Safe Handling Of Hazardous Drugs: 
Reviewing Standards for Worker Protection

In 2011, senior officials of the National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), and the Joint Commission collaborated on a letter sent to all hospital employers in the United States stating that hazardous drugs (HDs), such as antineoplastic drugs, can pose serious job-related health risks to workers if proper precautions are not used in handling the drugs.¹

This unusual action was taken to remind hospital employers that protecting the health of their employees is vitally important, according to NIOSH Director John Howard, MD, as well as OSHA Assistant Secretary of Labor David Michaels PhD, MPH, and the Joint Commission’s Senior Vice President of Healthcare Improvement Paul M. Schyve, MD.²³

Health care worker exposure to HDs, including antineoplastic agents, antiviral agents, biological modifiers, hormones, and other agents, has been a concern since the late 1970s. Despite decades of research and guidance on safe handling, including a comprehensive NIOSH Alert issued in 2004,⁴ health care workers still experience HD exposure. A NIOSH-sponsored
study published in 2010\(^5\) reexamined risk points from a 1999 study\(^6\) and showed similar levels of HD surface contamination in both compounding and administration areas. A 2010 study describes evidence of drug uptake and chromosomal changes in oncology workers\(^7\) and a 2012 study documents adverse reproductive events in nurses exposed to HDs in the workplace.\(^8\) The reproductive results are similar to those reported in a 2005 meta-analysis of the increased occurrence of toxic events among HD handlers.\(^9\) These recently published studies demonstrate little improvement over earlier studies indicating that healthy workers exposed to HDs may experience adverse effects.\(^10^-^12\)

Ongoing efforts are necessary to promote awareness of the health risks associated with this exposure to all health care workers involved in the handling of HDs and to assess whether the failure of existing programs is due to ineffective interventions or the lack of adherence to recommended precautions. This review focuses on existing guidance and some new activities of regulatory groups to improve adherence to safety precautions.

## Routes of Occupational Exposure

Many studies have documented both surface and worker contamination from HDs.\(^13^-^19\) Health care workers may breathe contaminated air or touch contaminated surfaces and take in HDs from the work environment through unprotected skin.\(^13^-^17,20\) Standard work practices for handling injectable drugs in vials and syringes can generate powder and liquid aerosols. These drug residues may contaminate the air and surfaces in the work area.\(^13^-^19,21\) A multisite 2005 study documented that many HD vials are delivered from the manufacturer with drug residue on the outside of the vials, creating yet another opportunity for contamination.\(^22\) A 2010 study looking at drug vials manufactured in Europe found similar results.\(^23\) Certain HDs have been shown to vaporize at room temperature, resulting in drug contamination of the air.\(^24^-^26\) Drug uptake also may occur through the ingestion of contaminated food or drink that is inappropriately located in or near drug-handling areas. The transfer of contaminated residues from hands to mouth may result in the ingestion of HDs. Needlesticks with HD-contaminated needles or cuts from glass fragments of vials or ampules may result in exposure by injection.

## Guidelines and Standards for Safe Handling of Hazardous Drugs

Since 1980, numerous organizations have issued guidelines for the safe handling of HDs. OSHA updated early guidelines in 1995,\(^27\) and made them available online in 1999.\(^28\) In 2004, NIOSH issued an alert, “Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings,” which reassessed the problem and existing guidance.\(^4\) The American Society of Health-System Pharmacists (ASHP) published updated and extensive guidelines on the safe handling of cytotoxic agents as a Technical Assistance Bulletin in 1990, and issued new guidelines on HDs in 2006.\(^29,30\) The 2006 guidelines were harmonized to the 2004 NIOSH Alert. To influence nursing practice and protect its members from exposure, the Oncology Nursing Society (ONS) published “Chemotherapy and Biotherapy Guidelines and Recommendations for Practice” and developed an extensive educational program.\(^31^-^33\) ONS’s latest recommendations harmonize with those of NIOSH and ASHP.

