Evaluation of Closed-system Transfer Devices in Reducing Potential Risk for Surface Contamination Following Simulated Hazardous-drug Preparation and Compounding

Abstract

Closed-system transfer devices mitigate occupational exposure risks associated with hazardous-drug handling. This study was conducted in a controlled laboratory to evaluate the effectiveness of a needle-free and a needle-based closed-system transfer device in minimizing surface contamination during simulated compounding, preparation, and administration. A needle-based and a needle-free closed-system transfer device underwent three trials per system. Each trial included reconstituting cyclophosphamide in a vial, withdrawing cyclophosphamide from the vial, and pushing cyclophosphamide into an intravenous bag. After every trial, wipe samples were collected from five sources: biological safety cabinet workbench (left and right sides), biological safety cabinet grill, biological safety cabinet airfoil, and technicians' gloves. Wipe samples were then analyzed using high-performance liquid chromatography with dual-mass spectrometry to measure cyclophosphamide concentrations. Surface contamination levels from 30 post-trial tests (15 per device) are reported, representing five different surface wipe samples from three trials for each device. Pre-trial samples of precleaned vials and work surfaces were obtained to ensure no cyclophosphamide contamination. Field blank samples were analyzed for quality-control purposes. Post-trial wipe sample analyses following each of the three needle-free trials did not detect cyclophosphamide on the biological safety cabinet workbench (both left/right), biological safety cabinet grill, biological safety cabinet airfoil, or the technician's gloves. For the needle-based closed-system transfer device, the wipe sample analyses after the first trial showed no contamination; however, cyclophosphamide was detected on the right biological safety cabinet workbench at concentrations of 0.223 ng/cm^2 and 0.021 ng/cm^2, respectively, following the second and third trials. No cyclophosphamide was found on the technician's gloves after any of the three needle-based closed-system transfer device trials. Based on surface contamination analyses, this study verified the ability of a needle-free closed-system transfer device in preventing the escape of cyclophosphamide during simulated compounding and preparation. Needle-free closed-system transfer devices warrant consideration for the handling of hazardous drugs.

S STABILITY | P PENETRATION | F FORMULATIVE | C CLINICAL STUDY | O OTHER

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Introduction

Over 18.1 million patients in 2018 were diagnosed with cancer, which is the second leading cause of death worldwide.[1,2] Given the rising global cancer burden along with the constant improvement/development of chemotherapy treatments, the number of patients receiving first-course chemotherapy is expected to increase over the next two decades, ranging from 9.8 to 15 million per year.[3] As chemotherapy becomes more prevalent, potential exposure of antineoplastic agents during preparation/administration pose an occupational hazard to over eight million healthcare workers annually, and frontline healthcare professionals face the highest risk.[4-6] Without appropriate precautions, oncology nurses, pharmacy personnel, and other clinical staff are at risk of acquiring acute or chronic adverse health conditions from exposure to antineoplastic drugs.[4-7]

The U.S. Center for Disease Control's (CDC) National Institute of Occupational Safety and Health (NIOSH) has classified multiple antineoplastic drugs to be hazardous based on their carcinogenicity, teratogenicity, reproductive toxicity, and/or organ toxicity when exposed to healthy cells.[8] NIOSH recommends the use of closed-system transfer devices (CSTDs) as part of a comprehensive program to mitigate exposure risk and prevent spillage.[9] NIOSH defines CSTDs as drug transfer devices that mechanically prohibit the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.[9] The United States Pharmacopeial Convention, Inc. (USP) in its latest guidelines for hazardous drug handling in the *United States Pharmacopeia (USP)* Chapter <800> requires CSTD use during antineoplastic administration and highly recommends CSTD use during hazardous-drug compounding.[10] Compared with more traditional methods (e.g., needle and syringe), CSTDs have shown increased efficiency and effectiveness in hazardous-drug handling through faster preparation times and lower surface contamination rates.[11-13]

CSTDs have been implemented throughout many oncology treatment centers since first cleared in 1997 (Carmel Pharma AB, Columbus, Ohio).[14,15] Recent biotechnological advances have yielded the development of needle-free CSTDs to protect healthcare professionals from needle-stick injuries, while ensuring the containment of hazardous drugs within a closed system during preparation and administration.[16] There exists a need to compare needle-free CSTDs against needle-based CSTDs and evaluate their ability to minimize occupational exposure risk associated with handling hazardous drugs.

