SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

October 7, 2016

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

Re: Insanitary Conditions at Compounding Facilities - Guidance for Industry; FDA-2016-D-2268-0002

The Society of Nuclear Medicine and Molecular Imaging's (SNMMI) more than 17,000 members set the standard for molecular imaging and nuclear medicine practice by creating guidelines, sharing information through journals and meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice.

SNMMI welcomes the publication of the draft guidance, Guidance for Industry: *Insanitary Conditions at Compounding Facilities*, to illuminate the current thinking of the Food and Administration (FDA) with respect to the compounding of sterile pharmaceuticals. SNMMI believes the draft guidance has the potential to provide valuable information and guidance to technical and physical condition requirements that are applicable to the safe compounding of sterile pharmaceuticals. SNMMI agrees and supports that sterile compounded radiopharmaceuticals must be fully compliant with the 501(a) (2) (A) adulteration provisions of the FD&C Act.

Sterile radiopharmaceuticals play a pivotal role in the current world of molecular Imaging. Approximately 18 million studies are performed yearly in Nuclear Medicine that rely on the administration of sterile radiopharmaceuticals. For many years SNMMI has played an active role as an advocate for the establishment of safe practices and procedures directed at ensuring the safety and quality of radiopharmaceuticals and the security of the radiopharmaceutical distribution system in support of the provision of medical imaging services.

The inclusion of radiopharmaceuticals in this guidance is of special interest to SNMMI considering the current exemption or exclusion of sterile compounded radiopharmaceuticals under the most recent version of the 2013 Drug Quality and Security Act.

On September 24, 2014, and April 28, 2015 the SNMMI along with other stakeholders participated in open discussions with the FDA to develop a rational approach to the regulatory oversight of radiopharmaceutical compounding. At this current time FDA regulatory rulemaking with respect to compounded sterile radiopharmaceutical is still in progress.

With the release of this draft guidance and in view of the current status of regulatory limbo with respect to FDA regulatory guidance for the sterile preparation and compounding of radiopharmaceuticals, SNMMI would like to bring forward specific concerns within the proposed draft guidance.

Sterile compounding of radiopharmaceuticals involves a consideration of shielding and other radiation safety practices that are well recognized in current Nuclear Pharmacy and Nuclear Medicine practice. We believe that

these unique considerations are not well addressed in the current proposed draft guidance. To illustrate this area of concern we have provided below some examples of recognized considerations unique to sterile radiopharmaceuticals which could be misconstrued as unsanitary conditions under the draft guidance document:

Line 137-138
Performing aseptic manipulations outside of an International Organization for Standardization Class 5 (ISO 5) area.

Comment: USP <797> allows generator elution in an ISO Class 8 area.

Lines 146-149
Moving quickly in the vicinity of open containers or instruments (e.g., needles). While conducting aseptic manipulations, ISO 5 airflow must be unidirectional to protect the product from contaminating particles. Quick movement of personnel disrupts the airflow and increases the risk of bringing lesser quality air into the ISO 5 area.

Comment: May be problematic when moving quickly related to ALARA (radiation dose is proportional to time, so limit time of exposure)

Line 150-155
Conducting aseptic manipulations or placing equipment/supplies in an area that blocks the movement of first pass air around an open container, whether before or after it is filled with sterile product. If unidirectional air over the critical surface is blocked, the area is no longer protected. If it is blocked by personnel conducting aseptic manipulations, contamination on personnel, particularly on exposed skin, could be introduced to the critical area.

Comment: May be problematic in a vertical flow hood, especially with lead shielding (L-block, syringe shield), angle of holding items, and other radiation equipment in the hood.

Line 160-162
Touching equipment or other surfaces (e.g., walls, telephone, floors) located outside of the ISO 5 area with gloved hands and then proceeding with aseptic manipulations without changing or sanitizing gloves.

Comment: May be problematic when handling vial shields, syringe shields, labels, etc.

SNMMI recognizes and agrees with the concepts of quality by design and continuous improvement as represented by the proposal of this draft guidance. In this vein, SNMMI has also been concerned with sanitary conditions and best practices for the sterile preparation and compounding of sterile radiopharmaceuticals and believes that current USP <797> also fails to adequately address the unique characteristics of these drug products. To address these issues SNMMI recognizes the United States Pharmacopeial (USP) Convention as an authoritative body with an established and appropriate process to permit expert input into the establishment of best practices for the sterile preparation and compounding of radiopharmaceuticals. To this end, SNMMI has developed a white paper that outlines a pathway for the development of appropriate guidelines for the sterile

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preparation and compounding of radiopharmaceuticals under a new and respectively dedicated USP chapter. We include this white paper in support of this letter.

In summary, we believe that the establishment of an expert USP committee with input from knowledgeable stakeholders, including representatives of the FDA, is the best way to move forward in developing appropriate guidance for the aseptic processing of sterile radiopharmaceuticals; so as to both ensure the safety of our patients and the continued availability of these drugs products for their medical care. We would appreciate the FDA's support and endorsement for this approach.

SNMMI appreciates the opportunity to comment on this draft guidance. As always, SNMMI is ready to discuss any of its comments or meet with FDA on 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,

Sally W. Schwarz

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