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Reduction in surface contamination with antineoplastic drugs in 22 hospital pharmacies in the US following implementation of a closed-system drug transfer device

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Abstract

Purpose—Surface contamination with the antineoplastic drugs cyclophosphamide, ifosfamide, and 5-fluorouracil was compared in 22 US hospital pharmacies following preparation with standard drug preparation techniques or the PhaSeal® closed-system drug transfer device (CSTD).

Methods—Wipe samples were taken from biological safety cabinet (BSC) surfaces, BSC airfoils, floors in front of BSCs, and counters and analyzed for contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil. Contamination was reassessed several months after the implementation of the CSTD. Surface contamination (ng/cm^2) was compared between the two techniques and evaluated with the Signed Rank Test.

Results—Using the CSTD compared to the standard preparation techniques, a significant reduction in levels of contamination was observed for all drugs (cyclophosphamide: p <0.0001; ifosfamide: p <0.001; 5-fluorouracil: p <0.01). Median values for surface contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil were reduced by 95%, 90%, and 65%, respectively.

Conclusions—Use of the CSTD significantly reduces surface contamination when preparing cyclophosphamide, ifosfamide, and 5-fluorouracil as compared to standard drug preparation techniques.

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Keywords

Antineoplastic agents; closed-system drug transfer device; surface contamination; drug preparation; hospital pharmacies; cyclophosphamide

Introduction

Over the last 20 years, several studies have been published showing environmental contamination with antineoplastic drugs in hospital pharmacies.[1–28] In addition, several studies have shown that antineoplastic drugs are inadvertently absorbed by healthcare workers through environmental exposure as determined by the presence of the parent compound and/or its metabolite(s) in their urine.[12,18,29–41]

Because of the hazardous properties of these drugs, adverse health effects such as cancer, fetal malformations, and fetal loss during pregnancy might occur.[42–62] Therefore, unnecessary occupational exposure to these drugs should be limited to reduce the risk of any associated health problems in healthcare personnel. Special mixing techniques, personal protective equipment and the use of Class II BSCs were introduced during the eighties.[63] Although overall exposure was reduced as a result of implementing these precautionary measures, significant environmental contamination, and antineoplastic drug exposure to hospital workers is still commonly observed in US hospitals.[3,4,26,28]

Due to the potential health risks of antineoplastic drugs, the increasing use of these drugs, and the continuing environmental contamination and employee exposure, the National Institute for Occupational Safety and Health (NIOSH) published an alert on anti-neoplastic and other hazardous drugs used in health-care settings.[64] Based upon the recommendations in the NIOSH Alert, the American Society of Health-System Pharmacists (ASHP) has published updated guidelines on the safe-handling of cytotoxic and hazardous drugs.[65]

The NIOSH Alert and ASHP guidelines make several recommendations to limit environmental contamination in an effort to limit unnecessary exposure of these drugs to healthcare workers. One recommendation is to consider the use of closed-system drug transfer devices (CSTD) when transferring the hazardous drugs from primary packaging (such as vials) to dosing equipment (such as infusion bags, bottles or pumps). Closed-systems allow for the containment of aerosolized or vaporized drug while limiting the potential for direct skin contact or inhalation from inadvertent release of drug to the environment.

In 2000, the PhaSeal® closed-system drug-transfer device (Carmel Pharma ab,)[a] was introduced in the US. Studies have shown that the implementation of this system resulted in a decrease of drug contaminants inside Class II BSCs and in the environment.[4,26,28,66] Most studies were conducted in one to three hospitals. In this study, the PhaSeal® CSTD was evaluated in 22 hospital pharmacies where the system was introduced over the period 2000–2005. Wipe samples were taken from potentially contaminated work surfaces. In all hospital pharmacies, the same type of surfaces were wiped and analyzed for cyclophosphamide, ifosfamide, and 5-fluorouracil contamination. Following the first round of sampling, the

PhaSeal® CSTD was introduced. After several months of preparation with the PhaSeal® CSTD, surface contamination was reassessed from the same surfaces. Surface contamination results were compared between the two techniques.

