Assessment Of A New Closed System Drug-Transfer Device At 13 U.S. Cancer Centers

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INTRODUCTION

Worker exposure to antineoplastic hazardous drugs (AHDs) has been a long standing concern.[1] Studies show that AHD surface contamination is prevalent in work areas where AHDs are mixed and administered and that marker AHDs are found in the urine of workers who handle these drugs.[2,3] Closed system drug-transfer devices (CSTDs), adjuncts used in mixing and administration, have been shown to reduce contamination and worker uptake of marker AHDs.[3] To date only one of the commercial CSTDs has been extensively studied and shown to be effective with results published in peer-reviewed journals.[4,5] The study presented here is the first to evaluate a new CSTD using a strict protocol for both mixing and administering AHDs to allow reliability of results across multiple sites.

OBJECTIVES

- Evaluate performance of the new CSTD in reducing surface contamination during mixing and administration of a set protocol of marker AHDs cyclophosphamide (CP) and 5-fluorouracil (5FU) using wipe sampling in participating U.S. cancer centers
- Compare the performance of the new CSTD to similar studies of another CSTD in the literature
- Determine user satisfaction/ease-of-use of the new CSTD

METHODS

- Study sites were recruited from the National Cancer Institute (NCI) designated Cancer Centers and the members of the Association of Community Cancer Centers (ACCC) in the U.S.
- Nineteen U.S. cancer centers were selected to participate in the study; six sites were omitted based on exclusion criteria, including failure to provide required pharmacy and nursing staff, pre-contaminated and/or exploded drug vials unrelated to the study device, and a failure to comply with the study protocol

A standardized protocol was followed by all participating centers:

- Wipe samples of predetermined surfaces were collected in mixing and infusion areas to determine existing levels of surface contamination at each site
- Stainless steel templates of 500cm^2 and 478.5cm^2 (for the chair arm) were placed over previously sampled surfaces, and specific amounts of AHDs were mixed and infused over the templates, using the new CSTD system
- Wipe samples from the templates were collected after the tasks were done and analyzed for both marker AHDs: CP and 5FU
- Results were reported as ng/cm^2 with the limit of detection (LOD) of 0.002 ng/sample
- Study participants completed a questionnaire on satisfaction/ease-of-use of the new CSTD

RESULTS

The preexisting CP and 5FU surface contamination found in both mixing and infusion areas was similar to that reported in literature with combined 67% (104/156) of wipe samples being contaminated. The infusion area had 78% (61/78) contaminated samples which is higher than in the literature. **See Table 1.**

Table 1. Initial sampling of contamination with 5FU + CP on pharmacy & administration area surfaces (ng/cm^2)

	Pharmacy						Administration area						Aggregate (per site)
Site No.	BSC Floor		BSC, Left		BSC, Right		Floor (right)		Floor (left)		Chair arm		% >LOD
	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU+CP
003	0.290	0.029	<0.002	0.003	<0.002	0.003	0.112	0.004	0.145	0.006	0.598	0.015	83
004	6.440	0.648	0.168	0.051	0.132	0.052	0.600	0.086	0.270	0.056	0.069	0.028	100
006	<0.002	0.061	<0.002	<0.002	<0.002	<0.002	0.025	0.007	0.013	0.005	0.034	0.021	58
008	0.516	0.126	19.880	0.035	2.960	0.031	0.013	0.005	0.010	0.005	0.056	0.005	100
009	<0.002	0.003	<0.002	<0.002	<0.002	<0.002	0.003	<0.002	<0.002	<0.002	0.007	0.007	33
010	<0.002	<0.002	0.006	<0.002	<0.002	<0.002	0.288	0.073	0.100	0.083	<0.002	0.007	50
012	0.212	0.018	0.045	0.004	0.037	0.003	0.004	<0.002	<0.002	<0.002	<0.002	<0.002	58
013	0.009	0.024	0.046	0.048	0.047	0.336	0.005	0.021	0.009	0.036	0.014	0.004	100
014	<0.002	<0.002	<0.002	0.007	<0.002	0.012	<0.002	0.012	<0.002	0.007	<0.002	0.007	42
016	0.120	0.010	0.127	<0.002	0.158	<0.002	3.480	0.246	3.880	0.023	0.301	0.270	83
017	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	0.002	<0.002	<0.002	0.006	<0.002	17
018	3.020	0.110	0.668	0.018	1.144	0.017	0.988	0.018	0.664	0.021	0.089	0.010	100
019	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	0.360	0.019	0.042	0.004	0.028	42
No. >LOD	7	9	7	7	6	7	10	11	9	10	10	11	104
No. Samples	13	13	13	13	13	13	13	13	13	13	13	13	156
% >LOD	54	69	54	54	46	54	77	85	69	77	77	85	67
Median	0.009	0.018	0.006	0.003	<0.002	0.003	0.019	0.013	0.016	0.014	0.014	0.007	
Min	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	
Max	6.440	0.648	19.880	0.051	2.960	0.336	3.480	0.360	3.880	0.083	0.598	0.083	

During the protocol 10g of CP + 5g of 5FU were mixed with the new CSTD. Overall contamination was reduced to 5.8% (9/156). Infusing 3.5g of CP and 3g of 5FU resulted in only 2 of 78 samples over the LOD (2.6%). **See Table 2**.

