

ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs

In 1985, the “ASHP Technical Assistance Bulletin on Handling Cytotoxic Drugs in Hospitals”¹ summarized published information on handling hazardous drugs, referred to as cytotoxics, as of July 1984. As more information became available on the types of hazardous agents that may represent a health risk to the occupationally exposed population, and as the handling of such substances became routine in hospitals, community pharmacies, home care settings, clinics, and physicians’ offices, the need to revise the Technical Assistance Bulletin became apparent.

Early concerns regarding occupational exposure to hazardous agents involved primarily drugs used in cancer therapy. Therefore, the terms “antineoplastics” (drugs used to treat neoplasms) and “chemotherapy” were used in early reports and guidelines. Although any chemical used therapeutically may be referred to as chemotherapy, this term is currently used, both in the medical and lay communities, to mean drug therapy of cancer. In an attempt to be more precise, many professionals adopted the term “cytotoxic” or “cell killer.” Not all antineoplastics, however, are cytotoxic, nor are all cytotoxics used exclusively in the treatment of cancer. “Cytotoxic” is often used to refer to any agent that may be genotoxic, oncogenic, mutagenic, teratogenic, or hazardous in any way. As our knowledge of the hazardous nature of many agents grows and as new hazardous agents (e.g., genotoxic biologicals and some biotechnological agents) continue to be developed, cytotoxic is a less appropriate term. In deference to the original Technical Assistance Bulletin, cytotoxic remains in the title of this revision. The remainder of the document, however, will refer exclusively to hazardous drugs or agents, except in very specific instances.

In January 1986, the Federal Occupational Safety and Health Administration (OSHA) released recommendations on safe handling of cytotoxic drugs by health-care personnel.² This revised Technical Assistance Bulletin includes information from these recommendations, modified by subsequent discussions with OSHA, and from published reports by the National Institutes of Health,³ the National Study Commission on Cytotoxic Exposure,⁴ and the American Medical Association’s (AMA) Council on Scientific Affairs,⁵ along with other published information on this issue as of June 1988.

The safe handling of hazardous drugs is an issue that must be addressed in health-care settings and one that may even affect, in a home care environment, persons other than the patient. Inasmuch as possible, the pharmacist should take the lead in establishing policies and procedures to ensure the proper handling of all hazardous drugs in any health-care setting. The recommendations contained in this Technical Assistance Bulletin should be applied to any area where hazardous drugs are handled. Procedures specific to noninstitutional care settings have been included where available.^{6–8} Because of the many questions about implementing the recommendations in the original Technical Assistance Bulletin, this revision contains detailed information in those areas of greatest concern. The recommendations contained here should be supplemented with the professional judgments of qualified staff and with newer information as it develops.

Hazardous Drug Dangers

The danger to health-care personnel from handling a hazardous drug stems from a combination of its inherent toxicity and the extent to which workers are exposed to the drug in the course of carrying out their duties. This exposure may be through inadvertent ingestion of the drug on foodstuffs (e.g., workers’ lunches), inhalation of drug dusts or droplets, or direct skin contact. Drugs that may represent occupational hazards include any that exhibit the following characteristics:

1. Genotoxicity [i.e., mutagenicity and clastogenicity (see Appendix A) in short-term test systems].
2. Carcinogenicity in animal models, in the patient population, or both, as reported by the International Agency for Research on Cancer (IARC).
3. Teratogenicity or fertility impairment in animal studies or treated patients.
4. Evidence of serious organ or other toxicity at low doses in animal models or treated patients.

The oncogenic and teratogenic effects of therapeutic doses of several antineoplastic agents are well established.^{9–13} The mutagenic properties of some cytotoxics, immunosuppressants, antiviral agents, and biological response modifiers have also been documented.¹⁴ The long-term effects (e.g., cancer, impaired fertility, and organ damage) of continued exposure to small amounts of one or more of such drugs remain undetermined.

For example, it is known that long-term use of potent immunosuppressive agents may result in the development of lymphoma. It is not known, however, at what drug level or over what period of time this may occur and how this correlates with possible drug levels achieved through occupational exposure during preparation and administration of hundreds or thousands of injectable and oral doses of these agents.

Studies have attempted to assess indirectly the potential exposure of hospital pharmacists and nurses to some hazardous drugs in several health-care settings including physicians’ offices.^{15–21} These studies examined the urine mutagenicity or evidence of chromosome damage in subjects who prepared or administered primarily antineoplastic injections. The mutagenicity and chromosome damage that were found were thought to document exposure to and absorption of the drugs that had been handled. An association may exist between carcinogenicity and chromosome breakage or mutagenicity. Therefore, one might conclude that handling hazardous drugs entails some danger to health-care personnel. These studies, although not conclusive, support the postulated occupational risks.

However, several reports make the situation slightly more ominous. Palmer and coworkers²² measured chromosome damage in 10 patients receiving chlorambucil. They found that the damage was cumulative and was related to both the daily dose and the duration of therapy. Another report²³ described permanent liver damage in three nurses who had worked 6, 8, and 16 years, respectively, on an

oncology ward. On the basis of histories, the investigators suggested that the liver injuries may have been related to the intensity and duration of exposure to certain toxic agents. The chlorambucil study involved therapeutic doses of drug, and three cases of liver damage is a small base for drawing any final conclusions. Nevertheless, this information is disturbing in view of the fact that many health-care workers prepare or administer hundreds or even thousands of doses of hazardous drugs during their careers. If low-dose exposure to these agents is cumulative, this exposure should be minimized by strict compliance with safe handling procedures.

The value of chromosome and mutagenicity studies as indicators of the occupational risks of exposure to hazardous drugs has been questioned.^{24–28} However, several researchers have employed more direct methods of determining whether or not workers have been exposed to and absorbed hazardous drugs handled in the customary manner. Demonstration that absorption has occurred would be strong support for the imposition of safety measures. (The absorption of hazardous drug is presumed to be a health risk.)

A letter²⁹ described a study that used the presence of thioethers in the urine as an indicator of exposure to alkylating agents (i.e., certain antineoplastic drugs). The mean urinary thioether concentration (UTC) was higher in a group of 15 oncology nurses after a 5-day rotation than it was when they returned to work after a 3-day leave ($p < 0.01$). There was no difference between the mean pre-exposure UTC and that of a group of 20 nurses who never handled antineoplastic drugs. Twelve of the 15 nurses wore gloves when handling the drugs; none wore any other form of protective apparel. Drug preparation procedures were not reported.

Using gas chromatography, Hirst's group³⁰ found cyclophosphamide in the urine of two nurses working in a cancer clinic who took no special precautions when handling the drug. They also demonstrated that cyclophosphamide can be absorbed through intact skin. On the other hand, another group of researchers³¹ looked for (but could not detect) platinum in the urine of 10 pharmacists and nurses who frequently prepared or administered cisplatin and other platinum-containing antineoplastic agents. However, these subjects employed several protective measures when working with the drugs; this may have influenced the results (and demonstrated the effectiveness of the safety precautions employed). Also, the assay method may not have been sensitive enough.

With a different type of approach, Neal et al.³² detected fluorouracil in the air of a drug preparation room and nearby office (where the drug was not prepared). A similar study³³ showed that routine drug manipulations in a horizontal laminar airflow hood contaminated the air in an intravenous admixture preparation room. Fluorouracil and cefazolin sodium were the test drugs employed.

Certain antineoplastic drugs have also been implicated in reproductive risks in humans. There have been reports of fetal loss or malformation occurring in pregnancies of women receiving drug therapy for cancer during the first trimester.³⁴ Two controlled, retrospective Finnish studies^{35,36} attempted to examine the relationship between occupational exposure to antineoplastics and reproductive risks in nurses. One study of nurses reported a statistically significant correlation between the birth of children with malformations and the nurses' preparation and administration of antineoplastics more than once a week during the first trimester of pregnancy. At the time of these nurses' exposure, few protective mechanisms were used.

The second study was done in cooperation with the U.S. National Institute for Occupational Safety and Health (NIOSH); it examined only the incidence of fetal loss and did not investigate the condition of live births. The study showed a significant association between fetal loss and occupational exposure to antineoplastic drugs during the first trimester. Both studies are subject to criticism regarding recall bias and determination of exposure data. Concern about exposure of pregnant workers to hazardous drugs, at least in the first trimester, is, however, valid in light of the reproductive risk reported with therapeutic exposure to certain antineoplastics. At therapeutic doses, these drugs have also been shown to suppress testicular function and spermatogenesis.^{37–39} While the relationship between occupational exposure to hazardous drugs and testicular dysfunction has not been assessed, this potential complication should be considered in light of the effects on treated patients.