Methods

Study design and sample collection

This study was conducted from June 2000 till May 2005 in 22 US hospital pharmacies who self reported that antineoplastic drugs are prepared according to national guidelines.[67,68] These guidelines include use of Class II BSCs, protective gloves, disposable gowns, and aseptic and negative-pressure mixing techniques using needle syringes defined as standard drug preparation techniques.

Surface contamination was assessed by taking wipe samples. Cyto Wipe Kits were used containing standardized supplies for sampling and wipe procedure (Exposure Control B.V.,[b]). Seventeen millilitres of 0.03 M NaOH solution was applied to each surface and then wiped using one tissue. A second tissue was used to remove the remaining liquid. Both tissue samples were immediately placed in a storage container, sealed, and placed in storage at −20°C or colder. When all samples were collected, they were shipped on dry ice to Exposure Control B.V. in The Netherlands for analysis. Trained persons were responsible to take the samples in one or more hospitals. To avoid bias, all samples within one hospital were taken by the same person.

Sampling surfaces included the BSC surfaces, BSC airfoils, floors in front of BSCs and counters. In some hospitals more than one surface, airfoil, floor or counter was tested due to the additional BSCs and counter-tops present in these institutions. If surfaces were not used for drug handling, wipe samples were not collected. The surface area wipes ranged from 300 to 11,050 cm^2.

After the first series of wipe samples were taken, the CSTD was introduced into the hospitals. Several months after use of the CSTD, wipe samples were taken from the same surfaces and contamination was reassessed.

The wipe samples were analyzed for cyclophosphamide, ifosfamide, and 5-fluorouracil contamination. These drugs were selected for monitoring because they were frequently used at most hospitals and documented sampling methods and sensitive analytical methods were available. If a drug was rarely used in a hospital, the wipe samples were not analyzed for the specific drug.

Sample preparation and analysis

Sample preparation was performed according to published procedures.[16,31,32,69] Each sample was analyzed for the presence of cyclophosphamide and ifosfamide by gas chromatography in tandem with mass spectroscopy-mass spectroscopy, and for 5-fluorouracil using reverse-phase HPLC with ultraviolet-light detection. Methods for both analyses were developed by Sessink et al.[16,31,32,69] The analytical detection limits for cyclophosphamide, ifosfamide and for 5-fluorouracil were 0.10, 0.10, and 20 ng/mL of

extract, respectively. This allowed detection of 16 ng of cyclophosphamide and ifosfamide and 3200 ng of 5-fluorouracil per sampling surface after sample processing and dilution with reagents for analysis. The drug recovery from the surfaces was >80% for cyclophosphamide and ifosfamide, and >95% for 5-fluorouracil.

Statistical methods

For each drug and surface, absolute amounts of contamination/cm^2 were compared between the two techniques using the Signed Rank Test. The Kruskal–Wallis Test was applied to assess differences of contamination between the sampling surfaces for each drug and for each technique separately. P-values of 0.05 or less were deemed significant. Data were characterized by median and range.

PhaSeal® CSTD

The system is composed of three components, the Injector, the Protector and the Connector. The syringe device is called the Injector and works with a double membrane that creates a dry connection in all interfaces with other components of the system. The Protector is the vial device that uses a sealed expansion chamber to maintain a neutral pressure during drug reconstitution. The Connector is the connection device used in all patient or infusion connections.

Results

During the test period, 114 samples were selected from 22 hospitals. The results of surface contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil are presented in the Tables 1–4. The results were separated into preparation according to standard preparation techniques and preparation with the CSTD. Measurements reported for each drug and each site are single measurements.

Using standard preparation techniques, contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil was recorded. Prior to the introduction of the CSTD, 78% of the wipe samples of the four surfaces tested positive for cyclophosphamide contamination, 54% tested positive for ifosfamide, and 33% tested positive for the presence of 5-fluorouracil. A significant difference in contamination for all drugs was observed between the four surfaces showing the BSC airfoils to be the most heavily contaminated (cyclophosphamide: $p < 0.01$; ifosfamide: $p < 0.05$; 5-fluorouracil: $p < 0.0001$).

