Identification and reduction of hazardous drug surface contamination through the use of a novel closed-system transfer device coupled with a point-of-care hazardous drug detection system

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Purpose: Minimizing hazardous drug (HD) contamination is critical for protecting the health of healthcare workers (HCWs) and patients. Alarmingly, widespread HD contamination has been documented across a variety of clinical settings. Quantitative wipe sampling presents significant time and cost barriers, resulting in routine monitoring adherence rates around 25%. Closed-system drug transfer devices (CSTDs) and qualitative point-of-care tests can be implemented to overcome these barriers.

Methods: In this study, we tested the effects of the BD PhaSeal Optima (Becton, Dickinson and Company), a recently introduced CSTD, on HD contamination at 2 chemotherapy infusion centers. Wipe samples were taken at 29 workstations at each location prior to and a year following CSTD implementation. Additionally, traditional liquid chromatography with mass spectrometry (LCMS/MS) analyses were compared against a novel lateral flow immunoassay HD testing device (BD HD Check; Becton, Dickinson and Company) to determine the validity of the qualitative assay.

Results: We found a 46% reduction in HD contamination after incorporating the CSTD into clinical workflows. Across time points and sites, HD contamination reported by the BD HD Check device was 91% accurate against LCMS/MS and 98% accurate within its limits of detection.

Conclusion: Collectively, the evaluated CSTD and lateral flow immunoassay device may help to reduce HD contamination and provide real-time measures of contamination, respectively. As part of a multifaceted approach, these devices may help minimize barriers to routine monitoring, ultimately improving the safety of HCWs and patients.

Keywords: antineoplastic agents, chemotherapy, closed-system transfer device, environmental monitoring, hazardous drugs, point-of-care testing

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Hazardous drugs (HDs) are compounds that pose a significant health risk to healthcare workers (HCWs) through their carcinogenic, teratogenic, reproductive toxic, organ toxic, or genotoxic properties.[1] One group of HDs encompasses antineoplastic, or anticancer, drugs utilized by HCWs in a variety of clinical settings. HD exposure, even at small concentrations, can cause adverse health outcomes such as internal organ damage, genetic mutations, increased rates of cancer, and higher rates of reproductive issues,[2-6] therefore posing significant health risks to those who are exposed. However, HD surface contamination in clinical settings can be widespread. High-touch surfaces (eg, countertops, computers, door handles), and drug preparation areas (eg, biological safety cabinets [BSCs], floors) have all tested positive for HD contamination.[7-9] HCWs working in both pharmacies and hospitals have been

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shown to be exposed to HDs, and a risk of spontaneous abortion among pregnant HCWs who handle HDs has been documented.[5,10-14] Being able to identify and mitigate these contamination risks is therefore paramount to ensure workplace safety.

The 2020 Safe to Touch Consensus Conference was convened to formulate surface contamination consensus statements and contamination monitoring protocols to help guide and unify contamination prevention/monitoring practices.[15] Facilities are encouraged to identify areas at high risk of contamination and implement both quick qualitative screenings and more specific quantitative analyses.[15] At a minimum, monitoring of central working areas of BSCs, the floors in front of BSCs, countertops, and door handles is recommended.[15] This is also in line with guidance from the Spanish Society of Hospital Pharmacists (SEFH), which advises routinely testing of between 1 and 5 HD contact points.[16] The SEFH also encourages facilities to use a common HD, such as cyclophosphamide (CYC), as a surrogate measure for overall HD contamination.[16] Only testing high-risk surfaces and a few common HDs may help institutions to overcome the financial barriers associated with routine monitoring and may aid in action planning; however, other interventions may help amplify these efforts.

To monitor HD contamination, facilities perform routine wipe studies[17,18] using expensive quantitative analyses like liquid chromatography with tandem mass spectrometry and inductively coupled plasma mass spectrometry (LCMS/MS). LCMS/MS results may take weeks to be reported,[15] prolonging possible exposure to contaminants and posing an ongoing occupational hazard. Therefore, having a rapid, qualitative point-of-care (POC) test that can identify the presence of HD residue may reduce time to decontamination, help minimize costly quantitative testing, and improve routine monitoring adherence above the current approximately 25%.[19] Lateral flow immunoassays (LFIAs) are one method of POC testing. LFIAs are portable devices that have been used in various clinical settings (eg, pregnancy testing). Becton, Dickinson and Company has released the only commercially available LFIA, the BD HD Check device, which can be used to test for several common HDs (doxorubicin [DOX], methotrexate [MTX], and CYC).[20] While LFIAs allow less sensitive analysis,[21] the demand for accurate, rapid POC tests will continue to drive advancement of LFIA technology. In combination with quantitative analyses, rapid, qualitative HD monitoring devices may improve worker safety in clinical settings.

