharmaceutical are FDA-approved products or components of FDA-approved products, or comply with an applicable USP or National Formulary (NF) monograph, if one exists. SNMMI also recommends that each bulk drug substance be manufactured in an

establishment registered with FDA under FDC Act Section 510, and should be accompanied by a valid certificate of analysis.

- **Inactive ingredients**
  SNMMI recommends that inactive ingredients used in the compounded radiopharmaceutical product comply with an applicable USP or NF monograph, if one exists.

- **Drugs on "Withdrawn or Removed" List**
  SNMMI recommends that a radiopharmaceutical (or any of its components) should not appear on FDA's list of drug products that have been withdrawn or removed from the market because they have been found to be unsafe or ineffective (21 C.F.R. § 216.24).

- **Demonstrable Difficulties for Compounding**
  The drug product is not identified by the FDA as one that presents demonstrable difficulties for compounding that can reasonably have a negative effect on the safety or effectiveness of that drug product.

- **Resale**
  SNMMI recommends that compounded radiopharmaceutical preparations should not be offered at wholesale or to other entities for resale, or further compounding.

SNMMI is ready to discuss any of its comments or meet with the FDA regarding the above issues. In this regard, please contact Susan Bunning, Director, Health Policy and Regulatory Affairs, by email at sbunning@snmmi.org or by phone at 703-326-1182.

Sincerely,

Hossein Jadvar, MD, PhD, MPH, MBA, FACNM
President-Elect
SNMMI