Using the CSTD, contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil was still observed, but the percentage of positive samples for all drugs was reduced. Sixty-eight percent of the wipe samples of the four surfaces tested positive for cyclophosphamide, 45% tested positive for ifosfamide, and 20% tested positive for 5-fluorouracil. However, compared to the standard preparation techniques, a significant reduction in levels of contamination was observed for all drugs (cyclophosphamide: $p < 0.0001$; ifosfamide: $p < 0.001$; 5-fluorouracil: $p < 0.01$). Median values for surface contamination with cyclophosphamide, ifosfamide, and 5-fluorouracil were reduced by 95%, 90%, and 65%, respectively. A significant difference in levels of contamination for all drugs was observed

between the four surfaces showing again the BSC airfoils to be the most heavily contaminated (cyclophosphamide: $p < 0.05$; ifosfamide: $p < 0.01$; 5-fluorouracil: $p < 0.0001$).

Discussion

The results of this study concur with the results of similarly conducted studies, which again show that needle and syringe preparation techniques do not prevent release of drugs during preparation in hospital pharmacies.[1–28] As a consequence, it is possible that healthcare workers are exposed to these harmful drugs resulting in adverse health effects.[42–62] As a result of the increasing concern, the NIOSH Alert sought to reduce environmental contamination and potential exposure to these drugs. This increased concern also led ASHP to update their existing guidelines concerning the safe-handling of cytotoxic and hazardous drugs.[65] One of the recommendations proposed in the ASHP guidelines is to use a CSTD.

In the US, four quantitative studies and one qualitative study have evaluated the use of a CSTD in reducing contamination of the workplace with anti-neoplastic drugs.[4,26,28,66,71] In addition two similar studies have been published in Europe.[19,25]

Connor et al. measured surface contamination for six months at 28 day intervals following implementation in a newly renovated pharmacy area.[4] Cyclophosphamide and ifosfamide were prepared using a CSTD, while 5-fluorouracil was prepared in the conventional manner. Overall, cyclophosphamide and ifosfamide levels were lower than 5-fluorouracil levels on a per gram basis.

Wick et al. examined cyclophosphamide and ifosfamide surface contamination in pharmacy and nursing areas following implementation of a CSTD for six months.[26] They reported reductions in both the percentage of wipe samples that were above the limit of detection and the concentration of the drugs in the wipe samples.

Harrison et al. evaluated surface contamination in three hospital pharmacies with cyclophosphamide and 5-fluorouracil.[28] Following a 12-week baseline collection of biweekly samples, a CSTD was implemented with both drugs, with 5-fluorouracil being prepared outside the BSC on a benchtop. The CSTD was used for 12 weeks and samples were collected biweekly. At the end of the 12 weeks, the drugs were again prepared using standard procedures. The surface contamination was significantly lower for cyclophosphamide with the use of the CSTD and there was no significant increase in 5-fluorouracil contamination when it was prepared outside the BSC with the CSTD.

Nyman et al. measured the concentration of cyclophosphamide and ifosfamide in a new hospital pharmacy following the use of a CSTD for six months for their preparation.[71] Twenty-one percent of cyclophosphamide and 12% of ifosfamide have levels of drug above the limit of detection. The authors conclude these values were below their historical controls for other sites.

Spivey and Connor employed a fluorescent compound to visually compare standard drug compounding and administration techniques with the use of a CSTD.[66] When viewed under UV light, all phases of the compounding and administration demonstrated visible

contamination with the fluorescent compound. However, 75 simulated procedures with the CSTD did not reveal any visible fluorescence.

Most previous studies were performed in one to three hospital pharmacies. The results of these studies are influenced by the study design such as the number of surfaces and drugs tested and the wipe sampling procedure. A disadvantage is that the results cannot be compared with each other due to the various methodologies employed in each study. To overcome these shortcomings, it is important to employ a uniform study design to be able to compare the results between the hospital pharmacies by selecting the same surfaces to be wiped, the same drugs to be tested, and the same sampling procedure in all hospital pharmacies. In some cases, surfaces were not sampled and drugs were not analyzed if the surface was not used for drug handling and/or the drug was rarely used. This would result in false negative findings. In addition, it is important that the time of wipe sampling after the introduction of the CSTD is long enough to offer the opportunity for potential contamination to accumulate to create a situation for a fair comparison with the pre-CSTD period. Hence, we have selected a period of at least several months. In an effort to evaluate these studies on a larger scale and to overcome the shortcomings mentioned, the CSTD was tested in 22 US hospitals.