This study's objective was to compare and evaluate a needle-free and needle-based CSTD for effectiveness in preventing surface contamination during simulated hazardous drug compounding activities. Wipe samples from work surfaces were collected and analyzed for surface contamination of cyclophosphamide following vial reconstitution, withdrawal of drug from the vial, and drug injection into an intravenous (IV) bag.

Materials and Methods

OUTCOME MEASURES

The outcome was cyclophosphamide surface contamination defined by the amount of cyclophosphamide (ng) detected on various work surfaces as well as the concentration of cyclophosphamide by surface area (ng/cm^2). Surface contamination was assessed following the use of a needle-free and needle-based CSTD during simulated compounding, preparation, and administration of cyclophosphamide.

MATERIALS

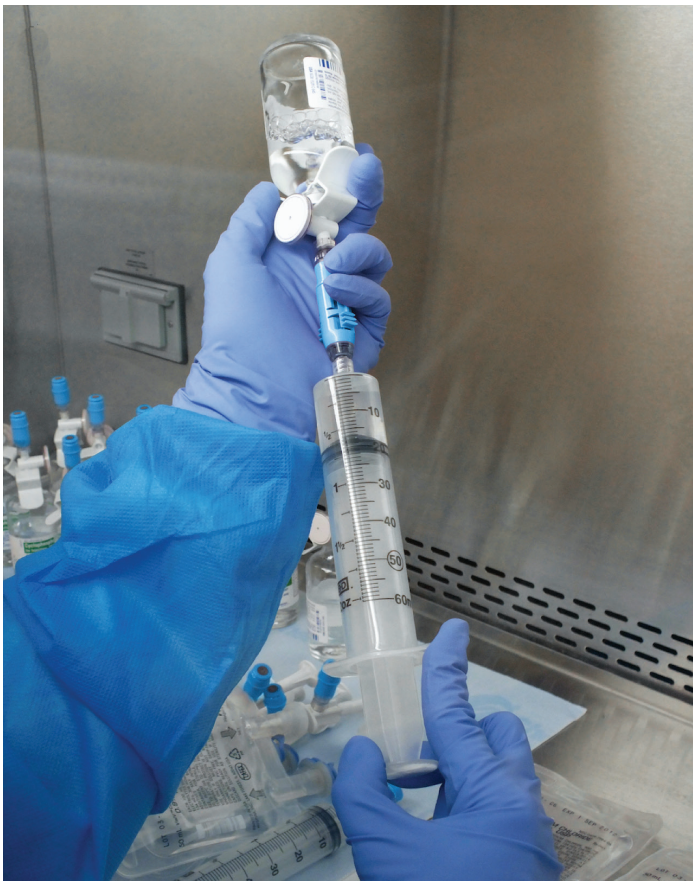
This preliminary investigation was conducted in a controlled laboratory (RJ Lee Group, Inc., Waynesburg, Pennsylvania) equipped with a Class 5 cleanroom (ISO14644-1) and a Class II (EN 12469 standard) biological safety cabinet (BSC) (Model NU-440-660, Series 30, Nuaire, Plymouth, Minnesota. The workspace was demarcated into four defined surfaces: two sides of the BSC workbench (left/right), the BSC grill, and the BSC airfoil. Cyclophosphamide was selected due to its common clinical use as well as the availability of a sensitive analytical method to detect trace levels of surface contamination. Vials of Cyclophosphamide Powder USP, one gram (Lot 2E765; Baxter Healthcare Corporation, Deerfield, Illinois) were used for the study.

Two CSTDs were evaluated; each system consisted of a vial access device, syringe adaptor, and IV bag spike. The needle-free CSTD (ChemoLock, ICU Medical, San Clemente, California) used was a single-motion, "click-to-lock" system that incorporated a CSTD vented (air-cleaning) vial access device (Lot 2648079, CL-70; ICU Medical), a CSTD needle-free syringe adaptor (Lot 2608114, CL2000S; ICU Medical), and an CSTD IV bag spike (Lot 2649838, CL-12; ICU Medical). The air-cleaning vial adaptor was equipped with a 0.22-micron filter that is permanently attached to the vial designed to equalize pressure in the vial and prevent the escape of hazardous drug while allowing air to escape. To connect the system and open the fluid path, the syringe was attached to the CSTD syringe adaptor and, as a single unit, was pushed into the mating CSTD port of the vial access device until an audible click was heard, ensuring that the locking mechanism was engaged (**FIGURE 1A**). The combined syringe and CSTD adaptor unit was disconnected from the vial access device port by pushing the two release clips on the sides of the adaptor to disengage the locking mechanism after the desired dosage of contents from the vial was drawn into the syringe. To administer cyclophosphamide into an IV bag (VisIV Container; ICU Medical) the drug-filled syringe and CSTD adaptor unit was pushed into the CSTD port of the IV bag spike, until the audible click was heard, ensuring a secure connection between the CSTD syringe and CSTD IV bag (**FIGURE 1B**). Disconnecting the system required pushing the two release clips on the sides of the adaptor and pulling away from the IV bag port.

