Revision Status of USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations

The U.S. Pharmacopeia (USP) 28 is the official source of Chapter <797> Pharmaceutical Compounding—Sterile Preparations. It is currently enforceable by the U.S. Food and Drug Administration (FDA). State boards of pharmacy have either adopted it into statute and regulations or are considering whether it should be adopted. The Joint Commission on Accreditation of Health Care Organizations (JCAHO) has also incorporated this chapter into their standards. <797> has generated many concerns in pharmacies and health care facilities because of its new enforceable status. Radiopharmaceuticals are considered a preparation or a compounded sterile product according to this chapter. The SNM Committee on Pharmacopeia together with the SNM Radiopharmaceutical Sciences Council communicated their concerns to the Sterile Compounding Committee (SCC) of the USP in the fall of 2004 (*1*).

As a result of comments received from SNM and many other organizations and individuals, the SCC of the USP met and approved proposed revisions to <797>. A summary of that proposal may be reviewed at the USP Web site: www.usp.org/standards/proposed797Revisions.html.

The revision of a chapter in the USP includes the involvement of the public. The 4-step process that the SCC used in the development and revision of <797> follows the general guidance given in the USP's journal, the *Pharmacopeial Forum* (*PF*). The following is a summary of the USP revision process used by the SCC:

1. The SCC considers internal (from USP volunteers and staff) and external (from public sources, "*PF* provides interested parties an opportunity to review and comment. . .") comments.
2. A draft containing both current official content and proposed revisions is published in *PF*.
3. A period of several weeks elapses for an opportunity to receive public comments.
4. The SCC reviews received comments, then determines whether additional revision is necessary before the next version is published in the *PF* as an Interim Revision Announcement (IRA) which bears a date for official USP adoption.

The cycle of steps 1–4 may be repeated; thus, 1 or more years could elapse between currently official <797> in USP 28 and the next official <797>. The next official <797> will appear either in an annual USP revision (e.g., USP 29 in 2006) or in 1 of the 2 semiannual

Sam C. Augustine, PharmD, is a member of the 2000–2005 Sterile Compounding Committee (SCC), of the Council of Experts of the United States Pharmacopeial Convention, Inc. SCC is the committee that is responsible for the establishment and revision of the general chapter titled "Pharmaceutical Compounding–Sterile Preparations" (<797>) of the United States Pharmacopeia (USP). Dr. Augustine is the only board-certified nuclear pharmacist to serve as a member of this committee. He was recently invited to participate in the mid-winter meeting of the Committee on Pharmacopeia, Radiopharmaceutical Sciences Council, SNM, to update members on the proposed revision of <797>. Dr. Augustine was also invited to present a talk on the aforementioned topic during the 2005 SNM Mid-Winter Meeting. He has provided a brief summary of the current revision status of <797>. As mentioned in his article, the full text of the proposed revision of <797> is scheduled for publication in the *Pharmacopeial Forum* this spring. The Committee on Pharmacopeia will continue to closely monitor further developments in proposed revisions to <797> and will communicate our concerns and comments to the USP, as necessary, especially where any proposed revision of <797> might encroach on our professional practice.

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supplements to each annual USP revision. The earliest possibility (but an unlikely probability) would be Supplement 2 to USP 28 in late 2005 (*2*).

The following proposed revisions that may affect radiopharmaceutical preparations were reproduced from the summary prepared by Dr. David Newton, who serves as the chair of the SCC. His complete summary of the proposed revisions can be accessed at the USP Web site. The following summaries include only a selection of these revisions, with changes and added language appearing in italics.

1. Definitions to differentiate preparations from products are provided at the end of the introduction to the chapter, as well as revised standards and clarifications of what constitutes sterile compounding.

   PREPARATION. *A preparation, or compounded sterile preparation, CSP,* is a sterile drug or nutrient prepared in a licensed pharmacy or other health care related facility pursuant to the order of a licensed prescriber, which may or may not contain sterile *products*.

   PRODUCT. A *product* is a commercially manufactured sterile drug or nutrient that has been evaluated for safety and efficacy by the U.S. Food and Drug Administration, FDA. *Products* are accompanied by full prescribing information, which is commonly known as the FDA-approved manufacturer's labeling or *product* package insert.

   Sterile compounding pertains to all pre-administration manipulations of CSPs, including compounding, storage, and transport, but not to administration of CSPs to patients.

   Sterile compounding differs from nonsterile compounding primarily by requiring the maintenance of sterility when compounding exclusively with sterile ingredients and components, and the achievement of sterility when compounding with unsterile ingredients and components.

   Use of sterile products is not subject to <797> unless their preparation, packaging, and storage deviates from their product package inserts, or their preparation requires sterilization (i.e., involves a high-risk level component).

2. The exemption for "immediate use" (this exemption was honored by the JCAHO in 2004):

   Three or fewer sterile products may be prepared in worse than ISO Class 5 air when there is no direct contact contamination, and administration begins within 1 hour and is completed within 12 hours of preparation.

3. Hazardous drugs:

   This new section addresses safety precautions and practices when hazardous drugs (e.g., those that can cause abortion, allergy, birth defects, blisters, burns, cancer, cytotoxicity, genetic damage, infertility, irritation, sensitivity, vital organ toxicity, or other adverse effects) are ingredients in CSPs. It refers to applicable state and federal guidelines and standards, and NIOSH Publication No. 2004-165 at www.cdc.gov/niosh/docs/2004-165/ for safe practices. This section refers PET compounding to USP <823>, and it contains a statement about safe practices for all other radioactive sterile compounding. Currently official <797> requires positive pressure for all sterile compounding, but that is wrong for compounding radioactive and other hazardous drugs.

4. Physical inspection:

   Direct visual inspection of highly radioactive CSPs is not required based on maintaining radiation exposures As Low As Reasonably Achievable (ALARA).

5. Storage and Beyond Use Dating:

   Technetium-99m/Molybdenum 99 generator systems shall be stored and eluted (operated) under conditions recommended by their manufacturers and applicable state and federal regulations.

The full revision of <797> should be published this spring in the *PF*. Comments on the revision should be directed to Dr. Claudia Okeke at cco@usp.org. Access the USP Web site for the date of publication of the full text in *PF*.

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REFERENCES

1. Hung JC. Exemption of radiopharmaceuticals from <797> from the SNM Committee on Pharmacopeia. *J Nucl Med.* 2004:45(10):13N,14N,16N.
2. The United States Pharmacopeial Convention, Inc. Web site. Available at www.usp.org/standards/proposed797Revisions.html. Accessed on February 15, 2005.