The results show the BSC airfoils to be the most heavily contaminated surfaces. This is not surprising because the airfoils are the surfaces where preparation activities are actively performed. Release of the drugs will result in high levels of contamination of airfoils and the gloves of the healthcare workers. Away from the preparation site, surfaces such as floor and counter will be less contaminated as observed in this study.

The results show that a reduction in environmental contamination can be achieved if the preparation is performed by using the CSTD. However, even with the use of the CSTD, environmental contamination was still observed. Possible sources contributing to this observation may include remaining contamination from the past and introduction of new contamination via external contamination on the drug vials. A US study has been published showing surface contamination of chemotherapy drug vials.[70] While the results of this 22 hospital study show reduction in contamination, the true reduction will always be clouded by how much contamination from the manufacturing process remains on the outsides of the vials. Contamination from drug vial surfaces may be transferred from the vials to the gloves of the healthcare worker and finally to the environment. Until there is an industry consensus or federal mandate to require provision of contamination-free vial exteriors, then healthcare workers will remain at risk of exposure.

Conclusion

The results of this study show the possibility to reduce environmental contamination with antineoplastic drugs in hospital pharmacies using the CSTD. A reduction in environmental contamination can contribute to a reduced exposure potential for healthcare workers in these areas. Compliance with current safe handling guidelines in the United States will also be enhanced through the use of a CSTD.

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Mention of company names and/or products does not constitute endorsement by the Centers for Disease Control and Prevention (CDC).

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Table 1

Contamination with cyclophosphamide (CP), ifosfamide (IP), and 5-fluorouracil (5FU) on BSC surfaces in 22 US hospital pharmacies (ng/cm^2)

Site, state and test periods				BSC Surface					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
1	CA	Jul-01	Mar-02	<0.03	<0.03	<0.03	0.09	<5.3	<5.3
2	CA	Jun-01	Dec-01	<0.01	0.03	0.18	0.02	<1.3	<0.9
				0.05	0.01	0.51	<0.01	<4.0	<0.9
3	CA	Jun-01	Jan-02	0.33	0.01	0.01	<0.01	3.0	<0.9
				0.01	<0.01	<0.01	<0.01	<1.4	<0.9
4	TX	Jan-02	Jun-02	0.47	0.02	0.18	0.72	<2.9	0.6
5	MA	Jan-02	Aug-02	0.63	1.90	5.03	0.80	<0.8	<0.8
6	MN	Oct-00	Feb-01	0.05	0.01	ns	ns	ns	ns
7	TX	Jun-00	Apr-01	0.06	<0.01	<0.02	<0.02	ns	ns
				<0.01	0.02	0.17	0.01	ns	ns
				11.44	0.03	ns	ns	ns	ns
8	OH	Mar-01	Oct-01	<0.01	0.03	ns	ns	<0.9	<0.8
9	UT	Nov-01	Jun-02	0.02	<0.02	<0.02	<0.02	<3.6	<3.6
10	CA	Aug-02	Feb-03	0.21	0.02	ns	ns	9.9	15.2
11	MI	Mar-04	Sep-04	<0.01	<0.01	<0.01	<0.01	<0.6	<0.6
				<0.01	<0.01	<0.01	<0.01	<0.6	<0.6
12	WI	Dec-03	Jul-04	0.01	<0.01	ns	ns	<2.2	<0.4
13	MD	Aug-04	Jan-05	4.31	0.07	0.04	<0.01	<0.5	<0.5
				17.19	0.04	0.23	<0.01	<0.5	<0.5
14	IL	Jul-04	Apr-05	0.13	0.02	0.02	<0.01	<1.1	<0.5
				0.97	0.01	<0.01	<0.01	<0.5	<0.5
15	ID	Nov-01	Jul-02	0.24	<0.01	ns	ns	17.2	<1.6
16	CA	Mar-02	Nov-02	0.23	5.41	<0.01	<0.01	<0.7	<0.7
				0.12	<0.01	<0.01	<0.01	<0.7	<0.7
				6.47	0.04	0.44	0.01	4.5	<0.7
17	MI	Apr-02	Nov-02	2.72	0.04	<0.01	0.01	<0.7	<0.7
18	NH	Jun-03	Jan-04	4.97	<0.01	<0.01	<0.01	<0.7	<0.7

