January 29, 2016

Ronald T. Piervincenzi, Ph.D.
Chief Executive Officer
United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, Maryland 20852-1790

RE: Chapter <797> Pharmaceutical Compounding—Sterile Preparations

Dear Dr. Piervincenzi:

The American Society of Clinical Oncology (ASCO) is pleased to submit these comments on proposed revisions to the U.S. Pharmacopeial Convention (USP) General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. ASCO is the national organization representing nearly 40,000 physicians and other healthcare professionals specializing in cancer treatment, diagnosis, and prevention. ASCO members are dedicated to conducting research that leads to improved patient outcomes and ensuring that evidenced-based practices for the prevention, diagnosis, and treatment of cancer are available to all Americans.

ASCO is deeply committed to ensuring patient safety through the proper and accurate delivery of anticancer medication. In 2013, ASCO, along with the Oncology Nursing Society (ONS), released an updated set of chemotherapy administration safety standards that focus on patient protection. Additionally, ASCO has convened a Task Force on Safe Handling of Chemotherapy to develop recommendations for updated safety standards focused on worker and patient protection from exposure to hazardous drugs. Most recently, in November 2015, ASCO and the National Institutes for Occupational Safety and Health (NIOSH) convened a multi-stakeholder workshop to address issues surrounding the safe handling of hazardous drugs.

There has been an alarming trend in which chapters under development by USP have failed to adequately account for the day-to-day operations of modern oncology practices with respect to substance, phrasing, and clarity. We strongly urge USP to accommodate the recommendations described below. We have reviewed the proposed revisions to Chapter <797>, and we support changes that work to align the laws and regulations governing the U.S. Food and Drug Administration (FDA) with documents produced by USP.
In lines 49 to 56 of proposed revisions to Chapter <797>, USP has proposed the following definition for reconstitution and dilution:

**Reconstitution or dilution:** Reconstituting or diluting a conventionally manufactured sterile product with no intervening steps strictly in accordance with the manufacturer’s labeling for administration to an individual patient is not considered compounding. However, aseptic technique must be followed during preparation, and procedures must be in place to minimize the potential for contact with nonsterile surfaces and introduction of particulate matter or biological fluids.

Any other reconstitution or dilution of a conventionally manufactured sterile product is considered compounding and must be performed in accordance with this chapter.

The proposal deviates from the FDA’s definition of compounding – as enacted by Congress – in ways that are likely to cause significant confusion and practical problems in oncology practices throughout the United States (Section 503A of the U.S. Food, Drug, and Cosmetic Act). We urge USP to revise the definition of reconstitution and dilution to better align with the FDA definition and to clarify that the vast majority of reconstitution and dilution activities that occur in modern oncology practices do not fall within the scope of compounding governed by <797>.

Specifically, USP should amend this definition with the addition and deletion described below to better align with the FDA’s definition of compounding and more clearly identify the reconstitution and dilution activities that are exempt from the requirements of <797>:

**Reconstitution or dilution:** Reconstituting or diluting a conventionally manufactured sterile product with no intervening steps strictly in accordance with the manufacturer’s labeling or other manufacturer directions consistent with that labeling for administration to an individual patient is not considered compounding. However, aseptic technique must be followed during preparation, and procedures must be in place to minimize the potential for contact with nonsterile surfaces and introduction of particulate matter or biological fluids.

Any other reconstitution or dilution of a conventionally manufactured sterile product is considered compounding and must be performed in accordance with this chapter.

In addition, we urge USP to expressly state in <797> that activities such as, but not limited to, the addition of prepared drug products to normal saline solution for administration to an individual patient are administration activities (lines 34-38) in the final version of <797>. For example, there should be clarity that the USP intends for activities such as adding a single oncology drug to a 50 cc bag of normal saline for administration to a specified patient in an outpatient oncology setting would typically fall within the scope of administration, reconstitution, or dilution that is excluded from the definition of compounding.

We also recommend that the Compounding Expert Committee and USP develop supporting materials or additional language that makes the distinctions described above exceedingly clear.
Additionally, the proposed revision to the chapter directs readers to Chapter <800> Hazardous Drugs – Handling in Healthcare Settings for compounding, personal protective equipment (PPE) (line 352), facility (lines 640-642), handling (line 1025), and storage (line 1025) requirements for hazardous drugs. Because comments to proposed revisions to Chapter <797> are due before the final version of Chapter <800> will be published, we are unable to provide comment on the appropriateness of this language.

For your convenience, we have summarized our comments in the attached submission template.

* * * * *

Thank you for the opportunity to comment on this proposal. If we can provide any information or expertise on issues involving hazardous drugs or other aspects of the operation of modern oncology practices, please contact Deborah Kamin by email at Deborah.Kamin@asco.org or by phone at (571) 483-1610.

Sincerely,

Julie M. Vose, MD, MBA, FASCO
ASCO President
**Comment Submission Template for:**
**General Chapter <797> Pharmaceutical Compounding—Sterile Preparations**
Revision proposed in *Pharmacopeial Forum* 41(6) Nov/Dec 2015
Send completed template to CompoundingSL@usp.org by January 31, 2016

<table>
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<tr>
<th>Commenter's Name:</th>
<th>Position:</th>
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| Julie M. Vose, MD, MBA, FASCO | President, American Society of Clinical Oncology | Deborah Kamin, RN, PhD  
Vice President – Cancer Policy  
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**General Comments:** There has been an alarming trend in which chapters under development by USP have failed to adequately account for the day-to-day operations of modern oncology practices with respect to substance, phrasing, and clarity. We strongly urge USP to accommodate the recommendations described below. We have reviewed the proposed revisions to Chapter <797>, and we support changes that work to align the laws and regulations governing the U.S. Food and Drug Administration (FDA) with documents produced by USP. Please see attached comment letter for our full comments.

[See next page.]
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<th>Section(s)</th>
<th>Line Number(s)</th>
<th>Existing text: (Provide the proposed text.)</th>
<th>Suggested change: (Provide the revised suggestion to replace the existing text.)</th>
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<th>Rationale / Scientific Evidence</th>
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<td>1</td>
<td>34-38</td>
<td><strong>Administration of medications:</strong> This chapter is not intended to address administration of sterile medications. Administration of sterile medications should be performed in accordance with the Centers for Disease Control and Prevention’s Safe Injection Practices and the manufacturer’s or compounder’s labeling of the sterile medication.</td>
<td>We urge USP to expressly state in &lt;797&gt; that activities such as, but not limited to, the addition of prepared drug products to normal saline solution for administration to an individual patient are administration activities in the final version of &lt;797&gt;. For example, there should be clarity that the USP intends for activities such as adding a single oncology drug to a 50 cc bag of normal saline for administration to a specified patient in an outpatient oncology setting would typically fall within the scope of administration, reconstitution, or dilution that is excluded from the definition of compounding.</td>
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