

Determining Sources of Workplace Contamination with Antineoplastic Drugs and Comparing Conventional IV Drug Preparation with a Closed System

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Abstract — Many procedures involved in the preparation and administration of hazardous drugs put health care workers at risk of exposure to these agents through leakage or accidental spills. The first objective of this study was to determine if the conventional needle/syringe technique has the potential to allow drugs to escape into the environment. The second objective was to evaluate if a closed system, PhaSeal, prevents inadvertent release of hazardous drugs. Fluorescein, a fluorescent indicator, was prepared as a dry powder and a 0.05% solution in empty drug vials. Each phase of the manipulation was photographed using UV light to visualize fluorescein leaks and spills. The procedures included reconstitution of a dry powder, drug transfer from the vial to an IV bag, simulated drug administration, and IV push administrations through an IV port. With the conventional needle/syringe technique, each phase of the manipulations resulted in visible fluorescein leakage into the environment. Fluorescein leakage ranged in size from less than 1 to 50 mm in diameter. The syringes, work surfaces, gloves, manifold ports, and IV bag ports exhibited fluorescein contamination. With PhaSeal, no leakage was observed during any phase of the manipulations. Using the conventional needle/syringe technique during preparation of a hazardous drug may lead to release of the agent into the work environment, posing a health risk to the worker. A closed system such as PhaSeal has the ability to confine hazardous drugs, substantially reducing or possibly eliminating drug exposures.

Key Words — antineoplastic drugs; closed system; environmental contamination; fluorescein

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The potential occupational hazards of many drugs, especially antineoplastic drugs, have been well documented.^{1–4} Several recent studies from the US and other countries indicate that contamination of work areas with hazardous drugs is commonplace.^{5–14} European studies have shown that health care workers excrete antineoplastic drugs in their urine, even when they have not actively handled the drugs, indicating that their exposure results from generalized contamination of the workplace.^{6,8,10,14} Given the fact that many of these drugs are genotoxic,¹⁵ known or suspected reproductive toxins,^{16,17} and known or suspected human carcinogens,¹⁸ elimination or reduction of workplace contamination is warranted.

Exposure studies in the 1980s resulted in the use of Class II biological safety cabinets (BSCs), which replaced the horizontal laminar flow devices used previously for drug preparation.^{19,20} This intervention greatly reduced worker exposure to hazardous drugs. However, with more sensitive and specific analytical techniques, it has been shown that workers who prepare and administer antineoplastic drugs continue to be at risk for exposure even when proper controls are in place.^{5–14}

A closed system has the potential to reduce environmental contamination by antineoplastic and other hazardous drugs.²¹ The PhaSeal system, manufactured by Carmel Pharma ab (Göteborg, Sweden), has been shown to be effective.

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Table 1

Simulated Drug Preparation and Administration Activities

Simulated Activity	Number of Procedures	
	Needle/Syringe	PhaSeal
Reconstitution of dry powder	10 vials x 2 (20)	10 vials x 2 (20)
Removal of solution from vial and transfer to IV bag	10 vials x 2 (20) 20 IV bags	10 vials x 2 (20) 20 IV bags
Simulated drug administration	10 IV bags	10 IV bags
Injection of drug solution into an IV port	5 IV ports	5 IV ports



Figure 1. The PhaSeal system attached to a 100 mL vial containing 80 mL fluorescein solution

neoplastic drug contamination in the environment and in patient urine.²⁵ The present study compared conventional needle/ syringe procedures with the use of a closed system to determine which procedures during drug preparation and administration are most likely to release drug particles into the environment. Fluorescein was used as the contamination detection agent.

MATERIALS AND METHODS

Fluorescein^a was prepared as a dry powder at 40 mg/100 mL vial^b and sealed with a rubber septum with a crimped cap to simulate a powdered drug for reconstitution. Alternatively, it was prepared as a 0.05% solution/ 80 mL saline in 100 mL vials and sealed as above.

The filled vials were scanned with UV light (UVP, Inc., San Gabriel, CA) to ensure that fluorescein had not contaminated the outside of the vials.

The PhaSeal system (see Figure 1) consists of a protector (P50), an injector (N31), a connector (C40), and an infusion adaptor (C71) and has been described previously.²² The drug preparation steps were carried out by an experienced pharmacy technician who had been trained in the use of the PhaSeal system. The administration steps were performed by an oncology nurse with minimal previous experience with the system before taking part in the

study.

All manipulations were performed in a BSC, simulating actual working conditions as closely as possible. A sterile plastic-backed drape was placed in the BSC before the start of each set of operations and scanned with UV light to detect any interfering fluorescence that might have originated from the pad. The manipulations were performed using room lighting. Following each procedure, the lights were turned off and the drape on the work surface and all equipment and gloves were scanned with UV light and photographed using a digital camera.

For the drug reconstitution study, 80 mL of saline was added to the vials containing the fluorescein powder. Two 20 mL aliquots were removed using (1) a 60 cc syringe fitted with an 18 g x 1 1/2" needle or (2) with the PhaSeal system. The 20 mL was then transferred to an IV bag containing 250 mL D5W.

