ASHP Guidelines on Handling Hazardous Drugs

In 1990, the American Society of Health-System Pharmacists (ASHP) published its revised technical assistance bulletin (TAB) on handling cytotoxic and hazardous drugs.[1] The information and recommendations contained in that document were current to June 1988. Continuing reports of workplace contamination and concerns for health care worker safety prompted the Occupational Safety and Health Administration (OSHA) to issue new guidelines on controlling occupational exposure to hazardous drugs in 1995.[2,3] In 2004, the National Institute for Occupational Safety and Health (NIOSH) issued the "NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings."[4] The following ASHP Guidelines on Handling Hazardous Drugs include information from these recommendations and are current to 2004.

Purpose

The purpose of these guidelines is to (1) update the reader on new and continuing concerns for health care workers handling hazardous drugs and (2) provide information on recommendations, including those regarding equipment, that have been developed since the publication of the previous TAB. Because studies have shown that contamination occurs in many settings, these guidelines should be implemented wherever hazardous drugs are received, stored, prepared, administered, or disposed.[2–7]

Comprehensive reviews of the literature covering anecdotal and case reports of surface contamination, worker contamination, and risk assessment are available from OSHA,[2,3] NIOSH,[4] and individual authors.[5–7] The primary goal of this document is to provide recommendations for the safe handling of hazardous drugs.

These guidelines represent the recommendations of many groups and individuals who have worked tirelessly over decades to reduce the potential harmful effects of hazardous drugs on health care workers. The research available to date, as well as the opinions of thought leaders in this area, is reflected in the guidelines. Where possible, recommendations are evidence based. In the absence of published data, professional judgment, experience, and common sense have been used.

Background

Workers may be exposed to a hazardous drug at many points during its manufacture, transport, distribution, receipt, storage, preparation, and administration, as well as during waste handling and equipment maintenance and repair. All workers involved in these activities have the potential for contact with uncontained drug.

Early concerns regarding the safety of workers handling potentially hazardous drugs focused on antineoplastic drugs when reports of second cancers in patients treated with these agents were coupled with the discovery of mutagenic substances in nurses who handled these drugs and cared for treated patients.[8,9] Exposure to these drugs in the workplace has been associated with acute and short-term reactions, as well as long-term effects. Anecdotal and case reports in the literature range from skin-related and ocular effects to flu-like symptoms and headache.[4,5,10–17] Two controlled surveys have reported significant increases in a number of symptoms, including sore throat, chronic cough, infections, dizziness, eye irritation, and headaches, among nurses, pharmacists, and pharmacy technicians routinely exposed to hazardous drugs in the workplace.[18,19] Reproductive studies on health care workers have shown an increase in fetal abnormalities, fetal loss, and fertility impairment resulting from occupational exposure to these potent drugs.[20–23] Antineoplastic drugs and immunosuppressants are some of the types of drugs included on lists of known or suspected human carcinogens by the National Toxicology Program[24] and the International Agency for Research on Cancer.[25] Although the increased incidence of cancers for occupationally exposed groups has been investigated with varying results,[26,27] a formal risk assessment of occupationally exposed pharmacy workers by Sessink et al.[28] estimated that cyclophosphamide causes an additional 1.4–10 cases of cancer per million workers each year. This estimate, which considered workplace contamination and worker contamination and excretion in combination with animal and patient studies, was based on a conservative exposure level. Connor et al.[29] found greater surface contamination in a study of U.S. and Canadian clinical settings than had been reported in European studies conducted by Sessink and colleagues.[30–32] Ensslin et al.[33] reported an almost fivefold greater daily average excretion of cyclophosphamide in their study than that reported by Sessink. These later findings could add 7–50 additional cancer cases per year per million workers to Sessink's estimate. From these and other studies that show variations in work practices and engineering controls,[34,35] it may be assumed that such variations contribute to differences in surface and worker contamination.

Routes of Exposure. Numerous studies showed the presence of hazardous drugs in the urine of health care workers.[30–34,36–41] Hazardous drugs enter the body through inhalation, accidental injection, ingestion of contaminated foodstuffs or mouth contact with contaminated hands, and dermal absorption. While inhalation might be suspected as the primary route of exposure, air sampling studies of pharmacy and clinic environments have often demonstrated low levels of or no airborne contaminants.[30–32,40] Recent concerns about the efficacy of the sampling methods[42] and the possibility that at least one of the marker drugs may be volatile[42–45] and thus not captured on the standard sampling filter leave the matter of inhalational exposure unresolved. Surface contamination studies do, however, suggest that dermal contact and absorption may be a primary route of exposure.[31,46] While some hazardous drugs are dermally absorbed, a 1992 report showed no detectable skin absorption of doxorubicin, daunorubicin, vincristine, vinblastine, or melphalan.[47] An alternative to dermal absorption is that surface contamination transferred to hands may be ingested via the hand-to-mouth route.[48,49] One or more of these routes might be responsible for workers' exposure.

Hazard Assessment. The risk to health care personnel from handling hazardous drugs is the result of a combination of the inherent toxicity of the drugs and the extent to which workers are exposed to the drugs in the course of their daily job activities. Both hazard identification (the qualitative evaluation of the toxicity of a given drug) and an exposure assessment (the amount of worker contact with the drug) are required to complete a hazard assessment. As the hazard assessment is specific to the safety program and safety equipment in place at a work site, a formal hazard assessment may not be available for most practitioners. An alternative is a performance-based, observational approach. Observation of current work practices, equipment, and the physical layout of work areas where hazardous drugs are handled at any given site will serve as an initial assessment of appropriate and inappropriate practices.[4]

Hazardous Drugs as Sterile Preparations

Many hazardous drugs are designed for parenteral administration, requiring aseptic reconstitution or dilution to yield a final sterile preparation. As such, the compounding of these products is regulated as pharmaceutical compounding by the *United States Pharmacopeia (USP)*, chapter 797.[50] The intent of chapter 797 is to protect patients from improperly compounded sterile preparations by regulating facilities, equipment, and work practices to ensure the sterility of extemporaneously compounded sterile preparations. Chapter 797 addresses not only the sterility of a preparation but also the accuracy of its composition. Because many hazardous drugs are very potent, there is little margin for error in compounding.

The initial version of chapter 797, released in early 2004, provided only minimal guidance for the handling of hazardous drugs, limiting this issue to a short discussion of chemotoxic agents in the document's section on aseptic technique. The chapter referred to standards established by the International Organization for Standardization (ISO)[51] that address the acceptable air quality (as measured by particulate counts) in the critical environment but failed to discuss airflow, air exchanges per hour, or pressure gradients of the ISO standards for cleanrooms and associated environments for compounding sterile products. The chapter did not describe the containment procedures necessary for compounding sterile hazardous agents, leaving it to the practitioner to simultaneously comply with the need to maintain a critical environment for compounded sterile products for patient safety while ensuring a contained environment for worker safety. The use of positive-pressure isolators for compounding hazardous drugs or placement of a Class II biological-safety cabinet (BSC) for use with hazardous drugs in a positive-pressure environment may result in airborne contamination of adjacent areas. Engineering assessment of designs of areas where this may occur should be done to address concerns of contaminant dissemination. Because hazardous drugs are also compounded in areas adjacent to patients and their family members (e.g., in chemotherapy infusion centers), inappropriate environmental containment puts them, as well as health care workers, at risk. Because *USP* review is a dynamic and ongoing process, future revisions are likely to address these concerns. Practitioners are encouraged to monitor the process and participate when appropriate.

Definition of Hazardous Drugs

The federal hazard communication standard (HCS) defines a hazardous chemical as any chemical that is a physical or health hazard.[52,53] A health hazard is defined as a chemical for which there is statistically significant evidence, based on at least one study conducted in accordance with established scientific principles, that acute or chronic health effects may occur in exposed employees. The HCS further notes that the term *health hazard* includes chemicals that are carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, and agents that produce target organ effects.

A 1990 ASHP TAB proposed criteria to determine which drugs should be considered hazardous and handled within an established safety program.[1] OSHA adopted these criteria in its 1995 guidelines, which were posted on its Web site in 1999.[2,3] The TAB's definition of hazardous drugs was revised by the NIOSH Working Group on Hazardous Drugs for the 2004 alert.[4] These definitions are compared in Table 1.

Each facility should create its own list of hazardous drugs based on specific criteria. Appendix A of the NIOSH alert contains related guidance and a sample list.[4] When drugs are purchased for the first time, they must be evaluated to determine whether they should be included in the facility's list of hazardous drugs. As the use and number of hazardous drugs increase, so too do the opportunities for health care worker exposure. Investigational drugs must be evaluated according to the information provided to the principal investigator. If the information provided is deemed insufficient to make an informed decision, the investigational drug should be considered hazardous until more information is available.

Recommendations

Safety Program. Policies and procedures for the safe handling of hazardous drugs must be in place for all situations in which these drugs are used throughout a facility. A comprehensive safety program must be developed that deals with all aspects of the safe handling of hazardous drugs. This program must be a collaborative effort, with input from all affected departments, such as pharmacy, nursing, medical staff, housekeeping, transportation, maintenance, employee health, risk management, industrial hygiene, clinical laboratories, and safety. A key element of this safety program is the Material Safety Data Sheet (MSDS) mandated by the HCS.[52,53] Employers are required to have an MSDS available for all hazardous agents in the workplace. A comprehensive safety program must include a process for monitoring and updating the MSDS database. When a hazardous drug is purchased for the first time, an MSDS must be received from the manufacturer or distributor. The MSDS should define the appropriate handling precautions, including protective equipment, controls, and spill management associated with the drug. Many MSDSs are available online through the specific manufacturer or through safety-information services.

