

# Pharmacy Purchasing & Products

Product News for Pharmacy Services, Purchasing, and IT

January 2007  
Vol.4 No.1  
www.pppmag.com



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www.pppmag.com

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NIOSH

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## Best Practices for the Handling of Hazardous Drugs

OVER THE PAST SEVERAL YEARS THE ISSUE OF THE SAFE handling of hazardous medications has received increasing interest among health care professionals. This article will describe a “best practice” approach to assist you in creating a system that protects both patients and health care workers. USP Chapter <797>, the National Institute for Occupational Safety and Health (NIOSH) hazardous drug alert, and the European Quality Standards for Oncology Pharmacy Services, as well as personal and professional observations, form the foundation for these best practice suggestions.<sup>1,4</sup> These recommendations are not intended to be all-encompassing, but they have been selected to address some of the most visible and important aspects of oncology practice.

**Environment:** Careful consideration should be given to the overall design of IV sterile product preparation areas for the compounding of hazardous medications. While the NIOSH alert represents guidelines only, it seems clear that the expected revisions for USP Chapter <797> will include elements of the NIOSH alert. When considering building a new facility or upgrading an existing facility, a prudent suggestion would include “over-engineering” the project against current standards. The European Standards, which have been in practice for four years, as well as the proposed <797> revisions, provide a good model upon which to build.

A best practice environment should include a separate cleanroom area for compounding hazardous medications. This area should meet all of the standards specified by the International Standards



Photo courtesy of Carmel Pharma, Inc.

The deployment of closed system drug transfer devices, like Carmel Pharma's PhaSeal (pictured here) provides an additional layer of worker protection.

Organization (ISO) for ISO Class 7 quality air.<sup>5,7</sup> In addition, to prevent the escape of hazardous medication into the workplace, this area should be negative pressure, preferably 0.01 inch water column or

greater, when compared with surrounding areas. This area should also be 100% vented to the outside. The anteroom feeding this area should also be ISO 7 air quality, as opposed to the expected ISO 8, since the hazardous medication preparation cleanroom is negative pressure, and the air quality being drawn into the room should be equivalent to the actual room air quality. The ideal design would be a facility that provides a common ISO 7 anteroom that feeds into both a negative pressure ISO 7 cleanroom for hazardous medications, as well as an ISO 7 positive pressure cleanroom for non-hazardous medications. Construction of a traditional hardwall facility may present significant facility design challenges, as well as significant expense. With many organizations facing difficult decisions in allocating limited capital dollars, a modular cleanroom design may provide a less costly opportunity to achieve a best practice environment.

**Equipment:** When compounding IV sterile preparations containing hazardous medications, an appropriate biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI) should be utilized. The BSC or isolator must be capable of maintaining an ISO 5 air quality environment under normal operating conditions and should be 100% vented to the outside.<sup>8</sup> This contaminated air exhaust vent should be situated at least 12 feet from ground level and should not be in close proximity to any doors, windows, or air-intake vents. When evaluating BSCs, it is important to understand the differences between Class I, Class II, and Class III units. Class I units are essentially fume hoods that protect the operator, but do not ensure asepsis. They have an open front with a minimum air flow velocity of 75 feet per min and HEPA-exhausted air. Class I BSCs are not acceptable for aseptic compounding. Class II BSCs protect personnel, as well as the product and environment. Class II BSCs have an open front, inward air flow with downward HEPA-filtered laminar flow, and HEPA-filtered exhaust. Class II units include four different types of BSCs: A1, A2, B1, and B2 units. Type A1 units produce a minimum inflow air velocity of 75 feet per minute; down flow is mixed with inflow; exhaust may be into the surrounding environment; and contaminated ducts are not surrounded by negative pressure. Type A2 differs from A1 with an inflow velocity of 100 feet per minute and negative pressure surrounding the plenums. Type B1 units have an inflow air velocity of 100 feet per minute; the down flow is uncontaminated re-circulated inflow; contaminated down flow is exhausted through a dedicated duct with HEPA filtration to the atmosphere; and all contaminated ducts are under negative pressure. Type B2 units differ from B1, with down flow drawn from external air and exhausted to the atmosphere without recirculation. Class III BSCs are completely contained units of gas-tight construction. Operation of the unit is conducted through attached rubber gloves and viewed through a non-opening window. The unit is maintained under negative pressure; intake air is HEPA filtered; and exhaust air is double HEPA-filtered or HEPA-filtered and incinerated. Class III BSCs are essentially isolators. A best practice recommendation for BSC use would be a Class II, type B2 unit.