To date, these reports provide the primary evidence that health-care workers exposed to hazardous drugs during the course of their work may be absorbing these drugs and may be at risk for adverse outcomes.

Additional research in this area is needed, but awareness of the problem has led to overall reduction of exposures, either by improved drug handling techniques or through the implementation of safety programs,^{40,41} and thus fewer exposed health-care workers are available for study. Definitive knowledge of the occupational dangers of handling hazardous drugs may someday be available through epidemiologic studies of health-care workers.

In theory, correct and perfect preparation and handling techniques will prevent drug particles or droplets from escaping from their containers while they are being manipulated. Our opinion is that near-perfect technique is uncommon; therefore, contamination of the workplace is likely and worker exposure may increase without protective equipment and other safety measures. This is particularly true, we think, in the absence of any structured training and quality-assurance programs covering the proper handling of hazardous drugs. (Such programs are most likely to be found in health-care settings where the preparation of hazardous drugs is centralized.) Beyond problems in technique, however, contamination also will occur from inevitable spills and from the breakage of hazardous drug containers. ASHP believes that the occupational dangers of exposure to hazardous drugs can be summarized as follows:

1. If hazardous drugs are handled in the same way as other less hazardous substances (e.g., potassium chloride solutions and multivitamin tablets), contamination of the work environment is almost certain to occur.
2. The limited data available suggest that this contamination may result in exposure to and absorption of the drugs by health-care personnel and others. The amount of drug absorbed by any one individual on any given day probably is very small, except for instances of excessive exposure.
3. However, if experience with the therapeutic use of hazardous drugs indicates that the damage is cumulative, individuals whose job responsibilities require them to prepare or administer large numbers of hazardous drug doses for long periods of time (e.g., oncology or transplant nurses and pharmacy intravenous service staff) are at greater risk.
4. Considering the above, the use of procedures, equipment, and materials that demonstrably or theoretically

reduce exposure to hazardous drugs in the health-care workplace is necessary.

The question remains: What safety precautions should be employed?

Safety Precautions

Ideally, the safety precautions employed to protect health-care workers handling hazardous drugs would be those whose efficacy and cost-effectiveness have been documented. Since these drugs have many different physical and chemical properties, research studies into environmental contamination and safety-garment penetration for all questionable drugs are problematic. However, several studies have attempted to demonstrate the effectiveness of certain recommended interventions. Hoy and Stump⁴² concluded that a commercial air-venting device, when used with appropriate technique, effectively reduced the release of drug aerosols during reconstitution of drugs packaged in vials. A study by Anderson et al.¹⁶ provides support for preparing hazardous drugs in a vertical laminar airflow biological safety cabinet (BSC) (NSF Class II;⁴³ see Appendix B) rather than a horizontal airflow clean air work station.

A more recent air-sampling study,⁴⁴ carried out in a hospital pharmacy work area where a Class II BSC was used to prepare cytotoxic drugs, detected no fluorouracil during the study period. The study was limited to one drug and two short study periods; the results indicate that a Class II BSC, in conjunction with stringent aseptic technique and recommended procedures for handling hazardous drugs, may reduce environmental contamination by these drugs.

While common sense suggests that the airflow characteristics of containment cabinets would provide greater worker protection than open airflow workstations, it should also suggest that the front opening of the Class II BSC might present potential for environmental contamination and increased worker exposure to hazardous agents. Indeed, as demonstrated by an industrial hygiene experiment,⁴⁵ a Class II BSC may cause occasional leakage toward the operator and into the environment if it is placed in an area of strong air drafts or frequent personnel traffic. The containment characteristics of the Class II BSC are compromised whenever the intake or exhaust grilles are blocked (e.g., by placing equipment or supplies on the front grille or too near the back exhaust) or by too much movement on the part of the operator.

Gloves are a major source of protection, whether the work is performed with or without a Class II BSC. The permeability of various glove materials to selected drugs has been examined.^{46–49} By using various methods to determine and quantitate penetration, researchers found that permeability of the glove material varied with the drug, contact time, and glove thickness. None of the glove materials tested was impervious to all drugs, and no material was statistically superior except as related to thickness. A thicker glove material is optimal. In addition, several glove materials showed variation in permeability within a manufacturer's lot. These studies do establish that gloves can provide protection against skin contact with the tested drugs, although the degree of protection has not been substantiated. Protection from skin contact is important since many of the problem drugs are skin irritants or even vesicants and, as Hirst et al.³⁰ showed, at least one (cyclophosphamide) is absorbed through the skin.

Only one study⁵⁰ looked at the permeability of gown

materials to drugs. Lab coats and disposable isolation gowns were penetrated immediately and were therefore inappropriate for study. Of the four other gown materials studied, Kaycel and nonporous Tyvek had greater permeability than the coated fabrics (Saranex-laminated Tyvek and polyethylene-coated Tyvek). As with gloves, permeability was drug specific. The investigators concluded that users of garments made of Kaycel and nonporous Tyvek should be aware of the potential of these materials for permeability to certain drugs. An earlier report⁵¹ supports the wearing of gloves and gowns. Additional research is needed in the area of protective garments and equipment. Since substantive data are still lacking, health-care professionals should choose protective measures on the basis of expert recommendations, professional judgment, and common sense as well as scientifically established facts.

Recommended Safe Handling Methods

The balance of this article presents our recommendations for policies, procedures, and safety materials for controlling, preparing, administering, containing, and disposing of hazardous drugs. The recommendations are given in a format that can be used either as a base for establishing safe handling methods or for evaluating existing procedures as part of a quality-assurance program. ASHP believes these recommendations represent a conservative but reasonable approach to the precautions that should be taken.

The recommendations are in the format of evaluation criteria organized into four groups. This format should be useful in establishing a quality-assurance system for all nontherapeutic aspects of hazardous drug use. Each group begins with a broad goal, followed by a set of specific criteria and recommendations for achieving the goal. The four goals reflect the following axioms for handling hazardous drugs:

1. Protect and secure packages of hazardous drugs.
2. Inform and educate all involved personnel about hazardous drugs and train them in the safe handling procedures relevant to their responsibilities.
3. Do not let the drugs escape from containers when they are manipulated (i.e., dissolved, transferred, administered, or discarded).
4. Eliminate the possibility of inadvertent ingestion or inhalation and direct skin or eye contact with the drugs.

The handling of hazardous drugs is a complex issue, and the advice of medical experts, occupational physicians, industrial hygienists, legal counsel, and others should be obtained when organizational policy is being established.

Goal 1. Accidental contamination of the health-care environment, resulting in exposure of personnel, patients, visitors, and family members to hazardous substances, is prevented by maintaining the physical integrity and security of packages of hazardous drugs.

1. Access to all areas where hazardous drugs are stored is limited to specified authorized staff.
2. A method should be present for identifying to personnel those drugs that require special precautions (e.g., cytotoxics).⁵² One way to accomplish this is to apply appropriate warning labels (see Figure 1) to all hazardous drug containers, shelves, and bins where the drug products are stored.

3. *A method of identifying, for patients and family members, those drugs that require special precautions in the home should be in place.* This may be accomplished in the health-care setting by providing specific labeling for discharge medications, along with counseling and written instructions. Providers of home care and supplies should develop similar labeling and instructional material for the protection of patients and their families.
4. *Methods for identifying shipping cartons of hazardous drugs should be required from manufacturers and distributors of these drugs.*
5. *Written procedures for handling damaged packages of hazardous drugs should be maintained.* Personnel involved in shipping and receiving hazardous drugs should be trained in these procedures, including the proper use of protective garments and equipment. Damaged shipping cartons of hazardous drugs should be received and opened in an isolated area (e.g., in a laboratory fume hood, if available, not in a BSC used for preparing sterile products). Protective apparel—disposable closed-front gown or coveralls, disposable utility gloves over disposable latex gloves, NIOSH-approved⁵³ air-purifying half-mask respirator (may be disposable) equipped with a high-efficiency filter, and eye protection—should be worn. Broken containers and contaminated packaging materials should be placed in the designated receptacles as described in this article.
6. *Facilities (e.g., shelves, carts, counters, and trays) for storing hazardous drugs are designed to prevent breakage and to limit contamination in the event of leakage.* Bins, shelves with barriers at the front, or other design features that reduce the chance of drug containers falling to the floor should be used. Hazardous drugs requiring refrigeration should be stored separately from nonhazardous drugs in individual bins designed to prevent breakage and contain leakage.
7. *Methods for transporting hazardous drugs to the health-care setting should be consistent with environmental protection and national or local regulations for transporting hazardous substances.* When hazardous drugs are being transported to the home care setting, appropriate containers (e.g., lined cardboard boxes) and procedures should be used to prevent breakage and contain leakage. Hazardous drug containers should be secured to prevent handling by unauthorized persons. Transportation vehicles should be kept locked at all times.