Drugs that have been identified as requiring safe handling precautions should be clearly labeled at all times during their transport and use. The HCS applies to all workers, including those handling hazardous drugs at the manufac-

Table 1.
Comparison of 2004 NIOSH and 1990 ASHP Definitions of Hazardous Drugs[a]

NIOSH[4]	ASHP[1]
Carcinogenicity	Carcinogenicity in animal models, in the patient population, or both as reported by the International Agency for Research on Cancer
Teratogenicity or developmental toxicity[b]	Teratogenicity in animal studies or in treated patients
Reproductive toxicity[b]	Fertility impairment in animal studies or in treated patients
Organ toxicity at low doses[b]	Evidence of serious organ or other toxicity at low doses in animal models or treated patients
Genotoxicity[c]	Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems)
Structure and toxicity profile of new drugs that mimic existing drugs determined hazardous by the above criteria	

[a]NIOSH = National Institute for Occupational Safety and Health, ASHP = American Society of Health-System Pharmacists.

[b]NIOSH's definition contains the following explanation: "All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 mg/day or a dose of 1 mg/kg/day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 micrograms/meter^3 after applying appropriate uncertainty factors. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry. Under all circumstances, an evaluation of all available data should be conducted to protect health care workers."

[c]NIOSH's definition contains the following explanation: "In evaluating mutagenicity for potentially hazardous drugs, responses from multiple test systems are needed before precautions can be required for handling such agents. The EPA evaluations include the type of cells affected and *in vitro* versus *in vivo* testing."

turer and distributor levels. Employers are required to establish controls to ensure worker safety in all aspects of the distribution of these drugs.

The outside of the vials of many commercial drugs are contaminated by the time they are received in the pharmacy.[30,54,55] Although the possibility has not been studied, the contamination may extend to the inside of the packing cartons and onto the package inserts placed around the vial within the carton. Such contamination would present an exposure risk to anyone opening drug cartons or handling the vials, including workers receiving open or broken shipping cartons or selecting vials to be repackaged at a distribution point (e.g., a worker at the drug wholesaler selecting hazardous drugs for shipping containers or a pharmacy worker dividing a hazardous drug in a multidose container for repackaging into single-dose containers). These activities may present risks, especially for workers who too often receive inadequate safety training. Housekeepers and patient care assistants who handle drug waste and patient waste are also at risk and are not always included in the safe handling training required by safety programs. Safety programs must identify and include all workers who may be at risk of exposure.

The packaging (cartons, vials, ampuls) of hazardous drugs should be properly labeled by the manufacturer or distributor with a distinctive identifier that notifies personnel receiving them to wear appropriate personal protective equipment (PPE) during their handling. Sealing these drugs in plastic bags at the distributor level provides an additional level of safety for workers who are required to unpack cartons. Visual examination of such cartons for outward signs of damage or breakage is an important first step in the receiving process. Policies and procedures must be in place for handling damaged cartons or containers of hazardous drugs (e.g., returning the damaged goods to the distributor using appropriate containment techniques). These procedures should include the use of PPE, which must be supplied by the employer. As there may be no ventilation protection in the area where damaged containers are handled, the use of complete PPE, including an NIOSH-certified respirator, is recommended.[56,57] As required by OSHA, a complete respiratory program, including proper training and fit testing, must be completed by all staff required to use respirators.[56] Surgical masks do not provide adequate protection from the harmful effects of these drugs.

Labeling and Packaging from Point of Receipt. Drug packages, bins, shelves, and storage areas for hazardous drugs must bear distinctive labels identifying those drugs as requiring special handling precautions. Segregation of hazardous drug inventory from other drug inventory improves control and reduces the number of staff members potentially exposed to the danger. Hazardous drugs should be stored in an area with sufficient general exhaust ventilation to dilute and remove any airborne contaminants.[4] Hazardous drugs placed in inventory must be protected from potential breakage by storage in bins that have high fronts and on shelves that have guards to prevent accidental falling. The bins must also be appropriately sized to properly contain all stock. Care should be taken to separate hazardous drug inventory to reduce potential drug errors (e.g., pulling a look-alike vial from an adjacent drug bin). Because studies have shown that contamination on the drug vial itself is a consideration,[30,54,55] all staff members must wear double gloves when stocking and inventorying these drugs and selecting hazardous drug packages for further handling. All transport of hazardous drug packages must be done in a manner to reduce environmental contamination in the event of accidental dropping. Hazardous drug packages must be placed in sealed containers and labeled with a unique identifier. Carts or other transport devices must be designed with guards to protect against falling and breakage. All individuals transporting hazardous drugs must have safety training that includes spill control and have spill kits immediately accessible. Staff handling hazardous drugs or cleaning areas where hazardous drugs are stored or handled must be trained to recognize the unique identifying labels used to distinguish these drugs and areas. Warning labels and signs must be clear to non-English readers. All personnel

who work with or around hazardous drugs must be trained to appropriately perform their jobs using the established precautions and required PPE.[52]

Environment. Hazardous drugs should be compounded in a controlled area where access is limited to authorized personnel trained in handling requirements. Due to the hazardous nature of these preparations, a contained environment where air pressure is negative to the surrounding areas or that is protected by an airlock or anteroom is preferred. Positive-pressure environments for hazardous drug compounding should be avoided or augmented with an appropriately designed antechamber because of the potential spread of airborne contamination from contaminated packaging, poor handling technique, and spills.

Only individuals trained in the administration of hazardous drugs should do so. During administration, access to the administration area should be limited to patients receiving therapy and essential personnel. Eating, drinking, applying makeup, and the presence of foodstuffs should be avoided in patient care areas while hazardous drugs are administered. For inpatient therapy, where lengthy administration techniques may be required, hanging or removing hazardous drugs should be scheduled to reduce exposure of family members and ancillary staff and to avoid the potential contamination of dietary trays and personnel.

Because much of the compounding and administration of hazardous drugs throughout the United States is done in outpatient or clinic settings with patients and their family members near the compounding area, care must be taken to minimize environmental contamination and to maximize the effectiveness of cleaning (decontamination) activities. The design of such areas must include surfaces that are readily cleaned and decontaminated. Upholstered and carpeted surfaces should be avoided, as they are not readily cleaned. Several studies have shown floor contamination and the ineffectiveness of cleaning practices on both floors and surfaces.[29,30,46] Break rooms and refreshment areas for staff, patients, and others should be located away from areas of potential contamination to reduce unnecessary exposure to staff, visitors, and others.

Hazardous drugs may also be administered in nontraditional locations, such as the operating room, which present challenges to training and containment. Intracavitary administration of hazardous drugs (e.g., into the bladder, peritoneal cavity, or chest cavity) frequently requires equipment for which locking connections may not be readily available or even possible. All staff members who handle hazardous drugs should receive safety training that includes recognition of hazardous drugs and appropriate spill response. Hazardous drug spill kits, containment bags, and disposal containers must be available in all areas where hazardous drugs are handled. Techniques and ancillary devices that minimize the risk of open systems should be used when administering hazardous drugs through unusual routes or in nontraditional locations.

Ventilation Controls. Ventilation or engineering controls are devices designed to eliminate or reduce worker exposure to chemical, biological, radiological, ergonomic, and physical hazards. Ventilated cabinets are a type of ventilation or engineering control designed for the purpose of worker protection.[4] These devices minimize worker exposure by controlling the emission of airborne contaminants. Depending on the design, ventilated cabinets may also be used to provide the critical environment necessary to compound sterile preparations. When asepsis is not required, a Class I BSC or a containment isolator may be used to handle hazardous drugs. When sterile hazardous drugs are being compounded, a Class II or III BSC or an isolator intended for aseptic preparation and containment is required.[4] Recommendations for work practices specific to BSCs and isolators are discussed later in these guidelines.

Class II BSCs. In the early 1980s, the Class II BSC was determined to reduce the exposure of pharmacy compounding staff to hazardous preparations, as measured by the mutational response to the Ames test by urine of exposed subjects.[58,59] Studies in the 1990s, using analytical methods significantly more specific and sensitive than the Ames test, indicated that environmental and worker contamination occurs in workplace settings despite the use of controls recommended in published guidelines, including the use of Class II BSCs.[29–35,37–41,60,61] The exact cause of contamination has yet to be determined. Studies have shown that (1) there is contamination on the outside of vials received from manufacturers and distributors,[30,54,55] (2) work practices required to maximize the effectiveness of the Class II BSC are neglected or not taught,[32,46] and (3) the potential vaporization of hazardous drug solutions may reduce the effectiveness of the high-efficiency particulate air (HEPA) filter in providing containment.[42–45] Studies of surface contamination have discovered deposits of hazardous drugs on the floor in front of the Class II BSC, indicating that drug may have escaped through the open front of the BSC onto contaminated gloves or the final product or into the air.[29–32]

Workers must understand that the Class II BSC does not prevent the generation of contamination within the cabinet and that the effectiveness of such cabinets in containing hazardous drug contamination depends on operators' use of proper technique.

Some Class II BSCs recirculate airflow within the cabinet or exhaust contaminated air back into the work environment through HEPA filters.[62] The Class II BSC is designed with air plenums that are unreachable for surface decontamination; the plenum under the work tray collects room dirt and debris that mix with hazardous drug residue when the BSC is operational.[1] Drafts, supply-air louvers, and other laminar flow equipment placed near the BSC can interfere with the containment properties of the inflow air barrier, resulting in contamination of the work environment.[63] More information on the design and use of Class II BSCs is available from the NSF International (NSF)/American National Standards Institute (ANSI) standard 49-04.[62] Recommendations for use of Class II BSCs are listed in Appendix A.

Alternatives to Class II BSCs. Alternatives to the open-front Class II BSC include the Class III BSC, glove boxes, and isolators. By definition, a Class III BSC is a totally enclosed, ventilated cabinet of leak-tight construction.[64] Operations in the cabinet are conducted through fixed-glove access. The cabinet is maintained under negative air pressure. Supply air is drawn into the cabinet through HEPA filters. The exhaust air is treated by double HEPA filtration or by HEPA filtration and incineration. The Class III BSC is designed for use with highly toxic or infectious material. Because of the costs of

purchasing and operating a Class III BSC, it is seldom used for extemporaneous compounding of sterile products.