Closed-system drug transfer devices (CSTDs) are another contamination reduction solution endorsed by the Safe to Touch Consensus Conference. A CSTD mechanically prevents environmental contamination through leakproof and airtight HD transfer, helping to lower occupational exposure hazards.[22,23] In a study following the National Institute for Occupational Safety and Health draft testing protocols, 2 commercial CSTDs, Equashield (Equashield LLC) and PhaSeal (Becton, Dickinson and Company), were shown to meet the acceptance criteria,[24] and various studies have demonstrated their efficacy in reducing HD contamination.[12,25-27] For example, a US-based study showed that use of the BD PhaSeal device significantly lowered contamination across 30 hospital pharmacies when compared to previous standard protocols.[14] Since that study, the original BD PhaSeal design has been reengineered to optimize ergonomics, performance, and ease of use by HCWs.[28,29] Its new features are designed to contain vapors and ensure airtight drug transfers. The BD PhaSeal Optima is currently novel to the literature—no peer-reviewed studies have demonstrated its efficacy in reducing HD contamination.

The primary aim of this study was to assess changes in surface contamination by using the BD PhaSeal Optima across 2 infusion centers at Emory Healthcare's Winship Cancer Institute, a National Cancer Institute–designated comprehensive cancer center. The secondary aim was to assess the result validity of the BD HD Check against quantitative wipe study analyses (via LCMS/MS). We hypothesized that utilization of the BD PhaSeal Optima would reduce HD contamination, and that on-site qualitative POC testing can be used in conjunction with quantitative analysis to provide a timelier, rapid assessment of HD contamination. The results of this study provide evidence for the BD PhaSeal Optima, as well as the expanded use of POC tests, as part of a robust, multifaceted HD surface contamination management program to help reduce occupational hazards for HCWs.

KEY POINTS

- The BD PhaSeal Optima closed-system transfer device was associated with a 46% reduction in contamination at 2 chemotherapy infusion centers.
- BD HD Check, a qualitative, rapid, point-of-care test, was 91% consistent with traditional quantitative analyses in reporting contamination.
- As part of a multifaceted approach, the BD PhaSeal Optima and BD HD Check may have the potential to reduce barriers to routine monitoring, which could ultimately protect employee and patient health.

Methods

Wipe sampling. Wipe samples were collected at 2 infusion pharmacies located at the Winship Cancer Institute Clifton Campus (location A) and the Winship Cancer Institute Buford Campus (location B). Per institutional protocols, pharmacy and nursing workstations are decontaminated using

PeridoxRTU sporicide (Contec, Inc., Spartanburg, SC) daily or after patient care concludes. To assess the change in residual HD contamination, wipe samples were taken with the BD HD Check Collection Kit at locations A and B both before and after the incorporation of CSTD technology into infusion center pharmacy and nursing workflows (Figure 1). Twenty-seven sites (eTable 1) were sampled at midday under dynamic conditions at each location. Surface samples measuring 929 cm^2 (1 ft × 1 ft) were collected using BD HD Check protocols. Each sample was aliquoted into two 1-mL aliquots that were used for quantitative and qualitative testing, respectively. These aliquots were sent in refrigerated coolers to Intertek (a commercial laboratory) for LCMS/MS testing, and the remainder were used for BD HD Check POC testing.

DOX, MTX, CYC, fluorouracil, paclitaxel (PAC), and docetaxel (DOC) were selected as the 6 HDs to test, but the volume of each HD used at the individual locations varied. In a given month, location A may prepare and administer 100 doses of DOX, 10 doses of MTX, 50 doses of CYC, 200 doses of fluorouracil, 100 doses of PAC, and 30 doses of DOC. Location B may prepare and administer 10 doses of DOX, 5 doses of MTX, 10 doses of CYC, 30 fluorouracil doses, 30 doses of PAC, and 10 doses of DOC.

