Hazardous Drugs

Controlling the risk in healthcare facilities

By Joseph W. Klancher, Mary Vorndran and William Weiss

ADVANCEMENTS IN PHARMACEUTICAL and biological technology have resulted in the introduction of an increasing number of hazardous drugs each year. NIOSH (2004) defines *hazardous drug* as "any drug identified by at least one of the following six criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, or new drugs that mimic existing hazardous drugs in structure or toxicity." The increase in drug volume has increased the potential for occupational exposure, which has prompted many healthcare organizations to reevaluate current controls.

In 2004, NIOSH published guidelines to prevent employee exposure to hazardous drugs during preparation, administration and disposal in healthcare facilities. These guidelines follow previously published guidelines from the Oncology Nursing Society (2003), the American Society of Healthcare Pharmacists (ASHP, 2000) and OSHA (1986). This article discusses how a large medical center conducted a risk assessment relative to hazardous drugs and systematically established organizational best practices.

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Characterizing the Risk

According to NIOSH (2004):

> [W]orkers may be exposed to a drug throughout its life cycle—from manufacture to transport and distribution, to use in healthcare or home care settings, to waste disposal. These workers include shipping and receiving personnel, pharmacists, and pharmacy technicians, nursing personnel, physicians, operating room personnel, environmental services personnel and workers in veterinary practices where hazardous drugs are used.

A growing body of scientific evidence indicates that exposures are occurring and being detected inside the bodies of healthcare workers. NIOSH (2004) cites a report by Harrison (2001) which states that six different drugs (cyclophosphamide, methotrexate, ifosfamide, epirubicin and cisplatin/carboplatin) were detected in the urine of healthcare workers by 13 of 20 investigations. NIOSH also documents five additional case studies.

Polovich, Blecher and Glynn-Tucker, et al. (2003) list 17 research studies on the occupational risks of healthcare workers with occupational exposure to hazardous drugs. Sessink and Bos (1999) report that long-standing control methods may be insufficient to protect healthcare workers from exposure to hazardous drugs.

In response to these reports, Mayo Clinic formed a Hazardous Drug Workgroup to evaluate the medical center's practices for handling hazardous drugs.

Evaluation Process

The evaluation process consisted of a three-step process:

1) Job hazard analyses (JHAs) in departments with potential exposure. These analyses led to recommendations and updates to the medical center's existing engineering, administrative and personal protection practices.

2) Systematic comparison of the medical center's internal control practices with the recommendations of NIOSH, OSHA, Oncology Nursing Society and ASHP.

3) Research, analysis and justification for instances where the medical center's internal control methods differ from the guidance documents.

Job Hazard Analyses

Each department in the medical center whose job functions involved potential employee exposure to hazardous drugs conducted a JHA. The departments included pharmacy, nursing, environmental services, linen and central services, facilities and

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waste management. Coordinators from the safety section worked with representatives from each department, who either performed tasks with potential exposure to hazardous drugs or who supervised those who performed such tasks. The JHA identified tasks that potentially exposed the employees to the hazardous materials. The workgroup evaluated job tasks, identified the types of PPE being worn, and documented the potential hazards involving contact with hazardous drugs or with blood and bodily fluids that may contain hazardous drugs.

Conducting the JHAs was a labor-intensive process. A safety coordinator and individuals from each participating department reviewed the actual tasks performed. This often involved observing employees performing the job tasks, as well as gathering further information from other employees who performed the same or similar tasks in different areas. All information gathered during the JHA was documented in a spreadsheet (Table 1, p. 26).

Once the JHA was documented, a work team from the department reviewed the information, discussed current work practices, and reviewed existing engineering, administrative and personal protection practices as they related to preparing, administering, cleaning up and disposing of hazardous drugs. All participating departments used this evaluation process to streamline and update current work practices and written policies; this also helped to establish a consistent work process that was used by individuals working in multiple locations.

Comparing Work Practices With Recommendations From External Sources

The JHA information was used to complete a compliance grid that summarized the recommendations from multiple external sources (NIOSH, 2004; OSHA, 1999; Polovich, et al., 2003; ASHP, 1990). The original compliance grid was a spreadsheet created to identify the multitude of recommendations reviewed. Each recommendation was identified on a separate line on the grid, with a notation made as to its source. The safety coordinator and the departmental work teams then reviewed each recommendation and noted whether the department was currently meeting that recommendation. If it was not, a notation was made as to whether it planned to do so in the future. A summary of the information gathered from each department was documented in the compliance grid (Figure 1, p. 27).