The drug preparation and administration steps performed were:

- Reconstitution of a dry powder;
- Removal of a drug solution from the vial;
- Transfer of a drug solution to an IV bag;
- Simulation of drug administration; and
- IV push of a drug solution into an IV port.

Depending on the type of activity, all manipulations were repeated between 5 to 20 times using separate equipment for each activity (see Table 1).

RESULTS

All types of procedures using the standard needle and syringe technique resulted in some level of environmental contamination (see Figures 2 to 4). Most fluorescein spots were relatively small (1 to 4 mm), but others were up to several centimeters.

Fluorescein leakage resulted from several activities. Withdrawing a needle from an overpressurized vial produced

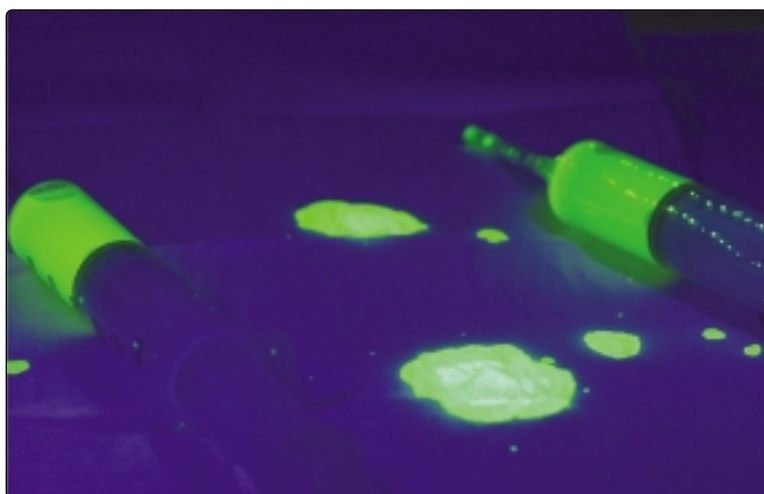


Figure 2. Leakage of fluorescein from a vial due to overpressurization following simulated drug reconstitution

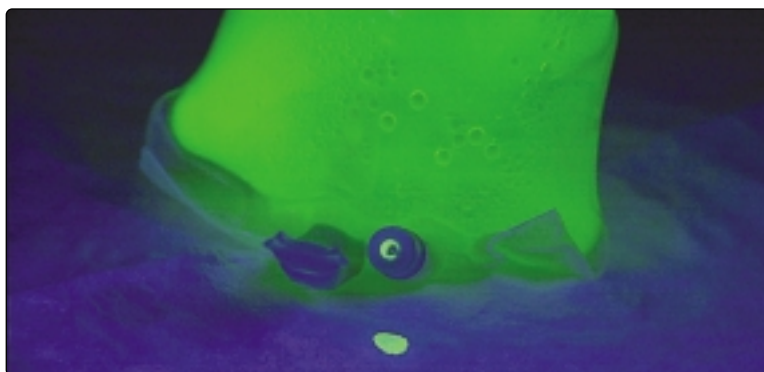


Figure 3. Leakage from an IV bag following the addition of 20 mL of fluorescein solution

some of the largest spots (see Figure 2), although smaller spots were common occurrences. Withdrawing a needle from the port of an IV bag often resulted in the formation of a drop of fluorescein solution on the port and drops on the drape (see Figure 3).

Both the simulated drug administration and the IV push of the solution into an IV port resulted in release of the fluorescein solution into the environment (see Figure 4). Although contamination was observed on the gloves of the workers, it was difficult to visualize with UV light because of glove material properties.

Studies with the PhaSeal system during 75 total manipulations did not demonstrate a single identifiable release of the fluorescein solution into the work environment (see Figures 5 to 7). No fluorescein drops were seen on the equipment, the gloves, or the drape following any of the operations.

DISCUSSION

The authors and other researchers have measured widespread environmental contamination in pharmacy and clinical areas with antineoplastic drugs, despite the use of Class II BSCs, even BSCs that vented to the outside environment.^{5–14} Given the demonstrated excretion of selected antineoplastic drugs by health care workers,^{6,8,10,14} it is obvious that levels of contamination by these drugs need to be reduced.

Health care workers are typically exposed to several drugs during the course of the workday.²⁶ Although numerous studies have documented various adverse health effects from exposure to antineoplastic drugs, the cumulative effect of exposure to several drugs over long periods of time is difficult to quantify. Nevertheless, exposure to hazardous drugs should be eliminated or reduced whenever possible.

Kromhout et al²⁵ have reported on leakage from various IV infusion systems using a fluorescent indicator and a visual scoring technique. By adding the indicator to bedpans before use, these researchers also showed that urine of patients containing excreted drug could be a source of environmental, worker, and patient contamination.

Sessink et al²² have shown that use of the PhaSeal system for one year without a BSC is sufficient to eliminate environmental contamination with cyclophosphamide and fluorouracil in a low-use hospital in Sweden. A six-month study in Belgium has demonstrated that PhaSeal reduced environmental contamination with cyclophosphamide in the pharmacy.¹⁴ This study also

reported that two activities, filling a cassette and priming tubing, resulted in leakage of fluorouracil to the environment.