Quantitative and qualitative wipe sample analyses. For quantitative analyses, samples were shipped in a refrigerated, labeled container to an independent commercial laboratory site (Intertek) for testing by LCMS/MS. Pre-CSTD sample analysis was completed on May 7, 2019, and post-CSTD analyses were conducted on June 3 and July 17, 2020. At both pre- and post-CSTD time points, DOX, MTX, CYC, fluorouracil, PAC, and DOC were extracted from the wipe swabs and classified by concentration into 4 groups: not detected (ND), <0.1 ng/cm^2 (low), 0.1 to ≤1.0 ng/cm^2 (medium), and >1.0 ng/cm^2 (high). The concentration ranges used match the same units and scale as the ChemoGLO reporting system (ChemoGLO, Chapel Hill, NC) and are similar to other published scales.[18] LCMS/MS thresholds are 0.003 ng/cm^2 for PAC, CYC, and MTX, 0.006 ng/cm^2 for DOX and DOC, and 0.012 ng/cm^2 for fluorouracil.

Using the same locations and workstations, wipe samples obtained at the before and after time points were also analyzed using the qualitative, rapid-response BD HD Check system. The BD HD Check system utilizes LFIA technology to report a positive/negative readout for DOX, MTX, and CYC contamination within minutes.[20] As such, the BD HD Check has limits of detection (LODs) for different HDs. The LOD (95% sensitivity/specificity) of HD Check is 0.1 ng/cm^2 for DOX and MTX and 0.5 ng/cm^2 for CYC.[30]

Statistical analysis. For LCMS/MS comparisons, raw HD contamination values were averaged, and their standard deviation was calculated (Tables 1 and 2). Analysis of variance (ANOVA) modeling was used to estimate the impact of CSTD implementation across HDs and sample sites for both the LCMS/MS data set (eTable 2) and the BD HD Check data set (not shown). Contamination percent reduction was calculated using relative bias (eTable 3). For specific model considerations and statistical descriptions, please see the eAppendix.

Results

Location A. ***Quantitative analysis: pre- and post-CTSD.*** Quantitative (LCMS/MS) analysis of DOX both before and after implementation of CSTDs from location A showed no detectible contamination across the 27 sites sampled (Table 1). At the pre-CSTD time point, low MTX concentrations were detected on a BSC and the area underneath a different BSC (2 of 27 sampled surfaces; 7%); however,

Figure 1. Schematic of testing methods showing the infusion locations, analyses, and timeline. Prior to implementation of the closed-system drug transfer device (CSTD) (PhaSeal Optima; Becton, Dickinson and Company) in May 2019, wipe samples of 29 surfaces at location A and location B were sampled using both liquid chromatography with tandem mass spectrometry (LCMS/MS), performed by the commercial laboratory Intertek, and the BD HD Check lateral flow immunoassay (LFIA) testing device (Becton, Dickinson and Company). About a year after implementation, posttest samples were obtained for the same sites tested previously and analyzed using the same methods in June and July 2020. HD indicates hazardous drug.

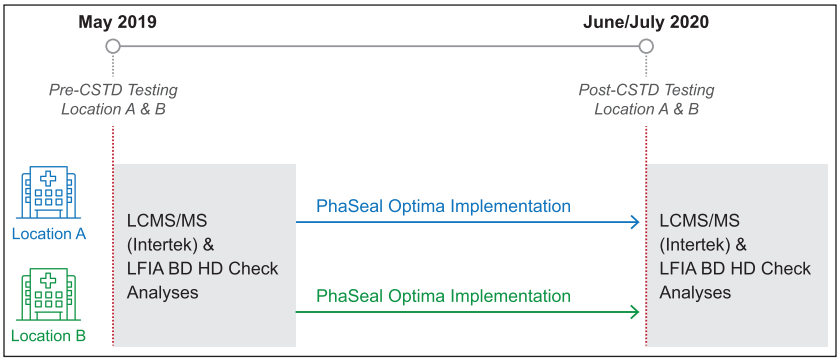

Table 1. HD Contamination at Infusion Center Location A in Pre- and Post-CSTD Testing[a,b,c]

