
Comparative Study of Syringe Contamination by Hazardous Drugs

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Abstract

Aim ▶ The purpose of this study was to compare surface contamination resulting from standard syringe plungers and cylinders compared to using the EQUASHIELD® Syringe Unit.

Method ▶ The contamination level of standard syringes was compared to that of EQUASHIELD® Syringe Units, after repeated pharmaceutical manipulations using an antineoplastic (Cyclophosphamide) drug.

Results ▶ Significant levels of up to 0.5 milligrams contamination were found on all sampled standard syringe plungers and cylinders. Significantly lower contamination levels were found on EQUASHIELD's fully enclosed Syringe Units.

Since the late 1970s numerous studies have documented the potential health risks associated with exposure to hazardous drugs in healthcare settings. Evidence has indicated that exposure to these dangerous substances can lead to acute and long term health complications such as infertility, miscarriage, birth defects, leukemia and other types of cancer. It has been clearly demonstrated that workers are in danger of exposure to these drugs at all contact stages, including drug manufacture, transport, distribution, receipt, storage, preparation, administration, waste handling, and equipment repair and maintenance (ASHP, 2006).

Identifying and quantifying possible sources of contamination is of great importance, as it can contribute to a better understanding of the issues involved in the safe handling of hazardous drugs, as well as to constant improvement of drug handling methods, the development of more effective protective equipment, and the establishment of better pharmacy and bedside compounding and administration safety policies and regulations.

The National Institute for Occupational Safety and Health (NIOSH, 2004) has recommended the use of an effective closed-system drug transfer device (CSTD) in order to facilitate safe, enclosed drug transfers and minimize the exposure to hazardous drugs and their adverse effects.

When examining surface contamination, studies using CSTDs have shown a significant reduction in contamination levels, yet detectable levels of hazardous substances were still found, suggesting that the systems are not entirely safe and that environmental contamination still places healthcare workers at risk of exposure.

In 2005, a study using a surface monitoring technique further explored environmental contamination, when it specifically examined the possibility of syringe plunger contamination during routine drug preparations at hospital pharmacies. Contamination by Cyclophosphamide was confirmed, quantified, and localized on a standard syringe plunger, in order to determine what quantity of the Cytotoxic agents come into contact with the operators' gloves (Favier, Gilles, Latour, Desage and Giammarile, 2005). Thus, results revealed a previously undetected route of exposure whereby drug residuals on the syringe plunger contaminate gloves and the work environment, and most alarmingly, place unprotected hospital staff who handle the syringe outside of the safety cabinet, at great danger.

The current study was designed to provide further evidence regarding the surface contamination on standard syringe plungers and barrels during routine drug preparation, using the prevalent Cyclophosphamide. The same agent was also used to quantify drug residuals detected on the inner wall of the syringe cylinders.

As all but one currently available CSTD use standard syringes, this study is significant in establishing the efficiency of these systems in minimizing exposure to hazardous drugs. The only CSTD that has addressed this route of exposure is a new device called EQUASHIELD®.

EQUASHIELD® is a new airtight, leak-proof closed system drug transfer device that prohibits the escape of hazardous drugs and vapors into the surrounding environment through an innovative pressure equalization mechanism. EQUASHIELD® addresses the issue of contamination through the syringe:

1. EQUASHIELD's Syringe Unit has a double jacket enclosure that seals the syringe barrel and isolates the syringe plunger's rod. Thus, EQUASHIELD's design ensures that contaminants remain fully contained, preventing any possibility of plunger and cylinder contact or exposure.
2. There is no direct contact between EQUASHIELD's plunger rod and the syringe cylinder.
3. The plunger rod's surface area in EQUASHIELD® is much smaller than that of a standard syringe plunger.
4. EQUASHIELD's plunger rod can never be detached from the syringe, whereas in standard syringes, the plunger can be pulled out of the barrel.