In 2007, the United States Pharmacopeial Convention released USP Chapter <797>, “Pharmaceutical Compounding—Sterile Preparations,” which became effective in 2008.\(^34\) This revision of the 2004 standard includes a section specific to the compounding of HDs and is coordinated with much of the 2004 NIOSH Alert. More importantly, USP Chapter <797> is an enforceable standard and establishes many of the NIOSH recommendations as requirements. The standards set by USP Chapter <797> are applicable in all settings in which sterile doses of HDs are compounded, not just hospitals and clinics. Revisions to USP Chapter <797> for the 2012 edition currently are proposed in Pharmacopeial Forum (PF) but are not yet approved by an Expert Committee.\(^35\) USP also is proposing a separate chapter on compounding HDs that will provide guidelines and recommendations to reduce the potential harmful effects of HDs on health care workers. A Hazardous Drugs Expert Panel has been commissioned to work with the 2010-2015 USP Compounding Pharmacy Expert Committee to prepare this chapter.\(^36\)

The Washington State Legislature required the State Department of Labor & Industries (L&I) to set requirements to protect workers who handle chemotherapy and other HDs. This landmark bill required L&I to adopt rules that are consistent with but do not exceed provisions in the 2004 NIOSH Alert on preventing occupational exposures to antineoplastic and other HDs in health care settings, as updated in 2010. L&I’s HDs rule was adopted on Jan. 3, 2012, and the rule will take effect in stages beginning Jan. 1, 2014.\(^37\)

## Continuing Exposure

Studies of surface and worker contamination conducted in the late 1990s and through 2010 have
continued to document HD exposure.5-12,17-19,21 A NIOSH-sponsored study from 2010 detected surface contamination with HDs in compounding and administration environments of all sites studied.5 The findings of the study included a correlation between the size and spatial design of the compounding area and the amount of surface contamination. Preliminary reports support the USP Chapter <797> design standard that requires an appropriate buffer area around the primary engineering control (PEC).34 One site studied in the 2010 NIOSH study had a smaller, less delineated compounding area and the investigators found a higher rate of surface contamination at that site. Surprisingly, the percentage of surfaces contaminated with HD residue in this study is almost identical to that found in a similar study published more than a decade earlier, in 1999.6 In both studies, 75% of surfaces sampled in the pharmacies were found to have residue of at least one of the marker HDs. This raises the question of whether the efforts of NIOSH and USP have made any difference with regard to HD contamination.

Additional concern was generated by a substudy within the NIOSH research. In this companion study, also published in 2010, investigators at the University of Maryland evaluated the chromosomal effects of select HDs in health care workers using fluorescence in situ hybridization.7 The DNA of exposed workers showed a statistically significant increased frequency of damage to chromosome 5 or 7 (P=0.01) and an increased frequency of damage to chromosome 5 alone (P=0.01). Myelodysplastic syndrome and acute myeloid leukemia are known to be associated with signature lesions in chromosomes 5, 7, and 11. These results provide additional evidence for harmful effects from occupational exposure to HDs.

A 2011 retrospective study of occupational exposures and pregnancy outcomes in 8,461 participants in the Nurses’ Health Study II found an associated 2-fold increased risk for spontaneous abortion with HD exposure.8 The authors of this study noted that even though awareness of HD exposure has increased, protocols to reduce exposure of health care personnel to these chemicals have been insufficient to eliminate the exposure.8 However, other researchers have postulated other reasons for continuing HD exposure, including workers’ lack of awareness of the issue; poor facility design; a lack of vigilance in work practices; poor adherence to the use of personal protective equipment (PPE); less than supportive attitudes by supervisory personnel; and inadequate time to compound and administer and properly care for