As with BSCs, it is important to select an isolator that best meets the needs of hazardous medication preparation.<sup>9</sup> There are numerous differences between isolators, including positive versus negative pressure, air flow dynamics (turbulent flow versus unidirectional), aseptic versus containment, and recirculation of air versus complete venting to the outside. Ideally, for hazardous medication preparation, a CACI with unidirectional air flow that is 100% vented to the outside should be utilized. For maximum safety, this unit should be situated in the ISO 7 negative pressure cleanroom reserved for hazardous medication

preparation. If this is not possible, at a minimum, it should be situated in a separate negative pressure room capable of at least 12 air exchanges per hour.

The deployment of closed system drug transfer devices (CSDTD) provides an additional layer of worker protection. These systems are designed to prevent the release of hazardous medications into the environment. Ideally, CSDTDs should be combined with a negative pressure cleanroom and a BSC or CACI. When considering CSDTDs, it is important to review the NIOSH definition of a closed system drug transfer device: “a mechanically closed system that prevents contamination of the drug product and prevents the escape of drug or drug vapors”.<sup>3</sup> This is a critical statement, since several commonly used drugs form volatile gas at normal conditions of room temperature and pressure. HEPA filtration or a 0.22-micron filter in a transfer device will not trap these gases. When evaluating CSDTDs, it is imperative to select a system that protects health care workers in all phases of the process, from initial vial entry to patient administration.

**Personal Protective Equipment:** The deployment of personal protective equipment (PPE) is a “last line of defense” for personnel engaged in handling hazardous medications. PPE should consist, at a minimum, of a polyethylene-coated gown with a solid front and closures in the back and with knitted, tight-fitting wrist cuffs. Eye protection should consist of a face shield or goggles that prevent spills or splashes from reaching the eyes. Gloves may be made from a variety of substances, but any gloves utilized for manipulation of hazardous medications should be certified and labeled as “chemotherapy gloves.” When working with hazardous medications, it is always advisable to practice “double gloving.”

**Personnel:** Given health care’s current focus on patient safety, the importance of best practices in oncology cannot be underestimated. Cytotoxic drugs have a narrow therapeutic index and their normal therapeutic effects cause toxicity. The pharmacology of these drugs can cause serious adverse events at standard dosages, which require cautious monitoring to prevent toxicity. Excessive dosing or cumulative cycle doses can have devastating outcomes for patients. These required drugs are often used in combination, which makes monitoring even more complex. Such complex systems are very vulnerable to medication errors. The physician, nurse, pharmacist, pharmacy technician, and other health care professionals must develop consistent policies and procedures, design multiple checkpoints within complex systems, ensure protocol integrity, factor in inpatient specific therapy, and maintain quality controls to assure patient safety.

Pharmacists, pharmacy technicians, physicians, and nurses must be certified or receive competency-based training in oncology. Nurses should be encouraged to complete the Oncology Nursing Society Certification program ([www.ons.org](http://www.ons.org)), while pharmacists should be encouraged to complete the Board of Pharmaceutical Specialty certification in oncology ([www.bpsweb.org](http://www.bpsweb.org)). Health care organizations should develop competency programs that test the employee’s ability to effectively understand all oncology policies and procedures. Competency programs should include didactic training that addresses medication order entry, reference sources, and reviewing problem orders and complex protocols. A written examination should verify didactic competency. ASHP has developed two resources, both available through ASHP ([www.ashp.org](http://www.ashp.org)) to help prepare pharmacy technicians and pharmacists in competency training: “Basics of

Aseptic Compounding Technique” and “Safe Handling of Hazardous Drugs.”