Site, state and test periods				BSC Surface					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
19	NH	Jun-03	Dec-03	0.08	0.02	<0.01	<0.01	<1.2	6.2
20	CA	Aug-03	May-04	0.05	<0.01	ns	ns	<0.5	<0.5
21	NY	Jul-04	Jan-05	ns	ns	ns	ns	ns	ns
22	IL	Jun-04	May-05	0.30	1.84	0.10	8.86	ns	ns
Median				0.13	0.02	0.01	0.01	0.5	0.3
Min				<0.01	<0.01	<0.01	<0.01	<0.5	<0.4
Max				17.19	5.41	5.03	8.86	17.2	15.2

[a]−preparation according to standard preparation techniques, + preparation with the CSTD, ns not sampled (the drug was rarely used at this site or the surface was not used for drug handling).

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Table 2

Contamination with cyclophosphamide (CP), ifosfamide (IP), and 5-fluorouracil (5FU) on BSC airfoils in 22 US hospital pharmacies (ng/cm^2)

Site, state and test periods				BSC Airfoil					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
1	CA	Jul-01	Mar-02	0.60	0.44	1.85	0.94	26.3	29.2
2	CA	Jun-01	Dec-01	0.05	0.15	0.18	0.13	11.9	<3.6
				0.04	1.81	0.67	<0.02	<5.3	102.6
3	CA	Jun-01	Jan-02	158.00	3.11	0.18	<0.18	<2.7	<1.8
4	TX	Jan-02	Jun-02	0.98	<0.03	1.20	3.24	8.8	<4.7
5	MA	Jan-02	Aug-02	60.08	17.15	24.28	5.09	<4.5	<4.5
6	MN	Oct-00	Feb-01	0.10	0.01	ns	ns	ns	ns
7	TX	Jun-00	Apr-01	9.94	11.72	<0.04	<0.04	ns	ns
				<0.02	0.02	1.18	0.02	ns	ns
				4.85	0.04	ns	ns	ns	ns
8	OH	Mar-01	Oct-01	<0.02	0.28	ns	ns	15.2	8.0
9	UT	Nov-01	Jun-02	0.06	<0.06	<0.06	<0.06	<10.7	<10.7
10	CA	Aug-02	Feb-03	0.16	0.03	ns	ns	56.6	11.1
11	MI	Mar-04	Sep-04	<0.02	<0.02	<0.02	<0.02	<3.5	<3.5
				<0.02	<0.02	<0.02	<0.02	<3.5	<3.5
12	WI	Dec-03	Jul-04	ns	ns	ns	ns	ns	ns
13	MD	Aug-04	Jan-05	80.72	1.29	8.09	0.02	<1.8	<1.8
				49.51	1.90	2.37	0.02	12.8	<1.8
14	IL	Jul-04	Apr-05	ns	ns	ns	ns	ns	ns
15	ID	Nov-01	Jul-02	0.99	<0.02	ns	ns	<2.4	<2.3
16	CA	Mar-02	Nov-02	10.64	7.03	<0.02	0.15	26.0	24.2
				27.71	<0.01	0.04	0.02	<4.0	<4.0
				19.08	2.14	0.39	0.20	13.2	<2.1
17	MI	Apr-02	Nov-02	2.87	0.68	0.52	0.6	<2.1	<1.5
18	NH	Jun-03	Jan-04	45.22	0.02	<0.02	<0.02	47.0	<2.4
19	NH	Jun-03	Dec-03	75.29	0.24	2.73	0.03	35.6	39.1
20	CA	Aug-03	May-04	12.09	0.02	ns	ns	<1.8	<1.9

