SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

November 29, 2018

Ravi Ravichandran, Ph.D.
Principal Scientific Liaison
U.S. Pharmacopeial Convention (USP)
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: SNMMI Comments on USP General Chapter <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging

Dear Dr. Ravichandran:

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) appreciates the opportunity to provide comments on the proposed general chapter <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging. SNMMI's more than 17,000 members set the standard for molecular imaging and nuclear medicine practice through the creation of clinical guidelines, sharing evidence-based medicine through journals and meetings, and leading advocacy on key issues that affect molecular imaging and therapy research and practice. SNMMI is pleased to offer comments on specific topics detailed below.

SNMMI commends the USP for creating a dedicated chapter for the provision of radiopharmaceuticals. We recognize the efforts of the expert panel to address the concerns of the nuclear medicine community with respect to unique considerations for preparation of sterile radiopharmaceuticals that were not adequately addressed under the sterile compounding chapter <797>. We applaud this effort to provide a reasonable and rational basis for the protection of patients from unsafe practices when preparing, compounding, dispensing, and repackaging radiopharmaceuticals. SNMMI recognizes that the creation of the new chapter USP <825> is the result of an extended process that started with the establishment of USP Chapter <797> "Pharmaceutical Compounding–Sterile Preparations," which became official in January 2004.

Immediately following the inception of <797>, there was widespread recognition within the Nuclear Medicine and Nuclear Pharmacy communities that radiopharmaceuticals were underserved by this founding chapter and specific standards based on the unique characteristics of radiopharmaceuticals were needed. This concern was immediately addressed by the USP with the recognition and inclusion of standards for compounded sterile radiopharmaceuticals in subsequent revisions <797> and ultimately to this proposed chapter <825>.

To quote David W. Newton, BS, PhD, FAPhA and Lawrence A. Trissel, BS, RPh, FASHP, founding chairman and member respectively of the 2000–2005 Sterile Compounding Committee (SCC) of the Council of Experts of the USP SCC that established the first <797> chapter on sterile compounding in 2004, in USP 27 –NF 22 in his, A Primer on USP Chapter <797> "Pharmaceutical Compounding–Sterile Preparations," and USP Process for Drug and Practice Standards, which outlined the intent of the founding USP<797> committee.

> **"The paramount concern of the SCC was the protection of patients from inadequate and unsafe compounding practices. Patient safety was the primary consideration. However, the SCC did consider the practicality of the specific Chapter <797> requirements because this too serves patient safety."**

All of the requirements in the initial 2004 USP Chapter <797> were considered by the SCC to be reasonable and achievable within current compounding practice settings to help ensure patient safety." [1]

As such, we consider the proposed standards appropriate for multi-dose distributive radiopharmaceutical compounding such as found in commercial nuclear pharmacies or distributive healthcare operations, complex radiopharmaceutical compounding with bulk components, and compounding with non-sterile ingredients. We suggest that these activities are adequately addressed by the proposed chapter with some minor revisions that are outlined at the end of this letter.

When taking into consideration the provision of patient care Dr. Newton and Mr. Trissell also indicated **"the practicality of the specific Chapter <797> requirements" must be considered "because this too serves patient safety".**[2]

We suggest that proposed chapter <825> is deficient with respect to the provision of radiopharmaceuticals for patient care as provided in current healthcare facilities that do not distribute radiopharmaceuticals outside their facility (i.e., only prepare sterile radiopharmaceuticals for single patient use in the same healthcare facility within the specified BUD).

Specifically, proposed chapter <825> establishes only two risk levels for sterile compounding. This does not accurately reflect the current standard of care in healthcare facilities with respect to the preparation of sterile radiopharmaceuticals and could result in an unreasonable burden for the provision of radiopharmaceuticals.

SNMMI understands that the two categories in the proposed <825> are intended to harmonize the proposed draft revision of general chapter <797>. We submit that chapter <797> is an appropriate standard for risks associated with regular pharmacy sterile compounding practices (e.g., compounding large unit batches of drug product stored for distribution with storage times routinely exceeding 18 hours). In contrast, radiopharmaceuticals are routinely prepared, compounded, and dispensed for use within 18 hours as dictated by their characteristics of radioactive decay thereby alleviating risks associated with extended storage and other practices anticipated in the proposed revision of <797>.

Therefore, we suggest that the USP consider the elimination of two risks levels for sterile radiopharmaceuticals and adopt the risk categories (low, medium, and high) as established in the initial <797> chapters. This approach would adequately address risk within reasonable escalating controls that accommodate the current accepted provision of radiopharmaceuticals in healthcare facilities.

We suggest standards for radiopharmaceuticals be established according to risk are necessary to address the unique considerations for radiopharmaceuticals and to aid Practioners as they implement policies for the provision of patient care whether in a healthcare facility (including clinics) or commercial distributive facility.

Our specific recommendations are as follows:

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[1] Newton, DW. Tressel LA. A Primer on USP Chapter <797> "Pharmaceutical Compounding–Sterile Preparations," and USP Process For Drug and Practice Standards. Intl J Pharm Compd. 2004. July-August 8 (4) 251-63.

[2] Newton, DW. Tressel LA. A Primer on USP Chapter <797> "Pharmaceutical Compounding–Sterile Preparations," and USP Process For Drug and Practice Standards. Intl J Pharm Compd. 2004. July-August 8 (4) 251-63.

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Immediate Use – Use within 1 hour, (excluding RBC kit prep), Non-Classified CDC guideline clean segregated area, non-sterile.
Garb: Shoe cover, dedicated clean lab coat, wash hands, sanitized gloves
FDA approved kit & materials preparation according to manufacturer with less than 3 sterile components (unless directed by manufacturer PI).

Low risk – Dose preparation (multi & single) in ISO-5 according to manufacturer instructions using FDA approved kit & materials, use within 6 hours, ≤3 components (unless directed by manufacturer PI), ISO-5 located in non-classified SCRA minimum - annual PEC certification
Cleaning schedule: Floors daily, PEC daily before prep
Garb: Non-sterile shoe cover, head cover, dedicated lab coat, wash hands, sterile sleeve, gloves in ISO-5.
Aseptic operator: Initial finger (3x initial –annual 1x), media fill = Initial-Annual

Medium risk – Preparation with minor deviations, multi-dose vial prep with BUD <18 hours, min ISO-5 with buffer ISO-8 (or better). Classified room certification and differential pressure check = annual certification, 6 month PEC certification
Cleaning schedule: Rooms daily, c/w-monthly, PEC daily
Garb: Shoe, head, clean-low particulate dedicated lab coat/coverall, buffer room glove, ISO-5 sterile glove, sterile sleeve.
Aseptic operator: Initial finger (3x initial –annual 1x), media fill = Initial-Annual
Bioburden Surface: PEC-daily, rooms –monthly
Bio burden air: Every 6 months.

High risk – Compounding with other than minor deviations, compounding with non-sterile components requiring sterilizing filtration, complex compounding (includes lyophilization), multi dose kit prep with BUD >18 hours. Follow existing draft USP<825>.

In support of these recommendations the SNMMI Committee on Radiopharmaceuticals is prepared to support and sponsor the collection and collation of current and historical data from entities that are currently and have historically prepared compounded sterile radiopharmaceuticals in order to analyze and interpolate environmental monitoring data with respect to final outcomes and risk under a scientifically sound determination.

Sincerely,

Satoshi Minoshima, MD, PhD
President