Frequently Asked Questions: The Regulation of Safe Handling Practices for Hazardous Drugs Used in the Treatment of Individuals with Cancer

The American Society of Clinical Oncology (ASCO) is committed to promoting and supporting research, guidance, and educational materials to help ensure the safety of professionals in the oncology workforce who handle or otherwise potentially come into contact with hazardous drugs. This document addresses frequently asked questions (FAQs) regarding the safe handling of hazardous drugs from an evidence-based perspective for our members’ consideration. The information in this document represents our opinion on best practices for our members based on previous position papers and our communications with the United States Pharmacopeia (USP). Since the USP documents discussed are in flux and different states and accrediting organizations may adopt USP in whole, in part, or not at all, we recommend that you contact your legal counsel to help you interpret what guidelines would be appropriate in your particular location and circumstances.

Previous ASCO comments on USP <797> and <800> may be found below.

ASCO Comments 2014
ASCO Comments 2015
ASCO Comments 2016
ASCO Comments 2018
ASCO Comments 2019

What is the USP and how are the USP’s standards enforceable?
The USP is a private, non-profit, scientific organization that sets standards for the safe and proper use of medications. The USP is not an enforcement agency, so the USP does not enforce adherence to any of its standards at the national or state level. Historically, the USP has focused on developing standards that define the content and purity of drugs and other substances. Some of these standards are incorporated by reference into the laws and regulations that the U.S. Food and Drug Administration (FDA) actively enforces.

The USP has developed standards in the areas of drug compounding and the safe handling of hazardous drugs. To date, we are not aware of any activity by the FDA to adopt or enforce these standards at the national level. In some instances, states have incorporated the USP’s standards in part or in whole within state requirements, most commonly within the regulation of pharmacies that are subject to the rules promulgated by state boards of pharmacy or other state public health regulatory or labor-related functions.

What is USP <800>?
USP General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings lays out requirements for receiving, storing, compounding, dispensing, administering, and disposing of sterile and non-sterile hazardous drug products and preparations. It aims to promote patient safety, worker safety, and environmental protection by reducing unintended exposure to hazardous drugs. The USP released a final version of it in December 2019. A Revision Bulletin became official on July 1, 2020, which further
defined “antineoplastic” (medications to treat cancer) hazardous drugs (HDs) as intended to refer to antineoplastic HDs included in Table 1 of the most current National Institute for Occupational Safety and Health (NIOSH) list. In general, NIOSH defines a hazardous drug as any drug that possesses one or more of the following six characteristics: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, or molecular similarity to a known hazardous drug. Using these criteria, the NIOSH list further stratifies hazardous drugs into three categories: 1) antineoplastic drugs, 2) non-antineoplastic hazardous drugs, and 3) drugs with reproductive effects.

**When will USP <800> be effective?**
The most current version is the Revision Bulletin that became effective on July 1, 2020.

**How can I obtain a copy of USP <800>?**
The USP now allows free downloads of USP <800> available [here](https://www.usp.org). The June 26, 2020, Revision may be found [here](https://www.usp.org).

**What work has ASCO done on standards for the oncology community for the safe handling of hazardous drugs?**
ASCO took an evidence-based approach to developing a set of standards on the topic and released ASCO Standards on the Safe Handling of Hazardous Drugs in January 2019. In the development of the standards, the search for evidence found no studies that addressed health outcomes as they related to the identified interventions of interest. Thus, ASCO largely endorsed the best practices for safe handling of hazardous drugs as issued by USP <800> with the exception of the following, which we believe require evidence review and consensus-based standards: medical surveillance, closed system transfer devices (CSTD), external ventilation of containment secondary engineering controls or containment segregated compounding areas, and alternative duties. The ASCO Standards can be found [here](https://www.asco.org).

**What is USP <797>?**
The USP developed General Chapter <797> Pharmaceutical Compounding – Sterile Preparations to prevent patient harm from contaminated compounded sterile preparations. The USP proposed revisions to USP <795> and <797> on September 1, 2021, available [here](https://www.usp.org). A May 14, 2022, Compounding Expert Committee Update on USP <795> and <797> stated that the comment period for these proposed revisions ended March 17, 2022. At an April 19, 2022, meeting, the USP Compounding Expert Committee announced conclusion of comment review and advancement to next steps to make the revisions official, where such revision is expected to publish in 2023. In the meantime, the USP stated that the current version of USP <797> (last revised in 2008) remains official.

**How can I obtain a copy of USP <797>?**
A subscription to the USP-NF or USP Compounding Compendium is required to view USP <797>. More information about those subscriptions can be found [here](https://www.usp.org) and [here](https://www.usp.org). Proposed revisions to USP <797> are publicly available and can be viewed [here](https://www.usp.org).