In order to assess its effectiveness in reducing plunger contamination and aerosol evaporation of drug residuals compared to standard syringes used by other CSTDs, surface contamination of standard syringe plungers and inner walls (barrels) were compared with EQUASHIELD® surface contamination during routine drug preparation procedures.

Method

The study examined two sources of contamination: the first test examined plunger contamination levels, whereas the second test examined the prevalence of syringe barrel residuals that can evaporate into the environment.

Plunger Contamination Test

A total of 24 syringes were used to test plunger contamination levels: 12 standard Becton Dickinson 60cc syringes, and 12 EQUASHIELD® 60cc syringes. Similarly, 24 sealable sampling cups, one for each syringe, were prepared according to the laboratory's recommendation.

All syringes and sampling cups were marked in advance with matching labels that included the following information: the syringe type (BD or ES); the number of manipulations (2M, 4M, or 8M); the serial number (1 to 12 for BD and 1-12 for ES); and an empty space to mark the CP serial number.

Comparative Study of Syringe Contamination by Hazardous Drugs

Cyclophosphamide dry substance (Baxter) was admixed in original containers with sodium chloride solution according to standard procedure, resulting in stock solutions with a concentration of 20mg/ml. pH values were measured for all solutions. All vials filled with Cyclophosphamide were marked with serial numbers.

A trained person performed 2, 4 or 8 manipulations with each of the standard and EQUASHIELD® syringes. In each manipulation 50cc Cyclophosphamide were aspirated from the vial into the syringe, and then emptied back into the vial.

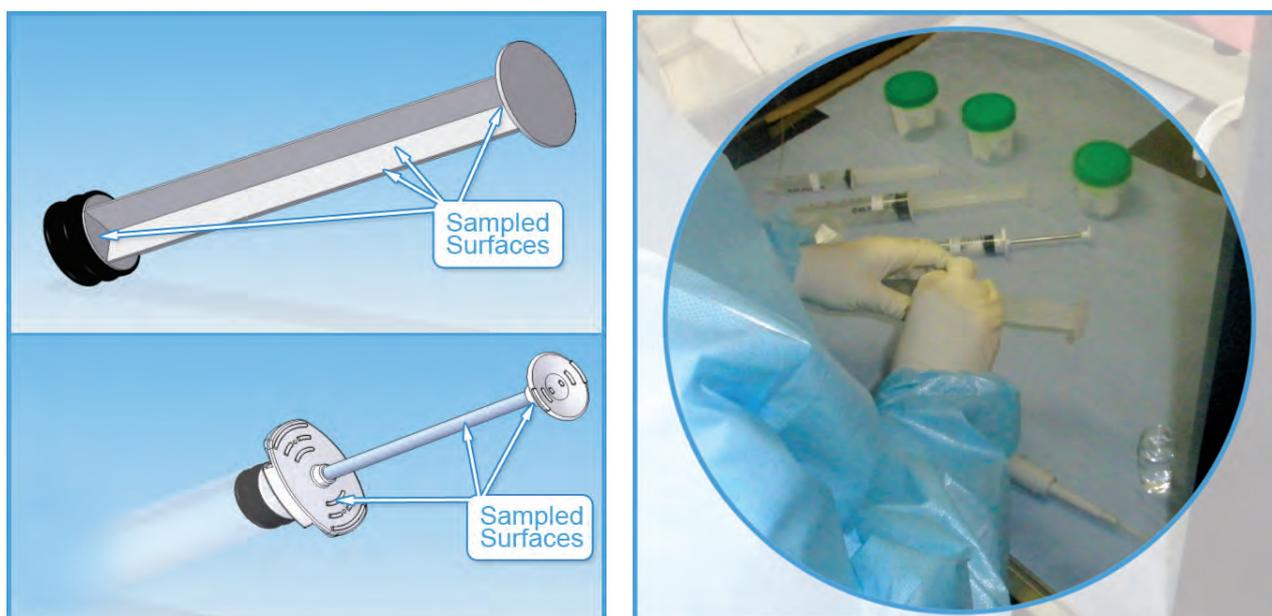
All manipulations were performed in a safety cabinet dedicated to the preparation of antineoplastic drugs, using paper sheets to cover the work area. After the completion of manipulations with each specific syringe, the paper sheet was replaced, gloves were changed and the work area was wiped with 0.1M NaOH followed by 2 Isopropanol before working with the next syringe.