Location A Sample Sites	DOX Pre LCMS & BD HD Check	DOX Post LCMS & BD HD Check	MTX Pre LCMS & BD HD Check	MTX Post LCMS & BD HD Check	CYC Pre LCMS & BD HD Check	CYC Post LCMS & BD HD Check	5FU Pre LCMS	5FU Post LCMS	PAC Pre LCMS	PAC Post LCMS	DOC Pre LCMS	DOC Post LCMS
Nurse station 1a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 1b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Patient side table 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse CPU 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Under HD waste bin 1	ND	ND	ND	ND	0.004[LOD]	0.003[LOD]	0.015	0.016	0.014	0.011	ND	ND
Under HD waste bin 2	ND	ND	ND FP	ND	0.011[LOD]	0.006[LOD]	0.268	0.309	3.594	0.008	0.008	ND
Under IV infusion stand 1	ND	ND	ND FP	ND	0.019[LOD]	0.015[LOD]	0.039	ND	0.043	ND	ND	ND
Under IV infusion stand 2	ND	ND	ND	ND	0.018[LOD]	0.014[LOD]	0.140	0.547	2.074	0.022	0.013	ND
Supply cart 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 2a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 2b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Patient side table 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse CPU 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Supply cart 2	ND	ND	ND	ND	ND	ND	0.023	0.049	ND	ND	ND	ND
BSC surface 1	ND	ND	0.004	ND	5.276 FN	0.005[LOD]	3.071	1.244	0.576	0.014	0.161	ND
BSC surface 2	ND	ND	ND	ND	0.093[LOD]	ND	4.653	22.203	0.015	ND	0.030	ND
Pass-through window 1	ND	ND	ND	ND	0.426[LOD]	0.004[LOD]	2.785	0.235	0.169	ND	0.117	ND
Pass-through window 2	ND	ND	ND	ND	0.014[LOD]	ND	0.198	1.203	ND	0.005	ND	ND
Under BSC 1	ND	ND	ND	ND	0.309[LOD]	0.044[LOD]	4.862	1.012	NR	ND	0.007	ND
Under BSC 2	ND	ND	0.006	ND	2.182 FN	0.072	49.471	1.950	NR	ND	0.031	0.006
Pharmacy prep area	ND	ND	ND	ND	0.02[LOD]	0.004[LOD]	ND	ND	ND	ND	ND	ND
Pharm chemo check 1	ND	ND	ND	ND	0.004[LOD]	ND	ND	ND	ND	ND	ND	ND

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Table 1. HD Contamination at Infusion Center Location A in Pre- and Post-CSTD Testing

Location A Sample Sites	DOX Pre	DOX Post	MTX Pre	MTX Post	CYC Pre	CYC Post	5FU Pre	5FU Post	PAC Pre	PAC Post	DOC Pre	DOC Post
	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS	LCMS	LCMS	LCMS	LCMS	LCMS
Pharm chemo check 2	ND	ND	ND	ND	0.006[LOD]	ND	ND	0.029	ND	ND	ND	ND
Pharm chemo check 3	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Chemo dispense station	ND	ND	ND	ND	0.008[LOD]	ND	0.141	0.014	ND	ND	ND	ND
Pharm entrance door	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ADC keyboard	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Average concentration	0.0000	0.0000	0.005	0.0000	0.5993	0.0186	5.4722	2.4009	0.9264	0.0120	0.0524	0.0060
Standard deviation	0.0000	0.0000	0.0014	0.0000	1.4638	0.0238	13.9827	6.2673	1.3888	0.0065	0.0613	0.0000

Abbreviations: ADC, automated dispensing cabinet; BSC, biological safety cabinet; CPU, computer; CSTD, closed-system drug transfer device; CYC, cyclophosphamide; DOX, doxorubicin; 5FU, fluorouracil; HD, hazardous drug; IV, intravenous; LCMS/MS, liquid chromatography with tandem mass spectrometry; LOD, limit of detection; ND, not detected; NR, no result.

[a]All numerical data are expressed as ng/cm2.

[b]Shading indicates ND (green), <0.1 (blue), 0.1 to ≤1.0 (yellow), or >1.0 (red) per ChemoGLO report categorizations.