FIGURE 1.

COMPONENTS OF THE NEEDLE-FREE CLOSED-SYSTEM TRANSFER DEVICE.

A. Locking Universal Vented Vial Access Device (CL-70) with the Spinning ChemoLock syringe adaptor (CL2000S)



B. Intravenous bag access using the Bag Spike with ChemoLock Additive Port and Dry Spike (CL-12)

The needle-based CSTD (PhaSeal; BD, Franklin Lakes, New Jersey) was a "push-turn-push" system that utilized a vial access device with a locking port (Lot 8290406, Protector P50; BD), a syringe adaptor with an enclosed needle (Lot 11020964 Injector Luer Lock N35; BD), and an IV bag spike with a locking CSTD port (Lot 9230585, Infusion adapter C100; BD). The vial access adaptor was equipped with barrier technology through a pressure-equalization device that is permanently attached to the vial to establish and maintain neutral pressure when air or fluid is injected into or aspirated from the vial. A disposable syringe was attached to the syringe adaptor, and as a single unit, was inserted into the CSTD port of the vial access device by a "push-turn-push" mechanism. The enclosed needle was pushed into the port to open the fluid path between the vial and syringe, allowing a sheath which covers the enclosed needle to retract simultaneously (FIGURE 2A). Once the desired dosage of the drug was drawn from the vial into the syringe, the coupled syringe and adaptor unit was disconnected by a "pull-turn-pull" mechanism to remove the mating components. To gain access to the IV bag, the drug-filled syringe and adaptor unit was inserted into the CSTD port of the IV bag spike, and the fluid path was opened and closed with the same methods used for vial access (FIGURE 2B).

STUDY PERSONNEL

A chemotherapy-certified pharmacy technician, previously trained in the use of each system, performed all simulated compounding and preparation activities. A Certified Industrial Hygienist (CIH) conducted all wipe sampling activities using standard techniques.[17]

STUDY PROCEDURES

Since drug residue can exist on exterior surfaces of drug vials due to the commercial manufacturing process,[18,19] manufacturing-related contamination was minimized using a multi-step decontamination procedure. This procedure included

separate applications of solutions containing detergent, sodium hypochlorite (NaOCl), and sodium thiosulfate/benzyl alcohol ($Na_2S_2O_3/C_7H_8O$), followed by wiping with lint-free towels and rinsing.[20] Surface wipe samples were collected for laboratory analysis from the vials after drying.

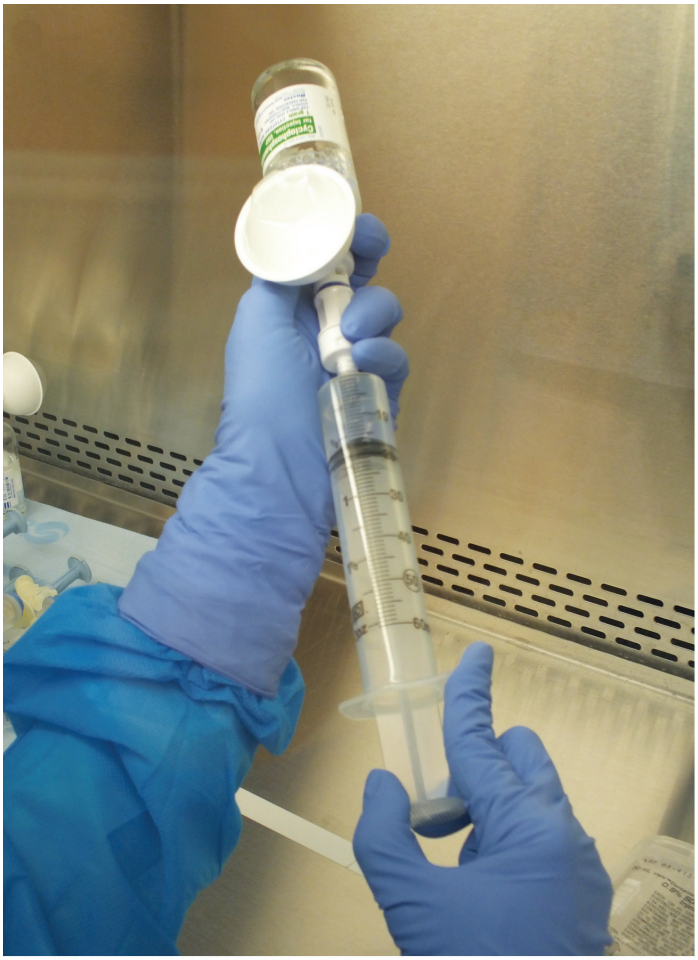
Before each device's evaluation, all four BSC surfaces were decontaminated using the same cleaning procedure for vial decontamination. A total of eight pre-trial wipe samples (four samples per device) were collected from the demarcated BSC surfaces and analyzed to determine if the surfaces were free from cyclophosphamide contamination prior to CSTD testing.