Less rigorous equipment with similar fixed-glove access include glove boxes and isolators. Although standardized definitions and criteria exist for glove boxes, these guidelines currently focus on applications in the nuclear industry and not on compounding hazardous drugs.[65] There are no standardized definitions or criteria for pharmaceutical compounding applications for this equipment and no performance standards determined by an independent organization to aid the purchaser in the selection process. NIOSH recommends that only ventilated engineering controls be used to compound hazardous drugs and that these controls be designed for containment.[4] NIOSH defines these controls and details their use and selection criteria as well as recommendations for airflow, exhaust, and maintenance. NIOSH further differentiates between ventilated engineering controls used for hazard containment that are intended for use with sterile products (aseptic containment) and those for use with nonsterile handling of hazardous drugs.[4]

An isolator may be considered a ventilated controlled environment that has fixed walls, floor, and ceiling. For aseptic use, supply air must be drawn through a high-efficiency (minimum HEPA) filter. Exhaust air must also be high-efficiency filtered and should be exhausted to the outside of the facility, not to the workroom. Workers access the isolator's work area, or main chamber, through gloves, sleeves, and air locks or pass-throughs. Currently available isolators have either unidirectional or turbulent airflow within the main chamber. For compounding sterile preparations, the filtered air and airflow must achieve an ISO class 5 (former FS-209E class 100) environment within the isolator.[50,51,66,67] Isolators for sterile compounding have become increasingly popular as a way to minimize the challenges of a traditional cleanroom and some of the disadvantages of the Class II BSC.[50,68–70] The totally enclosed design may reduce the escape of contamination during the compounding process. The isolator may be less sensitive to drafts and other laminar-airflow equipment, including positive-pressure environments. Issues unique to isolators include pressure changes when accessing the fixed-glove assembly, pressure changes in the main chamber when accessing the antechamber or pass-through, positive- versus negative-pressure isolators used to compound hazardous drugs, and ergonomic considerations associated with a fixed-glove assembly. Many isolators produce less heat and noise than Class II BSCs.[68] The Controlled Environment Testing Association has developed an applications guide for isolators in health care facilities.[71]

Isolators, like Class II BSCs, do not prevent the generation of contamination within the cabinet workspace, and their effectiveness in containing contamination depends on proper technique.[72] The potential for the spread of hazardous drug contamination from the pass-through and main chamber of the isolator to the workroom may be reduced by surface decontamination, but no wipe-down procedures have been studied. Surface decontamination may be more readily conducted in isolators than in Class II BSCs. (See *Decontamination, deactivation, and cleaning* for more information.)

Recirculating isolators depend on high-efficiency (HEPA or ultra-low penetrating air [ULPA]) filters. These filters may not sufficiently remove volatile hazardous drug contamination from the airflow. Isolators that discharge air into the workroom, even through high-efficiency filters, present exposure concerns similar to those of unvented Class II BSCs if there is a possibility that the hazardous drugs handled in them may vaporize. Isolators used for compounding hazardous drugs should be at negative pressure or use a pressurized air lock to the surrounding areas to improve containment. Some isolators rely on a low-particulate environment rather than laminar-airflow technology to protect the sterility of the preparations. Recommendations for use of Class III BSCs and isolators are summarized in Appendix B.

Closed-system drug-transfer devices. Closed-system drug-transfer devices mechanically prevent the transfer of environmental contaminants into the system and the escape of drug or vapor out of the system.[4] ADD-Vantage and Duplex devices are closed-system drug-transfer devices currently available for injectable antibiotics. A similar system that may offer increased environmental protection for hazardous drugs is a proprietary, closed-system drug-transfer device known as PhaSeal. This multicomponent system uses a double membrane to enclose a specially cut injection cannula as it moves into a drug vial, Luer-Lok, or infusion-set connector.

Several studies have shown a reduction in environmental contamination with marker hazardous drugs during both compounding and administration when comparing standard techniques for handling hazardous drugs with the use of PhaSeal.[73–78] It should be noted, however, that PhaSeal components cannot be used to compound all hazardous drugs.

In 1984, Hoy and Stump[79] concluded that a commercial air-venting device reduced the release of drug aerosols during reconstitution of drugs packaged in vials. The testing was limited to visual analysis. The venting device does not lock onto the vial, which allows it to be transferred from one vial to another. This practice creates an opportunity for both environmental and product contamination. Many devices labeled as "chemo adjuncts" are currently available. Many feature a filtered, vented spike to facilitate reconstituting and removing hazardous drugs during the compounding process. However, none of these devices may be considered a closed-system drug-transfer device, and none has been formally studied with the results published in peer-reviewed journals. As other products become available, they should meet the definition of closed-system drug-transfer devices established by NIOSH[4] and should be required to demonstrate their effectiveness in independent studies. Closed-system drug-transfer devices (or any other ancillary devices) are not a substitute for using a ventilated cabinet.

Personal Protective Equipment. *Gloves.* Gloves are essential for handling hazardous drugs. Gloves must be worn at all times when handling drug packaging, cartons, and vials, including while performing inventory control procedures and when gathering hazardous drugs and supplies for compounding a batch or single dose. During compounding in a Class II BSC, gloves and gowns are required to prevent skin surfaces from coming into contact with these agents. Studies of gloves indicate that many latex and nonlatex materials are effective protection against penetration and permeation by most hazardous drugs.[80–84] Recent concerns about latex sensitivity have prompted testing of newer glove materials. Gloves made of nitrile or neoprene rubber and polyurethane have been successfully tested using a battery of antineoplastic drugs.[82–84] The American Society for Testing and Materials (ASTM) has developed testing standards for assessing the

resistance of medical gloves to permeation by chemotherapy drugs.[85] Gloves that meet this standard earn the designation of "chemotherapy gloves." Gloves selected for use with hazardous drugs should meet this ASTM standard.

Connor and Xiang[86] studied the effect of isopropyl alcohol on the permeability of latex and nitrile gloves exposed to antineoplastic agents. During the limited study period of 30 minutes, they found that the use of isopropyl alcohol during cleaning and decontaminating did not appear to affect the integrity of either material when challenged with six antineoplastic agents.

In most glove-testing systems, the glove material remains static, in contrast to the stressing and flexing that occur during actual use. In one study designed to examine glove permeability under static and flexed conditions, no significant difference in permeation was reported, except in thin latex examination gloves.[87] Another study, however, detected permeation of antineoplastic drugs through latex gloves during actual working conditions by using a cotton glove under the latex glove.[88] The breakthrough time for cyclophosphamide was only 10 minutes. The authors speculated that the cotton glove may have acted as a wick, drawing the hazardous drug through the outer glove. Nonetheless, under actual working conditions, double gloving and wearing gloves no longer than 30 minutes are prudent practices.

Permeability of gloves to hazardous drugs has been shown to be dependent on the drug, glove material and thickness, and exposure time. Powder-free gloves are preferred because powder particulates can contaminate the sterile processing area and absorb hazardous drug contaminants, which may increase the potential for dermal contact. Hands should be thoroughly washed before donning gloves and after removing them. Care must be taken when removing gloves in order to prevent the spreading of hazardous drug contaminants.

Several studies have indicated that contamination of the outside of gloves with hazardous drug is common after compounding and that this contamination may be spread to other surfaces during the compounding process.[30–33,39] Studies have also shown that hazardous drug contamination may lead to dermal absorption by workers not actively involved in the compounding and administration of hazardous drugs.[30,88] The use of two pairs of gloves is recommended when compounding these drugs. In an isolator, one additional pair of gloves must be worn within the fixed-glove assembly.[68]

Once compounding has been completed and the final preparation surface decontaminated, the outer glove should be removed and contained inside the BSC. The inner glove is worn to affix labels and place the preparation into a sealable containment bag for transport. This must be done within the BSC. In the isolator, the fixed gloves must be surface cleaned before wiping down the final preparation, placing the label onto the preparation, and placing it into the pass-through. The inner gloves should be worn to complete labeling and to place the final preparation into a transport bag in the pass-through. The inner gloves may then be removed and contained in a sealable bag within the pass-through. If the final check is conducted by a second staff member, fresh gloves must be donned before handling the completed preparation.

During batch compounding, gloves should be changed at least every 30 minutes. Gloves (at least the outer gloves) must be changed whenever it is necessary to exit and re-enter the BSC. For aseptic protection of sterile preparations, the outer gloves must be sanitized with an appropriate disinfectant when reentering the BSC. Gloves must also be changed immediately if torn, punctured, or knowingly contaminated. When wearing two pairs of gloves in the BSC, one pair is worn under the gown cuff and the second pair placed over the cuff. When removing the gloves, the contaminated glove fingers must only touch the outer surface of the glove, never the inner surface. If the inner glove becomes contaminated, then both pairs of gloves must be changed. When removing any PPE, care must be taken to avoid introducing hazardous drug contamination into the environment. Both the inner and outer gloves should be considered contaminated, and glove surfaces must never touch the skin or any surface that may be touched by the unprotected skin of others. Gloves used to handle hazardous drugs should be placed in a sealable plastic bag for containment within the BSC or isolator pass-through before disposal as contaminated waste.

If an i.v. set is attached to the final preparation in the BSC or isolator, care must be taken to avoid contaminating the tubing with hazardous drug from the surface of the gloves, BSC, or isolator.

Class III BSCs and isolators are equipped with attached gloves or gauntlets. They should be considered contaminated once the BSC or isolator has been used for compounding hazardous drugs. For compounding sterile preparations, attached gloves or gauntlets must be routinely sanitized per the manufacturer's instructions to prevent microbial contamination. Hazardous drug contamination from the gloves or gauntlets may be transferred to the surfaces of all items within the cabinet. Glove and gauntlet surfaces must be cleaned after compounding is complete. All final preparations must be surface decontaminated by staff, wearing clean gloves to avoid spreading contamination.[68] Recommendations for use of gloves are summarized in Appendix C.

Gowns. Gowns or coveralls are worn during the compounding of sterile preparations to protect the preparation from the worker, to protect the worker from the preparation, or both. The selection of gowning materials depends on the goal of the process. Personal protective gowns are recommended during the handling of hazardous drug preparations to protect the worker from inadvertent exposure to extraneous drug particles on surfaces or generated during the compounding process.