A book of uniform labeling for standardized chemotherapy preparations can serve as a valuable reference when pharmacists are entering chemotherapy for similar protocols. Administrators of the chemotherapy program should continually update participants with new information regarding medications or changes in practice. The success of an oncology practice setting is dependant on a collaborative approach between all disciplines. Representatives from each discipline (physicians, nurses, pharmacy, environmental health, house-keeping, and safety) should be involved in developing policies and procedures. Key programmatic policies should include the safe handling of hazardous drugs, antineoplastic medication ordering, extravasation of chemotherapeutic agents, and medical surveillance. These policies should establish safe standards for the preparation, dispensing, transport, administration, and disposal of hazardous drugs.

Chemotherapy medication ordering should be limited to attending physicians, but may include oncology fellows, nurse practitioners, clinical pharmacists, or physician assistants (physician extenders). If any of these individuals are involved in chemotherapy ordering, their chemotherapy orders should always be co-signed by an attending physician before being considered valid orders. The chemotherapy pharmacist should help instruct fellows, interns, and residents on appropriate medication order writing during orientation to the oncology service. The pharmacist should review all chemotherapy orders prior to processing.

The primary duties of this pharmacist are:

- ▶ verification of chemotherapy protocols
- ▶ supportive therapy recommendations
- ▶ dose verification
- ▶ entering chemotherapy orders into the pharmacy information system
- ▶ patient outcome monitoring, and
- ▶ documentation in the patient medical record.

The pharmacist should verify all pertinent patient-specific information prior to processing chemotherapy. A second chemotherapy-certified pharmacist should also review the chemotherapy orders, patient laboratory parameters, verify doses, order entry, and final product preparation. If the pharmacist has any questions about protocol selection, doses, and/or treatment day, the pharmacist should contact the physician for clarification before proceeding with the chemotherapy. The pharmacist may request from the physician further documentation to support the regimen selected. The pharmacist should coordinate the administration of chemotherapy with the nurse and determine what type of venous access is available for that patient. The pharmacist and other health care professionals should always utilize two identifiers for the patient, such as name and date of birth.

The patient’s age, height, weight, and body surface area should be verified prior to processing chemotherapy orders and anytime there is greater than a 5% difference from the first treatment. Renal function should be evaluated with a chemistry panel and a calculated creatinine clearance. Total bilirubin, PT, PTT, total protein, and liver enzymes should be evaluated as indicators of liver function. Below-normal albumin may require a downward adjustment in creatinine clearance to compensate for compromised nutritional status. Finally, a complete blood count with absolute neutrophil count should be evaluated prior to each treatment cycle. An absolute neutrophil count greater than 1500 cell/mm<sup>3</sup> and a platelet count greater than 100 cell/mm<sup>3</sup> will be necessary for treatment. The patient’s age, prior

chemotherapy treatment, performance status, disease, and goals of therapy must be considered before a final dosing regimen is selected. When the goal of therapy is a cure, doses and schedules should be maintained at a minimum of 85% of optimal to provide the highest probability of success. Patient specific factors such as age, performance status, tolerability, and toxicity to treatment must be considered when adjusting treatment.

In general, the pharmacist should be responsible for the cognitive functions related to patient care. The pharmacy technician is instrumental in the compounding of chemotherapy. A pharmacy technician should prepare chemotherapy, thereby freeing the pharmacist to perform clinical duties. As previously noted, the pharmacy technician involved in hazardous medication preparation should be certified as competent to perform these duties. Competency should be verified by a written test, by media-fill testing to verify aseptic technique, by observation of simulated chemotherapy preparation utilizing fluorescein dye as a surrogate marker for chemotherapy, and by observation of compounding technique during normal working conditions. Competency should be verified for all new technicians and at least annually for all currently certified technicians.

**Medical Surveillance:** All employees that regularly come into contact with hazardous medications should be part of an organized medical surveillance program. This should include a baseline examination on hire or on assignment to an area that requires routine handling of hazardous medications. A follow-up examination should also be conducted annually or, at a minimum, every two years or after any incidence of acute exposure. Examinations should include a health assessment focused on systems that may indicate evidence of chemotherapy exposure, such as skin, hair, mucous membranes, and lymph system. In addition, selected laboratory tests, which may include a urinalysis, complete blood count with differential, and a comprehensive metabolic panel, should be conducted.