Figure 1. One example of a suitable warning label for cytotoxic and hazardous drugs. Other labels may be used.



For transporting hazardous drugs within the health-care setting, methods that do not cause breakage of or leakage from drug containers should be used. Conveyances that produce severe mechanical stress on their contents (e.g., pneumatic tubes) must not be used to transport hazardous drugs. The drugs must be securely capped or sealed and properly packaged and protected during transport to reduce further the chance of breakage and spillage in a public area such as a corridor or elevator. Adequate instruction and appropriate containers should be provided to patients for transporting discharge and home care medications that require special precautions.

Goal II. The preparation of hazardous drugs does not result in contamination of the health-care work environment or excessive exposure of personnel, patients, or family members to hazardous drug powders, dusts, liquids, or mists.

1. *Written policies and standard procedures for preparing hazardous drugs are maintained.*
 - a. They should include a method for identifying for health-care personnel the particular drugs covered by these policies.
 - b. Policies and procedures should be consistent with applicable government regulations, professional practice standards, and the recommendations of pharmaceutical manufacturers, hospital safety officers, and other knowledgeable parties.
 - c. Since several departments, such as pharmacy, nursing, transportation, maintenance, housekeeping, and medical staff, will be involved with some aspect of the hazardous drug handling issue, preparation of safe handling policies and procedures must be a collaborative effort. Pharmacy should take the lead in this effort.
 - d. All personnel who handle cytotoxic and other hazardous agents should have access to the procedures pertaining to their responsibilities. Deviations from the standard procedures must not be permitted except under defined circumstances.
2. *A method for orienting all involved personnel to the special nature of the hazardous drugs in question and the policies and procedures that govern their handling is present.*
 - a. The orientation should include, as appropriate, a discussion of the known and potential hazards of the drugs and explanation of all relevant policies. Training done in association with the orientation should cover all relevant techniques and procedures and the proper use of protective equipment and materials. The contents of the orientation program and attendance should be well documented and sufficient to meet “worker right to know” statutes and regulations.
 - b. While implementation of a safety program should reduce the risk of personnel exposure to hazardous drugs, the efficacy of such a program in protecting personnel during preparation or administration of these drugs has yet to be demonstrated. The limitations of such a program should be made known to hazardous drug handlers.
 - c. Until the reproductive risks (or lack thereof) associated with handling hazardous drugs within

- a safety program have been substantiated, staff who are pregnant or breast-feeding should be allowed to avoid contact with these drugs. Policies should be in effect that provide these individuals with alternative tasks or responsibilities if they so desire. In general, these policies should encourage personnel to solicit recommendations from their personal physicians regarding the need for restricted duties. In the case of personnel actively trying to conceive or father a child, a similar policy should be considered, and a specific time period (e.g., 3 months) should be agreed on. Legal counsel should be sought when establishing policies.
- d. Prospective temporary and permanent employees who may be required to work with hazardous drugs should be so notified and should receive adequate information about the policies and procedures pertaining to their use. This notification should be documented during the interview process and retained as part of the employment record for all employees.
 - e. All individuals handling hazardous drugs who do not have employee status (e.g., contract workers, students, residents, medical staff, and volunteers) should be informed through proper channels of the special nature of the drugs. If they choose to handle the hazardous drugs, then they will be expected to comply with established policies and procedures for preparing, administering, and containing hazardous drugs and their associated waste.
3. *A system for verifying and documenting acceptable staff performance of and conformance with established procedures is maintained.*
 - a. Methods of determining adherence to departmental safety program policies and procedures should be in place. Proper technique is essential to maintain the sterility of the product being manipulated and to reduce the generation of hazardous drug contaminants. Therefore, after initial training and at regular intervals, the knowledge and competence of personnel preparing and administering these drugs should be evaluated and documented. This evaluation should include written examinations and an observed demonstration of competence in the preparation and simulated administration of practice solutions. The monitoring of staff performance and the control of hazardous drugs usually are best achieved if the storage and preparation of the drugs are centralized within one area or department.
 - b. All personnel involved with the transportation, preparation, administration, and disposal of cytotoxic and hazardous substances should continually be updated on new or revised information on safe handling of cytotoxic and hazardous substances. Policies and procedures should be updated accordingly.
 4. *Sufficient information is maintained on safe use of the hazardous drugs in the work area.*
 - a. The pharmacy should provide access to information on toxicity, treatment of acute exposure (if available), chemical inactivators, solubility, and stability of hazardous drugs (including investigational agents) used in the workplace. This information should be in addition to information required to ensure patient safety during therapy with these drugs and to be in compliance with all applicable laws and regulations. The information must be easily and readily accessible to all employees where these drugs are routinely handled.
 - b. Currently, a large number of investigational agents that are potentially hazardous are under clinical study. Staff members should not prepare or administer any investigational agent unless they have received adequate information and instruction about the safe and correct use of the drug. The clinical protocol should include appropriate handling and disposal techniques, if available. When information is limited, pre-clinical data should be used to assess the health risk of the agent.
 5. *Appropriate engineering controls should be in place to protect the drug product from microbial contamination and to protect personnel and the environment from the potential hazards of the product.* These engineering controls should be maintained according to applicable regulations and standards.
 - a. Class 100 clean air work stations,⁵⁴ both horizontal and vertical airflow (with no containment characteristics), are inappropriate engineering controls for handling hazardous drugs because they provide no personnel protection and permit environmental contamination. Although there are no engineering controls designed specifically for the safe handling of hazardous chemicals as sterile products, Class II⁴³ contained vertical flow BSCs (biohazard cabinets) have been adopted for this use. Biohazard cabinetry is, however, designed for the handling of infectious agents, not hazardous chemicals. Therefore, the limitations of such cabinetry must be understood by purchaser and operator. Manufacturers, vendors, the National Sanitation Foundation (NSF), and some certifying agencies are appropriate sources of information regarding BSCs.
 - b. BSCs are available in three classes (Appendix B). Based on design, ease of use, and cost considerations, Class II contained vertical flow biohazard cabinetry is currently recommended for use in preparing sterile doses of hazardous drugs. Class II cabinetry design and performance specifications are defined in NSF Standard 49.⁴³ BSCs selected for use with hazardous drugs should meet NSF Standard 49 specifications to ensure the maximum protection from these engineering controls. NSF Standard 49 defines four types of Class II cabinetry, depending on the amount of contaminated air that is recirculated through high-efficiency particulate air (HEPA) filters within the cabinet (see Appendix B).

Selection criteria for Class II cabinetry should include the types and amounts of hazardous drugs prepared, the available location and amount of space, NSF Standard 49, any local requirements for handling hazardous materials and ducting contaminated air, and the cost of the

cabinet and related ventilation. Minimum recommendations are a Class II, Type A cabinet (recirculating a major portion of contaminated air through a HEPA filter and back into the cabinet and exhausting a minor portion, through a HEPA filter, to the workroom). In light of the continued development of hazardous drugs having differing physical properties, selection of a Type A cabinet that can be converted to a Type B3 (greater inflow velocity, contaminated ducts and plenums under negative pressure and vented to the outside) may be a prudent investment. There are currently no data to indicate that the use of an auxiliary charcoal filter is more effective in retaining hazardous drugs than the mandatory exhaust HEPA filter of the Type A cabinet.

Type B BSCs are designed to provide more personnel protection than Type A through their greater inflow velocities and required external exhaust of contaminated air. Types B1 (exhausting approximately 70% of the contaminated air to the outside through a HEPA filter) and B2 (exhausting 100% of the contaminated air to the outside through a HEPA filter) require outside exhaust ducts with auxiliary blowers. The Type B2 cabinet is preferred, but unavailability of adequate “makeup” air may eliminate it in favor of the Type B1. All exhaust ducting of any type of BSC must meet applicable codes and ordinances. Ducting into the “dead space” in the ceiling is inappropriate and may be illegal, because it may contaminate ventilation systems and promote contamination of the environment and personnel not directly involved in hazardous drug handling.

In the selection of any BSC, ceiling height should also be considered. Several manufacturers’ models have top-load HEPA filters. In workrooms with standard-height ceilings, the filters are difficult to access for certification, which may require that the entire BSC be moved when the filter must be replaced. Because of restrictions of space and cost, the 2-foot wide, Class II, Type A BSC may seem to be the only choice for smaller institutions, outpatient centers, and physician offices. There are, however, many limitations to the smaller cabinet. Because NSF testing facilities are not currently adaptable to 2-foot BSC models, no 2-foot BSC is NSF approved. Selection of a 2-foot cabinet should, therefore, include thorough investigation of cabinet design and knowledge of the reliability of the manufacturer. In all cases, the manufacturer’s 2-foot cabinet should not differ extensively from designs used for its NSF-approved larger models.