Guidelines for the safe handling of hazardous drugs 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.[1–4,89,90] Early recommendations for barrier protective gowns required that they be disposable and made of a lint-free, low-permeability fabric with a closed front, long sleeves, and tight-fitting elastic or knit cuffs.[1] Washable garments (e.g., laboratory coats, scrubs, and cloth gowns) absorb fluids and provide no barrier against hazardous drug absorption and permeation. Studies into the effectiveness of disposable gowns in resisting permeation by hazardous drugs found variation in the protection provided by commercially available materials. In an evaluation of polypropylene-based gowns, Connor[91] found that polypropylene spun-bond nonwoven material alone and polypropylene–polyethylene copolymer spun-bond provided little protection against permeation by a battery of aqueous-

and nonaqueous- based hazardous drugs. Various constructions of polypropylene (e.g., spun-bond/melt-blown/spun-bond) result in materials that are completely impermeable or only slightly permeable to hazardous drugs. Connor[91] noted that these coated materials are similar in appearance to several other nonwoven materials but perform differently and that workers could expect to be protected from exposure for up to four hours when using the coated gowning materials. Harrison and Kloos[92] reported similar findings in a study of six disposable gowning materials and 15 hazardous drugs. Only gowns with polyethylene or vinyl coatings provided adequate splash protection and prevented drug permeation. In a subjective assessment of worker comfort, the more protective gowns were found to be warmer and thus less comfortable. These findings agree with an earlier study that found that the most protective gowning materials were the most uncomfortable to wear.[93] Resistance to the use of gowns, especially by nurses during administration of hazardous drugs, has been reported.[94] The lack of comfort could cause resistance to behavioral change.

Researchers have looked at gown contamination with fluorescent scans, high-performance liquid chromatography, and tandem mass spectrometry.[39,95] In one study, researchers scanned nurses and pharmacists wearing gowns during the compounding and administration of hazardous drugs.[95] Of a total of 18 contamination spots detected, 5 were present on the gowns of nurses after drug administration. No spots were discovered on the gowns of pharmacists after compounding. In contrast, researchers using a more sensitive assay placed pads in various body locations, both over and under the gowns used by the subjects during compounding and administration of cyclophosphamide and ifosfamide.[39] Workers wore short-sleeved nursing uniforms, disposable or cotton gowns, and vinyl or latex gloves. More contamination was found during compounding than administration. Contamination found on the pads placed on the arms of preparers is consistent with the design and typical work practices used in a Class II BSC, where the hands and arms are extended into the contaminated work area of the cabinet. Remarkably, one preparer had contamination on the back of the gown, possibly indicating touch contamination with the Class II BSC during removal of the final product. While early guidelines do not contain a maximum length of time that a gown should be worn, Connor's[91] work would support a two- to three-hour window for a coated gown. Contamination of gowns during glove changes must be a consideration. If the inner pair of gloves requires changing, a gown change should be considered. Gowns worn as barrier protection in the compounding of hazardous drugs must never be worn outside the immediate preparation area. Gowns worn during administration should be changed when leaving the patient care area and immediately if contaminated. Gowns should be removed carefully and properly disposed of as contaminated waste to avoid becoming a source of contamination to other staff and the environment.

Hazardous drug compounding in an enclosed environment, such as a Class III BSC or an isolator, may not require the operator to wear a gown. However, because the process of handling drug vials and final preparations, as well as accessing the isolator's pass-throughs, may present an opportunity for contamination, the donning of a gown is prudent. Coated gowns may not be necessary for this use if appropriate gowning practices are established. Recommendations for use of gowns are summarized in Appendix D.

Additional PPE. Eye and face protection should be used whenever there is a possibility of exposure from splashing or uncontrolled aerosolization of hazardous drugs (e.g., when containing a spill or handling a damaged shipping carton). In these instances, a face shield, rather than safety glasses or goggles, is recommended because of the improved skin protection afforded by the shield.

Similar circumstances also warrant the use of a respirator. All workers who may use a respirator must be fit-tested and trained to use the appropriate respirator according to the OSHA Respiratory Protection Standard.[56,57] A respirator of correct size and appropriate to the aerosol size, physical state (i.e., particulate or vapor), and concentration of the airborne drug must be available at all times. Surgical masks do not provide respiratory protection. Shoe and hair coverings should be worn during the sterile compounding process to minimize particulate contamination of the critical work zone and the preparation.[50] With the potential for hazardous drug contamination on the floor in the compounding and administration areas, shoe coverings are recommended as contamination-control mechanisms. Shoe coverings must be removed with gloved hands when leaving the compounding area. Gloves should be worn and care must be taken when removing hair or shoe coverings to prevent contamination from spreading to clean areas. Hair and shoe coverings used in the hazardous drug handling areas must be contained, along with used gloves, and discarded as contaminated waste.

Work Practices. *Compounding sterile hazardous drugs.* Work practices for the compounding of sterile hazardous drugs differ somewhat with the use of a Class II BSC, a Class III BSC, or an isolator. Good organizational skills are essential to minimize contamination and maximize productivity. All activities not requiring a critical environment (e.g., checking labels, doing calculations) should be completed before accessing the BSC or isolator. All items needed for compounding must be gathered before beginning work. This practice should eliminate the need to exit the BSC or isolator once compounding has begun. Two pairs of gloves should be worn to gather hazardous drug vials and supplies. These gloves should be carefully removed and discarded. Fresh gloves must be donned and appropriately sanitized before aseptic manipulation.

Only supplies and drugs essential to compounding the dose or batch should be placed in the work area of the BSC or main chamber of the isolator. BSCs and isolators should not be overcrowded to avoid unnecessary hazardous drug contamination. Luer-Lok syringes and connections must be used whenever possible for manipulating hazardous drugs, as they are less likely to separate during compounding.

Spiking an i.v. set into a solution containing hazardous drugs or priming an i.v. set with hazardous drug solution in an uncontrolled environment must be avoided. One recommendation is to attach and prime the appropriate i.v. set to the final container in the BSC or isolator before adding the hazardous drug. Closed-system drug-transfer devices should achieve a dry connection between the administration set and the hazardous drug's final container. This connection allows the container to be spiked with a secondary i.v. set and the set to be primed by backflow from a primary nonhazardous solution. This process may be done outside the BSC or isolator, reducing the potential for surface contamination of the

i.v. set during the compounding process. A new i.v. set must be used with each dose of hazardous drug. Once attached, the i.v. set must never be removed from a hazardous drug dose, thereby preventing the residual fluid in the bag, bottle, or tubing from leaking and contaminating personnel and the environment.

Transport bags must never be placed in the BSC or in the isolator work chamber during compounding to avoid inadvertent contamination of the outer surface of the bag. Final preparations must be surface decontaminated after compounding is complete. In either the BSC or isolator, clean inner gloves must be worn when labeling and placing the final preparation into the transport bag. Handling final preparations and transport bags with gloves contaminated with hazardous drugs will result in the transfer of the contamination to other workers. Don fresh gloves whenever there is a doubt as to the cleanliness of the inner or outer gloves.

Working in BSCs or isolators. With or without ancillary devices, none of the available ventilation or engineering controls can provide 100% protection for the worker. Workers must recognize the limitations of the equipment and address them through appropriate work practices.[1] The effectiveness of Class II BSCs and isolators in containing contamination depends on proper technique.[72] Hazardous drug contamination from the work area of the isolator may be brought into the workroom environment through the pass-throughs or air locks and on the surfaces of items removed from the isolators (e.g., the final preparation). Surface decontamination of the preparation before removal from the isolator's main chamber should reduce the hazardous drug contamination that could be transferred to the workroom, but no wipe-down procedures have been studied. Surface decontamination may be accomplished using alcohol, sterile water, peroxide, or sodium hypochlorite solutions, provided the packaging is not permeable to the solution and the labels remain legible and intact. Recommendations for working in BSCs and isolators are summarized in Appendix E.

BSCs. Class II BSCs use vertical-flow, HEPA-filtered air (ISO class 5) as their controlled aseptic environment. Before beginning an operation in a Class II BSC, personnel should wash their hands, don an inner pair of appropriate gloves, and then don a coated gown followed by a second pair of gloves. The work surface should be cleaned of surface contamination with detergent, sodium hypochlorite, and neutralizer or disinfected with alcohol, depending on when it was last cleaned. For the Class II BSC, the front shield must be lowered to the proper level to protect the face and eyes. The operator should be seated so that his or her shoulders are at the level of the bottom of the front shield. All drugs and supplies needed to aseptically compound a dose or batch should be gathered and sanitized with 70% alcohol or appropriate disinfectant. Avoid exiting and reentering the work area. Being careful not to place any sterile objects below them, i.v. bags and bottles may be hung from the bar. All items must be placed well within the Class II BSC, away from the unfiltered air at the front barrier. By design, the intended work zone within the Class II BSC is the area between the front and rear air grilles. The containment characteristics of the Class II BSC are dependent on the airflow through both the front and back grilles; these grilles should never be obstructed. Due to the design of the Class II BSC, the quality of HEPA-filtered air is lowest at the sides of the work zone, so manipulations should be performed at least six inches away from each sidewall in the horizontal plane. A small waste–sharps container may be placed along the sidewall toward the back of the BSC. One study has suggested that a plastic-backed absorbent preparation pad in a Class II BSC may interfere with airflow,[39] but another study determined that use of a flat firm pad that did not block the grilles of the cabinet had no effect on airflow.[96] The use of a large pad that might block the front or rear grilles must be avoided. In addition, because a pad may absorb small spills, it may become a source of hazardous drug contamination for anything placed upon it. Preparation pads are not readily decontaminated and must be replaced and discarded after preparation of each batch and frequently during extended batch compounding. More information on the design and use of Class II BSCs is available from the NSF/ANSI standard 49-04.[62]

Isolators. For work in an isolator, all drugs and supplies needed to aseptically compound a dose or batch should be gathered and sanitized with 70% alcohol or appropriate disinfectant and readied for placement in the pass-through. A technique described in the literature involves the use of a tray that will fit into the pass-through.[97] A large primary sealable bag is placed over the tray. Labels and a second sealable (transport) bag, which is used to contain the final preparation, are placed into the primary sealable bag on the tray surface. Vials, syringes, needles, and other disposables are placed on top of the sealed bag. The enclosed tray is then taken into the main chamber of the isolator, where the drug and supplies are used to compound the dose. The contaminated materials, including the primary sealable bag, are removed using the closed trash system of the isolator, if so equipped, or sealed into a second bag and removed via the pass-through for disposal as contaminated waste. The dose is then labeled and placed into the second sealable bag for transport.