After the designated number of manipulations with each syringe was completed, the syringe was moved to a second safety cabinet and placed on a paper sheet. Special care was taken to prevent one syringe from touching another. A KimWipe saturated with 1ml water pH adjusted to 3.0 with HCl was applied to the plunger surfaces as illustrated in Figure 1 in order to determine the contamination level on each syringe plunger.

A total of 3 wipes were taken from each plunger and stored at -18°C until analysis. No longer than 40 minutes elapsed between the time a syringe was manipulated and the time it was wiped. After wiping was completed, syringes were placed in a closed disposal bin and the gloves and paper sheet were replaced. The pH values of the Cyclophosphamide in each vial was measured and recorded.

Recovery rates (101% for the wiping tests and 72% for the rinsing procedure) and standard deviation of the wiping process were determined in precursory validation of the process using syringes spiked with known amounts of Cyclophosphamide.

Figure 1



Cylinder Contamination Test

The second test, that was designed to evaluate contamination levels on the exposed inner walls of standard syringe barrels, used a total of 21 syringes of 3 different types from 2 manufacturers: 9 standard Becton Dickinson 20cc syringes, 9 standard Becton Dickinson 60cc syringes (Manufacturer A), and 3 standard Terumo 60cc syringes (Manufacturer B).

EQUASHIELD® cylinders were not tested for contamination because their syringe units are fully enclosed, presenting no risk of vapor and aerosol evaporation.

Manipulations using Cyclophosphamide were performed in the exact same manner as in the first test (see above description). Once the designated number of manipulations with each syringe was completed, 5ml of pH3 water was dripped into each of the four standard syringe quarters, and then poured into a flask that was then sealed and frozen at -18°C until analysis (see Figure 2 where colored water was used to demonstrate the actual procedure).

All samples were analyzed using a HPLC-MS/MS system consisting of an 1100 binary pump with a HTS-PAL autosampler equipped with a stack cooler for sample storage at 4°C until injection of $20\mu\text{L}$. As previously mentioned, this step was validated using spiked syringes to determine recovery rates and standard deviation of the process (Tuerk, Kiffmeyer, Kuss, Hahn, Stuetzer, Hadtstein, Heinemann, and Eickmann, 2010).

Figure 2



Results

The results of the first test indicated significant levels of contamination on standard syringe plungers; contamination levels on EQUASHIELD® syringe plungers were mostly negligible (see Table 1 and Figure 3). Contamination levels were not related to the number of manipulations performed with each syringe and could be detected as soon as after one manipulation.

Table 1 – Cyclophosphamide Plunger Total Contamination Levels (ng)

	Standard (STD)	EQUASHIELD®
Syringe 1(2 M)	273	U/D
Syringe 2 (4M)	30	U/D
Syringe 3 (8M)	11 ,022	U/D
Syringe 4 (2M)	U/D	U/D
Syringe 5 (4M)	3,960	2442
Syringe 6 (8M)	172 ,260	24
Syringe 7 (2M)	557 ,700	U/D
Syringe 8 (4M)	138 ,270	U/D
Syringe 9 (8M)	105 ,930	U/D
Syringe 10 (2M)	18 ,051	38
Syringe 11 (4 M)	170 ,940	U/D
Syringe 12 (8M)	82 ,170	23
Average	105 051.00	210.58
Median	50 111.00	U/D