- c. All Class II BSCs have an open front with inward airflow forming a “curtain” or barrier to protect the operator and the environment from contaminants released in the BSC work area. Because BSCs are subject to breaks in their containment properties if there is interference with the inward airflow through the work area access opening, placement of the BSC and operator training are critical. The placement of a BSC in an area with drafts or in close proximity to other airflow

devices (e.g., horizontal flow hoods, air conditioners, air vents, fans, and doors) may interfere with the inward airflow through the opening and may release contaminants into the workroom.

The horizontal motion of an operator’s arms in the opening may also result in similar workroom contamination. Because smaller BSCs are more sensitive to disruption of the inward airflow barrier, the use of a 2- to 3-foot BSC is associated with a greater risk of releasing contaminants than are larger cabinets and requires that the operator be more carefully trained and monitored. It is critical that all operators know the proper method for preparing hazardous drugs in a BSC and that they understand the limitations of BSCs.

- d. Class II BSCs should be certified according to specifications of NSF Standard 49 and Class 100 specifications of Federal Standard 209C.⁵⁴ Certification should take place on initial installation, whenever the cabinet is moved or repaired, and every 6 months thereafter. At present, there are no licensing requirements for individuals who certify Class II BSCs. It is, therefore, imperative that the pharmacist responsible for the intravenous preparation area be familiar with the certification requirements for Class II BSCs and the test procedures that should be performed.⁵⁵

All BSCs should be tested for the integrity of the HEPA filter, velocity of the work access airflow and supply airflow, airflow smoke patterns, and integrity of external surfaces of the cabinet and filter housings. Testing of the integrity of the HEPA filter generally ensures that the particulate count in the work area is less than that required to meet Class 100 conditions of Federal Standard 209C.⁵⁴ Class II, Type B1 BSCs may be prone to exceed Class 100 particle counts and should have routine particulate testing as part of the certification process. Individuals certifying the BSC should be informed of the hazardous nature of the drugs being prepared in the BSC and should wear appropriate protective apparel (see section 5g).

- e. BSCs should be cleaned and disinfected regularly to ensure a proper environment for preparation of sterile products. For routine cleanups of surfaces between decontaminations, water should be used (for injection or irrigation) with or without a small amount of cleaner. If the contamination is soluble only in alcohol, then 70% isopropyl or ethyl alcohol may be used in addition to the cleaner. In general, alcohol is not a good cleaner, only a disinfectant, and its use in a BSC should be limited. The BSC should be disinfected with 70% alcohol before any aseptic manipulation is begun. The excessive use of alcohol should be avoided in BSCs where air is recirculated (i.e., Class II, Type A, B3, and, to a lesser extent, B1) because alcohol vapors may build up in the cabinet.

A lint-free, plastic-backed disposable liner may be used in the BSC to facilitate spill cleanup. Problems with the use of such a liner include introduction of particulates into the work area,

“lumping” of a wet liner that causes unsteady placement of drug containers, poor visibility of spills, and creation of additional contaminated disposables. If used, the liner should be changed frequently and whenever it is overtly contaminated.

- f. The BSC should be operated with the blower turned on continuously, 24 hours a day, 7 days a week. Hazardous drug aerosols and spills generated in the work area of the BSC routinely accumulate in the deposits of room dust and particles under the work tray. These contaminants are too heavy to be transported to the HEPA filter located at the top of the cabinet. In addition, the plenums in all of the BSCs currently available in the United States become contaminated during use; these plenums cannot be accessed for washing. Turning off the blower may allow contaminated dust to recirculate back into the workroom, especially if other sources of air turbulence, such as horizontal hoods, air intakes, air conditioners, and fans, are located near the BSC. Whether or not the BSC is vented to the outside, the downward airflow velocity is insufficient to move and “trap” room dust, spill debris, and other contaminants on the HEPA filter. If it is necessary to turn off a BSC, first the entire cabinet, including all parts that can be reached, should be thoroughly cleaned with a detergent that will remove surface contamination and then rinsed (see section 5g). Once the BSC is clean, the blower may be turned off and the work access opening of the BSC and the HEPA exhaust area may be covered with impermeable plastic and sealed with tape to prevent any contamination from inadvertently escaping from the BSC. The BSC must be sealed with plastic whenever it is moved or left inoperative for any period of time.
- g. The BSC should be decontaminated on a regular basis (ideally at least weekly) and whenever there is a spill or the BSC is moved or serviced, including for certification. While NSF Standard 49 recommends decontamination with formaldehyde to remove biohazard contamination, chemical (drug) contamination is not removed by such treatment. Currently, no single reagent will deactivate all known hazardous drugs; therefore, decontamination of a BSC used for such drugs is limited to removal of contamination from a nondisposable surface (the cabinet) to a disposable surface (e.g., gauze or towels) by use of a good cleaning agent that removes chemicals from stainless steel.

The cleaning agent selected should have a pH approximating that of soap and be appropriate for stainless steel. Cleaners containing chemicals such as quaternary ammonium compounds should be used with caution, because they may be hazardous to humans and their vapors may build up in any BSC where air is recirculated (see section 5e). Similar caution should be used with any pressurized aerosol cleaner; spraying a pressurized aerosol into a BSC may disrupt the protective containment airflow, damage the HEPA filter, and cause an accumulation of the propellant

within a BSC where air is recirculated, resulting in a fire and explosion hazard.

During decontamination, the operator should wear a disposable closed-front gown, disposable latex gloves covered by disposable utility gloves, safety glasses or goggles, a hair covering, and a disposable respirator, because the glass shield of the BSC occasionally must be lifted (see 5j). The blower must be left on, and only heavy toweling or gauze should be used in the BSC to prevent it from being “sucked” up the plenum and into the HEPA filter.

Decontamination should be done from top to bottom (areas of lesser contamination to greater) by applying the cleaner, scrubbing, and rinsing thoroughly with distilled or deionized water. All contaminated disposables should be contained in sealable bags for transfer to larger waste containers. The HEPA filter must not become wet during cleaning of the protective covering (e.g., grille front). This covering, therefore, should not be cleaned with spray cleaners while it is in place. Removable parts of the BSC should be cleaned within the containment area of the BSC and should not be removed from the cabinet. The work tray usually can be lifted and placed against the back wall for cleaning of the undersurface of the tray and exposure of the very bottom (or sump) of the BSC.

The drain spillage trough area collects room dust and all spills, so it is the most heavily contaminated area and must be thoroughly cleaned (at least twice with the cleaning agent). The trough provides limited access to the side and back plenums; surfaces should be cleaned as high as possible. BSCs have sharp metal edges, so disposable utility gloves are more durable and appropriate than surgical latex gloves for decontamination. Gloves should be changed immediately if torn. All plenum surfaces must be rinsed well, with frequent changes of water and gauze. If the BSC is equipped with a drainpipe and valve, it may be used to collect rinse water. The collection vessel used must fit well around the drain valve and not allow splashing. Gauze may be used around the connection to prevent aerosol from escaping. The collection vessel must have a tight-fitting cover, and all rinse water (and gauze, if used) must be disposed of as contaminated waste. The outside of the BSC should be wiped down with cleaner to remove any drip or touch contamination.

Cleaner and rinse containers are generally contaminated during the procedure and should remain in the BSC during cleaning or be placed on a plastic-backed, absorbent liner outside the BSC. All bottles must be discarded as contaminated waste after decontamination of the BSC. All protective apparel (e.g., gown, gloves, goggles, and respirator) should be discarded as contaminated waste. Work area surfaces should be disinfected with 70% alcohol before any aseptic operation is begun. With good planning, decontamination of a 4-foot BSC should take about 1 hour.

- h. Because of its design and decontamination limitations, the BSC should be considered a contaminated environment and treated as such. The use of the BSC should be restricted to the preparation of sterile dosage forms of hazardous drugs. Access to the BSC should be limited to authorized personnel wearing appropriate protective clothing.
- i. If a BSC previously used for biologicals will be adopted for use with hazardous drugs, the BSC should be completely decontaminated of biohazardous agents by use of NSF Standard 49 decontamination techniques. Both HEPA filters should be replaced and the cabinet tested against the *complete* requirements of NSF Standard 49 Appendix B and the particulate limitations of Class 100 conditions of Federal Standard 209C. A BSC used for hazardous drugs that will be recycled for use with hazardous drugs in another section of the institution or in another institution must be surface decontaminated (as described in section 5g), sealed (as in section 5f), and carefully transported to its new location before the filters are replaced (as in section 5j). Once in its new location, the BSC must be recertified.
- j. The HEPA filters of the BSC must be replaced whenever they restrict required airflow velocity or if they are overtly contaminated (e.g., by a breach in technique that causes hazardous drug to be introduced onto the clean side of the supply HEPA filter). Personnel and environmental protection must be maintained during replacement of a contaminated HEPA filter. Because replacement of a HEPA filter generally requires breaking the integrity of the containment aspect of the cabinet, this procedure may release contamination from the filter into the pharmacy or intravenous preparation area if carried out in an inappropriate manner.