Connor et al¹³ have shown that the PhaSeal system reduced overall contamination with cyclophosphamide and ifosfamide compared to fluorouracil contamination without the use of PhaSeal. This study was carried out over a 6-month period in the US, in a high-usage ambulatory pharmacy following a complete renovation of the work area. The present study supports the findings of these previous studies with PhaSeal and demonstrates the potential for release of drug solutions into the environment using the standard needle/syringe technique.

CONCLUSIONS

The use of the standard needle/syringe technique for the preparation of antineoplastic and other hazardous drugs has the potential to release drug solutions into the work environ-

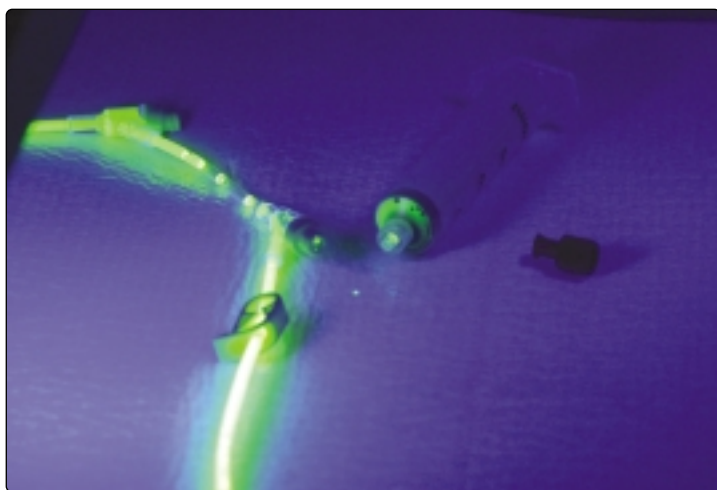


Figure 4. Leakage of fluorescein solution from an IV port following disconnection of syringe



Figure 5. A PhaSeal protector and injector following simulated drug reconstitution

ment. All phases of drug preparation and administration were shown to result in leakage of the fluorescein solution and contamination of equipment and work surfaces. With PhaSeal, no indication of release of the test solution was seen in any of the 75 manipulations performed.

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PRODUCT NOTES

- a. Sigma Chemical Company; St. Louis, MO.
- b. Lab Products, Inc.; Houston, TX.

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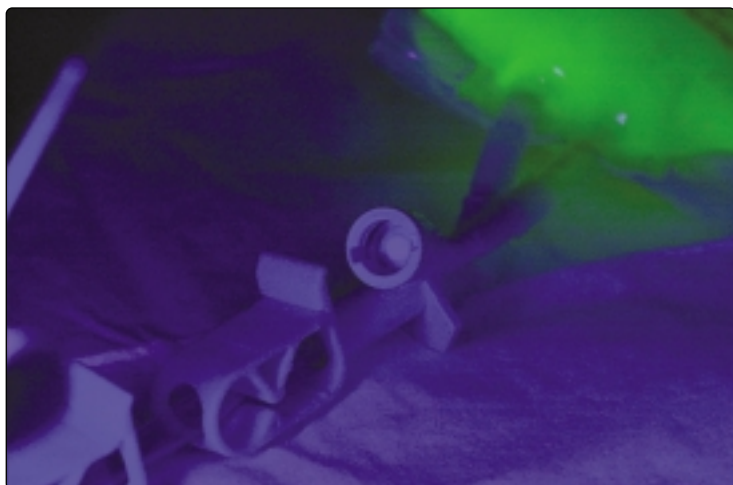


Figure 6. A PhaSeal spike following transfer of 20 mL fluorescein solution to an IV bag

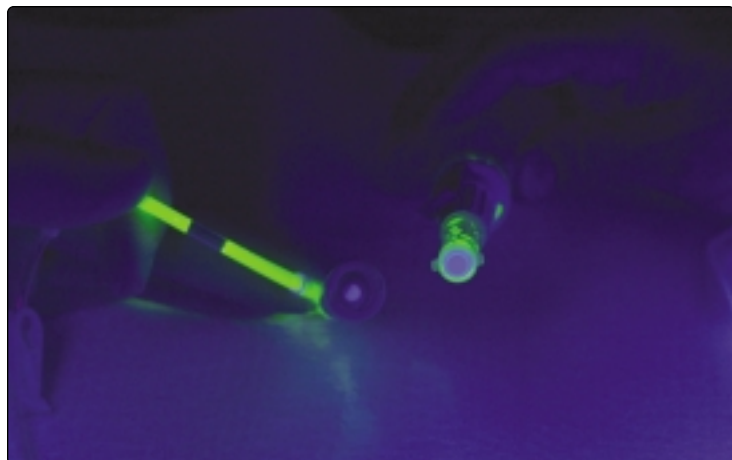


Figure 7. A PhaSeal injector and connection following an IV push

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