During each trial, keeping within the demarcated areas of the BSC, the technician performed all simulated compounding activities using personal protective equipment (PPE) and cleanroom garb, including coveralls, shoe covers, hair covers, surgical face mask, splash-proof gowns with tight-fitting cuffs, and chemotherapy-protective nitrile inner gloves. Three consecutive individual trials were performed for each system utilizing the same BSC, yielding a total of six separate trials. The technician donned a new pair of nitrile outer gloves at the beginning of every trial. Each trial included four preparation cycles to simulate hazardous drug compounding and preparation in a pharmacy setting. To start a preparation cycle, 1) the technician inserted the CSTD vial spike into the one-gram cyclophosphamide vial and reconstituted with 50 mL of 0.9% sodium chloride, resulting in a concentration of 20 mg/mL, according to the drug and CSTD instructions of use; 2) an IV bag was accessed with the CSTD bag spike and placed on the BSC workbench, ensuring that the access ports were inside the demarcated area; 3) the technician attached the CSTD syringe adapter to the syringe, withdrew 48 mL of reconstituted cyclophosphamide

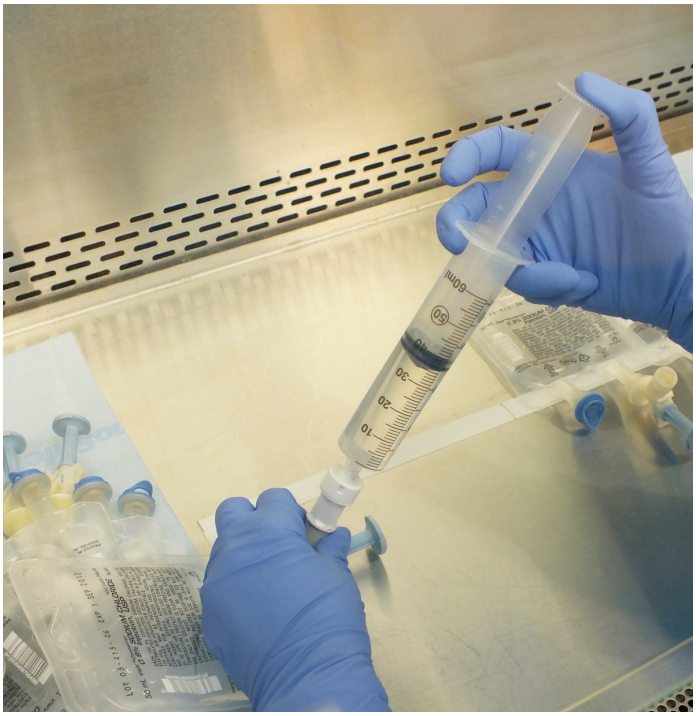
FIGURE 2.

COMPONENTS OF THE NEEDLE-BASED CLOSED-SYSTEM TRANSFER DEVICE.

A. Protector vial access device with external chamber (P50) and Injector Luer Lock (N35) syringe adaptor



B. Intravenous bag access using the Infusion Adaptor (C100) IV bag spike and Injector Luer Lock (N35) syringe adaptor



from the vial, and 4) transferred three separate volumes of 16 mL into the IV bag, disconnecting the syringe from the bag after each 16-mL transfer. Every preparation cycle thus included one connection to the vial with three transfers to the bag. Therefore, the CSTD syringe combination made four connections in total. A total of four preparation cycles with separate CSTD syringe combinations were required per trial, utilizing four reconstituted vials of cyclophosphamide and four IV bags. Given that three trials per CSTD were completed, the technician utilized 36 CSTD components and performed 36 fluid transfers totaling 576 mL of solution containing 11.52 g of cyclophosphamide.