[c]Positive/negative readings on the lateral flow immunoassay device (BD HD Check; Becton, Dickinson and Company) were congruent with LCMS/MS results unless otherwise noted with superscript FN (false negative), FP (false positive), or LOD (incongruent read that fell below the BD HD Check LOD).

during post-CSTD testing, no MTX contamination was detected, resulting in no contaminated surfaces and a reduction in the average contamination concentration (Table 1).

CYC contamination was much more widespread. During pre-CSTD testing, 14 of 27 surfaces (52%) tested for CYC contamination exceeded detectable levels (Table 1). Four of these workstation surfaces, 2 under BSC areas, a BSC surface, and a pharmacy pass-through, reached medium to high CYC concentrations (Table 1). After CSTD implementation, all CYC-contaminated surfaces showed a reduction in CYC concentrations: 5 surfaces had no detectable contamination, and the other 9 surfaces all fell into the low contamination range (Table 1). Overall, post-CSTD readings showed a reduction in the number of contaminated surfaces to 9 of 27 (33%) and a reduction in the average CYC concentration from 0.5993 ng/cm^2 to 0.0186 ng/cm^2 (Table 1).

Detectable quantities of fluorouracil were found on 12 of 27 surfaces (44%) at location A. In post-CSTD screening, 6 of these surfaces showed a reduction in fluorouracil levels: 2 surfaces shifted into lower concentration groups, and 1 surface showed no detectable contamination (Table 1). The other 6 surfaces found to be contaminated in pre-CSTD testing showed an increase in fluorouracil levels in post-CSTD analyses, with 1 surface escalating from medium to high contamination and another showing an increase in the contaminant concentration from 4.653 ng/cm^2 to 22.203 ng/cm^2. There was also 1 surface that did not test positive during pre-CSTD testing but tested positive at low concentrations in post-CSTD analyses (Table 1). The post-CSTD analyses therefore did not show an overall reduction in the number of contaminated surfaces (it remained at 12 of 27; 44%), but the average level of fluorouracil contamination was reduced from 5.4722 ng/cm^2 to 2.4009 ng/cm^2 (Table 1).

PAC was initially detected on 7 of 27 workstation surfaces (26%); of

Table 2. HD Contamination at Infusion Center Location B in Pre- and Post-CSTD Testing[a,b,c]

Location B Sample Sites	DOX Pre LCMS & BD HD Check	DOX Post LCMS & BD HD Check	MTX Pre LCMS & BD HD Check	MTX Post LCMS & BD HD Check	CYC Pre LCMS & BD HD Check	CYC Post LCMS & BD HD Check	5FU Pre LCMS	5FU Post LCMS	PAC Pre LCMS	PAC Post LCMS	DOC Pre LCMS	DOC Post LCMS
Nurse station 1a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 1b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Patient side table 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse CPU 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Under HD waste bin 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Under HD waste bin 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Under IV infusion stand 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Under IV infusion stand 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Supply cart 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 2a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse station 2b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Patient side table 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Nurse CPU 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Supply cart 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
BSC surface 1	ND	ND	ND	ND	ND	ND	ND	0.013	ND	0.033	ND	ND
BSC surface 2	ND	ND	ND	ND	ND	0.022[LOD]	0.612	0.019	ND	0.054	ND	ND
Pass-through window 1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Pass-through window 2	ND	ND	ND	ND	ND	0.003[LOD]	0.012	ND	ND	ND	ND	ND
Under BSC 1	ND	ND	ND	ND	ND	ND FP	ND	ND	ND	ND	ND	ND
Under BSC 2	ND	ND	ND	ND	ND	ND FP	ND	ND	ND	ND	ND	ND
Pharmacy prep area	ND	ND	ND	ND	ND	ND	0.203	ND	ND	ND	ND	ND
Pharm chemo check 1a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Pharm chemo check 1b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

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Table 2. HD Contamination at Infusion Center Location B in Pre- and Post-CSTD Testing

