Special REPORT

Closed-System Drug Delivery

A closed-system approach to the isolation of hazardous drugs was developed in Sweden in the 1990s. The portable device (PhaSeal, Carmel Pharma) was designed to prevent drug leakage and aerosolization during preparation and administration. Several elements in the PhaSeal design work to contain the drug. A protector with a flexible bulb fits onto the drug vial and equalizes air pressure in the vial during drug preparation when air or diluent are injected or withdrawn. The system's double membrane is designed to prevent leaks during drug transfers and disconnections. The injector element uses a needle that is never exposed, preventing needle-stick injuries and avoiding leakage during injection. The connector allows for a dry-spike connection.

Widely used in Europe, the PhaSeal system was evaluated in the United States at the University of Texas M.D. Anderson Cancer Center in Houston.[90] The PhaSeal System was used to prepare cyclophosphamide and ifosfamide; fluorouracil, the control drug, was prepared using standard methods. Investigators concluded that the use of the device together with BSCs "appeared to contain surface contamination resulting from the preparation" of the test drugs.[90] They stated that the system "may offer a solution" to reducing occupational exposure of healthcare workers to antineoplastic agents, and, "combined with other safe handling practices, should make the work environment safe for healthcare personnel."[90]

A recent study at the University of Utah Hospitals and Clinics, Salt Lake City, demonstrated both a reduction in the level of surface contamination in the pharmacy and the levels of 2 cytotoxic drugs excreted in the urine of pharmacy and nursing personnel after using the PhaSeal system for 6 months.[44] Studies in other countries have also demonstrated a reduction in surface contamination following use of the PhaSeal system.[91-93]

Formulations, Packaging and Transport

Changes in formulations and packaging may also reduce the potential for healthcare worker exposure to hazardous drugs. For example, by reducing the number of manipulations required in drug preparation, the opportunity for exposure is decreased. Ideally, hazardous drugs would be packaged in ready-to-use versions, such as prefilled syringes or contained transfer devices such as ADD-vantage or Mini-Bag Plus systems. The exacting nature of dosing chemotherapy, however, precludes many of these methods for reducing exposure. Most drug packaging is designed to maintain the integrity of the product or guarantee its sterility. Only a few containers or dispensing products are designed with the safety of the healthcare worker in mind.

There are some practical considerations that should result in improved safety for healthcare workers:

- Avoid ampules whenever possible. Choose drugs provided in vials, which eliminate the handling of sharps and also reduce spilling of drugs during disposal. In one study, the substitution of fluorouracil vials for ampules resulted in a significant reduction in glove contamination.[27]
- Choose nonreactive plastic polymer vials over glass whenever possible to reduce exposure from breakage of hazardous drug containers, especially in transport from manufacturer and distributor. According to OSHA guidelines, hazardous drugs should be transported in containers designed to avoid breakage. Personnel involved in transporting hazardous drugs should be trained in spill procedures, including sealing off the contaminated area and calling for appropriate assistance.[12]
- Choose liquid formulations over powder whenever available. This reduces the number of times a drug is handled during preparation.
- In high-volume pharmacies, choose multi-dose vials with PhaSeal to reduce the number of manipulations, cost and the environmental impact of disposal.
- For oral formulations, choose drugs provided from the manufacturer in unit-dose packaging.
- Select oral formulations that are either coated tablets or capsules, or tablets with "core drug" to reduce the risk of drug powder being released from drug containers.
- Manufacturers should provide oral drugs as liquid formulations to reduce the need for compounding suspensions from oral tablets.

Information and Training

According to the OSHA Hazard Communication Standard, everyone involved in the preparation, administration, and disposal of hazardous drugs must receive information and training about the workplace risks and safe-handling practices.[94] The information should be provided when the employee is first assigned to an area where hazardous drugs are present, and refresher information and training should be given annually. Training also should include proper use of Material Safety Data Sheets.

OSHA recommends that knowledge and competence of personnel be evaluated after the first orientation or training session, and then annually—or more often if required.[12] In evaluating the employee's knowledge and performance techniques, trainers should use nonhazardous drug solutions, such as fluorescein, that will fluoresce under UV light.[95]

The training program needs to be thorough and job-specific (such as pharmacy or nursing), and should include at least the following elements:

- Drugs listed as hazardous: what specific drugs require special handling and how they are labeled.
- Potential carcinogenic and reproductive health risks to workers who are exposed to some hazardous drugs.
- How workers can be exposed while performing their jobs.
- Requirements for drug storage, including the location of vials and prepared drugs.
- The use of personal protective equipment, including the types of PPE and when they should be worn.
- How to minimize exposure during preparation and administration.
- Safe-handling requirements during hazardous drug transport.
- Requirements for disposal of hazardous waste products, including PPE; needles, syringes, and other paraphernalia used in preparation and administration; and patient waste products.
- Procedures for spill cleanup. According to the OSHA guidelines, incidental spills and breakage should be cleaned up immediately by properly protected and trained personnel.[12] The area should be identified with a warning sign to limit access to the area.
- Requirements for record-keeping, including drug preparation logs and employee health status.

If new information becomes available, it should be provided immediately to employees. When a different job assignment involves new risks, the employee should receive fresh training and information about the hazards.

Waste Handling

Safety measures used in the handling and disposing of hazardous waste products are as essential as the precautions