DETECTION OF SURFACE CONTAMINATION

Surface contamination was assessed with wipe sample analyses prior to the first trial of each device and following the completion of each device trial. A total of eight pre-trial wipe samples were collected (one sample from four demarcated BSC surfaces per device) and analyzed (FIGURE 3A). Post-trial wipe samples were collected from all four BSC surfaces and the technician's gloves which were replaced after every trial (FIGURE 3B). A total of 30 post-trial wipe samples (five samples following each device trial) were analyzed in this study. The amount of area sampled from each BSC surface was 400 cm^2 for both pre- and post-trial wipe samples.

Wipe samples were obtained using sampling media kits (RJ Lee Group, Inc.) and analyzed using generally accepted industrial hygiene techniques.[17] All wipe samples were stored at or below minus 70°C before laboratory preparation. Samples were analyzed using a HPLC-MS/MS (Sciex API 4000 Mass Spectrometer, Framingham, Massachusetts), with a Shimadzu 10VP LC System (Columbia, Maryland) following a validated methodology. Field blank samples (sampling media not wiped on surfaces) were submitted along with survey samples for quality control. The limit of detection for cyclophosphamide was two nanograms (ng) per sample.

Results

PRE-STUDY WIPE SAMPLE RESULTS

No cyclophosphamide was detected on the exterior of the vials sampled following decontamination and prior to use.

PRE-TRIAL WORK AREA SURFACE WIPE SAMPLE RESULTS

On the BSC workbench (right), at a concentration of 0.008 ng/cm^2 prior to the needle-free CSTD trials, 3.3 ng of cyclophosphamide was detected, whereas no cyclophosphamide was measured on any of the surfaces prior to the needle-based CSTD trials (TABLE 1).

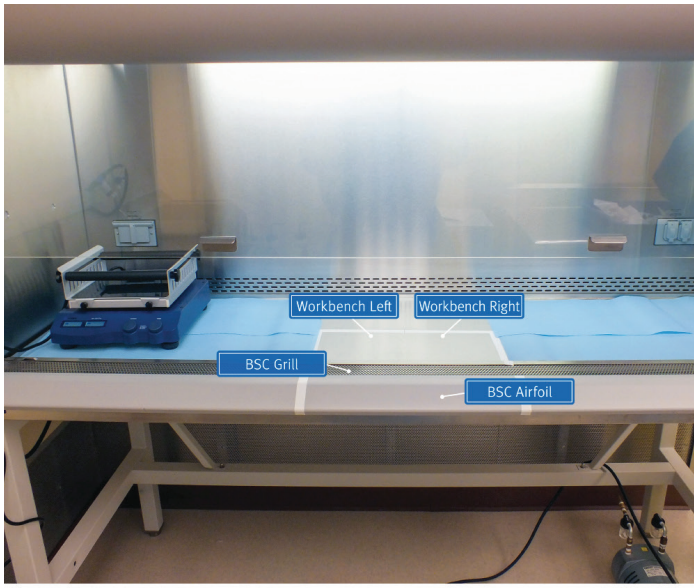
POST-TRIAL SURFACE WIPE SAMPLE RESULTS

Following each needle-free CSTD trial, no cyclophosphamide was detected on any BSC work surface (TABLE 2). Wipe sample analyses following trials 2 and 3 of the needle-based CSTD measured cyclophosphamide concentrations of 0.223 ng/cm^2 and 0.021 ng/cm^2 on the right workbench, respectively. No cyclophosphamide was detected on the technician's gloves following any of the CSTD trials (TABLE 2).

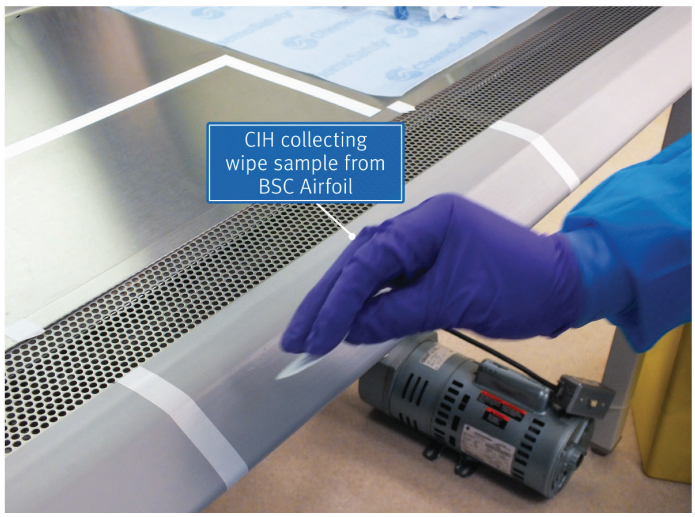
FIGURE 3.