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<tr>
<th>NIOSH</th>
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<tr>
<td>Carcinogenicity</td>
<td>Carcinogenicity in animal models, in the patient population, or both, as reported by the International Agency for Research on Cancer</td>
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<tr>
<td>Teratogenicity or developmental toxicity</td>
<td>Teratogenicity in animal studies or in treated patients</td>
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<tr>
<td>Reproductive toxicity</td>
<td>Fertility impairment in animal studies or in treated patients</td>
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<tr>
<td>Organ toxicity at low doses</td>
<td>Evidence of serious organ or other toxicity at low doses in animal models or treated patients</td>
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<tr>
<td>Genotoxicity</td>
<td>Genotoxicity (ie, mutagenicity and clastogenicity in short-term test systems)</td>
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<td>Structure and toxicity profile of new drugs that mimic existing drugs determined hazardous by the above criteria</td>
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ASHP, American Society of Health-System Pharmacists; NIOSH, National Institute for Occupational Safety and Health

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patients. In a 2006 review of the HD safe-handling literature, the authors reported the common finding that policies and procedures for handling HDs are in place but that employees who are directly involved in the preparation and administration of HD are not compliant. Possibly, the fact that HD precautions are referred to as guidelines instead of practice standards or rules promotes a lack of employer and individual worker concern.

NIOSH actively continues to increase awareness of this issue by maintaining Safety and Health Topic pages online: “Hazardous Drug Exposures in Health Care” and “Occupational Exposure to Antineoplastic Agents.” These pages provide links to extensive background information, the latest studies, updates on related activities, and NIOSH publications.

**Barriers**

Although many studies document continuing HD contamination and worker exposure, few have attempted to identify why the efforts to improve worker safety have not been successful. A recent study of nurses sought to explain this issue. The purpose of the study was to examine relationships among factors affecting nurses’ use of HD safe-handling precautions and to identify factors that promote or hinder the use of precautions. In a study with a cross-sectional, correlation design, 165 nurses from oncology centers throughout the United States who reported handling chemotherapy completed a mailed survey. Instruments measured the use of HD precautions and various factors thought to influence the use of precautions. Despite the fact that nurses were knowledgeable about chemotherapy exposure, overall use of precautions during administration and disposal of these drugs was low. The following factors were predictive of higher use of precautions: fewer patients per day per nurse, fewer barriers (eg, availability and convenience of PPE), and a better workplace safety climate (eg, training provided, supervisors’ encouragement of precaution use, and expectations that policies are followed). These findings have important implications because factors in the workplace environment seem to be the most important influences on safe-handling practices.

**Defining HDs**

A number of drug types that are potent and toxic in patients have the potential to cause adverse effects in persons who are occupationally exposed to them. Although the cytotoxic potential of the alkylating agents is of primary concern, there are multiple mechanisms by which drugs cause hazardous effects. In 1990, ASHP attempted to categorize these drugs in its “Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs,” for the first time using the term hazardous drug in reference to drugs that involve risks from occupational exposure. The terminology was selected to be inclusive of the types of drugs with safety concerns and to be compatible with the then newly developed OSHA Hazard Communication Standard (HCS).

The HCS is intended to ensure that workers who are at risk for exposure to hazardous chemicals in the workplace are informed of the specific hazardous chemicals, their associated health and safety hazards, and the appropriate protective measures to be taken. The HCS (CFR 1910.1200) has been updated to align with the UN Globally Harmonized System of Classification and Labeling of Chemicals (GHS), Revision 3. This rule became effective on May 25, 2012. The revised HCS defines a hazardous chemical as any chemical that is classified as a physical hazard or a health hazard, a simple asphyxiant, combustible dust, pyrophoric gas, or hazard not otherwise classified. It further defines a health hazard as a chemical that is classified as posing one of the following hazardous effects: acute toxicity (any route of exposure); skin corrosion or irritation; serious eye damage or irritation; respiratory or skin sensitization; germ cell mutagenicity; carcinogenicity; reproductive toxicity; specific target organ toxicity (single or repeated exposure); or aspiration hazard. The criteria for determining whether a chemical is classified as a health hazard are detailed in Appendix A to §1910.1200—Health Hazard Criteria.