**How are USP <797> and <800> Related?**
USP <797> provides standards for compounding of sterile preparations while USP <800> provides standards for the safe handling of hazardous drugs to minimize exposure risks for personnel who come
into contact with the hazardous drugs. USP <797> promotes the protection of the sterility of the drug, e.g., free from contaminants and consistent in intended identity, strength and potency and includes a number of requirements, including responsibilities of compounding personnel, training, environmental monitoring, storage and testing of finished preparations. Together, USP <797> and <800> establish an environment for compounding drugs that reduces contamination risk and aims to increase safety for healthcare personnel, patients and the environment.

Are there any substantive concerns with USP <797> from the perspective of community-based practices?
The recently proposed revisions to USP <797> may exempt certain activities that commonly occur in physician oncology practices, such as mixing and diluting activities that are consistent with the product labeling instructions, from the requirements of the chapter. Oncology drugs still should be prepared with aseptic technique, but the requirements in USP <797> seem more applicable to bulk compounding and are overly burdensome for most oncology practices.

Do community-based oncology practices “compound” as defined by the USP?
Since its initial development, the USP has been working with associations such as ASCO to better align USP <800> with USP <795> and <797> that were intended to apply only when a practitioner is “compounding”, i.e., not dispensing final dosage forms according to FDA-approved labeling. Accordingly, Section 1.4 of proposed USP <797> states: “Compounding does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling. Preparing a conventionally manufactured sterile product in accordance with the directions in the manufacturer’s approved labeling is out of scope of this chapter only if: 1. The product is prepared as a single dose for an individual patient; and 2. The approved labeling includes information for the diluent, the resultant strength, the container closure system, and storage time.”

In addition, the USP issued an FAQ for USP <800> that clarified that “For hazardous drugs, this means only when a practitioner is “compounding” (as that term is defined in <795> and <797>) would <800> be applicable.”

ASCO has contended that these statements from the USP should exempt community sites of care from both USP <797> and <800> compounding requirements, including USP <800> engineering controls (so long as the site of care does not perform activities other than in alignment with USP <797> Section 1.4).

How can USP standards be adopted?
State and local governments, federal agencies, or private accreditation organizations, including certain specialty pharmacies or pharmacy groups, could adopt USP standards in whole or in part at any time. At the state level, adoption could arise either by action through the state legislature or by action taken by a state agency, board of medicine, or board of pharmacy. Although the USP has set a specific implementation date, state or private entities could establish implementation dates that start before or after the USP’s recommendation.

What is NIOSH and how are its standards enforceable?
The National Institute for Occupational Safety and Health (NIOSH) is part of the Centers for Disease Control and Prevention (CDC) and is responsible for conducting research and making recommendations for the prevention of work-related injury and illness. NIOSH is not an enforcement agency. A few states have incorporated NIOSH standards within state laws, and in these instances, enforcement is the responsibility of the state governments.

What is the NIOSH Alert?
The NIOSH Alert is a document entitled “Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings” that NIOSH published in 2004. NIOSH also maintains a list of hazardous drugs, and the most recent version of that document (“NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings”) was released in 2010, 2012, and 2014. In 2016, a new format was developed for the 2014 list of hazardous drugs, which is available here. On May 1, 2020, NIOSH proposed the 2020 NIOSH List of Hazardous Drugs in Healthcare Settings for public comment. However, the 2016 List remains official until NIOSH finalizes and publishes the 2020 List.

How can I obtain a copy of the NIOSH Alert?
The NIOSH Alert can be accessed here.

What other materials has NIOSH developed on safe handling?
NIOSH maintains a list of recent scientific articles about occupational exposure to hazardous drugs on their website and has developed supplementary materials. NIOSH released a draft protocol for testing the efficacy of Closed System Transfer Devices (CSTDs) that function by vapor containment (“A Vapor Containment Performance Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs”) on September 8, 2015. On January 19, 2016, NIOSH issued a request for information for developing a similar protocol for CSTDs that use air filtering technology (“Request for Information on Development of a Performance Test Protocol for Closed System Transfer Devices That Incorporate Air-Cleaning Technology to Provide Worker Protection During Pharmacy Compounding and Administration of Hazardous Drugs”). In January 2015, NIOSH released a draft document “Current Intelligence Bulletin: Reproductive Risks Associated with Hazardous Drug Exposures in Healthcare Workers and Recommendations for Reducing Exposures.”

What is OSHA and are its standards enforceable?
The Occupational Safety and Health Administration (OSHA) is a division of the United States Department of Labor. OSHA requires compliance with the latest U.S. Public Health Service guidelines for standards. NIOSH recommendations contain the latest U.S. Public Health Service guidelines.

An OSHA state by state organizational hazardous drug guideline map can be found here.