Before replacement of a HEPA filter contaminated with hazardous drugs, the BSC service agent should be consulted for a mutually acceptable procedure for replacing and subsequently disposing of a contaminated HEPA filter. One procedure would include moving the BSC to a secluded area or using plastic barriers to segregate the contaminated area. Protective clothing and equipment must be used by the servicer. The BSC should be decontaminated before filter replacement (see section 5g). The contaminated filters must be removed, bagged in thick plastic, and prepared for disposal in a hazardous waste dump site or incinerator licensed by the Environmental Protection Agency (EPA).

When arranging for disposal, precise terms should be used to describe the hazard (e.g., “toxic chemicals” or “chemical carcinogens,” not “cytotoxic” or “chemotherapy”) to ensure that contractors are not inadvertently misled in the classification of the hazard. Disposal of an entire contaminated BSC should be approached in the same manner. The filters should be removed, bagged, and disposed of separately from the BSC. If no available service company will

arrange for removal of the filter (or entire BSC) and its ultimate disposal, a licensed hazardous waste contractor should be used. The use of triple layers of thick plastic (e.g., 2-mil low-linear or 4-mil plastic) for initial covering of the filter or cabinet and then the construction of a plywood crate for transport to an EPA-licensed hazardous waste dump site or incinerator is suggested.

- 6. *Engineering controls should be supplemented with personal protective apparel and other safety materials.* Policies and procedures should be in place to ensure that these materials are used properly and consistently.
 - a. Workers should wear powder-free, disposable surgical latex gloves of good quality when preparing hazardous drugs. Selection criteria for gloves should include thickness (especially at the fingertips where stress is the greatest), fit, length, and tactile sensation. While no glove material has been shown to be impervious to all hazardous drugs or to be statistically superior in limiting drug penetration, thickness and time in contact with drug are crucial factors affecting permeability.^{47–49}

The practice of double gloving is supported by research that indicates that many glove materials vary in drug permeability even within lots;^{48,49} therefore, double gloving is recommended. This recommendation is based on currently available research findings. Evidence to show that single gloves are sufficiently protective might make this recommendation unnecessary. In general, surgical latex gloves fit better, have appropriate elasticity for double gloving and maintaining the integrity of the glove-gown interface, and have sufficient tactile sensation (even during double gloving) for stringent aseptic procedures.
 - b. Powdered gloves increase the particulate level in the filtered air environment of the BSC and leave a powder residue on the surfaces of supplies, final product, and the hands that may absorb contamination generated in the BSC; therefore, powdered gloves should be avoided. The use of sterile gloves is unnecessary during operations involving nonsterile surfaces. Hands must be thoroughly washed and dried before gloves are donned and when a task or batch is completed. If only powdered gloves are available, all powder must be washed off the outside of the outer glove before any operation is begun, and hands should be washed once gloves have been removed.
 - c. Two pairs of fresh gloves should be put on when beginning any task or batch. The outer glove should be changed immediately if contaminated. Both gloves should be changed if the outer glove is torn, punctured, or overtly contaminated with drug (as in a spill) and every hour during batch operations. During removal of gloves, care should be taken to avoid touching the inside of the glove or the skin with the contaminated glove fingers. To limit transfer of contamination from the BSC into the work area, outer gloves should be removed after each batch and should be placed in “zipper”-closure plastic bags or other sealable containers for disposal.
 - d. The worker should wear a protective disposable gown made of lint-free, low-permeability fabric

- with a solid front, long sleeves, and tight-fitting elastic or knit cuffs when preparing hazardous drugs. Washable garments are immediately penetrated by liquids and therefore provide little, if any, protection. In addition, washable garments require laundering and thus potentially expose other personnel to contamination.
- e. When double gloving, one glove should be placed under the gown cuff and one over. The glove-gown interface should be such that no skin on the arm or wrist is exposed. Gloves and gowns should not be worn outside the immediate preparation area. On completion of each task or batch, the worker should, while wearing outer gloves, wipe all final products with gauze. The outer gloves should then be removed and placed, along with the gauze, in a sealable container (e.g., a zipper-closure plastic bag) within the BSC. All waste bags in the BSC should be sealed and removed for disposal. The gown should be removed and placed in a sealable container before removal of the inner gloves. The inner gloves should be removed last and placed in the container with the gown.
 - f. Workers who are not protected by the containment environment of a BSC should use respiratory protection when handling hazardous drugs. Respiratory protection should be an adjunct to and not a substitute for engineering controls.
 - g. Surgical masks of all types provide no respiratory protection against powdered or liquid aerosols of hazardous drugs.
 - h. In situations where workers may be exposed to potential eye contact with hazardous drugs, an appropriate plastic face shield or splash goggles should be worn. Eyewash fountains should be available in areas where hazardous drugs are routinely handled. Inexpensive alternatives include an intravenous bag of 0.9% sodium chloride solution (normal saline) or irrigation bottle of water or saline with appropriate tubing.
7. *Proper manipulative technique to maintain the sterility of injectable drugs and to prevent generation of hazardous drug contaminants is used consistently.*
- a. Proper manipulative technique must be taught to all workers who will be required to prepare hazardous drugs.⁵⁶ Preparers should demonstrate competence in these techniques once training has been completed and at least annually thereafter.
 - b. Systems to ensure that these techniques are adhered to should exist, along with systems to ensure patient safety by providing that drugs are properly selected, calculated, measured, and delivered.
 - c. The work area should be designed to provide easy access to those items necessary to prepare, label, and transport final products; contain all related waste; and avoid inadvertent contamination of the work area.
 - d. Maintenance of proper technique requires an organized approach to the preparation of sterile doses of hazardous drugs in a BSC. All drug and nondrug items required for completing a dose or batch and for containing the waste should be assembled and placed in the BSC; care should be taken not to overload the BSC work area. All calculations and any label preparation should be completed at this time. Appropriate gowning, hand washing and gloving (or glove changing), and glove washing should be completed before any manipulations are begun. Unnecessary moving in and out of the BSC should be avoided during aseptic manipulations.
 - e. Syringes and intravenous sets with Luer-lock type fittings should be used for preparing and administering hazardous drug solutions, since they are less prone to accidental separation than friction fittings. Care must be taken to ensure that all connections are secure. Syringes should be large enough so that they are not full when containing the total drug dose. This is to ensure that the plunger does not separate from the syringe barrel. Doses should be dispensed in several syringes when this problem arises.
 - f. The contents of an ampul should be gently tapped down from the neck and top portion of the ampul before it is opened. The ampul should be wiped with alcohol before being opened. A sterile gauze pad should be wrapped around the neck of the ampul when it is opened.
 - g. Substantial positive or negative deviations from atmospheric pressure within drug vials and syringes should be avoided.
 - h. For additional worker protection, equipment such as venting devices with 0.2- μm hydrophobic filters and 5- μm filter needles or “straws” may be used. It is critical that the worker be proficient with these devices before using them with hazardous drugs. Improper use of these devices may result in increased, rather than decreased, risk of exposure.
 - i. Final products should be dispensed in ready-to-administer form. If possible, intravenous administration sets should be attached to the bag or bottle in the BSC and primed with plain fluid before the hazardous drug is added. However, if total volume is a concern, intravenous sets may be primed with diluted drug solution, which is discarded into an appropriate container within the BSC. Potential disadvantages to this approach include difficulty in selecting the appropriate administration set when several methods of administering hazardous drugs exist, potential contamination of the outside of the intravenous set, and the risk of the intravenous set becoming dislodged from the bag or bottle during transport.
 - j. The outside of bags or bottles and intravenous sets (if used) should be wiped with moist gauze to remove any inadvertent contamination. Entry ports should be wiped with sterile, alcohol-dampened gauze pads and covered with appropriate seals or caps.
 - k. Final products should be placed in sealable containers (e.g., zipper-closure plastic bags) to reduce the risk of exposing ancillary personnel or contaminating the environment. Containers should be designed such that damage incurred during storage or transport is immediately visible and any leakage is fully contained. For offsite transport, appropriate storage conditions