ASHP has used similar criteria to define HDs. Data on the side effects of a drug are collected during both the drug’s premarket investigational phase and its clinical use. These data reasonably may be used to infer health hazards in workers occupationally exposed to the drug. As such, ASHP proposed the following criteria to define HDs:

- genotoxicity (ie, mutagenicity and clastogenicity in short-term test systems);
- carcinogenicity in animal models, in the patient population, or in both, as reported by the International Agency for Research on Cancer;
- teratogenicity or fertility impairment in animal studies or in treated patients; and
- evidence of serious organ or other toxicity at low doses in animal models or treated patients.

ASHP’s criteria for HDs were revised by NIOSH for the 2004 Hazardous Drug Alert. The NIOSH 2004 and ASHP 1990 definitions of HDs are compared in Table 1.
of HDs, which supports both the HCS and the NIOSH Alert definitions: Drugs are classified as hazardous if studies in animals or humans indicate that exposures to them have a potential to cause cancer, developmental or reproductive toxicity, or harm to organs.\textsuperscript{34}

NIOSH has adopted a mechanism both to review its HD criteria and to judge newly FDA-approved drugs against these criteria on a regular basis. The review process for the addition of the new listings is described in the \textit{Federal Register}.\textsuperscript{49} The updated “NIOSH List of Anti-neoplastic and Other Hazardous Drugs in Healthcare Settings 2012” can be found on the NIOSH website.\textsuperscript{50}

\textbf{Recommendations}

Recommendations for the safe handling of HDs have been available since the early 1980s. As more research has been conducted and more groups have been involved, the recommendations have been coordinated in an attempt to provide uniformity. Each group, however, has a somewhat different focus. The NIOSH Alert and OSHA Technical Manuals are broad guidelines; the ONS “Chemotherapy and Biotherapy Guidelines” focus on administration and patient safety information; ASHP addresses pharmacists’ concerns; and USP Chapter <797> deals exclusively with sterile compounding.

All guidelines agree that to reduce exposure to HDs in the occupational setting, a comprehensive safety program must be developed that deals with all aspects of drug handling—from selection and receipt of the product to storage, compounding, administration, spill control, and waste management. Key components of such a program are administrative, environmental

\begin{table}
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\caption{Comparison of the NIOSH, ASHP, and USP Chapter <797> Recommendations for the Hazardous Drug Compounding Environment}
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 & NIOSH & ASHP & USP Chapter <797> \\
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\textbf{Storage environment} & Store HDs separately from other drugs in an area with sufficient general exhaust ventilation to dilute and remove any airborne contaminants. & Segregate HD inventory and store in an area with sufficient general exhaust ventilation to dilute and remove any airborne contaminants. & HDs shall be stored separately from other inventory, preferably within a containment area such as a negative-pressure room. \\
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\textbf{Compounding} & Prepare HDs in an area that is devoted to that purpose alone and is restricted to authorized personnel. & HDs should be compounded in a controlled area where access is limited to authorized personnel trained in handling requirements. & HDs shall be prepared in a PEC, which shall be placed in an ISO class 7 area that is physically separated from other preparation areas. \\
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\textbf{Ventilation} & Where feasible, exhaust 100\% of the filtered air to the outside. & Because of the hazardous nature of these preparations, a contained environment where air pressure is negative relative to that of the surrounding areas or that is protected by an air lock or anteroom is preferred. & Storage: area should have exhaust ventilation of at least 12 air changes per hour. Compounding: optimally at negative pressure relative to adjacent positive-pressure ISO class 7 or better ante-areas. \\
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\textbf{ASHP, American Society of Health-System Pharmacists; HDs, hazardous drugs; ISO, International Organization for Standardization; NIOSH, National Institute for Occupational Safety and Health; PEC, primary engineering control; USP, United States Pharmacopeia}

Based on references 4, 30, and 34.
Table 3. Comparison of NIOSH, ASHP, and USP Chapter <797> Recommendations for Primary Engineering Controls