Location B Sample Sites	DOX Pre	DOX Post	MTX Pre	MTX Post	CYC Pre	CYC Post	5FU Pre	5FU Post	PAC Pre	PAC Post	DOC Pre	DOC Post
	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS & BD HD Check	LCMS	LCMS	LCMS	LCMS	LCMS	LCMS
Pharm chemo check 2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Chemo dispense station	ND	ND	ND	ND	ND	ND	0.018	ND	ND	ND	ND	ND
Pharm entrance door	0.01[LOD]	ND FP	ND	ND	ND	ND	0.106	ND	ND	ND	ND	ND
ADC keyboard	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Average concentration	0.010	0.000	0.000	0.000	0.000	0.013	0.190	0.016	0.000	0.044	0.000	0.000
Standard deviation	0.000	0.000	0.000	0.000	0.000	0.013	0.248	0.004	0.000	0.015	0.000	0.000

Abbreviations: ADC, automated dispensing cabinet; BSC, biological safety cabinet; CPU, computer; CSTD, closed-system drug transfer device; CYC, cyclophosphamide; DOX, doxorubicin; 5FU, fluorouracil; HD, hazardous drug; IV, intravenous; LCMS, liquid chromatography with tandem mass spectrometry; LOD, limit of detection; ND, not detected; NR, no result.

[a]All numerical data are expressed as ng/cm2.

[b]Shading indicates ND (green), <0.1 (blue), 0.1 to ≤1.0 (yellow), or >1.0 (red) per ChemoGLO report categorizations.

[c]Positive/negative readings on the BD HD Check lateral flow immunoassay device (Bectom, Dickinson and Company) were congruent with LCMS/MS results unless otherwise noted with superscript FN (false negative), FP (false positive), or LOD (incongruent read that fell below the BD HD Check LOD).

these contaminated surfaces, 3 had low concentrations, 2 had medium concentrations, and 2 had high concentrations (Table 1). All surfaces that tested positive for PAC in pre-CSTD analyses showed reduced PAC levels in post-CSTD analyses, with 4 categorized in low concentration ranges and 3 surfaces having no detectable contamination (Table 1). One surface that had nondetectable quantities on pre-CSTD testing was contaminated at a low level (0.005 ng/cm^2) on post-CSTD testing, resulting in a final post-CSTD total of 5 of 27 contaminated surfaces (18%) and a reduction in average contamination from 0.9264 ng/cm^2 to 0.012 ng/cm^2 (Table 1).

Finally, 7 of the 27 surfaces assayed for DOC tested positive at either low or medium concentrations (26%) (Table 1). All 7 surfaces showed reductions in DOC concentrations in post-CSTD analyses, with 6 surfaces reading nondetectable, leaving just 1 contaminated surface (1/27; 4%) (Table 1). Average contamination concentration was therefore reduced from 0.0524 ng/cm^2 to 0.006 ng/cm^2 (Table 1).

Qualitative analysis: pre- and post-CSTD. Across all workstations assessed for DOX, MTX, and CYC during both pre- and post-CSTD screening, a total of 162 readings by the BD HD Check were obtained. Twenty-three of the 25 positive LCMS/MS readings were concentrations lower than the BD HD Check LOD; however, the BD HD Check accurately identified 3 of these instances (12%) (Table 1). Finally, of 137 negative LCMS/MS readings, 135 (98.5%) were accurately identified by the BD HD Check device. This brought the device's overall accuracy against LCMS/MS to 85.2% (138 correct readings out of a total of 162 readings) and accuracy within its LOD to 97.1% (135 correct readings out of a total of 139 LCMS/MS readings within the BD HD Check device's LOD).

Location B. ***Quantitative analysis: pre- and post-CSTD and follow-up.*** LCMS/MS analyses for MTX and DOC at both pre- and post-CSTD time points did not indicate any

surface contamination (Table 2). Low DOX contamination was reported on the pharmacy door tested in pre-CSTD analysis (1 of 27 samples; 3.7%), but the contaminant level was lowered to nondetectable during post-CSTD testing (Table 2). During pre-CSTD analysis, there was no detectible CYC contamination; however, 2 of 27 sampled surfaces (7.4%), a BSC surface and a pharmacy pass-through window, showed low levels of contamination in post-CSTD testing, increasing the average contamination level to 0.013 ng/cm^2 (Table 2). This trend was repeated with PAC contamination as well: While no surfaces were initially contaminated, 2 of 27 BSC surface sites (7.4%) had contamination in post-CSTD analysis, which raised the average contamination level to 0.044 ng/cm^2 (Table 2). Finally, fluorouracil contamination was observed on 5 of 27 surfaces (18%) initially, and all but 1 of those surfaces did not show subsequent contamination during post-CSTD analysis; for the 1 surface that still showed contamination in post-CSTD testing, the level of fluorouracil contamination was lowered from medium to low. However, 1 surface with no detectable contamination during pre-CSTD analysis showed contamination after CSTD implementation, bringing the number of contaminated surfaces in post-CSTD testing to 2 of 27 (7%) (Table 2). Additionally, the average fluorouracil contamination concentration decreased from 0.190 ng/cm^2 to 0.016 ng/cm^2 (Table 2).