Table 2. Post-CSTD sampling of contamination with 5FU + CP on pharmacy & administration area surfaces (ng/cm^2)

	Pharmacy						Administration area						Aggregate (per site)
Site No.	BSC Floor		BSC, Left		BSC, Right		Floor (right)		Floor (left)		Chair arm		% >LOD
	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU	CP	5FU+CP
003	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
004	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
006	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
008	ND	ND	ND	ND	ND	ND	ND	0.002	ND	ND	ND	ND	8
009	0.002	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	8
010	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
012	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
013	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
014	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.003	ND	8
016	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0
017	0.002	ND	0.003	ND	0.003	ND	ND	ND	ND	ND	ND	ND	25
018	0.004	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	8
019	ND	ND	ND	2.600	ND	0.386	ND	ND	ND	ND	ND	ND	17
No. >LOD	3	0	1	1	1	1	0	1	0	0	1	0	9
No. Samples	13	13	13	13	13	13	13	13	13	13	13	13	156
% >LOD	23	0	8	8	8	8	0	8	0	0	8	0	5.8
Median	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	
Min	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	
Max	0.004	<0.002	0.003	2.600	0.003	0.386	<0.002	0.002	<0.002	<0.002	0.003	<0.002	

Comparison to peer-reviewed literature

Only two multi-site studies, both done with the initial CSTD PhaSeal®, were sufficiently similar in methods and reporting of results to allow a reasonable comparison with the new CSTD. The 5FU and CP surface contamination found in the current 13 U.S. site study with the new CSTD is less than reported with PhaSeal® in 22 U.S. sites in a 2011 publication (**Table 3**). When compared with a second published study of compounding CP with PhaSeal® in 30 U.S. sites, the new CSTD in 13 U.S. sites resulted in less contamination overall (**Table 4**).

Table 3. Contamination with 5FU and CP in Halo® wipe samples in 13 U.S. cancer center pharmacies compared with PhaSeal® in 22 U.S. hospital pharmacies [ref 4 Tables 1 + 3]

	Halo®						PhaSeal® (ref 4 – tables 1 + 3)			
	BSC Floor		BSC, Left		BSC, Right		BSC Floor		BSC Surface	
	5FU[a]	CP	5FU	CP	5FU	CP	5FU	CP	5FU	CP
Median	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	0.3	0.01	0.3	0.02
Minimum	<0.002	<0.002	<0.002	<0.002	<0.002	<0.002	<0.6	<0.01	<0.4	<0.01
Maximum	0.004	<0.002	0.003	2.600	0.003	0.386	22.3	16.33	15.2	5.41

BSC = biological safety cabinet [a] Values for 5FU and CP are presented as ng/cm^2

Table 4. Contamination with CP in Halo® wipe samples in 13 U.S. cancer center pharmacies compared with PhaSeal® in 30 U.S. hospital pharmacies [ref 5 Table 1]

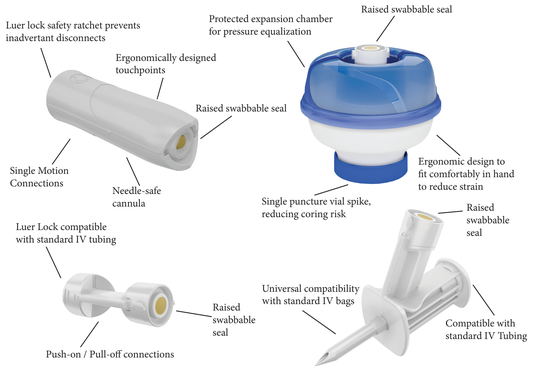
	Halo®			PhaSeal® (ref 5 Table 1)	
	BSC Floor	BSC, Left	BSC, Right	BSC Floor	BSC Surface
	CP[a]	CP	CP	CP	CP
Median	<0.002	<0.002	<0.002	0.08	0.02
Minimum	<0.002	<0.002	<0.002	<0.01	<0.01
Maximum	<0.002	2.600	0.386	4.13	38.59

BSC = biological safety cabinet [a] Values for 5FU and CP are presented as ng/cm^2

Satisfaction survey

To assess the CSTD's impact on workload, acceptance and ease of use, participants were given a survey to rate the new CSTD on a scale of 1 to 5 (1 being extremely dissatisfied and 5 being extremely satisfied), 18/26 clinicians scored Halo® as a 5 with the other 8 clinicians scoring a 4.

Halo® Test Device



Halo® by Corvida Medical®

DISCUSSION

Comparison of the wipe sampling data in Tables 1 & 2 shows a significant decrease in overall surface contamination with the new CSTD, demonstrating that it is an effective method of reducing surface contamination not only in the mixing of AHDs but also in their administration. This is the first study to focus on measuring existing surface contamination in the AHD infusion area, where spills and leaks at the delivery site are likely to occur, and assessing the performance of a CSTD directly at those sites.

CONCLUSION

The new CSTD reduced surface contamination by the marker AHDs during both mixing and administration. Compared to the published results of another CSTD, the new CSTD is superior in reducing surface contamination with marker AHDs as determined by wipe sampling of similar surfaces. Participants reported the new CSTD was easy-to-use which would support consistent and proper use of the CSTD.

REFERENCES

1. NIOSH (National Institute for Occupational Safety and Health). 2004. NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. DHHS (NIOSH) Publication No. 2004-165

2. Suspiro A, Prista J. 2011. Biomarkers of occupational exposure to anticancer agents: A minireview. Tox Lett 207:42–52

3. Wick C, Slawson MH, Jorgenson JA, Tyler LS. 2003. Using a closed-system protective device to reduce personnel exposure to antineoplastic agents. Am J Health-Syst Pharm 60:2314–20

4. Sessink PJ, Connor TH, Jorgenson JA, Tyler TG. 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 Practice. 2011; 17:39-48

5. Sessink PJM, Trahan J, Coyne JW. Reduction in surface contamination with cyclophosphamide in 30 hospital pharmacies following implementation of a closed-system drug transfer device. Hosp Pharm. 2013; 48:204-212

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