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Understanding the **New Proposed USP Chapter <800>**

Each year, approximately eight million US health care workers are potentially exposed to hazardous drugs (HDs).[1] The subject of worker exposure to HDs (ie, chemotherapy, antineoplastics, cytotoxics, etc) has been discussed since the early 1970s, when chemotherapy was mixed on countertops or in horizontal laminar airflow workbenches that blew HD-contaminated air into the room, directly at compounding personnel. In 2004, the National Institute of Occupational Safety and Health (NIOSH) published the NIOSH Alert, Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings, 11 months after the publication of the 2004 version of USP Chapter <797>. In the 2008 revision of USP Chapter <797>, a specific section was devoted to the preparation of hazardous drugs, which defined several key requirements, including[2]:

1. Appropriate primary and secondary engineering controls to ensure sterility and drug containment
2. The use of personal protective equipment (PPE), regardless of engineering control employed
3. Training of compounding personnel to include at least the following:
   - Safe aseptic manipulation practices;
   - Negative pressure techniques when utilizing a biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI);
   - Correct use of closed system drug-transfer devices (CSTDs);
   - Containment, cleanup, and disposal procedures for breakages and spills; and
   - Treatment of personnel contact and inhalation exposure
4. Training of personnel who perform routine custodial waste removal and cleaning activities in storage and preparation areas for HDs in appropriate procedures to protect themselves and prevent contamination.

These requirements are limited, however, as they do not address the full scope of HD exposure. Not all HDs are sterile; as such, the hazards of non-sterile compounding require delineation as well.

New Proposed USP <800>

On March 28, 2014, USP posted the new proposed *General Chapter <800> Hazardous Drugs–Handling in Healthcare Settings* on their Web site (available at http://www.usp.org/usp-nf/notices/compounding-notice).[3] This chapter identifies the requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administering HDs to properly protect patients, health care personnel, and the environment. General Chapter <800> was published electronically in the May–June issue of *Pharmacopeial Forum* (PF). Public review and comments will be accepted through July 31, 2014.

Proposed USP Chapter <800> identifies the requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administering hazardous drugs to properly protect patients, health care personnel, and the environment.

An important strategy to minimize occupational exposure to HDs is to ensure containment to as low a limit as reasonably achievable (ALARA). The concept of ALARA, a radiation safety principle, can be borrowed for use related to HD containment. As defined in Title 10, Section 20.1003 of the Code of Federal Regulations (10 CFR 20.1003),

> *ALARA is an acronym for "as low as (is) reasonably achievable," which means making every reasonable effort to maintain exposures to ionizing radiation as far below the dose limits as practical, consistent with the purpose for which the licensed activity is undertaken, taking into account the state of technology, the economics of improvements in relation to state of technology, the economics of improvements in relation to benefits to the public health and safety, and other societal and socioeconomic considerations, and in relation to utilization of nuclear energy and licensed materials in the public interest.*[4]

By replacing the references to radiation and nuclear energy with the term HDs, the ALARA principle accurately explains the essence of proposed chapter <800>. Adopting the strategies laid out in USP <800> will enable hospitals to ensure that health care workers manipulating HDs are exposed only to amounts of contamination in line with the concept of ALARA.

Understanding Hazardous Drug Exposure

Since the first reported HD exposures, one of the roadblocks to achieving HD safety compliance has been the lack of documented evidence that HDs cause harm to health care workers. There is no clear, reportable number of deaths of health care workers who have developed cancer as a result of handling HDs at the workplace; few registries exist in the US that track employment, cancer outcomes, or reproductive outcomes of health care workers exposed to HDs, so accurate counts remain elusive. While to date there is no conclusive proof of the link between HD exposure and cancer in health care workers, the data on reproductive risk, notable biological marker effects, and recent specific chromosomal aberrations is too much to ignore.

In 2010, an investigative reporter, Carol Smith, endeavored to put a human face on the problem by recounting the tribulations of Sue Crump, a Seattle-area pharmacist who died at age 55 of pancreatic cancer.[5] The reporter chronicled Crump's experience mixing chemotherapy in hospital settings, which Crump believed was a causative factor in her cancer. The impact of this report resulted in the Washington State legislature passing two HD rules in 2012, one detailing handling requirements and the other requiring a registry to track workers who handle HDs and adverse events they had experienced.[6,7] Certainly this is a positive development, and underscores the need for additional resources to track occupational exposure and cancer throughout the US.