This technique does not address contamination on the isolator gloves or gauntlets. Additional work practices may include cleaning off the gloves or gauntlets and final preparation after initial compounding and before handling the label and second sealable bag. Care must be taken when transferring products out of the pass-through and disposing of waste through the pass-through or trash chute to avoid accidental contamination.

Aseptic technique. Stringent aseptic technique, described by Wilson and Solimando[98] in 1981, remains the foundation of any procedure involving the use of needles and syringes in manipulating sterile dosage forms. This technique, when performed in conjunction with negative pressure technique, minimizes the escape of drug from vials and ampuls. Needleless devices have been developed to reduce the risk of blood-borne pathogen exposure through needle sticks. None of these devices has been tested for reduction of hazardous drug contamination. The appropriateness of these devices in the safe handling of hazardous drugs has not been determined.

In reconstituting hazardous drugs in vials, it is critical to avoid pressurizing the contents of the vial. Pressurization may cause the drug to spray out around the needle or through a needle hole or a loose seal, aerosolizing the drug into the work zone. Pressurization can be avoided by creating a slight negative pressure in the vial. Too much negative pressure, however, can cause leakage from the needle when it is with-

drawn from the vial. The safe handling of hazardous drug solutions in vials or ampuls requires the use of a syringe that is no more than three-fourths full when filled with the solution, which minimizes the risk of the plunger separating from the syringe barrel. Once the diluent is drawn up, the needle is inserted into the vial and the plunger is pulled back (to create a slight negative pressure inside the vial), so that air is drawn into the syringe. Small amounts of diluent should be transferred slowly as equal volumes of air are removed. The needle should be kept in the vial, and the contents should be swirled carefully until dissolved. With the vial inverted, the proper amount of drug solution should be gradually withdrawn while equal volumes of air are exchanged for solution. The exact volume needed must be measured while the needle is in the vial, and any excess drug should remain in the vial. With the vial in the upright position, the plunger should be withdrawn past the original starting point to again induce a slight negative pressure before removing the needle. The needle hub should be clear before the needle is removed.

If a hazardous drug is transferred to an i.v. bag, care must be taken to puncture only the septum of the injection port and avoid puncturing the sides of the port or bag. After the drug solution is injected into the i.v. bag, the i.v. port, container, and set (if attached by pharmacy in the BSC or isolator) should be surface decontaminated. The final preparation should be labeled, including an auxiliary warning, and the injection port covered with a protective shield. The final container should be placed, using clean gloves, into a sealable bag to contain any leakage.[1]

To withdraw hazardous drugs from an ampul, the neck or top portion should be gently tapped.[98] After the neck is wiped with alcohol, a 5-µm filter needle or straw should be attached to a syringe that is large enough that it will be not more than three-fourths full when holding the drug. The fluid should then be drawn through the filter needle or straw and cleared from the needle and hub. After this, the needle or straw is exchanged for a needle of similar gauge and length; any air and excess drug should be ejected into a sterile vial (leaving the desired volume in the syringe); aerosolization should be avoided. The drug may then be transferred to an i.v. bag or bottle. If the dose is to be dispensed in the syringe, the plunger should be drawn back to clear fluid from the needle and hub. The needle should be replaced with a locking cap, and the syringe should be surface decontaminated and labeled.

Training and demonstration of competence. All staff who will be compounding hazardous drugs must be trained in the stringent aseptic and negative-pressure techniques necessary for working with sterile hazardous drugs. Once trained, staff must demonstrate competence by an objective method, and competency must be reassessed on a regular basis.[99]

Preparation and handling of noninjectable hazardous drug dosage forms. Although noninjectable dosage forms of hazardous drugs contain varying proportions of drug to nondrug (nonhazardous) components, there is the potential for personnel exposure to and environmental contamination with the hazardous components if hazardous drugs are handled (e.g., packaged) by pharmacy staff. Although most hazardous drugs are not available in liquid formulations, such formulations are often prescribed for small children and adults with feeding tubes. Recipes for extemporaneously compounded oral liquids may start with the parenteral form, or they may require that tablets be crushed or capsules opened. Tablet trituration has been shown to cause fine dust formation and local environmental contamination.[100] Procedures for the preparation and the use of equipment (e.g., Class I BSCs or bench-top hoods with HEPA filters) must be developed to avoid the release of aerosolized powder or liquid into the environment during manipulation of hazardous drugs. Recommendations for preparation and handling of noninjectable hazardous drug dosage forms are summarized in Appendix F.

Decontamination, deactivation, and cleaning. Decontamination may be defined as cleaning or deactivating. Deactivating a hazardous substance is preferred, but no single process has been found to deactivate all currently available hazardous drugs. The use of alcohol for disinfecting the BSC or isolator will not deactivate any hazardous drugs and may result in the spread of contamination rather than any actual cleaning.[30,47]

Decontamination of BSCs and isolators should be conducted per manufacturer recommendations. The MSDSs for many hazardous drugs recommend sodium hypochlorite solution as an appropriate deactivating agent.[101] Researchers have shown that strong oxidizing agents, such as sodium hypochlorite, are effective deactivators of many hazardous drugs.[102,103] There is currently one commercially available product, SurfaceSafe (SuperGen, Dublin, CA), that provides a system for decontamination and deactivation using sodium hypochlorite, detergent, and thiosulfate neutralizer. A ventilated cabinet that runs continuously should be cleaned before the day's operations begin and at regular intervals or when the day's work is completed. For a 24-hour service, the cabinet should be cleaned two or three times daily. Cabinets used for aseptic compounding must be disinfected at the beginning of the workday, at the beginning of each subsequent shift (if compounding takes place over an extended period of time), and routinely during compounding.

Appropriate preparation of materials used in compounding before introduction into the Class II BSC or the pass-through of a Class III BSC or isolator, including spraying or wiping with 70% alcohol or appropriate disinfectant, is also necessary for aseptic compounding.

The Class II BSC has air plenums that handle contaminated air. These plenums are not designed to allow surface decontamination, and many of the contaminated surfaces (plenums) cannot be reached for surface cleaning. The area under the work tray should be cleaned at least monthly to reduce the contamination level in the Class II BSC (and in isolators, where appropriate).

Surface decontamination may be accomplished by the transfer of hazardous drug contamination from the surface of a nondisposable item to disposable ones (e.g., wipes, gauze, towels). Although the outer surface of vials containing hazardous drugs has been shown to be contaminated with hazardous drugs,[30,54,55] and hazardous drug contamination has been found on the outside of final preparations,[30] no wipe-down procedures have been studied. The amount of hazardous drug contamination placed into the BSC or isolator may be reduced by surface decontamination (i.e., wiping down) of hazardous drug vials. While no wipe-down procedures have been studied, the use of gauze moistened with alcohol, sterile water, peroxide, or sodium hypochlorite solutions

may be effective. The disposable item, once contaminated, must be contained and discarded as contaminated waste.

Administration of hazardous drugs. Policies and procedures governing the administration of hazardous drugs must be jointly developed by nursing and pharmacy for the mutual safety of health care workers. These policies should supplement policies designed to protect patient safety during administration of all drugs. All policies affecting multiple departments must be developed with input from managers and workers from the affected areas. Extensive nursing guidelines for the safe and appropriate administration of hazardous drugs have been developed by the Oncology Nursing Society[90,104] and OSHA.[2,3] Recommendations for reducing exposure to hazardous drugs during administration in all practice settings are listed in Appendix G.

Spill management. Policies and procedures must be developed to attempt to prevent spills and to govern cleanup of hazardous drug spills. Written procedures must specify who is responsible for spill management and must address the size and scope of the spill. Spills must be contained and cleaned up immediately by trained workers.

Spill kits containing all of the materials needed to clean up spills of hazardous drugs should be assembled or purchased (Appendix H). These kits should be readily available in all areas where hazardous drugs are routinely handled. A spill kit should accompany delivery of injectable hazardous drugs to patient care areas even though they are transported in a sealable plastic bag or container. If hazardous drugs are being prepared or administered in a nonroutine area (e.g., home setting, unusual patient care area), a spill kit and respirator must be obtained by the drug handler. Signs should be available to warn of restricted access to the spill area.

Only trained workers with appropriate PPE and respirators should attempt to manage a hazardous drug spill. All workers who may be required to clean up a spill of hazardous drugs must receive proper training in spill management and in the use of PPE and NIOSH-certified respirators.

The circumstances and handling of spills should be documented. Staff and nonemployees exposed to a hazardous drug spill should also complete an incident report or exposure form and report to the designated emergency service for initial evaluation.

All spill materials must be disposed of as hazardous waste.[105] Recommendations for spill cleanup procedure are summarized in Appendix I.

Worker contamination. Procedures must be in place to address worker contamination, and protocols for medical attention must be developed before the occurrence of any such incident. Emergency kits containing isotonic eyewash supplies (or emergency eyewashes, if available) and soap must be immediately available in areas where hazardous drugs are handled. Workers who are contaminated during the spill or spill cleanup or who have direct skin or eye contact with hazardous drugs require immediate treatment. OSHA-recommended steps for treatment are outlined in Appendix J.

Hazardous Waste Containment and Disposal. In 1976, the Resource Conservation and Recovery Act (RCRA) was enacted to provide a mechanism for tracking hazardous waste from its generation to disposal.[106] Regulations promulgated under RCRA are enforced by the Environmental Protection Agency and apply to pharmaceuticals and chemicals discarded by pharmacies, hospitals, clinics, and other commercial entities. The RCRA outlines four "characteristics" of hazardous waste[107] and contains lists of agents that are to be considered hazardous waste when they are discarded.[108] Any discarded drug that is on one of the lists (a "listed" waste) or meets one of the criteria (a "characteristic" waste) is considered hazardous waste. The listed drugs include epinephrine, nicotine, and physostigmine, as well as nine chemotherapy drugs: arsenic trioxide, chlorambucil, cyclophosphamide, daunomycin, diethylstilbestrol, melphalan, mitomycin C, streptozocin, and uracil mustard. They require handling, containment, and disposal as RCRA hazardous waste.