The workgroup then reviewed the grid and summarized the information from each department into three categories: 1) issues being accomplished; 2) issues that a department intends to comply with yet has not fully implemented; and 3) issues a department is not planning to adopt. The workgroup met many times to discuss the issues, their categories, current practices and procedures of each department.

The guidelines were separated into nearly 140 total line item recommendations. Of those:

- 110 items were practices currently in compliance;
- 20 items were compliance recommended but not fully implemented;
- 10 items were compliance not recommended.

Figure 2 (p. 28) presents an excerpt from the compliance grid.

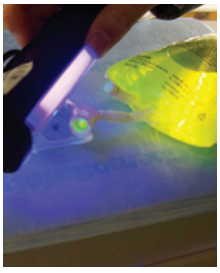
Research, Analysis & Justification

After identifying where the medical center's current practices differed from those recommended in the guidelines, the workgroup conducted research to analyze the differences, justify changes to current practices and identify where the guidelines were not justified in a given work setting. This involved liter-

Table 1

Example of Job Hazard Analysis (Pharmacy, Receiving)

Tasks of the job	Potential hazards	Recommended controls
Unstack red bins	Containers not recognized as having hazardous contents	Ensure that all hazardous products are labeled as hazardous. Define a list of hazardous drugs.
Unpack from bins	Broken product—skin exposure, inhalation	Gloves (nitrile, other chemo rated) gowns, goggles.
Unwrap containers	Broken product—skin exposure, inhalation	Leave in sealed bag until transported to chemo room. Gloves (nitrile, other chemo rated) gowns, goggles.
Scan or enter product	Broken product—skin exposure, inhalation	Transport to chemo room in a dedicated hard-sided delivery tote. Gloves (nitrile, other chemo rated) gowns, goggles
Carry or cart over to chemo room	Spill/break—skin, inhalation	Label all cytotoxic, chemos, etc., as hazardous drugs. Gloves (nitrile, other chemo rated) gowns, goggles.
Stock chemo room shelves	Spill/break—skin, inhalation	Provide containment on a shelving bin large enough to contain breakage, also lips on shelving. Gloves (nitrile, other chemo rated) gowns, goggles.
Spills	Spill/break—skin, inhalation	Follow chemo spill procedure—nitrile gloves, gown, respirator, goggles.



In testing the closed-system drug preparation and administration systems, safety, nursing and pharmacy personnel performed several simulations using fluorescein dye as a surrogate for actual drugs.

ature searches and collaboration with experts in the fields of industrial hygiene, occupational medicine, drug research, pharmacy/toxicology, glove certification, drug deactivation and destruction, infection control, industrial laundry and hazardous waste. The workgroup also conducted product searches and contacted several product manufacturers for additional information regarding the efficacy and appropriateness of their products in the medical center's work environment.

Closed-System Evaluation

The group also completed an end-user trial and human factors analysis of a closed-system drug preparation and administration system. In addition, it facilitated end-user testing of PPE and spill control equipment. This evaluation was set up in outpatient and inpatient areas at the medical center. This included pharmacy preparation and nursing administration of actual hazardous drug preparations and simulated activities using fluorescein dye preparations. The goal was to determine whether the system was robust enough to be implemented institution-wide and meet the needs of several different practice areas.

Distributor representatives provided training and were on site to assist with the preparation and administration of actual hazardous preparations. Safety, nursing and pharmacy personnel performed several simulations using fluorescein dye as a surrogate for actual drugs. Ultraviolet lighting was used to assess contamination after performing the simulated activities in various situations. Users completed evaluation forms to assess the products for human factor and safety implications. The workgroup also conducted group feedback meetings to review and assess the evaluations. Notable outcomes included the following:

- The system can reduce worker exposures if used with perfect technique; however, it was quite easy to use the system in a manner that will not impart the intended protection.
- Potential for contamination was observed during testing and trialing of the closed system.
- The expectation of workers maintaining perfect technique with this system was deemed unrealistic given its current design.
- The system reintroduced needles into a medication administration process that is currently needleless.
- The system cannot be used on all hazardous drug product preparations.

Based on these findings, the workgroup did not recommend implementation of the system.