BIOLOGICAL SAFETY CABINET WORKBENCH AND WIPE SAMPLE COLLECTION.

A. Demarcated areas of BSC work area



B. Wipe sample collection



QUALITY-CONTROL (FIELD BLANK) WIPE SAMPLE RESULTS

No cyclophosphamide was detected on the field blank samples.

Discussion

Considering the increasing focus on hazardous-drug exposure in oncology and oncology pharmacy settings, this study utilizes an effective method to analyze surface contamination following simulated preparation and IV administration of cyclophosphamide. More importantly, this study shows that when compared to a needle-based CSTD, a needle-free CSTD is similarly capable of minimizing cyclophosphamide surface contamination following simulated compounding, preparation, and administration.

TABLE 1.

SUMMARY OF PRE-TRIAL SAMPLE RESULTS.

		PRIOR TO NEEDLE-FREE CSTD EVALUATION		PRIOR TO NEEDLE-BASED CSTD EVALUATION	
Work Area Surface	Area, (cm^2)	CP, (ng)	CP Concentration, (ng/cm^2)	CP, (ng)	CP Concentration, (ng/cm^2)
Workbench left	400	nd	<0.005	nd	<0.005
Workbench right	400	3.33	0.008	nd	<0.005
BSC Grill	400	nd	<0.005	nd	<0.005
BSC Airfoil	400	nd	<0.005	nd	<0.005

Note: Cyclophosphamide levels and concentrations in each column were from wipe samples taken from four work area surfaces prior to the separate evaluation of each device in their three respective consecutive trials under the same BSC.
BSC = biological safety cabinet; CSTD = closed-system transfer device; CP = cyclophosphamide; nd = not detected (<2.0 ng/sample).

A low level of cyclophosphamide was detected on the BSC workbench before the needle-free system evaluation, whereas no contamination was observed following any of the needle-free trials. This indicates that the cyclophosphamide detected prior to these trials was reduced to undetectable levels due to the wipe sampling process, and no detectable contamination resulted from the CSTD use. At the end of the second needle-based CSTD trial, the technician observed that the internal needle was unintentionally exposed. A small component of the syringe adaptor appeared to have cracked, and a fluid droplet was observed on the tip of the needle (**FIGURE 4**). The cyclophosphamide detected following the second trial could potentially be attributed to this crack. However, no droplet was visually observed on any work area surface, and the remaining two needle-based trials were conducted without issues. Overall, the needle-based system was also effective in reducing detectable contamination, which is comparable to several studies reporting the system's ability to reduce surface contamination levels of hazardous drugs when compared to standard preparation techniques (i.e., needle and syringe).[12,21-24] Adding to the growing body of evidence, needle-free systems yield similarly favorable surface contamination results to that of a needle-based CSTD, with a lower risk of occupational hazards.[16] With a needle-free system, needlestick injury risk is non-existent, whereas needle-based CSTDs still potentiate the possibility of occupational needlestick injury even with the "enclosed" needle design.

USP Chapter <800> highlights a comprehensive set of guidelines for handling hazardous drugs, and includes environment quality and control, appropriate PPE, work practice, personnel

TABLE 2.

SUMMARY OF POST-TRIAL SAMPLE RESULTS.

DEVICE TYPE	WORK AREA SURFACE	AREA (CM^2)	POST-TRIAL 1		POST-TRIAL 2		POST-TRIAL 3	
			CP, ng	CP Concentration (ng/cm^2)	CP, ng	CP Concentration (ng/cm^2)	CP, ng	CP Concentration (ng/cm^2)
Needle-free CSTD	Gloves	n/a	nd	n/a	nd	n/a	nd	n/a
	Workbench left	400	nd	<0.005	nd	<0.005	nd	<0.005
	Workbench right	400	nd	<0.005	nd	<0.005	nd	<0.005
	BSC Grill	400	nd	<0.005	nd	<0.005	nd	<0.005
	BSC Airfoil	400	nd	<0.005	nd	<0.005	nd	<0.005
Needle-based CSTD	Gloves	n/a	nd	na	nd	n/a	nd	n/a
	Workbench left	400	nd	<0.005	nd	<0.005	nd	<0.005
	Workbench right	400	nd	<0.005	89.1	0.223	8.56	0.021
	BSC Grill	400	nd	<0.005	nd	<0.005	nd	<0.005
	BSC Airfoil	400	nd	<0.005	nd	<0.005	nd	<0.005

Note: Each set of "post-trial" results represents cyclophosphamide surface contamination identified by wipe samples taken from five work surfaces after the completion of each trial. Each device was evaluated separately with three consecutive trials (1 to 3).
BSC = biological safety cabinet; CSTD = closed-system transfer device; CP = cyclophosphamide; n/a = not applicable; nd = not detected (<2.0 ng/sample).