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Site, state and test periods				BSC Airfoil					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
21	NY	Jul-04	Jan-05	ns	ns	ns	ns	ns	ns
22	IL	Jun-04	May-05	76.04	15.23	<0.03	7.13	ns	ns
Median				3.86	0.20	0.29	0.03	5.3	1.8
Min				<0.02	0.01	<0.02	<0.02	<1.8	<1.5
Max				158.00	17.15	12.14	7.13	56.6	102.6

[a]−preparation according to standard preparation techniques, + preparation with the CSTD, ns not sampled (the drug was rarely used at this site or the surface was not used for drug handling).

Table 3

Contamination with cyclophosphamide (CP), ifosfamide (IP), and 5-fluorouracil (5FU) on floors in front of BSCs in 22 US hospital pharmacies (ng/cm^2)

Site, state and test periods				Floor in front of BSC					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
1	CA	Jul-01	Mar-02	ns	ns	ns	ns	ns	ns
2	CA	Jun-01	Dec-01	0.01	0.01	0.01	<0.01	1.8	<0.8
				<0.01	0.06	0.01	<0.01	<1.1	<0.8
3	CA	Jun-01	Jan-02	ns	ns	ns	ns	ns	ns
4	TX	Jan-02	Jun-02	0.14	<0.01	<0.01	<0.01	<0.7	<0.7
5	MA	Jan-02	Aug-02	0.93	0.60	0.92	0.29	<0.7	<0.7
6	MN	Oct-00	Feb-01	0.01	0.01	ns	ns	ns	ns
7	TX	Jun-00	Apr-01	0.13	0.63	<0.01	<0.01	ns	ns
				<0.01	<0.01	0.06	0.04	ns	ns
				4.02	0.01	ns	ns	ns	ns
8	OH	Mar-01	Oct-01	<0.01	0.01	ns	ns	<0.8	<0.7
9	UT	Nov-01	Jun-02	0.03	<0.02	<0.02	<0.02	<3.6	<3.6
10	CA	Aug-02	Feb-03	0.01	0.01	ns	ns	<0.6	4.6
11	MI	Mar-04	Sep-04	0.01	<0.01	<0.01	0.01	<0.7	<0.7
				<0.01	<0.01	<0.01	<0.01	<0.7	<0.7
12	WI	Dec-03	Jul-04	0.18	0.01	ns	ns	1.8	<0.7
13	MD	Aug-04	Jan-05	23.06	4.47	0.49	0.22	<0.7	<0.7
				34.76	16.33	0.14	0.34	<0.7	<0.7
14	IL	Jul-04	Apr-05	0.09	0.31	0.21	0.20	1.2	<0.7
				0.68	1.43	<0.01	0.04	1.5	<0.7
15	ID	Nov-01	Jul-02	0.01	<0.01	ns	ns	<0.7	<0.7
				0.01	<0.01	ns	ns	<0.7	<0.7
16	CA	Mar-02	Nov-02	0.40	<0.01	<0.01	0.01	4.5	<0.7
				0.26	0.06	<0.01	0.02	<0.7	<0.7
				4.21	0.26	1.26	0.08	<0.7	9.4
17	MI	Apr-02	Nov-02	4.54	0.56	1.00	0.23	1.7	7.2
18	NH	Jun-03	Jan-04	0.68	<0.01	<0.01	<0.01	22.1	<0.6

Site, state and test periods				Floor in front of BSC					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
19	NH	Jun-03	Dec-03	0.38	0.11	0.03	0.02	2.4	2.3
20	CA	Aug-03	May-04	0.64	0.02	ns	ns	<0.7	<0.7
21	NY	Jul-04	Jan-05	<0.01	0.06	<0.01	<0.01	14.8	22.3
22	IL	Jun-04	May-05	9.48	2.58	0.89	5.71	ns	ns
Median				0.14	0.01	0.01	0.02	0.4	0.3
Min				<0.01	<0.01	<0.01	<0.01	<0.6	<0.6
Max				34.76	16.33	1.26	5.71	22.1	22.3

[a]−preparation according to standard preparation techniques, + preparation with the CSTD, ns not sampled (the drug was rarely used at this site or the surface was not used for drug handling).