**Cleaning and Decontamination:** Many studies have documented chemotherapy surface contamination in preparation and administration work areas.<sup>10</sup> These areas, which include work surfaces, must be decontaminated and cleaned on a periodic basis, or workers will continue to be exposed to hazardous medications. A best practice recommendation is to clean and decontaminate work surfaces before and after each activity and at the end of each shift. The following is a good decontamination sequence: a cationic soap solution, followed by a dilute sodium hypochlorite solution, followed by an inactivating agent such as sodium thiosulfate (to prevent discoloration of stainless steel). In addition, it has been demonstrated that many chemotherapy vials come directly from the manufacturer with surface contamination present on the vial.<sup>11,12</sup> All chemotherapy vials should be decontaminated with sodium hypochlorite wipes prior to shelving the product. When chemotherapy vials are initially unpacked and wiped down, full PPE should be utilized, just as if chemotherapy were being prepared. It is also a best practice recommendation for all health care workers to thoroughly wash their hands after removing PPE.

**Spill Management:** Chemotherapy spills may occur during preparation, transport, or administration of chemotherapy. Spill kits should be located in all areas where chemotherapy is prepared and administered. The goal is to implement processes to prevent hazardous spills when possible. All staff preparing, administering, or transporting chemotherapy should be trained in spill management.

Once a spill has occurred, the nearest spill kit should be obtained. PPE, including a chemotherapy-resistant gown, shoe covers, eye protection, and two pair of chemotherapy-certified gloves, should be utilized. Contain the spill by draping a chemotherapy mat or absorbent pad over the spill area. If the spill is in a patient care area, relocate the patients away from the spill. Limit access to the spill area by posting a "Hazardous Drug" sign. All personnel involved in clean up of a spill must be trained. If trained, spills less than 5 mL may be cleaned by staff responsible for the spill. If the spill is greater than 5 mL, it is generally best practice to call environmental services to handle the spill. If the spill is on a patient or staff member, remove the contaminated clothing and immediately wash the skin with soap and water for 20 minutes. If splashed in the eyes, rinse with water for 15 minutes. An eye wash or eye bath should be located in all areas where splash risk may occur. Immediate medical attention should be provided. Spills should be cleaned with alkaline detergent and decontaminated with sodium hypochlorite and neutralized with sodium thiosulfate. Blot or wipe the area with disposable towels and place all contaminated materials in a chemotherapy disposable bag and dispose of it as chemotherapy waste. If glass is present, do not pick it up by hand. Instead, use the hard plastic scoop supplied in most spill kits. Any contaminated linen should also be placed in a chemotherapy-labeled bag for special cleaning.

**Waste Handling:** All hazardous drug waste must be disposed of according to guidelines published by the organization's Department of Environmental Health and Safety, as well as any applicable state regulations. Chemotherapy waste must be handled separately from other hospital trash. A licensed medical waste contractor should be retained to remove this waste on a regular basis. Generally, the contractor incinerates hazardous drug waste at a licensed facility. As always, when handling hazardous waste, full PPE should be worn. Contaminated materials can include ampoules, vials, bags, bottles, tubing, unused doses, chemotherapy mats, and isolated chemotherapy body fluids. All material used in preparation and administration of chemotherapy must be disposed of in a labeled and sealable chemotherapy container. All sharps should be placed in a puncture-proof labeled chemotherapy container. All containers should be closed to minimize the escape of any chemotherapy vapors. In addition, the following chemotherapeutic agents require special handling to meet Environmental Protection Agency standards: P-listed arsenic trioxide or bulk amounts of U-listed drugs. These drugs must be disposed of at a RCRA-permitted incinerator.<sup>13</sup>

**Conclusion:** The safe and effective handling of hazardous drugs requires the implementation of the proper equipment and carefully thought-out policies and procedures. By following the best practice recommendations presented in this article, you can provide your patients with safer care and your employees with a safer work environment, thereby realizing two top-of-mind objectives for any leader in health-system pharmacy. ■



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