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<tr>
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<th>NIOSH</th>
<th>ASHP</th>
<th>USP Chapter &lt;797&gt;</th>
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<td>PECs</td>
<td>• Aseptic containment ventilation control class II BSC-type B2 is preferred. • Class III BSC or CACI.</td>
<td>• Class II BSC-type B2 with outside exhaust is preferred. • Total exhaust is required if the HD is known to be volatile. • Class III BSC or CACI.</td>
<td>• BSC or CACI that meets or exceeds the standards for CACI in USP Chapter &lt;797&gt;.</td>
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<td>Ventilation</td>
<td>• Do not use a ventilated cabinet that recirculates air inside the cabinet or exhausts air back into the room environment if a drug is volatile.</td>
<td>• Without special design considerations, class II BSCs are not recommended in traditional, positive-pressure clean rooms.</td>
<td>• BSCs and CACIs optimally should be 100% vented to the outside air through HEPA filtration.</td>
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ASHP, American Society of Health-System Pharmacists; BSC, biological safety cabinet; CACI, compounding aseptic containment isolator; HD, hazardous drug; HEPA, high-efficiency particulate air; NIOSH, National Institute for Occupational Safety and Health; PEC, primary engineering control; USP, United States Pharmacopeia

Based on references 4, 30, and 34.

Engineering, and work practice controls, as well as PPE. These components are based on principles of industrial hygiene that have been successfully used to mitigate risks from other occupational exposures.51

**Administrative Controls**

Administrative controls include policies, procedures, staff education and training, validation of competency, and medical surveillance. All aspects of HD handling must be identified, staff performance expectations clearly defined, methods for validating staff competency determined, and processes for the ongoing monitoring of adherence to policies judiciously established.

USP Chapter <797> emphasizes administrative controls for the safe compounding of HDs by mandating conditions that protect health care workers and other personnel in preparation and storage areas. Additional requirements include extensive training of all personnel involved in the storage, handling, and disposal of these drugs. USP Chapter <797> reinforces the OSHA and NIOSH recommendations by requiring training before the preparation or handling of hazardous compounded sterile preparations, and by mandating that the effectiveness of training be verified by testing workers on specific HD preparation techniques. Ongoing training must be documented at least annually. The components of the training program are specified to include didactic overview of HDs and their mutagenic, teratogenic, and carcinogenic properties. The training program must address each new HD that enters the marketplace. Training in work practices also must include the following: aseptic manipulation; negative-pressure technique; correct use of safety equipment; containment, clean-up, and disposal procedures for breakages and spills; and treatment of personnel for contact and inhalation exposures.

OSHA and NIOSH include medical surveillance in their safety program recommendations. Medical surveillance involves collecting and interpreting data to detect changes in the health status of working populations potentially exposed to hazardous substances. In 2007, NIOSH released “Workplace Solution: Medical Surveillance for Health Care Workers Exposed to Hazardous Drugs,” which provides directions for establishing such a program and the elements that should be included.52

USP Chapter <797> requires that all compounding personnel with reproductive capability confirm in writing that they understand the risks associated with handling HDs. Although USP Chapter <797> mandates this only for personnel responsible for compounding, prudent practice dictates that the requirement should extend to all personnel who handle HDs along the chain of custody.
Table 4. Comparison of NIOSH, OSHA, ASHP, and USP Chapter <797> Recommendations for PPE