- (e.g., refrigerated, padded, and locked carriers) should also be used.
- l. Excess drug should be returned to the drug vial whenever possible or discarded into a closed container (empty sterile vial). Placing excess drug in any type of open container, even while working in the BSC, is inappropriate. Discarding excess drug into the drainage trough of the BSC is also inappropriate. These practices unnecessarily increase the risk of exposure to large amounts of hazardous drug.
 - m. All contaminated materials should be placed in leakproof, puncture-resistant containers within the contained environment of the BSC and then placed in larger containers outside the BSC for disposal. To minimize aerosolization, needles should be discarded in puncture-resistant containers without being clipped.
8. *Procedures for the preparation and dispensing of noninjectable dosage forms of hazardous drugs are established and followed.*
- a. Although noninjectable dosage forms of hazardous drugs contain varying proportions of drug to nondrug (nonhazardous) components, there is potential for personnel exposure and environmental contamination with the hazardous components. Procedures should be developed to avoid the release of aerosolized powder or liquid into the environment during manipulation of these drugs.
 - b. Drugs designated as hazardous should be labeled or otherwise identified as such to prevent their improper handling.
 - c. Tablet and capsule forms of these drugs should not be placed in automated counting machines, which subject them to stress and may introduce powdered contaminants into the work area.
 - d. During *routine handling* of hazardous drugs and contaminated equipment, workers should wear one pair of gloves of good quality and thickness.
 - e. The counting and pouring of hazardous drugs should be done carefully, and clean equipment dedicated for use with these drugs should be used. Contaminated equipment should be cleaned initially with water-saturated gauze and then further cleaned with detergent and rinsed. The gauze and rinse should be disposed of as contaminated waste.
 - f. During *compounding* of hazardous drugs (e.g., crushing, dissolving, and preparing an ointment), workers should wear low-permeability gowns and double gloves. Compounding should take place in a protective area such as a disposable glove box. If compounding must be done in the open, an area away from drafts and traffic must be selected, and the worker should use appropriate respiratory protection.
 - g. When hazardous drug tablets in unit-of-use packaging are being crushed, the package should be placed in a small sealable plastic bag and crushed with a spoon or pestle; caution should be used not to break the plastic bag.
 - h. Disposal of unused or unusable oral or topical dosage forms of hazardous drugs should be performed in the same manner as for hazardous injectable dosage forms and waste.
9. *Personnel know the procedures to be followed in case of accidental skin or eye contact with hazardous drugs.*
- a. Each health-care setting should have an established first aid protocol for treating cases of direct contact with hazardous drugs, many of which are irritating or caustic and can cause tissue destruction. Medical care providers in each setting should be contacted for input into this protocol. The protocol should include immediate treatment measures and should specify the type and location of medical followup and work-injury reporting. Copies of the protocol, highlighting emergency measures, should be posted wherever hazardous drugs are routinely handled.
 - b. Hazardous drug work areas should have a sink (preferably with an eyewash fountain) and appropriate first aid equipment to treat accidental skin or eye contact according to the protocol.
 - c. In settings where hazardous drug handlers are offsite (e.g., home use), protocols must be part of orientation programs, and copies of the procedures should be immediately accessible to handlers, along with appropriate first aid equipment and emergency phone numbers to call for followup and reporting.
10. *All hazardous drugs are labeled with a warning label stating the need for special handling.*
- a. A distinctive warning label with an appropriate CAUTION statement should be attached to all hazardous drug materials, consistent with state laws and regulations. This would include, for example, syringes, intravenous containers, containers of unit-dose tablets and liquids, prescription vials and bottles, waste containers, and patient specimens that contain hazardous drugs.
 - b. The hazardous drugs discussed in this Technical Assistance Bulletin are chemical hazards and *not* infectious hazards. Because the term “biohazard” refers to an infectious hazard, the use of this term or the biohazard symbol (in any variation) on the label of drugs that are chemical hazards is inappropriate and may be misleading to staff and contract workers who are familiar with the biohazard symbol. An example of a suitable label is shown in Figure 1.
 - c. All staff and contract workers should be informed about the meaning of the label and the special handling procedures that have been established.
 - d. In settings where patients or their families will be responsible for manipulating these drugs, they should be made aware of the need for special handling and the reasons behind it.
- Goal III. Procedures for administering hazardous drugs prevent the accidental exposure of patients and staff and contamination of the work environment.**
1. *A method for informing and training health-care professionals in these procedures is maintained.*
 - a. Only individuals trained to administer hazardous drugs should be allowed to perform this function. Training programs should contain information on the therapeutic and adverse effects of these

drugs and the potential, long-term health risk to personnel handling them. Each individual's knowledge and technique should be evaluated before administration of these drugs. This should be done by written examination and direct observation of the individual's performance.

2. *Standard procedures for the safe administration of hazardous drugs are established and followed.* These procedures ensure the safety of both the patient and health-care personnel.

- a. Intravenous administration sets (e.g., vented, nonvented, and minidrip) and infusion devices appropriate for use with the final product should be selected.
- b. Syringes and intravenous sets with Luer-lock fittings should be used whenever possible.
- c. Preparation of the final product for administration should take place in a clean, uncluttered area separate from other activities and excessive traffic. A plastic-backed absorbent liner should be used to cover the work area to absorb accidental spills. A single pair of disposable latex gloves and a disposable gown should be worn. The glove and gown cuffs should be worn in a manner that produces a tight fit (e.g., loose glove tucked under gown cuff; tight glove fitted over gown cuff). Hands must be thoroughly washed before gloves are donned.

Administration sets should be attached with care (if not attached during drug preparation). Administration sets and devices should be monitored for leakage.

- d. Priming of intravenous sets should not allow any drug to be released into the environment. Hazardous drug solutions may be "piggybacked" into primary intravenous solutions and primed by retrograde flow of the primary solution into the secondary tubing. All Y-site connections should be taped securely. Alternatively, the intravenous set may be primed with plain solution before the hazardous drug solution bag or bottle is connected. Some intravenous sets can be primed so that the fluid enters the medication port of the intravenous bag. The priming fluid may also be discarded into a sealable plastic bag containing absorbent material if care is taken not to contaminate the sterile needle tip. Likewise, a sterile gauze pad should be placed close to the sterile needle tip when air is expelled from a syringe. The syringe plunger should first be drawn back to withdraw liquid from the needle before air is expelled. Care should be taken not to contaminate the sterile needle with gauze fibers or microorganisms.
- e. Intravenous containers designed with venting tubes should not be used. If such containers must be used, gauze should be placed over the tube when the container is inverted to catch any hazardous drug solution trapped in the tube. If containers with solid stoppers are used, any vacuum present should be eliminated before the container is attached to a primary intravenous or to a manifold. If a series of bags or bottles is used to deliver the drug, the intravenous set should be discarded with each container because removing

the spike from the container is associated with a greater risk of environmental contamination than priming an intravenous set. (Use of secondary sets for administration of hazardous drugs reduces the cost of this recommendation and the risk of priming.)

- f. A plastic-backed absorbent liner should be placed under the intravenous tubing during administration to absorb any leakage and prevent the solution from spilling onto the patient's skin. The use of sterile gauze around any "push" sites will reduce the likelihood of releasing drug into the environment.
 - g. The use of eye protection (safety glasses or goggles) during work with hazardous drugs, especially vesicants, should be considered. Work at your waist level, if possible; avoid working above the head or reaching up for connections or ports.
 - h. All contaminated gauze, syringes, intravenous sets, bags, bottles, etc., should be placed in sealable plastic bags and placed in a puncture-resistant container for removal from the patient-care area.
 - i. Gloves should be discarded after each use and immediately if contaminated. Gowns should be discarded on leaving the patient-care area and immediately if contaminated. Hands must be washed thoroughly after hazardous drugs are handled.
 - j. Gloves should be worn when urine and other excreta from patients receiving hazardous drugs are being handled. Skin contact and splattering should be avoided during disposal. While it may be useful to post a list of drugs that are excreted in urine and feces and the length of time after drug administration during which precautions are necessary, an alternative is to select a standard duration (e.g., 48 hours) that covers most of the drugs and is more easily remembered.
 - k. Disposable linen or protective pads should be used for incontinent or vomiting patients. Nondisposable linen contaminated with hazardous drug should be handled with gloves and treated similarly to that for linen contaminated with infectious material. One procedure is to place the linen in specially marked water-soluble laundry bags. These bags (with the contents) should be prewashed; then the linens should be added to other laundry for an additional wash. Items contaminated with hazardous drugs should not be autoclaved unless they are also contaminated with infectious material.
3. *Appropriate apparel and materials needed to protect staff and patients from exposure and to protect the work environment from contamination are readily available.* Supplies of disposable gloves and gowns, safety glasses, disposable plastic-backed absorbent liners, gauze pads, hazardous waste disposal bags, hazardous drug warning labels, and puncture-resistant containers for disposal of needles and ampuls should be conveniently located for all areas where hazardous drugs are handled. Assembling a "hazardous drug preparation and administration kit" is one way to furnish nursing and medical personnel with the mate-

rials needed to reduce the risk of preparing and administering a hazardous drug.

