



February 28, 2017

Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, Maryland 20993

Re: DRAFT GUIDANCE: Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies and Federal Facilities – Guidance for Industry

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) would like to provide the following recommendations with respect to the FDA's Draft Guidance on Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies and Federal Facilities. The Society, composed of 17,000 members, works to set standards for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals, hosting meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice.

The society offers the following comments and recommendations:

- Page 2. The guidance does not address "Production of positron emission tomography (PET) drugs." SNMMI agrees that production of common PET drugs, such as F 18 fludeoxyglucose Injection, is manufacturing (in contrast to compounding). However, SNMMI has concerns about how Ga-68 kits (e.g. DOTATATE) are classified. The FDA has repeatedly stated verbally, albeit not in writing, that reconstitution of FDA-approved kits with Ga-68 from a DMF Ge-68 generator is practice of pharmacy/medicine rather than manufacturing. This guidance should be revised to address PET drugs that are prepared from kits (analogous to Tc-99m kits or In-111 kits).
- Page 2. The guidance does not address "Compounding or repackaging of radiopharmaceuticals by entities that are not State-licensed nuclear pharmacies or Federal facilities". Thus, it does not appear that this guidance would apply to the preparation/compounding of radiopharmaceuticals by nuclear medicine physicians (and their supervised designees) in a hospital-based nuclear medicine departments or nuclear medicine clinics. SNMMI believes this could be potentially interpreted by inspectors that "compounding" of radiopharmaceuticals is not, in fact, permitted in such facilities. The society understands that this draft guidance is intended to differentiate 503A-like compounding from 503B outsourcing facility compounding (which is the subject of a separate draft guidance document). Nonetheless, physician-supervised compounding in a hospital nuclear medicine department or clinic should be included in this guidance.
- Page 4-5. The definition/description of "minor deviation." SNMMI understands that it is very difficult to define (e.g., place limits on what activities constitute) minor deviations, so examples are given. Currently, however, there could be a broad range of interpretations as to what does, and what does not, constitute a "minor deviation." **SNMMI strongly recommends that the FDA work with the United States Pharmacopeia (USP) expert committees responsible for radiopharmaceuticals and compounding to develop a more precise definition (and possibly a more comprehensive list of examples) of "minor deviation."**

- Page 7. In item 7, the guidance states that the radiopharmaceutical is compounded in compliance with USP general chapter <795> or <797> “(except for BUD)”. SNMMI believes FDA needs to provide additional explanation and clarity on this item. As it is currently written, it is unclear what FDA means regarding “except for BUD.” Does it mean that FDA would support a longer BUD than described in USP <795> or <797>? Or does it mean that FDA would require a shorter BUD? If so, on what basis? To serve patient need, especially at some geographic distance, extension of manufacturer’s “use by _ hours” statements in the package inserts of radiopharmaceutical kits is required. These “use by” extensions should be viewed the same as minor deviations. In 2011 SNMMI developed and approved “Recommendations for Beyond-Use Dates (BUD) for Tc-99m Radiopharmaceuticals.” See: http://snmmi.files.cms-plus.com/docs/BUDs_for_Tc99m_radiopharmaceuticals_1382109507530_1.pdf

Again, SNMMI recommends that that FDA work with the USP expert committees responsible for radiopharmaceuticals and compounding to develop appropriate BUDs for compounded radiopharmaceuticals.

- Page 7-8. Item 9 describes prohibition of compounding essentially copies of FDA-approved radiopharmaceuticals, except if it is on the FDA shortage list, it is no longer marketed for reasons not related to safety, or the prescribing practitioner requests a change that produces a clinical difference for an identifiable individual patient. SNMMI appreciates the inclusion of this provision and supports its addition to the guidance.
- SNMMI recommends that FDA encourage the USP to develop a public standard for the compounding of sterile radiopharmaceuticals (i.e., a separate chapter). Previously, SNMMI’s Committee on Radiopharmaceuticals provided comments to the USP to encourage the establishment of a separate expert committee for radiopharmaceuticals and the development of a separate compounding chapter for radiopharmaceuticals. These recommendations are explained in detail in a white paper that was sent to the USP by the SNMMI President Sally Schwarz on September 29, 2016. See: http://snmmi.files.cms-plus.com/SNMMI-USP-Recommendations-Final_2016.pdf

We encourage the FDA to consider the SNMMI recommendations outlined in the white paper. We also recommend that the FDA withhold further development of guidance documents related to radiopharmaceutical compounding, including both of the draft guidance documents published on December 29, 2016. Instead, we believe the FDA should be an active participant in the USP standards-setting process. By actively supporting the USP process and foregoing its own standards through guidance documents until after the USP public standard process, FDA efforts will lead to stronger, more comprehensive standards that are easy to understand, follow, and enforce.

SNMMI is broadly supportive of the direction of this guidance. **As previously stated, SNMMI strongly recommends that FDA work with USP to develop a common understanding of activities defined and involved in the compounding of radiopharmaceuticals.**

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SNMMI appreciates the opportunity to comment on the Compounding and Repackaging of Radiopharmaceuticals by State-Licensed Nuclear Pharmacies and Federal Facilities **Draft Guidance**. SNMMI is ready to discuss any of its comments or meet with the FDA regarding the above issues. In this regard, please contact Caitlin Kubler, Senior Manager, Regulatory Affairs, by email at ckubler@snmmi.org or by phone at 703-326-1190.

Sincerely,

A handwritten signature in black ink that reads "Sally W. Schwarz". The signature is written in a cursive, flowing style.

Sally Schwarz, MS, RPh, BCNP
SNMMI President