Average HD contamination concentrations overall were relatively low in both pre- and post-CSTD testing. While CYC and PAC concentrations were slightly elevated in post-CSTD testing relative to pre-CSTD testing levels, the concentrations themselves remained in the lowest range. For all the other HDs tested, contamination levels were either maintained as undetectable or were reduced from pre-CSTD levels (Table 2).

Qualitative analysis: pre- and post-CSTD. Of the total of 162 LCMS/MS readings for DOX, MTX, and CYC contamination at location B, 3 showed surface contamination and 159 showed no contamination. The BD HD Check device did not report any of the LCMS/MS-reported contamination (0 of 3 LCMS/MS-positive reads); however, all HD concentrations were below the BD HD Check LOD (Table 2). Conversely, the BD HD Check accurately assessed 98.1% (156/159) of LCMS/MS-negative results. This brought the BD HD Check device's accuracy against LCMS/MS to 96.3% (156 correct readings out of 162 total readings) and accuracy within its LOD to 98.1% (156 correct readings out of 159 LCMS/MS readings within the BD HD Check LOD) (Table 2).

Statistical analysis. The ANOVA model provided overall trends of HD contamination reduction for instances where contamination was observed. Sample sites, HDs, and implementation time point contamination averages varied significantly within their groups. There was also a significant sample site by HD interaction (all P values < 0.0001; eTable 2). Overall, implementation of the BD PhaSeal Optima resulted in a 46% reduction in LCMS/MS-reported HD contamination (P < 0.0001, eTable 3). No statistically significant decrease was observed in the BD HD Check results (not shown).

Discussion

At both location A and location B, the number of contaminated surfaces, as well as contamination concentrations, were lower during post–CSTD implementation testing for a majority of the HDs. Of the 5 HDs associated with contamination at location A in pre-CSTD testing, 4 (MTX, CYC, PAC, and DOC) were identified as contaminating fewer surfaces in post-CSTD testing, and contamination concentrations were reduced for all 4 drugs (Table 1). Location B had fewer contaminated surfaces in post-CSTD screening for DOX and fluorouracil (2 HDs out of 6 total HDs; 33.3%), while testing for MTX and DOC showed no contaminated surfaces in either pre- or post-CSTD testing. During postimplementation testing, contamination concentrations were also found to be relatively low for all HDs tested at location B (Table 2). Therefore, the implementation of the BD PhaSeal Optima CSTD was associated with a statistically significant reduction in contamination (eTable 3). Use of the BD Phaseal Optima CSTD and routine 6-month LCMS/MS wipe sampling of pharmacy and nursing areas has continued, allowing area risk assessment and creation of necessary action plans. This approach has be effective in prolonged contamination prevention, emphasizing, in part, the important role of CSTDs such as the BD Phaseal Optima in HD-handling workflows.

Some exceptions to these reductions were seen in in both locations. At location A, the number of fluorouracil-contaminated surfaces did not change between pre- and postimplementation testing. The preparation of fluorouracil, along with other home infusion HDs, requires steps at our facility that do not utilize CSTDs. These steps may increase the risk of HD contamination and may help explain why fluorouracil contamination (number of surfaces and concentrations) was higher than for other HDs at both locations (Tables 1 and 2). While this study did not explicitly examine other variables that may contribute to contamination, the 2020 Safe to Touch Consensus report acknowledged that factors such as manufacturer container design and safety labeling may also play a role.[15] Exceptions illustrate the need for ongoing frequent environmental monitoring and decontamination practices.