The RCRA allows for the exemption of "empty containers" from hazardous waste regulations. Empty containers are defined as those that have held U-listed or characteristic wastes and from which all wastes have been removed that can be removed using the practices commonly employed to remove materials from that type of container and no more than 3% by weight of the total capacity of the container remains in the container.[109] Disposal guidelines developed by the National Institutes of Health (NIH) and published in 1984 coined the term "trace-contaminated" waste using the 3% rule.[110] Note that a container that has held an acute hazardous waste listed in §§261.31, 261.32, or 261.33(e), such as arsenic trioxide, is not considered empty by the 3% rule,[111] and that spill residues from cleanup of hazardous agents are considered hazardous waste.[105]

In addition, many states are authorized to implement their own hazardous waste programs, and requirements under these programs may be more stringent than those of the EPA. State and local regulations must be considered when establishing a hazardous waste policy for a specific facility.

General categories of hazardous waste found in health care settings would include trace-contaminated hazardous waste, bulk hazardous waste, hazardous drugs not listed as hazardous waste, and hazardous waste and mixed infectious–hazardous waste.

Trace-contaminated hazardous drug waste. By the NIH definition of trace chemotherapy waste,[110] "RCRA-empty" containers, needles, syringes, trace-contaminated gowns, gloves, pads, and empty i.v. sets may be collected and incinerated at a regulated medical waste incinerator. Sharps used in the preparation of hazardous drugs should not be placed in red sharps containers or needle boxes, since these are most frequently disinfected by autoclaving or microwaving, not by incineration, and pose a risk of aerosolization to waste-handling employees.

Bulk hazardous drug waste. While not official, the term *bulk hazardous drug waste* has been used to differentiate containers that have held either (1) RCRA-listed or characteristic hazardous waste or (2) any hazardous drugs that are not RCRA empty or any materials from hazardous drug spill cleanups. These wastes should be managed as hazardous waste.

Hazardous drugs not listed as hazardous waste. The federal RCRA regulations have not kept up with drug development, as there are over 100 hazardous drugs that are not listed as hazardous waste, including hormonal agents. In some states, such as Minnesota, these must be managed as hazardous waste. In other states, organizations should manage these drugs as hazardous waste as a best- management practice until federal regulations can be updated.

Hazardous waste and mixed infectious–hazardous waste. Most hazardous waste vendors are not permitted to

manage regulated medical waste or infectious waste; therefore, they cannot accept used needles and items contaminated with squeezable, flakable, or drippable blood. Organizations should check carefully with their hazardous waste vendors to ensure acceptance of all possible hazardous waste, including mixed infectious waste, if needed. Once hazardous waste has been identified, it must be collected and stored according to specific EPA and Department of Transportation requirements.[112] Properly labeled, leakproof, and spill-proof containers of nonreactive plastic are required for areas where hazardous waste is generated. Hazardous drug waste may be initially contained in thick, sealable plastic bags before being placed in approved satellite accumulation containers. Glass fragments should be contained in small, puncture-resistant containers to be placed into larger containers approved for temporary storage.

Waste contaminated with blood or other body fluids must not be mixed with hazardous waste. Transport of waste containers from satellite accumulation to storage sites must be done by individuals who have completed OSHA-mandated hazardous waste awareness training.[113,114] Hazardous waste must be properly manifested and transported by a federally permitted hazardous waste transporter to a federally permitted hazardous waste storage, treatment, or disposal facility.[115] A licensed contractor may be hired to manage the hazardous waste program. The waste generator, however, may be held liable for mismanagement of hazardous waste. Investigation of a contractor, including verification of possession and type of license, should be completed and documented before a contractor is engaged. More information on hazardous waste disposal is available at www.hercenter.org.

Alternative Duty and Medical Surveillance. A comprehensive safety program for controlling workplace exposure to hazardous drugs must include engineering controls, training, work practices, and PPE. Such safety programs must be able to identify potentially exposed workers and those who might be at higher risk of adverse health effects due to this exposure. Because reproductive risks have been associated with exposure to hazardous drugs, alternative duty should be offered to individuals who are pregnant, breast-feeding, or attempting to conceive or father a child. Employees' physicians should be involved in making these determinations.

All workers who handle hazardous drugs should be routinely monitored in a medical surveillance program.[2–4,90,104] Medical surveillance involves the collection and interpretation of data for the purpose of detecting changes in the health status of working populations. Medical surveillance programs involve assessment and documentation of symptom complaints, physical findings, and laboratory values (such as a blood count) to determine whether there is a deviation from the expected norms. Descriptions of medical surveillance programs for hazardous drug handlers are presented in the literature.[90,104] NIOSH encourages employees who handle hazardous drugs to participate in medical surveillance programs that are provided in the workplace.[4] Limited resources may preclude the implementation of a comprehensive medical surveillance program for health care workers who are exposed to hazardous drugs. In the absence of an institutional medical surveillance program, NIOSH encourages workers handling hazardous drugs to inform their personal health care providers of their occupation and possible hazardous drug exposure when obtaining routine medical care.[4]

Conclusion

These guidelines represent the recommendations of many groups and individuals who have worked tirelessly over decades to reduce the potential of harmful effects on health care workers exposed to hazardous drugs. No set of guidelines on this topic, however comprehensive, can address all the needs of every health care facility. Health care professionals are encouraged to rely on their professional judgment, experience, and common sense in applying these recommendations to their unique circumstances and to take into account evolving federal, state, and local regulations, as well as the requirements of appropriate accrediting institutions.

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Appendix A—Recommendations for Use of Class II BSCs

1. The use of a Class II BSC must be accompanied by a stringent program of work practices, including training, demonstrated competence, contamination reduction, and decontamination.
2. Only a Class II BSC with outside exhaust should be used for compounding hazardous drugs; type B2 total exhaust is preferred. Total exhaust is required if the hazardous drug is known to be volatile.[4]
3. Without special design considerations, Class II BSCs are not recommended in traditional, positive-pressure cleanrooms, where contamination from hazardous drugs may result in airborne contamination that may spread from the open front to surrounding areas.
4. Consider using closed-system drug-transfer devices while compounding hazardous drugs in a Class II BSC; evidence documents a decrease in drug contaminants inside a Class II BSC when such devices are used.[4]
5. Reduce the hazardous drug contamination burden in the Class II BSC by wiping down hazardous drug vials before placing them in the BSC.

Appendix B—Recommendations for Use of Class III BSCs and Isolators

1. Only a ventilated cabinet appendix to protect workers and adjacent personnel from exposure and to provide an aseptic environment may be used to compound sterile hazardous drugs.
2. Only ventilated cabinets that are designed to contain aerosolized drug product within the cabinet should be used to compound hazardous drugs.
3. The use of a Class III BSC or isolator must be accompanied by a stringent program of work practices, including operator training and demonstrated competence, contamination reduction, and decontamination.
4. Decontamination of the Class III BSC or isolator must be done in a way that contains any hazardous drug surface contamination during the cleaning process.
5. Appropriate decontamination within the cabinet must be completed before the cabinet is accessed via pass-throughs or removable front panels.
6. Gloves or gauntlets must not be replaced before completion of appropriate decontamination within the cabinet.
7. Surface decontamination of final preparations must be done before labeling and placing into the pass-through.
8. Final preparations must be placed into a transport bag while in the pass-through for removal from the cabinet.

Appendix C—Recommendations for Use of Gloves

1. Wear double gloves for all activities involving hazardous drugs. Double gloves must be worn during any handling of hazardous drug shipping cartons or drug vials, compounding and administration of hazardous drugs, handling of hazardous drug waste or waste from patients recently treated with hazardous drugs, and cleanup of hazardous drug spills.
2. Select powder-free, high-quality gloves made of latex, nitrile, polyurethane, neoprene, or other materials that meet the ASTM standard for chemotherapy gloves.
3. Inspect gloves for visible defects.
4. Sanitize gloves with 70% alcohol or other appropriate disinfectant before performing any aseptic compounding activity.
5. Change gloves every 30 minutes during compounding or immediately when damaged or contaminated.
6. Remove outer gloves after wiping down final preparation but before labeling or removing the preparation from the BSC.
7. Outer gloves must be placed in a containment bag while in the BSC.
8. In an isolator, a second glove must be worn inside the fixed-glove assembly.
9. In an isolator, fixed gloves or appendix must be surface cleaned after compounding is completed to avoid spreading hazardous drug contamination to other surfaces.
10. Clean gloves (e.g., the clean inner gloves) should be used to surface decontaminate the final preparation, place the label onto the final preparation, and place it into the pass-through.
11. Don fresh gloves to complete the final check, place preparation into a clean transport bag, and remove the bag from the pass-through.
12. Wash hands before donning and after removing gloves.
13. Remove gloves with care to avoid contamination. Specific procedures for removal must be established and followed.
14. Gloves should be removed and contained inside the Class II BSC or isolator.
15. Change gloves after administering a dose of hazardous drugs or when leaving the immediate administration area.
16. Dispose of contaminated gloves as contaminated waste.

Appendix D—Recommendations for Use of Gowns

1. Gowns should be worn during compounding, during administration, when handling waste from patients recently treated with hazardous drugs, and when cleaning up spills of hazardous drugs.
2. Select disposable gowns of material tested to be protective against the hazardous drugs to be used.
3. Coated gowns must be worn no longer than three hours during compounding and changed immediately when damaged or contaminated.
4. Remove gowns with care to avoid spreading contamination. Specific procedures for removal must be established and followed.
5. Dispose of gowns immediately upon removal.
6. Contain and dispose of contaminated gowns as contaminated waste.
7. Wash hands after removing and disposing of gowns.