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<tr>
<th>General handling</th>
<th>NIOSH/OSHA</th>
<th>ASHP</th>
<th>USP Chapter &lt;797&gt;</th>
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<tr>
<td>• Use double gloving for all activities involving HDs.</td>
<td>• Wear double gloves for all activities involving HDs.</td>
<td>• HDs shall be handled with caution at all times with the use of appropriate chemotherapy gloves during receiving, distributing, stocking, taking inventory, preparing for administration, and disposal.</td>
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<td>OSHA: • Protective equipment, including PPE for eyes, face, head, and extremities, protective clothing, respiratory devices, and protective shields and barriers shall be provided, used, and maintained in a sanitary and reliable condition wherever it is necessary by reason of hazards of processes or environment, chemical hazards, radiological hazards, or mechanical irritants encountered in a manner capable of causing injury or impairment in the function of any part of the body through absorption, inhalation, or physical contact.</td>
<td>• Guidelines for the safe handling of HDs recommend the use of gowns for compounding in the BSC, administration, spill control, and waste management to protect the worker from contamination by fugitive drug generated during the handling process.</td>
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<tr>
<th>Receiving and storage</th>
<th>NIOSH/OSHA</th>
<th>ASHP</th>
<th>USP Chapter &lt;797&gt;</th>
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<td>• Wear chemotherapy gloves, protective clothing, and eye protection when opening containers to unpack HDs.</td>
<td>• Gloves must be worn at all times when drug packaging, cartons, and vials are handled, including during the performance of inventory control procedures and the gathering of HDs.</td>
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<th>Compounding</th>
<th>NIOSH/OSHA</th>
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<td>• Wear PPE (including double gloves and protective gowns) while reconstituting and admixing drugs.</td>
<td>• Select disposable gowns of material tested to be protective against the HDs to be used.</td>
<td>• Sterile compounding: • Shoe covers, head and facial hair covers (eg, beard covers in addition to face masks), and face masks; a nonshedding gown that has sleeves that fit snugly around the wrists and is enclosed at the neck; sterile powder-free gloves.</td>
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<td>• Make sure that gloves are labeled as chemotherapy gloves.</td>
<td>• Coated gowns must not be worn for longer than 3 hours during compounding and must be changed immediately when damaged or contaminated.</td>
<td>Hazardous drug compounding: • Appropriate PPE shall be worn during compounding in a BSC or CACI and during the use of CSTDs. PPE should include gowns, face masks, eye protection, hair covers, shoe covers or dedicated shoes, double gloving with sterile chemotherapy-type gloves, and compliance with manufacturers' recommendations when a CACI is used.</td>
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<td>• Use disposable gowns made of polyethylene-coated polypropylene material (which is nonlinting and nonabsorbent).</td>
<td>• Gowns worn as barrier protection in the compounding of HDs must never be worn outside the immediate preparation area.</td>
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<th>Administration</th>
<th>NIOSH/OSHA</th>
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<tr>
<td>• Wear PPE (including double gloves, goggles, and protective gowns) for all activities associated with drug administration.</td>
<td>• Gowns worn during administration should be changed when the patient care area is left and immediately if contaminated.</td>
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ASHP, American Society of Health-System Pharmacists; BSC, biological safety cabinet; CACI, compounding aseptic containment isolator; CSTD, closed-system drug-transfer device; HD, hazardous drugs; NIOSH, National Institute for Occupational Safety and Health; OSHA, Occupational Safety and Health Administration; PEC, primary engineering control; PPE, personal protective equipment; USP, United States Pharmacopeia

Based on references 4, 28, 30, and 34.
ENVIRONMENTAL AND ENGINEERING CONTROLS

The 2008 revision to USP Chapter <797> contains extensive mandates to improve the environment in which sterile doses of HDs are compounded. These directives are designed to increase safety for patients by reducing the potential for the microbial contamination of sterile dosage forms, and to improve worker safety by addressing design concerns in traditional, positive-pressure compounding environments. Table 2 compares the NIOSH, ASHP, and USP Chapter <797> recommendations for the environment in which HDs are compounded.4,30,34

HDs must be stored separately from other inventory in a manner to prevent contamination and exposure of personnel. Because of the concerns of volatilization at room temperature, storage is preferably within a containment area such as a negative-pressure room with sufficient exhaust ventilation and at least 12 air changes per hour (ACPH) to dilute and remove airborne contaminants.

An International Organization for Standardization (ISO) Class 5 PEC is required for HD compounding to prevent microbial contamination of sterile preparations and to protect workers and the environment by preventing the escape of HD aerosols or residue. Appropriate PECs for compounding sterile HD preparations include Class II biological safety cabinets (BSCs) and compounding aseptic containment isolators (CACIs) that meet or exceed the standards set forth in USP Chapter <797>.