Recommendations

Of the 140 recommendations analyzed, the workgroup concluded that the medical center was in compliance with 110, recommended that steps be taken to come into compliance with 20 others and concluded that compliance with 10 others was not warranted.

The workgroup used the analysis to establish items for inclusion in the medical center's institutional hazardous drug handling policy. The following discussion describes key elements of the medical center's institutional policy and reviews those items the workgroup concluded did not warrant compliance.

Policy Recommendations

Following is a list of items identified as essential to the medical center's hazardous drug handling policy.

Hazardous drug workgroup. The medical center shall designate a multidisciplinary workgroup to establish and review institutional policies and practices for the safe preparation and handling of hazardous drugs.

Hazard assessments. All affected departments

shall perform hazard assessments to identify situations where hazardous drug exposure may occur and to identify required equipment, PPE and safe work practices not specified in this policy. These assessments shall be reevaluated by each department at least every 3 years.

Hazardous drug list. Pharmacy services shall establish evaluation criteria and maintain a list of new and existing formulary and investigational drugs designated as *hazardous*. The hazardous drug list shall be updated whenever a new hazardous drug is identified.

Labeling. All hazardous drugs dispensed by pharmacy services will bear a label indicating special precaution where necessary. This label serves a dual purpose as it also indicates that disposal as hazardous waste is required.

Ready-to-use preparation. Whenever possible, hazardous drugs shall be dispensed in a ready-to-use form.

Gowns. Polyethylene coated or other impermeable gowns shall be used whenever required by the hazard assessment to prevent hazardous drug exposure to the arms and torso. Gowns used for protection from hazardous drugs shall meet the following criteria:

- be made of material at least as protective as spunbonded/meltblown material;
- have long sleeves with a knit cuff;
- have a full front.

Gloves. Gloves approved for use with hazardous drugs shall be worn whenever required by the hazard assessment. Gloves used for protection from hazardous drugs shall meet the following criteria:

- be tested as nonpermeable to cytotoxic materials;
- be made from latex-free material;
- be changed between patients and tasks;
- be changed at least every hour.

Spill response. Spills involving hazardous drugs shall be remediated by the department in control of the hazardous drug. If the spill is larger than the department can safely clean up, then the institutional operator should be notified to summon the spill team. (Note: Because the quantity of liquid is nearly always quite small, the workgroup believes it is appropriate to allow trained departmental staff to remediate.)

Spill kits. Affected departments shall ensure that appropriately equipped spill kits are readily available wherever hazardous drugs are received, prepared, transported, administered or disposed. Hazardous drug spill kits shall contain the following items:

- gloves (exam, nitrile);
- bags (yellow, chemo waste);
- towel (white, professional)
- bag (clear plastic 24 in. x 33 in.)
- gown or tie back (nonsterile);
- full face shield;
- chlorinated towelette (8 in. x 10 in.);
- absorbent pillow.

Biological safety cabinets. All forms of hazardous drugs requiring sterile preparation shall be prepared in Class II B cabinets. Hazardous drugs not requiring sterile preparation shall be prepared in fume hoods with dedicated exhaust or Class II B biological safety cabinets.

Waste disposal. Hazardous drug waste shall be bagged and disposed of in hard-sided covered containers. Hazardous drug waste containers shall be labeled in accordance with EPA requirements. Hazardous drug waste shall be incinerated.

Decontamination. When cleaning spills and areas potentially contaminated with hazardous drugs (e.g., pharmacy preparations areas), an oxidizing agent (e.g., 0.5% bleach solution) shall be used.

Items Not Warranting Compliance

As noted, based on the workgroup's current understanding and assessment of the risks of handling hazardous drugs in this medical center's

Figure 1

Compliance Grid (Excerpt)

Preventing Occupational Exposures to Antineoplastic and other Hazardous Drugs in Healthcare Settings
Working Document 03/07/2005