FIGURE 4.

NEEDLE-BASED SYSTEM WITH UNINTENTIONALLY EXPOSED NEEDLE AND VISIBLE FLUID DROPLET AS OBSERVED BY THE TECHNICIAN AT THE END OF THE SECOND TRIAL.

training, and engineering controls such as ventilated BSCs.[10] As CSTD implementation becomes a growing priority among administrators and health systems striving for *USP* Chapter <800> compliance, it is important to consider newer strategies for handling hazardous drugs, specifically with CSTD systems offering improved features, such as membrane-to-membrane connection systems and vial access adaptor technologies designed to better protect end-users from workplace exposure.

Device ease of use, suitability, and safety are important factors to consider when evaluating CSTDs. A recent study evaluated ease-of-use between three CSTDs — one needle-free and two needle-based devices — during hazardous drug preparation and administration, and reported that nursing staff and pharmacy technicians preferred the needle-free system over the other two devices when provided with open-ended, Likert-scale questionnaires.[11] Furthermore, pharmacy technicians and nursing staff are at risk for developing cumulative stress-induced injuries stemming from repetitive motions such as opening and closing vial caps, attaching vials to syringes in addition to drawing and pushing solutions from vials to IV bags.[25,26] Thus, user friendliness metrics based on minimizing stressful repetitive motions, as reported by end-users, should also be prioritized when comparing various CSTDs.

This study has several limitations. First, even with the substantial number of transfer steps, the sample size was small, limiting the statistical evaluation and comparison of the relative effectiveness in preventing surface contamination. Second, there is a lack of a universal performance standard for evaluating this adjunct engineering control. Lastly, cyclophosphamide as a nitrogen mustard derivative is a single class of cytotoxic agents and may not be representative of all commonly used antineoplastic drugs.

Conclusion

It is evident that without the use of CSTDs, frontline oncology professionals are at increased risk of occupational exposure during hazardous-drug handling. Using a standardized methodology for surface contamination analysis, this study verified the ability of a needle-free CSTD to mechanically prevent the escape of cyclophosphamide outside of the CSTD during simulated compounding and preparation, as shown by undetectable cyclophosphamide levels following wipe sample analyses on work surfaces. These findings suggest that needle-free systems warrant thorough consideration in the effort aimed at creating safer hazardous-drug handling practices in oncology infusion areas. Future large-scale clinical studies are necessary to evaluate the effectiveness and ease-of-use of needle-free CSTDs.

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References

1. World Health Organization. International Agency for Research on Cancer. Press Release. *Latest global cancer data: Cancer burden rises to 18.1 million new cases and 9.6 million cancer deaths in 2018. [WHO Website.] September 12, 2018*. Available at: www.who.int/cancer/PRGlobocanFinal.pdf. Accessed March 2021.
2. Roser M, Ritchie H. *Cancer. Our World in Data: OurWorldinData.org, 2015; [Internet], 2015*. Available at: https://ourworldindata.org/cancer. Accessed March 2021.
3. Wilson BE, Jacob S, Yap ML et al. Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: A population-based study. *Lancet Oncol.* 2019; 20(6): 769–780.
4. Boiano JM, Steege AL, Sweeney MH. Adherence to safe handling guidelines by health care workers who administer antineoplastic drugs. *J Occup Environ Hyg.* 2014; 11(11): 728–740.
5. Polovich M, Clark PC. Factors influencing oncology nurses' use of hazardous drug safe-handling precautions. *Oncol Nurs Forum.* 2012; 39(3): E299–E309.
6. Polovich M. Minimizing Occupational Exposure to Antineoplastic Agents. *J Infus Nurs.* 2016; 39(5): 307–313.
7. Graeve CU, McGovern PM, Alexander B et al. Occupational Exposure to Antineoplastic Agents. *Workplace Health Saf.* 2017; 65(1): 9–20.