Table 4

Contamination with cyclophosphamide (CP), ifosfamide (IP), and 5-fluorouracil (5FU) on counters in 22 US hospital pharmacies (ng/cm^2)

Site, state and test periods				Counter					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
1	CA	Jul-01	Mar-02	0.19	0.08	0.04	<0.03	<5.3	<5.3
2	CA	Jun-01	Dec-01	<0.01	<0.01	0.35	<0.01	<2.1	<1.4
3	CA	Jun-01	Jan-02	0.07	0.18	0.02	<0.02	<2.7	<1.8
4	TX	Jan-02	Jun-02	ns	ns	ns	ns	ns	ns
5	MA	Jan-02	Aug-02	<0.59	0.12	<0.44	0.13	<0.6	<0.6
6	MN	Oct-00	Feb-01	<0.01	<0.01	ns	ns	ns	ns
7	TX	Jun-00	Apr-01	<0.01	0.29	<0.02	<0.02	ns	ns
				<0.01	<0.01	0.01	<0.01	ns	ns
				0.04	<0.01	ns	ns	ns	ns
8	OH	Mar-01	Oct-01	<0.01	0.01	ns	ns	1.1	<2.2
9	UT	Nov-01	Jun-02	ns	ns	ns	ns	ns	ns
10	CA	Aug-02	Feb-03	0.01	<0.01	ns	ns	<1.1	<1.1
11	MI	Mar-04	Sep-04	<0.01	0.05	<0.01	<0.01	<0.8	<0.8
				<0.01	<0.01	<0.01	<0.01	<1.0	<1.0
12	WI	Dec-03	Jul-04	<0.02	<0.01	ns	ns	<2.7	5.2
13	MD	Aug-04	Jan-05	48.95	0.09	0.87	<0.01	<0.8	<0.8
				122.27	0.20	1.20	0.01	<0.8	<0.8
14	IL	Jul-04	Apr-05	ns	ns	ns	ns	ns	ns
15	ID	Nov-01	Jul-02	0.02	<0.02	ns	ns	6.7	<2.7
16	CA	Mar-02	Nov-02	0.10	<0.01	<0.01	<0.01	<0.6	<0.6
				0.01	<0.01	<0.01	<0.01	<0.7	<0.7
				7.58	0.51	14.19	0.06	11.4	<0.8
17	MI	Apr-02	Nov-02	41.34	0.90	6.44	0.05	<5.3	<0.8
				0.04	0.04	0.14	0.02	4.1	<0.8
				0.02	0.03	0.07	0.01	<0.7	<0.7
				0.01	0.01	0.34	<0.01	<0.8	<0.8
18	NH	Jun-03	Jan-04	6.81	<0.01	<0.01	<0.01	<0.8	<0.8

Site, state and test periods				Counter					
Site	**State**	**Test −[a]**	**Test +[a]**	**CP−**	**CP+**	**IP−**	**IP+**	**5FU−**	**5FU+**
19	NH	Jun-03	Dec-03	0.59	0.01	0.02	<0.01	50.5	5.9
20	CA	Aug-03	May-04	ns	ns	ns	ns	ns	ns
21	NY	Jul-04	Jan-05	0.03	0.33	0.01	0.01	228.7	5.8
				<0.01	0.52	0.01	0.01	14.7	9.0
				1.36	0.03	<0.02	<0.02	36.4	186.8
22	IL	Jun-04	May-05	8.00	0.36	0.25	1.18	ns	ns
Median				0.03	0.03	0.02	0.01	0.8	0.5
Min				<0.01	<0.01	<0.01	<0.01	<0.6	<0.6
Max				122.27	0.90	14.19	1.18	228.7	186.8

[a]−preparation according to standard preparation techniques, + preparation with the CSTD, ns not sampled (the drug was rarely used at this site or the surface was not used for drug handling).