Isolators are recommended as a PEC in both the NIOSH Alert and the ASHP HD guidelines. The USP Chapter <797> revision sets performance standards for isolators used to compound sterile preparations, for compounding aseptic isolators (CAIs), and for isolators used to compound sterile HD preparations (CACIs). To meet the criteria of USP Chapter <797>, an isolator must provide isolation from the room and maintain ISO Class 5 air quality within the cabinet during dynamic operating conditions. CAI and CACI air quality must be documented by particle counts during compounding operations and during transfer of material in and out of the isolator. Recovery time to ISO Class 5 air in the main chamber must be documented after material is transferred into and out of the main chamber. Work practices must be developed to reduce disruption of the air quality in the isolator and to minimize recovery time.

A CACI meeting all these conditions, as detailed in USP Chapter <797>, is exempt from the requirement that it be placed in an ISO Class 7 buffer area. For HD compounding, however, the compounding area must maintain negative pressure and have a minimum of 12 ACPH.

A Class II BSC has an open front and depends on an air barrier to prevent HD contamination from escaping the cabinet.53 This air barrier can be compromised by worker technique, allowing escape of the contaminated air.54 The design of this type of cabinet is questionable for product protection because the air barrier is composed of air coming from the buffer area around the BSC. As air is pulled into the BSC, poor air quality in the buffer area may compromise the ISO Class 5 compounding environment within the Class II BSC. A Class II BSC or CACI that does not meet the conditions listed in USP Chapter <797> must be placed in an area that is physically separated from other compounding areas and have air quality of ISO Class 7. Optimally, this area should be at negative pressure relative to adjacent positive-pressure ISO Class 7 or better ante-areas, thus providing inward airflow to contain airborne drug. It also is optimal for a PEC used for compounding sterile HD preparations to be vented to the outside air through high-efficiency particulate air (HEPA) filtration.

All environments in which sterile preparations are compounded must be provided with HEPA-filtered air from outside the environment. The PEC may not be the sole source of HEPA-filtered air and it may not provide more than 50% of the ACPH in that environment. The ISO Class 7 buffer area and the ante-area must be supplied with HEPA-filtered air providing at least 30 ACPH. The NIOSH, ASHP, and USP Chapter <797> recommendations for HD PECs are compared in Table 3.4,30,34

WORK PRACTICE CONTROLS

Work practices must be designed to minimize the generation of HD contamination and maximize the containment of inadvertent contamination that occurs during routine handling or in the event of a spill. The compounding techniques described by Wilson and Solimando continue to be the standard for any procedure in which needles and syringes are used to manipulate sterile dosage forms of HDs.55 These techniques, when performed accurately, minimize the escape of drugs from vials and ampules.

Many adjunct devices have been developed to reduce the generation of contamination during the compounding process. Vented needles with 0.2-micron hydrophobic filters were designed to reduce the powder and liquid drug residues that escape from vials through standard vented needles. Dispensing pins with small spikes and hydrophobic filters were introduced
to make the compounding process more efficient. One study documented the effectiveness of one of these devices, but the investigators used only visual inspection because no sensitive drug assays were available at the time of the study.56

Since then, sensitive, drug-specific assays have been developed that provide a means to validate work practice controls at different work sites. The persistent presence of contamination in hospitals and pharmacies generated interest in adjunct devices, generically named in the 2004 NIOSH Alert as “closed-system drug-transfer devices” (CSTDs). NIOSH defines a CSTD as a device that mechanically prevents the transfer of environmental contaminants into the system and the escape of hazardous concentrations of drug or vapor from the system.4 USP Chapter <797> similarly defines CSTDs as “vial transfer systems that allow no venting or exposure of hazardous substance to the environment.” USP Chapter <797> further states that CSTDs must be used within the ISO Class 5 environment of a BSC or a CACI.