Another primary aim of this study was to assess the accuracy of the BD HD Check. Across all locations, drugs, and time points, and disregarding the BD HD Check LOD, the overall accuracy of the BD HD Check against traditional LCMS/MS analyses was 90.7% (294 accurate BD HD Check reading out of 324 total readings; false-positive rate, 1.5% [5/324]; false-negative rate, 7.7% [25/324]) (Tables 1 and 2). However, 23 of the 30 incongruent BD HD Check readings were due to concentrations that fell below the BD HD Check LOD. Therefore, if only data falling within

the LOD are considered, the overall BD HD Check accuracy was 97.7% (291 accurate readings within LOD out of 298 readings within LOD; false-positive rate, 1.7% [5/298]; false-negative rate, 0.7% [2/298]). Given that the BD HD Check readings were overwhelmingly consistent with quantitative analyses, it could serve as a useful real-time measurement tool to supplement traditional LCMS/MS tests.

Recognized limitations of this study relate to study size, CSTD risks, and compliance measures. Our study only sampled a handful of surfaces at 2 facilities; scaling up would demonstrate whether the patterns we observed in this study are generalizable. Oncology centers across the country are required to risk-assess various dosage forms for compatibility and safety with CSTDs. In cases of incompatibility, CSTDs may not be utilized, meaning some sources of contamination may never be entirely eliminated. Furthermore, the BD PhaSeal Optima is a membrane-based CSTD that utilizes luer-lock mechanisms,[29,31] which have the inherent risk of unlocking and leading to unintentional HD spills outside the CSTD membrane.[32] Also, assessments of CSTD compliance were not performed throughout the duration of the study, so measures of CSTD compliance cannot be correlated to the observed reduction in contamination.

This study assessed the efficacy of the latest-generation BD PhaSeal Optima CSTD and the accuracy of the rapid POC test, the BD HD Check, across both nursing and pharmacy practice areas where HDs are handled. CSTD implementation may be associated with a reduction in the number and concentration of contaminated surfaces across 2 separate chemotherapy infusion centers. We also demonstrated that use of the HD Check accurately reported over 90% of the LCMS/MS wipe sample results. To date, CSTD use is widely recommended during HD compounding and administration and organizations like the United States Pharmacopeia have highlighted its importance in combating HD contamination in clinical settings.[17] CSTDs should be part of overarching initiatives, which may also include rapid POC tests, to reduce contamination. Currently, the BD HD Check system is the only rapid HD detection system that can provide results in less than 10 minutes[20] and can detect contamination from 3 common HDs: MTX, CYC, and DOX. As a supplement to other approaches, the HD Check could be used as a real-time measure for decontamination efforts, and as a quicker monitoring device for patient, employee, and environmental safety. Therefore, our study provides support for using both the BD PhaSeal Optima CSTD and BD HD Check as part of a multifaceted approach to ensure a safer clinical environment.

Future studies can build on our work to universalize testing standards by assessing expanded HD surface contamination protocols. There is currently no global standardization on HD risk assessment and no tiered action planning protocols in response to various levels of detected HDs. Our study adopted and supported the use of concentration ranges laid out by ChemoGLO and other publications as a global standard for HD contamination detection ranges.[18] We observed delineation between categories that aligned with LCMS/MS data, and in future studies, this could be used to establish graded action planning responses. Additionally, our study elucidated crude HD contamination risks for different sample sites that facilities could use to target routine monitoring practices (eTable 4). Future studies should also assess more robust contamination prevention protocols, such as using POC tests at regular intervals, in order to maintain routine monitoring[15] and determine effective prevention strategies. Several publications have demonstrated reductions or elimination of HD contamination after routine monitoring,[10,33] and use of the BD HD Check has the potential to reduce some costs associated with frequent wipe sampling. Finally, compliance with prevention/monitoring protocols, as well as patient/employee satisfaction, should be recorded in future studies as well.

Conclusion

Collectively, the evaluated CSTD and lateral flow immunoassay device may help to reduce HD contamination and provide real-time measures of contamination, respectively. As part of a multifaceted approach, these devices may help minimize barriers to routine monitoring, ultimately improving the safety of HCWs and patients.

Disclosures

Support for technical writing assistance, provided by FORCE Communications, was provided by Becton, Dickinson and Company (BD). BD worked in conjunction with FORCE Communications and Dr. Brechtelsbauer to perform statistical analysis but had no additional role in study design, data collection, decision to publish, or manuscript preparation. Dr. Brechtelsbauer has provided consulting services for BD.

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