		NIOSH (2004)	ONS (2003)	OSHA (1986, rev 94)	ASHP (1990)		Pharm	Nursing	Env Svcs	Linen Central Services
Employee Involvement	Employee Input.	x			x		y	y	y	y
Workplace Analysis	Initial hazard assessment	x					y	y	y	y
	Periodic evaluation of drugs, equipment, training, policies and procedures.	x					y	y	y	y
	Comply with U S Environmental Protection Agency/Resource Conservation and Recovery Act	x		x	x		y	y	y	y
Drug Inventory	Written Drug Inventory (including investigational drugs)	x	x	x	x		y		-	-
MSDS Info	Material Safety Data Sheets (MSDSs) or other information	x	x	x	x		y	y	y	y
Training	Provide training to employees on the recognition, evaluation and control of hazardous drugs.	x	x	x	x		y	y	y	y

x = recommended; y = currently comply; - = not applicable

Figure 2

Example of Compliance Summary

Prepare workers for the possibility that spills might occur while they are handling containers (even when packaging is intact during routine activities), and provide them with appropriate PPE.	X		
Make sure that medical products have labeling on the outsides of containers that will be understood by all workers who will be separating hazardous from nonhazardous drugs.	X		
Wear chemotherapy gloves [ASTM in press], protective clothing, and eye protection when opening containers to unpack hazardous drugs. Such PPE protects workers and helps prevent contamination from spreading if damaged containers are found.	X - Hospital Pharmacy	X - OP Pharmacy, currently no eye protection or chemo gloves	
Wear chemotherapy gloves to prevent contamination when transporting the vial or syringe to the work area.			X - we do not allow gloved hands in public areas which would include transit. Drugs should be transported in clean outer containers.
Store hazardous drugs separately from other drugs, as recommended by ASHP [1990] and other chemical safety standards.	X		
Store and transport hazardous drugs in closed containers that minimize the risk of breakage.	X		
Make sure the storage area has sufficient general exhaust ventilation to dilute and remove any airborne contaminants.	X		
Depending on the physical nature and quantity of the stored drugs, consider installing a dedicated emergency exhaust fan that is large enough to quickly purge airborne contaminants from the storage room in the event of a spill and prevent contamination in adjacent areas.	X - Chemo areas are currently under negative pressure. G10 is capable of being placed in Purge mode.		

Based on its analysis, the workgroup recommended a 1-hour changeout schedule for gloves or a change whenever torn, punctured or contaminated.

healthcare facilities, it concluded that several items do not warrant compliance.

Receiving & Storage

•**Guidelines.** Wear chemotherapy gloves to prevent contamination when transporting the vial or syringe to the work area.

Workgroup response. The workgroup did not recommend gloved hands in public areas, including transit. The group viewed wearing gloves in public areas to be a poor practice. The public or other staff members cannot distinguish clean gloves from dirty gloves, so this practice can create a perception of poor hygiene. Drugs should be transported in clean zip bags and placed in hard-sided containers, which eliminates the need for gloved hands.

Drug Preparation & Administration

•**Guidelines.** Use double gloving for all activities involving hazardous drugs. Make sure that the outer glove extends over the cuff of the gown.

Workgroup response. This analysis concluded that double gloving outside the hospital pharmacy is not warranted. In areas outside the hospital pharmacy, glove requirements should be based on permeation rather than on the number of gloves used. NIOSH concluded that glove thickness was most important and, therefore, recommended double gloving. However, the level of risk reduction from double gloving has not been substantiated in the literature. Had there been issues with glove tearing, double gloving would have been a consideration. Within the hospital pharmacy, double gloving is used to protect the worker from unknowingly contaminating areas outside the hood or the outside of the patient's product. This is accomplished by removing the outer glove before wiping down the product, then removing it from the hood. The outer layer of gloves is at the highest risk of contamination and is removed before exiting the hood.

•**Guidelines.** Change gloves every 30 minutes or when torn, punctured or contaminated.

Workgroup response. Based on its analysis, the work group recommended a 1-hour changeout schedule for gloves or a change whenever torn, punctured or contaminated. Most glove permeation studies use > 480 minutes with no permeation under continuous contact as a key measure.

This measure is consistent with the workgroup's proposed internal glove criteria. The glove permeation studies establish worst-case scenarios that greatly exceed any scenario that could be anticipated in a healthcare setting.

•**Guidelines.** Double bag contaminated equipment and chemotherapy waste.

Workgroup response. Double bagging equipment was not recommended as no scientific evidence indicates that this practice significantly reduces risk. The workgroup concluded that bags used in spill kits are of sufficient thickness to prevent breakage.

•**Guidelines.** Consider using devices such as closed-system transfer devices. Such systems limit the potential for generating aerosols and exposing workers to sharps.

