SNM Responds to Proposed USP <797> Revisions

On August 15 the SNM submitted comments to the U.S. Pharmacopeia (USP) regarding the proposed revisions of USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. The proposed revisions of <797> appeared in the *USP Pharmacopeial Forum (PF), Journal of Standards Development and Official Compendia Revision*, 2006(May–June);32. The SNM document was supplemented by 2 reference attachments. One attachment was a set of comments by James A. Ponto, MS, a member of the SNM Committee on Pharmacopeia. The second was a PDF of an article by Mark Thomas, MS; Michael D. Sanborn, MS; and Rick Couldry, MS; on "IV admixture contamination rates: traditional practice sites vs. a class 1000 cleanroom" (*Am J Health-Syst Pharm*. 2005;62:2386–2392). The full texts of both attachments are available at: http://interactive.snm.org/index.cfm?PageID=5466. The full text of the proposed revisions is available at: www.usp.org/USPNF/pf/generalChapter797.html. Included here is the text of the main comment document submitted by the SNM.

Comments on Proposed Revisions USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations

Radiopharmaceutical Sciences Council Committee on Pharmacopeia
Society of Nuclear Medicine

The Society of Nuclear Medicine (SNM)—an international scientific and professional organization of more than 16,000 members dedicated to promoting the science, technology and practical applications of molecular imaging/nuclear medicine—appreciates the opportunity to submit comments regarding the concerns of the nuclear medicine community with the proposed revisions of USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. The following comments were developed by the members of the Radiopharmaceutical Sciences Council (RPSC) Committee on Pharmacopeia, with the collaboration of representatives from the RPSC Committee on Radiopharmaceuticals, SNM and SNM/Technologist Section leadership.

GENERAL COMMENTS

Radiopharmaceuticals as CSPs

We are in general agreement with the establishment of a separate section titled "Radiopharmaceutical as CSPs" within the proposed revisions of <797>. We propose, however, that the SCC consider creation of an entirely new category for short-lived radiopharmaceuticals, an intermediate category between "Immediate Use" and "Low-Risk," designated "Same-Day CSPs." This proposal is in agreement with a suggestion made previously by James Ponto (Attachment 1).

As suggested by Mr. Ponto, the requirements for Same-Day CSPs would be:

- Personnel training and media fill challenge testing.
- Handling in a properly functioning ISO 5 hood (in a limited access room but not necessarily in a clean room).
- Good aseptic technique, especially no contact contamination on the critical surfaces (but not necessarily donning clean room garments and following other clean room procedures).

Mr. Ponto's proposal is supported by a recent article (Attachment 2) that demonstrates that proper training in aseptic technique is more important than the physical environment when preparing admixtures for i.v. administration (Attachment 2). Perhaps most importantly, we feel that the creation of a new category better reflects the unique nature of short-lived radiopharmaceuticals.

Definitions of Compounding, Dispensing, and Preparation

The SNM encourages the USP to refine the definitions of compounding, dispensing, and preparation of radiopharmaceuticals within <797> such that these definitions are consistent with existing USP monographs and FDA regulations. Furthermore, the Society believes that the preparation of a radiopharmaceutical by combining sterile components as described on the package insert should be excluded from the definition of compounding.

Personnel Training and Competency in Aseptic Manipulation Skills

The SNM strongly believes the most important safety measure in the preparation of sterile drugs is the proper training of competent personnel in aseptic technique. Therefore, we support the development of competencies and outcomes for personnel, activities, and facilities. However, we request that <797> refrain from overly prescriptive requirements regarding the means by which these competencies and outcomes are achieved.

Performance-based Compounding Guidelines

As with Personnel Training, the SNM feels that compounding guidelines should be performance-based, not prescriptive, thus allowing for more or less stringent controls depending on the specific compounding activity. Therefore, we support the use of the word "should," but object to the word "must" throughout <797>.

Impact Evaluation on Enforcement and/or Compliance of <797>

As indicated above, the proposed revisions of <797> contain several references to activities that "must" be performed, rather than "should" be performed. This prescriptive language, combined with the fact that USP chapters numbered less than 1000 are enforceable, creates an environment in which <797> standards are essentially a set of de-facto regulations.

With this in mind, the SNM firmly believes <797> should be evaluated by the Office of Management and Budget (OMB) for its impact on enforcement or compliance of compounding practice standards by the FDA, Centers for Medicare & Medicaid Services, State Boards of Pharmacy, as well as various healthcare institutions and practitioners (e.g., individual pharmacies, hospitals, and clinics, etc.).

Patient Care & Patient Safety

The SNM is deeply concerned that implementation of <797> in its present form will have a significant (negative) impact on both patients and the health care system. The costs of renovating existing facilities to bring them into compliance with <797> will significantly increase the costs of drugs, including radiopharmaceuticals, and these increased costs will necessarily be passed on to patients. In some cases, nuclear medicine departments may not be able to absorb these costs and will be forced to close, resulting in delays in diagnosis or reliance on less effective but more readily available technologies.

SPECIFIC COMMENTS

1. As the term "ante-area" is not defined in the "Definitions" section and is indistinguishable from the defined term "anteroom" used throughout <797>, the SNM suggests only one term be used to avoid confusion.
2. Add a definition for the term "Biological Safety Cabinet, Class III (BSC)." This term appears on line #554, but is not explained within the "Definitions" section (the definition of "Biological Safety Cabinet, Class II [BSC] can be found on lines #125-128.)
3. Consolidate the names in lines #129-130 (i.e., Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area).
4. The name and definition for the term "Cleanroom" as listed in lines #133-137 seem to be perplexing. If the meaning of term "Cleanroom" is different from those for the terms (i.e., Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area), what should the classification be of the room air in a "Cleanroom"? If it should be ISO Class 7, what are the differences between the definitions of "Cleanroom" and "Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area"?
5. Add a definition for the term "Compounding" that is consistent with the FDA.
6. Add a definition for the term "Dispensing."
7. The term "expiration date" appears numerous times (e.g., line #256, lines #659-660, line #1337); however it is not defined in the "Definitions" section.
8. Add a definition for the term "Hazardous Drug."
9. Line #625—please define the term "Type B2 BSC."
10. The statement in line #626 (i.e., "[CAI] located in an ISO Class 8 . . .") is inconsistent with the stipulation in line #914 (i.e., "CAIs must be placed in an ISO Class 7 . . .").
11. What risk level should be assigned to the compounding process for radiolabeling of autologous leukocytes (white blood cells) given that the blood from which the leukocytes are isolated is not sterile and cannot be sterilized without destroying the leukocytes?
12. Figure 1—Define the term "Buffer Zone" as it appears in the upper floor plan of Figure 1?

In summary, the Society of Nuclear Medicine applauds and supports reasonable regulation(s) that improve patient safety. Radiopharmaceuticals, however, provide unique challenges in their preparation and dispensing, and the proposed document is confusing regarding these challenges. Because Nuclear Medicine/Pharmacy has a documented safety record and the short-lived radiopharmaceuticals do not fit well within the proposed revision of <797>, we propose the creation of a new category, Same-Day CSPs, as per the suggestion of James Ponto. We also urge that the SCC seriously consider the potential impact of the proposed changes in <797> both in terms of increased patient costs and very real potential of discontinued service in some areas of the United States.

Thank you for offering us an opportunity to express our concerns and comments with regard to the proposed revisions to <797>. We sincerely hope that you and the members of SCC would consider the above comments and suggestions. Thank you for your time and consideration.

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