4. *Personnel know the procedures to be followed in case of accidental skin or eye contact with hazardous drugs. (See Goal II9.)*

Goal IV. The health-care setting, its staff, patients, contract workers, visitors, and the outside environment are not exposed to or contaminated with hazardous drug waste materials produced in the course of using these drugs. (See Figure 2 for proposed flow chart for handling contaminated items.)

1. *Written policies and procedures governing the identification, containment, collection, segregation, and disposal of hazardous drug waste materials are established and maintained. All health-care workers who handle hazardous drugs or waste must be oriented to and must follow these procedures.*
2. *Throughout institutional health-care facilities and in alternative health-care settings, hazardous drug waste materials are identified, contained, and segregated from all other trash.*
 - a. Hazardous drug waste should be placed in specially marked (specifically labeled CAUTION: HAZARDOUS CHEMICAL WASTE) thick plastic bags or leakproof containers. These receptacles should be kept in all areas where the drugs are commonly used. All and only hazardous drug waste should be placed in them. Receptacles used for glass fragments, needles, and syringes should be puncture resistant. Hazardous drug waste should not be mixed with any other waste. Waste containers should be handled with uncontaminated gloves.
 - b. Health-care personnel providing care in a patient's home should have with them all the equipment and supplies necessary to contain properly any hazardous drug waste that is generated during the visit. Contaminated needles and syringes, intravenous containers, intravenous sets, and any

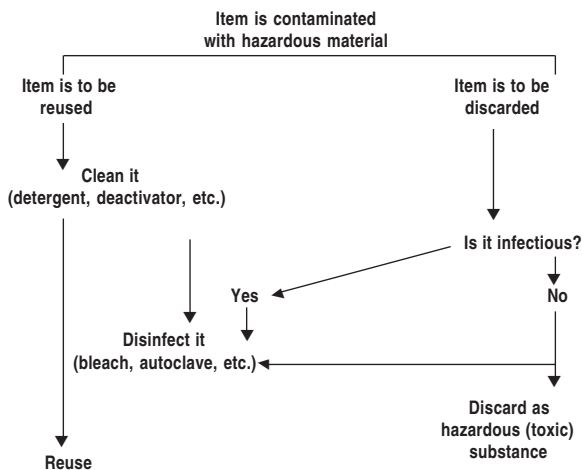


Figure 2. Proposed flow chart for handling chemical hazards versus biohazards. Disinfection of a disposable item contaminated with both infectious and hazardous material may not be necessary, depending on the degree of infectious hazard (e.g., human immunodeficiency virus versus *Escherichia coli*) and depending on the method of disposal (e.g., burial versus incineration).

broken ampuls should be placed in leakproof, puncture-resistant containers. Gloves, gowns, drug vials, etc., should be sealed in specially labeled (CAUTION: HAZARDOUS CHEMICAL WASTE) thick plastic bags or leakproof containers. All waste should be removed from the patient's home and transported to a designated area. Additional precautions should be taken during transport, including temporary storage in a spill-resistant container and ensuring that the vehicle is locked at all times. Hazardous waste should be securely stored at a designated area until it is picked up for appropriate disposal. Patients or their caregivers should be instructed on methods for the proper handling of excreta from patients receiving hazardous drugs.

- c. Unless restricted by state or local regulations, hazardous drug waste may be further divided into trace and bulk-contaminated waste, if desired, to reduce costs of disposal. As defined by the EPA, bulk-contaminated materials are solutions or containers whose contents weigh more than 3% of the capacity of the container.^{57,58} For example, empty intravenous containers and intravenous administration sets usually are considered trace waste; half-empty vials of hazardous drugs and unused final doses in syringes or intravenous containers are considered bulk-contaminated waste. If trace and bulk-contaminated waste are handled separately, bulk-contaminated waste should be segregated into more secure receptacles for containment and disposal as toxic waste. While this may allow for less expensive overall disposal of hazardous waste, it also requires close monitoring of the containment and segregation process to prevent the accidental discarding of a bulk-contaminated container into a trace-waste receptacle.
- d. All hazardous waste collected from drug preparation and patient-care areas should be held in a secure place in labeled, leakproof drums or cartons (as required by state or local regulation or disposal contractor) until disposal. This waste should be disposed of as hazardous or toxic waste in an EPA-permitted, state-licensed hazardous waste incinerator. Transport to an offsite incinerator should be done by a contractor licensed to handle and transport hazardous waste. (While licenses are generally required to transport infectious waste as well as hazardous waste, these are different classes of contractors and may not be interchangeable. Verification of possession and type of license should be documented before a contractor is engaged.)
- e. If access to an appropriately licensed incinerator is not available, transport to and burial in an EPA-licensed hazardous waste dump site is an acceptable alternative. While there are concerns that destruction of carcinogens by incineration may be incomplete, newer technologies and stringent licensing criteria have improved this disposal method. (Again, the existence and type of license should be verified before use of a contract incinerator.)
- f. Chemical deactivation of hazardous drugs should

- be undertaken only by individuals who are thoroughly familiar with the chemicals and the procedures required to complete such a task. The IARC recently published a monograph describing methods for chemical destruction of some cytotoxic (antineoplastic) drugs in the laboratory setting.⁵⁹ The chemicals and equipment described, however, are not generally found in the clinical setting, and many of the deactivating chemicals are toxic and hazardous. Most procedures require the use of a chemical fume hood. The procedures are generally difficult, and the deactivation is not always complete. Serious consideration should be given to the negative aspects of chemical deactivation before one commits to such a course of action.
3. *Materials to clean up spills of hazardous drugs are readily available and personnel are trained in their proper use.* A standard cleanup protocol is established and followed.
 - a. “Spill kits” containing all materials needed to clean up spills of hazardous drugs should be assembled or purchased. These kits should be readily available in all areas where hazardous drugs are routinely handled. If hazardous drugs are being prepared or administered in a nonroutine area (home setting or unusual patient-care area), a spill kit should be obtained by the drug handler. The kit should include two pairs of disposable gloves (one outer pair of utility gloves and one inner latex pair); low permeability, disposable protective garments (coveralls or gown and shoe covers); safety glasses or splash goggles; respirator; absorbent, plastic-backed sheets or spill pads; disposable toweling; at least two sealable thick plastic hazardous waste disposal bags (prelabeled with an appropriate warning label); a disposable scoop for collecting glass fragments; and a puncture-resistant container for glass fragments.
 - b. All individuals who routinely handle hazardous drugs must be trained in proper spill management and cleanup procedures. Spills and breakages must be cleaned up immediately according to the following procedures. If the spill is not located in a confined space, the spill area should be identified and other people should be prevented from approaching and spreading the contamination. Wearing protective apparel from the spill kit, workers should remove any broken glass fragments and place them in the puncture-resistant container. Liquids should be absorbed with a spill pad; powder should be removed with damp disposable gauze pads or soft toweling. The hazardous material should be completely removed and the area rinsed with water and then cleaned with detergent. The spill cleanup should proceed progressively from areas of lesser to greater contamination. The detergent should be thoroughly rinsed and removed. All contaminated materials should be placed in the disposal bags provided and sealed and transported to a designated containment receptacle.
 - c. Spills occurring in the BSC should be cleaned up immediately; a spill kit should be used if the volume exceeds 150 ml or the contents of one drug vial or ampul. If there is broken glass, utility gloves should be worn to remove it and place it in the puncture-resistant container located in the BSC. The BSC, including the drain spillage trough, should be thoroughly cleaned. If the spill is not easily and thoroughly contained, the BSC should be decontaminated after cleanup. If the spill contaminates the HEPA filter, use of the BSC should be suspended until the cabinet has been decontaminated and the HEPA filter replaced. (See Goal II 5j.)
 - d. If hazardous drugs are routinely prepared or administered in carpeted areas, special equipment is necessary to remove the spill. Absorbent powder should be substituted for pads or sheets and left in place on the spill for the time recommended by the manufacturer. The powder should then be picked up with a small vacuum unit reserved for hazardous drug cleanup. The carpet should then be cleaned according to usual procedures. The vacuum bag should be removed and discarded or cleaned, and the exterior of the vacuum cleaner should be washed with detergent and rinsed before being covered and stored. The contaminated powder should be discarded into a sealable plastic bag and segregated with other contaminated waste materials. Alternatively, inexpensive wet or dry vacuum units may be purchased for this express use and used with appropriate cleaners. All such units are contaminated, once used, and must be cleaned, stored, and ultimately discarded appropriately (i.e., like BSCs).
 - e. The circumstances and handling of spills should be documented. Health-care personnel exposed during spill management should also complete an incident report or exposure form.
 4. *Hazardous drug waste is disposed of in accordance with all applicable state, federal, and local regulations for the handling of hazardous and toxic waste.*
 - a. Regulatory agencies such as the EPA and state solid and hazardous waste agencies and local air and water quality control boards must be consulted regarding the classification and appropriate disposal of drugs that are defined as hazardous or toxic chemicals. EPA categorizes several of the antineoplastic agents (including cyclophosphamide and daunorubicin) as toxic wastes, while many states are more stringent and include as carcinogens certain cytotoxic drugs (azathioprine) and hormonal preparations (diethylstilbestrol and conjugated estrogens). EPA also allows exemptions from toxic waste regulations for “small quantity generators,”⁵⁷ whereas certain states do not. It is critical to research these regulations when disposal procedures are being established.