Workgroup response. Medical center staff evaluated and pilot tested the only currently available closed-system drug preparation and administration system; this included a rigorous human factors and safety analysis. As noted, the system did not meet expectations and was not recommended.

Routine Cleaning, Decontaminating, Housekeeping & Waste Disposal

•**Guidelines.** Clean work surfaces with an appropriate deactivation agent (if available) and cleaning agent before and after each activity and at the end of the work shift.

Workgroup response. The use of a diluted (1:10) bleach solution in the pharmacy and for spill response was recommended. The workgroup concluded that the pharmacy areas have a higher likelihood of contamination than other areas in the hospital. Bleach is an oxidizer and will deactivate many (but not all) hazardous drugs. Standard cleaning methods were recommended for patient rooms, as it is believed that mechanical removal is sufficient

to protect workers in these areas. Clean up of spills in patient rooms would include the use of a bleach solution as well.

•**Guidelines.** Consider double washing all linens used by patients receiving cytotoxic medications.

Workgroup response. Double washing is an undefined term and its efficacy has not been substantiated in the literature. Therefore, this item was not recommended for implementation.

Medical Surveillance

•**Guidelines.** Use a worker's past exposure history as a surrogate measure of potential exposure intensity.

Workgroup response. The workgroup could not quantify past exposure history and considered it impractical to do so. Thus, it did not recommend adopting this guideline.

•**Guidelines.** Include a complete blood count with differential and a reticulocyte count in the baseline and periodic laboratory tests. These may be helpful as an indicator of bone marrow reserve.

Workgroup response. It was concluded that periodic labs are not efficacious unless following a known exposure or suggestive history/exam.

•**Guidelines.** Monitor the urine of workers who handle hazardous drugs with a urine dipstick or a microscopic examination of the urine for blood (Brown, Esper, Kelleher, et al., 2001). Several antineoplastic agents are known to cause bladder damage and blood in the urine of treated patients.

Workgroup response. Urinalysis is nonspecific and of limited usefulness. Chromosome analysis is not a clinical test. Therefore, routine urinalysis was not recommended.

Lessons Learned

During this project, the workgroup learned several important lessons. For example, the process of reviewing the various hazardous drug recommendations and guidelines is tedious and cannot be accomplished quickly. In addition, the size of the medical institution will dictate the scope of the project and the number of people who need to be consulted and involved. Furthermore, the evaluation and its results will not necessarily be identical from institution to institution; therefore, the evaluation must be performed from the perspective of how operations function within a particular medical institution.

It is also important to select the proper team to review and evaluate the guidelines. The workgroup recommends creating a multidisciplinary team representing areas affected by the guidelines to facilitate the process, conduct the evaluations and make recommendations for organizational response. The key to success in this case was the involvement of individuals who understood the work practices within their specific areas of expertise. These individuals either knew existing work practices within their areas or knew how to get the answers. These individuals were also instrumental in performing JHAs for their areas and were able to identify and initiate improvements within their departments.

Working through this process, the workgroup encountered varying degrees of resistance from those affected. Some individuals had differences of opinion regarding what the guidelines stated and what they felt the guidelines meant. Others were resistant to changing current practices. Much of this resistance was likely related to the fact that the recommendations were guidelines rather than regulations—many individuals believed that they did not apply to the medical center's practice. Finally, the group learned that the process of performing the risk assessments and making recommendations based on them helped establish common ground and facilitate consensus.

Based on this experience, the workgroup concluded that establishing an institutional hazardous drug list is critical to the success of implementing NIOSH recommendations throughout the life cycle of the drug. Having such a list enables departments to identify when it is necessary to follow hazardous precautions.

Although NIOSH establishes six drug characteristics (carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, or new drugs that mimic existing hazardous drugs in structure or toxicity) to be considered when determining which drugs should be included on a hazardous drug list, interpreting and operationalizing those criteria are difficult. Therefore, the drug list is a top priority and is an ongoing process in any organization.

The workgroup formed for this process will continue to meet periodically. The members of each multidisciplinary work team will continue to evaluate their work practices in respect to how individuals in their work areas perform tasks involving hazardous drugs as well. Everyone involved realizes this is an ongoing process that will continue to evolve as new discoveries are made and work practices are improved. ■

It is important to select the proper team to review and evaluate the guidelines. A multidisciplinary team representing areas that are affected by the guidelines is recommended.

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