Appendix E—Recommendations for Working in BSCs and Isolators

1. The use of a Class II or III BSC or isolator must be accompanied by a stringent program of work practices, including operator training and demonstrated competence, contamination reduction, and decontamination.
2. Do not place unnecessary items in the work area of the cabinet or isolator where hazardous drug contamination from compounding may settle on them.
3. Do not overcrowd the BSC or isolator.
4. Gather all needed supplies before beginning compounding. Avoid exiting and reentering the work area of the BSC or isolator.
5. Appropriate handling of the preparation in the BSC or pass-through of the isolator, including spraying or wiping with 70% alcohol or another appropriate disinfectant, is necessary for aseptic compounding.
6. Reduce the hazardous drug contamination burden in the BSC or isolator by wiping down hazardous drug vials before placing them in the BSC or isolator.
7. Transport bags must never be placed in the BSC or the isolator work chamber during compounding to avoid inadvertent contamination of the outside surface of the bag.
8. Final preparations should be surface decontaminated within the BSC or isolator and placed into the transport bags in the BSC or in the isolator pass-through, taking care not to contaminate the outside of the transport bag.
9. Decontaminate the work surface of the BSC or isolator before and after compounding per the manufacturer's recommendations or with detergent, sodium hypochlorite solution, and neutralizer.
10. Decontaminate all surfaces of the BSC or isolator at the end of the batch, day, or shift, as appropriate to the workflow. Typically, a BSC or isolator in use 24 hours a day would require decontamination two or three times daily. Disinfect the BSC or isolator before compounding a dose or batch of sterile hazardous drugs.
11. Wipe down the outside of the Class II BSC front opening and the floor in front of the BSC with detergent, sodium hypochlorite solution, and neutralizer at least daily.
12. Seal and then decontaminate surfaces of waste and sharps containers before removing from the BSC or isolator.
13. Decontamination is required after any spill in the BSC or isolator during compounding.
14. Seal all contaminated materials (e.g., gauze, wipes, towels, wash or rinse water) in bags or plastic containers and discard as contaminated waste.
15. Decontamination of the Class III BSC or isolator must be done in a way that contains any hazardous drug surface contamination during the cleaning process.
16. Appropriate decontamination within the cabinet must be completed before the cabinet is accessed via the pass-throughs or removable front panels.
17. Gloves or gauntlets must not be replaced before completion of appropriate decontamination within the cabinet.
18. Surface decontamination of final preparations must be done before labeling and placing into the pass-through.
19. Final preparations must be placed into a transport bag while in the pass-through for removal from the cabinet.

Appendix F—Recommendations for Compounding and Handling Noninjectable Hazardous Drug Dosage Forms

1. Hazardous drugs should be labeled or otherwise identified as such to prevent improper handling.
2. Tablet and capsule forms of hazardous drugs should not be placed in automated counting machines, which subject them to stress and may introduce powdered contaminants into the work area.
3. During routine handling of noninjectable hazardous drugs and contaminated equipment, workers should wear two pairs of gloves that meet the ASTM standard for chemotherapy gloves.[85]
4. Counting and pouring of hazardous drugs should be done carefully, and clean equipment should be dedicated for use with these drugs.
5. Contaminated equipment should be cleaned initially with gauze saturated with sterile water; further cleaned with detergent, sodium hypochlorite solution, and neutralizer; and then rinsed. The gauze and rinse should be contained and disposed of as contaminated waste.
6. Crushing tablets or opening capsules should be avoided; liquid formulations should be used whenever possible.
7. During the compounding of hazardous drugs (e.g., crushing, dissolving, or preparing a solution or an ointment), workers should wear nonpermeable gowns and double gloves. Compounding should take place in a ventilated cabinet.
8. Compounding nonsterile forms of hazardous drugs in equipment designated for sterile products must be undertaken with care. Appropriate containment, deactivation, and disinfection techniques must be utilized.
9. Hazardous drugs should be dispensed in the final dose and form whenever possible. Unit-of-use containers for oral liquids have not been tested for containment properties. Most exhibit some spillage during preparation or use. Caution must be exercised when using these devices.
10. Bulk containers of liquid hazardous drugs, as well as specially packaged commercial hazardous drugs (e.g., Neoral [manufactured by Novartis]), must be handled carefully to avoid spills. These containers should be dispensed and maintained in sealable plastic bags to contain any inadvertent contamination.
11. Disposal of unused or unusable noninjectable dosage forms of hazardous drugs should be performed in the same manner as for hazardous injectable dosage forms and waste.

Appendix G—Recommendations for Reducing Exposure to Hazardous Drugs During Administration in All Practice Settings[104]

Intravenous administration

1. The use of gloves, gown, and face shield (as needed for splashing) is required.
2. Gather all necessary equipment and supplies, including PPE.
3. Use needleless systems whenever possible.
4. Use Luer-Lok fittings for all needleless systems, syringes, needles, infusion tubing, and pumps.
5. Needleless systems may result in droplets leaking at connection points; use gauze pads to catch leaks.
6. Designate a workplace for handling hazardous drugs.
7. Have a spill kit and hazardous drug waste container readily available.
8. Procedure for gowning and gloving: Wash hands, don first pair of gloves, don gown and face shield, and then don second pair of gloves. Gloves should extend beyond the elastic or knit cuff of the gown. Double-gloving requires one glove to be worn under the cuff of the gown and the second glove over the cuff.
9. Always work below eye level.
10. Visually examine hazardous drug dose while it is still contained in transport bag.
11. If hazardous drug dose appears intact, remove it from the transport bag.
12. Place a plastic-backed absorbent pad under the administration area to absorb leaks and prevent drug contact with the patient's skin.
13. If priming occurs at the administration site, prime i.v. tubing with an i.v. solution that does not contain hazardous drugs or by the backflow method.
14. Place a gauze pad under the connection at injection ports during administration to catch leaks.
15. Use the transport bag as a containment bag for materials contaminated with hazardous drugs, drug containers, and sets.
16. Discard hazardous drug containers with the administration sets attached; do not remove the set.
17. Wash surfaces that come into contact with hazardous drugs with detergent, sodium hypochlorite solution, and neutralizer, if appropriate.
18. Wearing gloves, contain and dispose of materials contaminated with hazardous drugs and remaining PPE as contaminated waste.
19. Hazardous drug waste container must be sufficiently large to hold all discarded material, including PPE.
20. Do not push or force materials contaminated with hazardous drugs into the hazardous drug waste container.
21. Carefully remove, contain, and discard gloves. Wash hands thoroughly after removing gloves.

Intramuscular or subcutaneous administration

1. The use of double gloves is required.
2. Gather all necessary equipment and supplies, including PPE.
3. Use Luer-Lok safety needles or retracting needles or shields.
4. Syringes should have Luer-Lok connections and be less than three-fourths full.
5. Designate a workplace for handling hazardous drugs.
6. Have a spill kit and hazardous drug waste container readily available.
7. Procedure for gloving: Wash hands; don double gloves.
8. Always work below eye level.
9. Visually examine hazardous drug dose while still contained in transport bag.
10. If hazardous drug dose appears intact, remove it from the transport bag.
11. Remove the syringe cap and connect appropriate safety needle.
12. Do not expel air from syringe or prime the safety needle.
13. After administration, discard hazardous drug syringes (with the safety needle attached) directly into a hazardous drug waste container.
14. Wearing gloves, contain and dispose of materials contaminated with hazardous drugs.
15. Do not push or force materials contaminated with hazardous drugs into the hazardous drug waste container.
16. Carefully remove, contain, and discard gloves.
17. Wash hands thoroughly after removing gloves.

Oral administration

1. Double gloves are required, as is a face shield if there is a potential for spraying, aerosolization, or splashing.
2. Workers should be aware that tablets or capsules may be coated with a dust of residual hazardous drug that could be inhaled, absorbed through the skin, ingested, or spread to other locations and that liquid formulations may be aerosolized or spilled.
3. No crushing or compounding of oral hazardous drugs may be done in an unprotected environment.
4. Gather all necessary equipment and supplies, including PPE.
5. Designate a workplace for handling hazardous drugs.
6. Have a spill kit and hazardous drug waste container readily available.
7. Procedure for gloving: Wash hands and don double gloves.
8. Always work below eye level.
9. Visually examine hazardous drug dose while it is still contained in transport bag.
10. If hazardous drug dose appears intact, remove it from the transport bag.
11. Place a plastic-backed absorbent pad on the work area, if necessary, to contain any spills.
12. After administration, wearing double gloves, contain and dispose of materials contaminated with hazardous drugs into the hazardous drug waste container.
13. Do not push or force materials contaminated with hazardous drugs into the hazardous drug waste container.
14. Carefully remove, contain, and discard gloves.
15. Wash hands thoroughly after removing gloves.

Appendix H—Recommended Contents of Hazardous Drug Spill Kit

1. Sufficient supplies to absorb a spill of about 1000 mL (volume of one i.v. bag or bottle).
2. Appropriate PPE to protect the worker during cleanup, including two pairs of disposable gloves (one outer pair of heavy utility gloves and one pair of inner gloves); nonpermeable, disposable protective garments (coveralls or gown and shoe covers); and face shield.
3. Absorbent, plastic-backed sheets or spill pads.
4. Disposable toweling.
5. At least two sealable, thick plastic hazardous waste disposal bags (prelabeled with an appropriate warning label).
6. One disposable scoop for collecting glass fragments.
7. One puncture-resistant container for glass fragments.

Appendix I—Recommendations for Spill Cleanup Procedure

General

1. Assess the size and scope of the spill. Call for trained help, if necessary.
2. Spills that cannot be contained by two spill kits may require outside assistance.
3. Post signs to limit access to spill area.
4. Obtain spill kit and respirator.
5. Don PPE, including inner and outer gloves and respirator.
6. Once fully garbed, contain spill using spill kit.
7. Carefully remove any broken glass fragments and place them in a puncture-resistant container.
8. Absorb liquids with spill pads.
9. Absorb powder with damp disposable pads or soft toweling.
10. Spill cleanup should proceed progressively from areas of lesser to greater contamination.
11. Completely remove and place all contaminated material in the disposal bags.
12. Rinse the area with water and then clean with detergent, sodium hypochlorite solution, and neutralizer.
13. Rinse the area several times and place all materials used for containment and cleanup in disposal bags. Seal bags and place them in the appropriate final container for disposal as hazardous waste.
14. Carefully remove all PPE using the inner gloves. Place all disposable PPE into disposal bags. Seal bags and place them into the appropriate final container.
15. Remove inner gloves; contain in a small, sealable bag; and then place into the appropriate final container for disposal as hazardous waste.
16. Wash hands thoroughly with soap and water.
17. Once a spill has been initially cleaned, have the area recleaned by housekeeping, janitorial staff, or environmental services.