These devices provide some of the benefits of the earlier devices, but with the added protection that they can be locked into place on the drug vial. CSTD components also provide protection during the administration of IV push and IV infusion doses that previously had not been available. Numerous studies using markers for HDs have demonstrated the effectiveness of CSTDs in reducing HD contamination in the workplace.19-21 At clinical practice sites representing inpatient and outpatient compounding and administration, the implementation of a CSTD reduced surface contamination significantly compared with standard practice.19-21,57

In facilities that prepare a low volume of HDs, the use of 2 tiers of containment (eg, a CSTD within a BSC or a CACI that is located in a non-negative-pressure room) is acceptable. The NIOSH Alert specifies that CSTDs should be used only within a ventilated cabinet.

Neither USP Chapter <797> nor NIOSH has developed performance standards for any device marketed as a CSTD. Because the configurations of available CSTDs vary from that of the tested device, it is unclear how effective these devices are in reducing environmental contamination resulting from the compounding and administration of HDs. Any device marketed as a CSTD should be clinically tested.

**Personal Protective Equipment**

In addition to environmental and engineering controls, PPE is required to provide a barrier between the health care worker and HDs during episodes of potential contact. A recent Canadian study examined dermal contamination of workers compounding and checking HDs and having contact with surfaces in HD work areas. Workers’ hands were wiped with a premoistened tissue and the tissues then were analyzed for marker drugs. Of 18 wipes tested, 28% had measurable levels of cyclophosphamide and methotrexate.58 Although the sample was small, this study supports the need for workers to wear gloves whenever they handle HDs or are in an area where HDs are handled. PPE is especially important during administration, spill control, handling of drug waste, and handling of patient waste because no PECs are in place for these activities. All PPE should be selected for effectiveness. Glove and gown materials should be capable of withstanding permeation by a variety of HDs.59-61 Several HDs require nonaqueous diluents for patient use and may permeate PPE more readily than others. ASHP and NIOSH recommend coated gowns for use with HDs.4,30 This recommendation was recently emphasized in an Institute for Safe Medication Practices (ISMP) Safety Brief that reported on a “chemo” gown being used for preparing a dose of iron dextran injection.62 The drug was sprayed onto the gown and penetrated it. A follow-up report noted that the FDA considers gowns to be medical devices.61 Companies that do not claim a gown has been tested for use with HDs and who do not describe it as a surgical gown are exempt from the requirement for 510(k) submission. It is important that, in the absence of a standard, PPE be selected according to the criteria developed by ASHP and NIOSH based on several peer-reviewed studies.60,61

The American Society for Testing and Materials (ASTM) has developed a standard for testing chemotherapy gloves (D 6978-05) that is specific to a battery of chemotherapy drugs and duration of exposure.64 There is no such standard for gowns or gowning materials to be tested for permeation by sample chemotherapy or other HDs. ASTM F739-07 is a test method for permeation by liquids and gases through protective clothing materials under conditions of continuous contact.65 This ASTM standard neither specifies drugs or concentrations to be tested nor has a performance standard for an acceptable resistance to permeation. Using provisions of both ASTM standards may be an appropriate testing method but that has not been determined. A comparison of PPE recommendations is presented in Table 4.4,28,30,54

During sterile compounding, barrier garments must be worn to prevent the shedding of human skin and hair cells and the deposition of mucus or respiratory residue into the compounding area. USP Chapter <797> specifies that compounding garb must include the following: dedicated shoes or shoe covers, face masks, head and...
working with OSHA and the Joint Commission to promote employer and employee awareness of safety. USP Chapter <797> has elevated many of the NIOSH recommendations to a standard, ensuring compliance with at least the compounding segment of safety program controls. USP also plans a separate chapter on HD compounding to further emphasize the issue. Washington State has promulgated an HD rule that will take effect in 2014, providing the first regulation of its kind in the United States. New generations of health care workers need to be educated about the risks of handling HDs and the importance of training in the proper techniques to reduce their exposure. Health care workers must promote continued vigilance about this important safety issue. In a discussion on the fragmented concept of safety, health care administration expert Gerald Goodman notes: Change requires a focus on safety, not occupational safety or patient safety, but just safety.68

**References**


Please visit pharmacypracticenews.com for our educational review on Closed System Transfer Devices for Safe Handling of Injectable Drugs.