8. Department of Health and Human Services. Centers for Disease Control and Prevention. The National Institute for Occupational Safety and Health. *NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016*. [NIOSH Website.] September 2016. Available at: www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf?id=10.26616/NIOSHPUB2016161. Accessed March 2021.
9. Department of Health and Human Services. Centers for Disease Control and Prevention. The National Institute for Occupational Safety and Health. *NIOSH Alert. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings.* [NIOSH Website.] 2004. Available at: www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf?id=10.26616/NIOSHPUB2004165. Accessed March 2021.
10. United States Pharmacopeial Convention, Inc. *United States Pharmacopeia–National Formulary.* Rockville, MD. *USP* General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings. [USP Website.] 2017. Available at: www.usp.org/sites/default/files/usp/document/our-work/healthcare-quality-safety/general-chapter-800.pdf. Accessed March 2021.
11. Nurgat ZA, Lawrence M, Elhassan TA et al. Comparison of closed system transfer devices for turnaround time and ease of use. *J Oncol Pharm Pract.* 2019; 25(5): 1142–1151.
12. Favier B, Labrosse H, Gilles-Afchain L et al. The PhaSeal® system: Impact of its use on workplace contamination and duration of chemotherapy preparation. *J Oncol Pharm Pract.* 2012; 18(1): 37–45.
13. Sessink PJ, Connor TH, Jorgenson JA et al. Reduction in surface contamination with antineoplastic drugs in 22 hospital pharmacies in the US following implementation of a closed-system drug transfer device. *J Oncol Pharm Pract.* 2011; 17(1): 39–48.
14. U.S. Food and Drug Administration. 510(K) *Summary of Safety and Effectiveness*. FDA Approval. [FDA Website.] 1998. Available at: www.accessdata.fda.gov/CDRH510K/K123213.pdf. Accessed March 2021.
15. Sessink PJ, Rolf M-AE, Rydèn NS. Evaluation of the PhaSeal Hazardous Drug Containment System. *Hospital Pharmacy* 1999; 34(11): 1311–1317.
16. Zock MD, Soefje S, Rickabaugh K. Evaluation of surface contamination with cyclophosphamide following simulated hazardous drug preparation activities using two closed-system products. *J Oncol Pharm Pract.* 2011; 17(1): 49–54.
17. Connor TH, Zock MD, Snow AH. Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. *J Occup Environ Hyg*. 2016; 13(9): 658–667.
18. Power LA, Sessink PJ, Gesy K et al. Hazardous drug residue on exterior vial surfaces: Evaluation of a commercial manufacturing process. *Hosp Pharm*. 2014; 49(4): 355–362.
19. Touzin K, Bussiéres J-F, Langlois E et al. Cyclophosphamide contamination observed on the external surfaces of drug vials and the efficacy of cleaning on vial contamination. *Ann Occup Hyg.* 2008; 52(8): 765–771.
20. United States Department of Labor. Occupational Safety and Health Administration. *Controlling Occupational Exposure to Hazardous Drugs.* [OSHA Website.] 2016. Available at: www.osha.gov/hazardous-drugs/controlling-occex#decontamination. Accessed March 2021.
21. Harrison BR, Peters BG, Bing MR. Comparison of surface contamination with cyclophosphamide and fluorouracil using a closed-system drug transfer device versus standard preparation techniques. *Am J Health Syst Pharm*. 2006; 63(18): 1736–1744.
22. Wick C, Slawson MH, Jorgenson JA et al. Using a closed-system protective device to reduce personnel exposure to antineoplastic agents. *Am J Health Syst Pharm.* 2003; 60(22): 2314–2320.
23. Nyman HA, Jorgenson JA, Slawson MH. Workplace contamination with antineoplastic agents in a new cancer hospital using a closed-system drug transfer device. *Hospital Pharmacy*. 2007; 42(3): 219–225.
24. Siderov J, Kirsa S, McLauchlan R. Reducing workplace cytotoxic surface contamination using a closed-system drug transfer device. *J Oncol Pharm Pract*. 2010; 16(1): 19–25.
25. Penkala S, El-Debal H, Coxon K. Work-related musculoskeletal problems related to laboratory training in university medical science students: A cross sectional survey. *BMC Public Health*. 2018; 18(1): 1208.
26. Davis KG, Kotowski SE. Prevalence of musculoskeletal disorders for nurses in hospitals, long-term care facilities, and home health care: A comprehensive review. *Hum Factors.* 2015; 57(5): 754–792.

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