Also in 2010, two important studies were published in the *Journal of Occupational and Environmental Medicine*. The first study, partially funded by NIOSH, evaluated antineoplastic drug exposure of health care workers at three university-based US health care centers, and reported continuing surface contamination in pharmacy and nursing areas despite HD handling guidelines.[8] The second study reported damage to health care workers' chromosomes that are linked to secondary cancers in treated patients, specifically tAML (acute myeloid leukemia with gene translocation) and tMDS (myelodysplastic syndromes with gene translocation).[9] These studies prompted NIOSH, OSHA, and TJC to jointly draft a letter discussing the safe use of HDs, which was sent on April 8, 2011 to all US hospitals.[10] Its message was to remind hospital and health care employers that HDs, such as antineoplastic drugs, pose serious health risks to workers when proper handling precautions are not followed.

Exposure to HDs, both directly and indirectly, is an occupational hazard for a large number of health care workers, **and it is vital that everyone who is at risk educate themselves about Chapter <800> and the actions they can take to protect themselves.**

NIOSH Hazardous Drug Handling Guidance

After the 2010 article on pharmacist Sue Crump was published, OSHA noted, "Although this is an important safety and health issue, OSHA has not considered a standard to specifically address hazardous drugs in the health care setting."[5] In fact, OSHA has not addressed this topic since posting their 1995 HD handling guidance document to the Web in 1999.[11,12] Although many hospital leaders rely on the OSHA Web site for information on HDs in the workplace, the site contains little information detailing surface contamination studies and no information on the use of CSTDs.

Many states operate their own OSHA programs, and some states are following Washington's lead in this effort. Maryland[13] and North Carolina[14] have action in progress, and California passed an HD bill in October 2013.[15] However, because state OSHA initiatives all vary somewhat, state rules may not ensure the consistency of practice standards necessary to effectively deal with the problem of HD exposure in the health care setting.

Hundreds of studies have been published discussing HD exposure since the 2004 NIOSH Alert. The NIOSH Web site maintains a list of all the studies related to HD exposure (available at http://www.cdc.gov/niosh/topics/antineoplastic/pubs.html).

While limited evidence exists in the literature concerning occupational cancer related to antineoplastic agents,[16] adverse effects on fertility and reproductive health continue to be identified in a number of studies, mainly in female nurses.[17]

USP Chapter <800> provides extensive and consistent position statements on all aspects of HD handling; thus, adopting the requirements in USP <800> will improve and standardize practice nationwide. **TABLE 1**[18] highlights some of the major differences between the current requirements in USP Chapter <797> and the proposed version of USP Chapter <800>.

(Continues on page 24)

TABLE 1

Comparison of USP <797> and New Proposed USP <800>[18]

USP <797> Pharmaceutical Compounding—Sterile Preparations	**Proposed General Chapter USP <800> Hazardous Drugs**—Handling in Healthcare Settings
Applies to sterile compounding only	Applies to sterile and non-sterile compounding
Applies from receipt of inventory up to start of drug administration	Applies from receipt of inventory through drug administration
All HDs should be stored separately in an area with 12 ACPH and 0.01" w.c. negative to adjacent space	Antineoplastic HDs must be stored separately from non-HDs in an area with 12 ACPH and 0.01" w.c. negative to adjacent space unless coated, final-manufactured dosage forms are clearly labeled as HDs and safety strategies are detailed in policies and procedures
Exemption for low-volume compounding	No low-volume exemption
CSTD use is a ***should***	CSTD use is a ***shall*** during administration, when dosage form permits
Defines PECs for HD sterile compounding	Defines PECs for non-sterile and sterile HD compounding Allows manipulation of HDs that do not produce aerosols (eg, coated tablets or capsules) outside of C-PEC
Prohibits SCA for HD compounding Requires BSC to be housed in ISO class 7 room air that is 0.01" w.c. negative	Permits SCA for HDs provided CACI/BSC in area that has 12 ACPH and 0.01" W.C. negative; maximum BUD 12 hours
Does not require environmental and medical surveillance	Requires environmental and medical surveillance

ACPH = air changes for hour; BSC = biological safety cabinet; BUD = beyond-use date; C-PEC = containment primary engineering control; CACI = compounding aseptic containment isolators; HD = hazardous drug; PECs = primary engineering controls; SCA = segregated compounding area; w.c. = water column.

(Continued from page 7)

Summary

Exposure to HDs, both directly and indirectly, is an occupational hazard for a large number of health care workers, and it is vital that everyone who is at risk educate themselves about Chapter <800> and the actions they can take to protect themselves. Do the strategies detailed in the new proposed chapter reduce exposures to HDs as low as reasonably achievable? To weigh in, please visit the USP Web site to download and read the proposed chapter. This is your opportunity to submit feedback and constructive suggestions to the expert committee to help strengthen the chapter and properly protect yourself and your colleagues from contamination. ■

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