Spills in a BSC or isolator

1. Spills occurring in a BSC or isolator should be cleaned up immediately.
2. Obtain a spill kit if the volume of the spill exceeds 30 mL or the contents of one drug vial or ampul.
3. Utility gloves (from spill kit) should be worn to remove broken glass in a BSC or an isolator. Care must be taken not to damage the fixed-glove assembly in the isolator.
4. Place glass fragments in the puncture-resistant hazardous drug waste container located in the BSC or discard into the appropriate waste receptacle of the isolator.
5. Thoroughly clean and decontaminate the BSC or isolator.
6. Clean and decontaminate the drain spillage trough located under the Class II BSC or similarly equipped Class III BSC or isolator.
7. If the spill results in liquid being introduced onto the HEPA filter or if powdered aerosol contaminates the "clean side" of the HEPA filter, use of the BSC or isolator should be suspended until the equipment has been decontaminated and the HEPA filter replaced.

Appendix J—OSHA-Recommended Steps for Immediate Treatment of Workers with Direct Skin or Eye Contact with Hazardous Drugs[3]

1. Call for help, if needed.
2. Immediately remove contaminated clothing.
3. Flood affected eye with water or isotonic eyewash for at least 15 minutes.
4. Clean affected skin with soap and water; rinse thoroughly.
5. Obtain medical attention.
6. Document exposure in employee's medical record and medical surveillance log.
7. Supplies for emergency treatment (e.g., soap, eyewash, sterile saline for irrigation) should be immediately located in any area where hazardous drugs are compounded or administered.

Glossary

Antineoplastic drug: A chemotherapeutic agent that controls or kills cancer cells. Drugs used in the treatment of cancer are cytotoxic but are generally more damaging to dividing cells than to resting cells.[4]

Aseptic: Free of living pathogenic organisms or infected materials.[4]

Biological-safety cabinet (BSC): A BSC may be one of several types.[4]

Class I BSC: A BSC that protects personnel and the work environment but does not protect the product. It is a negative-pressure, ventilated cabinet usually operated with an open front and a minimum face velocity at the work opening of at least 75 ft/min. A class I BSC is similar in design to a chemical fume hood except that all of the air from the cabinet is exhausted through a high-efficiency particulate air (HEPA) filter (either into the laboratory or to the outside).

Class II BSC: A ventilated BSC that protects personnel, the product, and the work environment. A Class II BSC has an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow

for product protection, and HEPA-filtered exhausted air for environmental protection.

Type A1 (formerly type A): These Class II BSCs maintain a minimum inflow velocity of 75 ft/min, have HEPA-filtered down-flow air that is a portion of the mixed down-flow and inflow air from a common plenum, may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy, and may have positive-pressure contaminated ducts and plenums that are not surrounded by negative-pressure plenums. They are not suitable for use with volatile toxic chemicals and volatile radionucleotides.

Type A2 (formerly type B3): These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered down-flow air that is a portion of the mixed down-flow and inflow air from a common exhaust plenum, may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy, and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, they must be exhausted through properly functioning exhaust canopies.

Type B1: These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered down-flow air composed largely of uncontaminated, recirculated inflow air, exhaust most of the contaminated down-flow air through a dedicated duct exhausted to the at-mosphere after passing it through a HEPA filter, and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for work involving minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, the work must be done in the directly exhausted portion of the cabinet.

Type B2 (total exhaust): These Class II BSCs maintain a minimum inflow velocity of 100 ft/min, have HEPA-filtered down-flow air drawn from the laboratory or the outside, exhaust all inflow and down-flow air to the atmosphere after filtration through a HEPA filter without recirculation inside the cabinet or return to the laboratory, and have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted negative-pressure ducts and plenums. These cabinets may be used with volatile toxic chemicals and radionucleotides.

Class III BSC: A BSC with a totally enclosed, ventilated cabinet of gastight construction in which operations are conducted through attached rubber gloves and observed through a nonopening view window. This BSC is maintained under negative pressure of at least 0.50 in of water gauge, and air is drawn into the cabinet through HEPA filters. The exhaust air is treated by double HEPA filtration or single HEPA filtration–incineration. Passage of materials in and out of the cabinet is generally performed through a dunk tank (accessible through the cabinet floor) or a double-door pass-through box (such as an autoclave) that can be decontaminated between uses.

Chemotherapy drug: A chemical agent used to treat diseases. The term usually refers to a drug used to treat cancer.[4]

Chemotherapy glove: A medical glove that has been approved by FDA for use when handling antineoplastic drugs.[4]

Chemotherapy waste: Discarded items such as gowns, gloves, masks, i.v. tubing, empty bags, empty drug vials, needles, and syringes used while preparing and administering antineoplastic agents.[4]

Closed system: A device that does not exchange unfiltered air or contaminants with the adjacent environment.[4]

Closed-system drug-transfer device: A drug-transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.[4]

Cytotoxic: A pharmacologic compound that is detrimental or destructive to cells within the body.[4]

Deactivation: Treating a chemical agent (such as a hazardous drug) with another chemical, heat, ultraviolet light, or another agent to create a less hazardous agent.[4]

Decontamination: Inactivation, neutralization, or removal of toxic agents, usually by chemical means.[4] Surface decontamination may be accomplished by the transfer of hazardous drug contamination from the surface of a nondisposable item to disposable ones (e.g., wipes, gauze, towels).

Disinfecting: Removal of viable organism from surfaces using 70% alcohol or other appropriate disinfectant prior to compounding of sterile hazardous drugs.

Engineering controls: Devices designed to eliminate or reduce worker exposures to chemical, biological, radiological, ergonomic, or physical hazards. Examples include laboratory fume hoods, glove bags, retracting syringe needles, sound-dampening materials to reduce noise levels, safety interlocks, and radiation shielding.[4]

Genotoxic: Capable of damaging DNA and leading to mutations.[4]

Glove box: A controlled environment work enclosure providing a primary barrier from the work area. Operations are performed through sealed gloved openings to protect the worker, the ambient environment, and/or the product.[4]

Hazardous drug: Any drug identified by at least one of the following six criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, and new drugs that mimic existing hazardous drugs in structure or toxicity.[4]

Hazardous waste: Any waste that is an RCRA-listed hazardous waste [40 C.F.R. 261.30-.33] or that meets an RCRA characteristic of ignitability, corrosivity, reactivity, or toxicity as defined in 40 C.F.R. 261.21-.24.[4]

Health care settings: All hospitals, medical clinics, outpatient facilities, physicians' offices, retail pharmacies, and similar facilities dedicated to the care of patients.[4]

Health care workers: All workers who are involved in the care of patients. These include pharmacists, pharmacy technicians, nurses (registered nurses, licensed practi-

cal nurses, nurses' aides, etc.), physicians, home health care workers, and environmental services workers (housekeeping, laundry, and waste disposal).[4]

HEPA filter: Filter rated 99.97% efficient in capturing particles 0.3-µm in diameter.[4]

Horizontal-laminar-airflow hood (horizontal-laminar-airflow clean bench): A device that protects the work product and the work area by supplying HEPA-filtered air to the rear of the cabinet and producing a horizontal flow across the work area and out toward the worker.[4]

Isolator: A device that is sealed or is supplied with air through a microbially retentive filtration system (HEPA minimum) and may be reproducibly decontaminated. When closed, an isolator uses only decontaminated interfaces (when necessary) or rapid transfer ports for materials transfer. When open, it allows for the ingress and egress of materials through defined openings that have been designed and validated to preclude the transfer of contaminants or unfiltered air to adjacent environments. An isolator can be used for aseptic processing, for containment of potent compounds, or for simultaneous asepsis and containment. Some isolator designs allow operations within the isolator to be conducted through a fixed-glove assembly without compromising asepsis or containment.[4]

Aseptic isolator: A ventilated isolator designed to exclude external contamination from entering the critical zone inside the isolator.[4]

Aseptic containment isolator: A ventilated isolator designed to meet the requirements of both an aseptic isolator and a containment isolator.[4]

Containment isolator: A ventilated isolator designed to prevent the toxic materials processed inside it from escaping to the surrounding environment.[4]

Laboratory coat: A disposable or reusable open-front coat, usually made of cloth or other permeable material.[4]

Material safety data sheet: Contains summaries provided by the manufacturer to describe the chemical properties and hazards of specific chemicals and ways in which workers can protect themselves from exposure to these chemicals.[4]

Mutagenic: Capable of increasing the spontaneous mutation rate by causing changes in DNA.[4]

Personal protective equipment (PPE): Items such as gloves, gowns, respirators, goggles, and face shields that protect individual workers from hazardous physical or chemical exposures.[4]

Respirator: A type of PPE that prevents harmful materials from entering the respiratory system, usually by filtering hazardous agents from workplace air. A surgical mask does not offer respiratory protection.[4]

Risk assessment: Characterization of potentially adverse health effects from human exposure to environmental or occupational hazards. Risk assessment can be divided into five major steps: hazard identification, dose–response assessment, exposure assessment, risk characterization, and risk communication.[4]

Surface decontamination: Transfer of hazardous drug contamination from the surface of nondisposable items to disposable ones (e.g., wipes, gauze, towels). No procedures have been studied for surface decontamination of hazardous drug contaminated surfaces. The use of gauze moistened with alcohol, sterile water, peroxide, or sodium hypochlorite solutions may be effective. The disposable item, once contaminated, must be contained and discarded as hazardous waste.

Ventilated cabinet: A type of engineering control designed for purposes of worker protection (as used in these guidelines). These devices are designed to minimize worker exposures by controlling emissions of airborne contaminants through (1) the full or partial enclosure of a potential contaminant source, (2) the use of airflow capture velocities to capture and remove airborne contaminants near their point of generation, and (3) the use of air pressure relationships that define the direction of airflow into the cabinet. Examples of ventilated cabinets include BSCs, containment isolators, and laboratory fume hoods.[4]

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