Other Hazardous Drug Issues

The handling of hazardous drugs, some of which are defined by the EPA as toxic chemicals, has implications that go beyond the health-care setting. Disposal of hazardous materials and toxic chemicals continues to be a controversial issue of which the disposal of hazardous drugs is but a small part. The EPA currently issues permits for both burial and

incineration of hazardous waste. Some such facilities may purport to possess permits to handle these types of hazardous agents when, in fact, they do not meet the requirements or are only in the initial stages of obtaining permits. It is imperative that health-care facilities verify the license or permit status of any contractor used to remove or dispose of infectious or hazardous waste. In addition, many hazardous drugs are excreted unchanged or as equally toxic metabolites. The amount of hazardous drug transferred to the environment (primarily through the water supply) from this source may exceed that resulting from the hospital trash pathway. No good methods for reducing this source of contamination are currently known.

Definitive risks of handling these drugs may never be fully determined without epidemiologic data from a national registry of handlers of hazardous drugs (and chemicals). There is no method available for routine monitoring of personnel for evidence of hazardous drug exposure. Tests for the presence of mutagens or chromosomal damage are not drug specific and are of value only in controlled studies. Chemical analysis of urine for the presence of hazardous drugs at the sensitivity level needed to detect occupational exposure is limited to a few drugs and is not yet commercially available.

This document is designed to identify areas of risk in the handling of hazardous drugs and to provide recommendations for reducing that risk. A safety program should be coupled with a strong quality-assurance program that periodically evaluates and verifies staff adherence to and performance of the established safe handling policies and procedures. Until some type of external monitoring of exposure levels from handling hazardous drugs is commercially available, development of and compliance with a safety program remain the most logical means for minimizing occupational risk.

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Appendix A—Glossary

- Biohazard:** An infectious agent presenting a real or potential risk to humans and the environment.
- Carcinogen:** Any cancer-producing substance.
- Chemotherapy:** The treatment of disease by chemical means; first applied to use of chemicals that affect the causative organism unfavorably but do not harm the patient; currently used to describe drug (chemical) therapy of neoplastic diseases (cancer).
- Clastogenic:** Giving rise to or inducing disruption or breakage, as of chromosomes.
- Contamination:** The deposition of potentially dangerous material where it is not desired, particularly where its presence may be harmful or constitute a hazard.
- Cytotoxic:** Possessing a specific destructive action on certain cells; used commonly in referring to antineoplastic drugs that selectively kill dividing cells.
- Decontamination:** Removal, neutralization, or destruction of a toxic (harmful) agent.
- Exposure:** The condition of being subjected to something, as to chemicals, that may have a harmful effect. Acute exposure is exposure of short duration, usually exposure of heavy intensity; chronic exposure is long-term exposure, either continuous or intermittent, usually referring to exposure of low intensity.
- Genotoxic:** Damaging to DNA; pertaining to agents (radiation or chemical substances) known to damage DNA, thereby causing mutations or cancer.
- Hazardous:** Dangerous; risky; representing a health risk.
- Mutagen:** Chemical or physical agent that induces or increases genetic mutations by causing changes in DNA.
- Plenum:** Space within a biohazard cabinet where air flows;

plenums may either be under positive (greater than atmospheric pressure) or negative pressure, depending on whether the air is “blown” or “sucked” through the space.

Respirator: A National Institute of Occupational Safety and Health (NIOSH) approved, air-purifying half-mask respirator equipped with a high-efficiency filter; may be disposable (discarded after the end of its recommended period of use).

Trough: Drain spillage trough; an area below the biological safety cabinet’s work surface, provided to retain spillage from the work area.

Utility Gloves: Heavy, disposable gloves, similar to household latex gloves.

Appendix B—Classification of Biohazard Cabinetry (Biological Safety Cabinets)⁴³

Class I: A ventilated cabinet for personnel and environmental protection, with an unrecirculated inward airflow away from the operator.

Note: The cabinet exhaust air is treated to protect the environment before it is discharged to the outside atmosphere. This cabinet is suitable for work with low- and moderate-risk biological agents when no product protection is required.

Class II: A ventilated cabinet for personnel, product, and environmental protection, having an open front with inward airflow for personnel protection, high-efficiency particulate air (HEPA) filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection.

Note: When toxic chemicals or radionuclides are used as adjuncts to biological studies or pharmaceutical work, Class II cabinets designed and constructed for this purpose should be used.

- **Type A (formerly designated Type 1):** Cabinets that (1) maintain minimum calculated average inflow velocity of 75 feet per minute (fpm) through the work area access opening; (2) have HEPA-filtered downflow air from a common plenum (i.e., plenum from which a portion of the air is exhausted from the cabinet and the remainder is supplied to the work area); (3) may exhaust HEPA-filtered air back into the laboratory; and (4) may have positive-pressure-contaminated ducts and plenums. Type A cabinets are suitable for work with low- to moderate-risk biological agents in the absence of volatile toxic chemicals and volatile radionuclides.
- **Type B1 (formerly designated Type 2):** Cabinets that (1) maintain a minimum (calculated or measured) average inflow velocity of 100 fpm through the work area access opening; (2) have HEPA-filtered downflow air composed largely of uncontaminated recirculated inflow air; (3) exhaust most of the contaminated downflow air through a dedicated duct exhausted to the atmosphere after it passes through a HEPA filter; and (4) have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. Type B1 cabinets are suitable for work with low- to moderate-risk biological agents. They may also be used with biological agents treated with minute quantities of toxic chemicals and trace amounts of radionuclides required as an adjunct to microbiological studies if work is done in the directly exhausted portion of the cabinet or if the chemicals or radionuclides will not interfere with the work when recirculated in the downflow air.

- **Type B2 (sometimes referred to as “total exhaust”):** Cabinets that (1) maintain a minimum (calculated or measured) average inflow velocity of 100 fpm through the work area access opening; (2) have HEPA-filtered downflow air drawn from the laboratory or the outside air (i.e., downflow air is not recirculated from the cabinet exhaust air); (3) exhaust all inflow and down-flow air to the atmosphere after filtration through a HEPA filter without recirculation in the cabinet or return to the laboratory room air; and (4) have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted (nonrecirculated through the work area) negative-pressure ducts and plenums. Type B2 cabinets are suitable for work with low- to moderate-risk biological agents. They may also be used with biological agents treated with toxic chemicals and radionuclides required as an adjunct to microbiological studies.
- **Type B3 (sometimes referred to as “convertible cabinets”):** Cabinets that (1) maintain a minimum (calculated or measured) average inflow velocity of 100 fpm through the work area access opening; (2) have HEPA-filtered downflow air that is a portion of the mixed downflow and inflow air from a common exhaust plenum; (3) discharge all exhaust air to the outdoor atmosphere after HEPA filtration; and (4) have all biologically contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. Type B3 cabinets are suitable for work with low- to moderate-risk biological agents treated with minute quantities of toxic chemicals and trace quantities of radionuclides that will not interfere with the work if recirculated in the downflow air.
- **Other Types:** Other cabinets may be considered Class II if they meet these requirements for performance, durability, reliability, safety, operational integrity, and cleanability.

Class III: A totally enclosed, ventilated cabinet of gas-tight construction. Operations in the cabinet are conducted through attached rubber gloves. The cabinet is maintained under negative air pressure of at least 0.5 inch (12.7 mm) water gauge (wg). 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.

This Technical Assistance Bulletin was reviewed in 1996 by the Council on Professional Affairs and by the ASHP Board of Directors and was found to still be appropriate.

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