SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

March 23, 2015

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 Follow Up

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.

During our stakeholder meeting on September 24, 2014, you asked us for comments on the possibility of CGMPs for nuclear medicine. Nuclear pharmacy is a specialty practice of pharmacy, distinct, and separate from manufacturing. A nuclear pharmacy is also distinct from a Positron Emission Tomography (PET) drug production facility.

PET drug production facilities produce the radioisotope using established standards of practice, which permit minimal specified variables, but the manufacturing of PET drug does not allow nor permit deviation from approved applications. PET drugs are manufactured via Current Good Manufacturing Practice (CGMP), in adherence with 21 Code of Federal Regulations Part 212.

After the PET drug is produced, it is sent to the nuclear pharmacy to be dispensed into individual patient doses, and then delivered to licensed authorized user physicians. Nearly all PET drugs are manufactured for procedures ordered at least one day in advance (in accordance with typical manufacturing processes), due to the chronic nature of illnesses in which PET drugs are used for imaging. It is standard practice to manufacture a PET drug batch, within specified activity concentration limits, each time to meet the needs of the patient population and associated examination logistics.

However, radiopharmaceutical kits are often prepared with little or no advanced notice. Radiopharmaceutical kits are prepared this way to meet the needs of a distinct patient population. The patient population may be experiencing chest pain, pulmonary emboli, or brain death. Activity concentrations are prepared to meet the needs of patients who are examined in close proximity to a radiopharmacy, typically in a metro area, as well as rural facilities,

sometimes two or three hours away in another state. Since the majority of radiopharmaceuticals used today in nuclear medicine practice are acquired from generator produced radioisotopes, it is not feasible to prepare radiopharmaceutical kits, with the same activity concentration, at the same time every day as is typical in manufacturing. In addition, procedures conducted in nuclear medicine practice cannot be readily anticipated or routinely produced, as they are not used for chronic illnesses, but for emergent illnesses (both outpatient and inpatient). In these scenarios it is not always possible to estimate when a patient will require an imaging study.

As such, the vast majority of radiopharmaceuticals are not prepared in large batches with long shelf lives, but rather small quantities with short shelf lives. Due to the short half-life of commonly used diagnostic radiopharmaceuticals, the standard of practice Beyond-Use Date (BUD) is usually measured by a few hours, not days. The quick turnaround time between preparation, transport, and administration commonly experienced in standard nuclear pharmacy practice does not allow as much time for microbial growth to the same degree as with compounded sterile preparations with long BUDs.

Individual states Board of Pharmacy are responsible for the regulation and oversight of nuclear pharmacy. As an example, State Boards of Pharmacy routinely inspect pharmacies for compliance with the USP <797> Chapter on Sterile Compounding. Radiopharmaceutical preparations are dispensed from a nuclear pharmacy, according to a patient prescription, as prescribed solely by licensed medical authorized users, who are listed on a facility's Federal or State radioactive materials license.

Some states allow radiopharmaceuticals to be dispensed to an authorized user "for Office Use". In these situations, it is the physician's responsibility, under the Practice of Medicine and Radioactive Material (RAM) licensing guidelines, to keep an exact record of each radiopharmaceutical dose a patient receives under their respective care, thereby insuring complete traceability in case of patient adverse reaction or drug recall.

Although there are general guidelines and standards of practice for patient radiopharmaceutical administered dosages, authorized user physicians commonly prescribe individual dosages for their patients. Doses are often adjusted by the authorized user physician in consideration of a patient's body habitus, medical condition, or other clinical considerations. Here again, the patient, physician, pharmacist triad is illustrated as the fundamental basis of current practice of nuclear pharmacy, distinct and separate from manufacturing.

We are grateful for the time and attention you are giving to nuclear medicine compounding and preparation. Do not hesitate to contact us should you have additional questions. For your convenience, attached is the previous letter we sent to you commenting on some of the other areas of concern.

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 phone at 703-326-1182.

SOCIETY OF
NUCLEAR MEDICINE
AND MOLECULAR IMAGING

Respectfully submitted,

Virginia Pappas, CAE
Chief Executive Officer