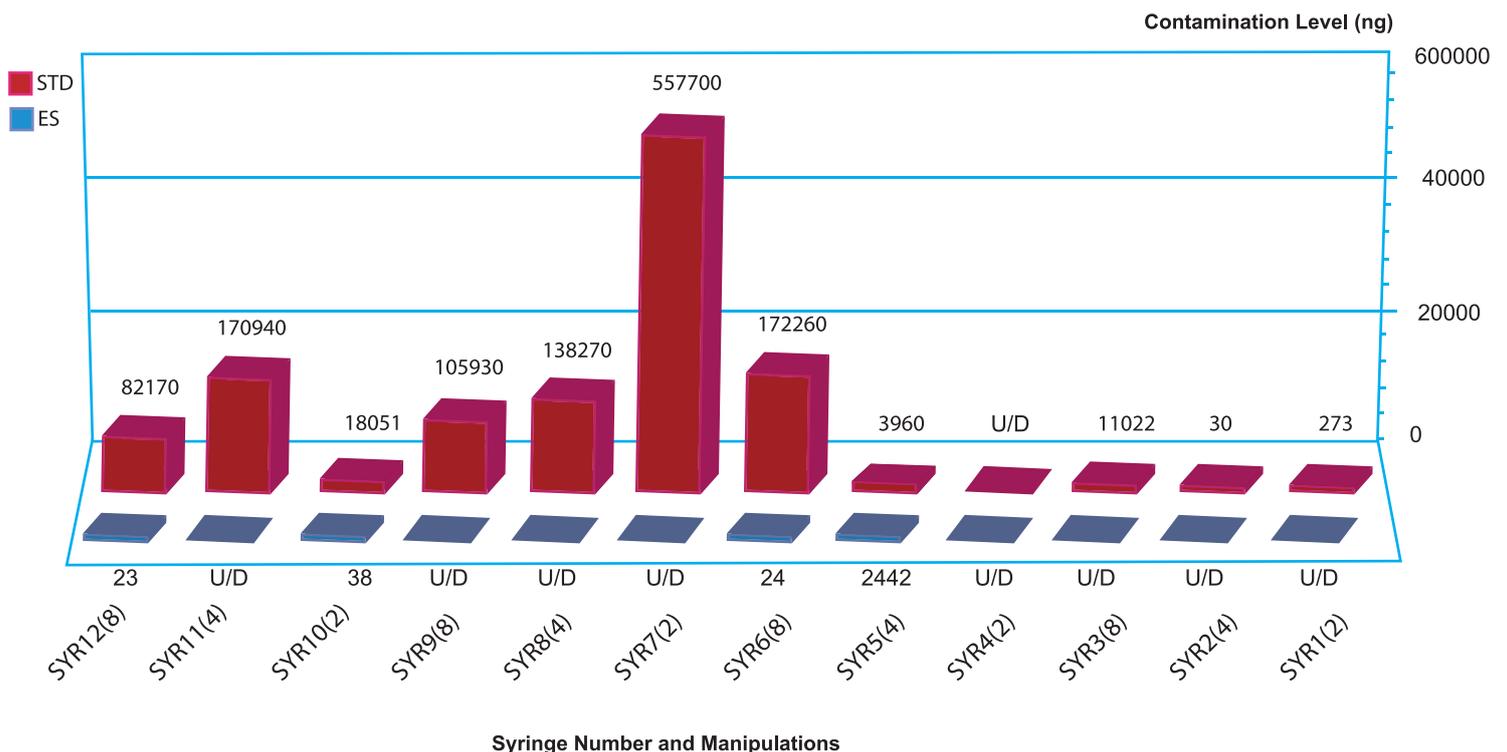
- 2, 4 and 8 are the number of manipulations.
- U/D-Undetectable contamination levels.

Sample analysis revealed significantly greater levels of contamination on standard syringe plungers.

Figure 3: Cyclophosphamide Plunger Contamination Levels (ng)

Plunger Contamination Levels (ng)

Standard (STD) syringes compared to EQUASHIELD® (ES) Syringe Units during routine drug preparation with Cyclophosphamide



Comparative Study of Syringe Contamination by Hazardous Drugs

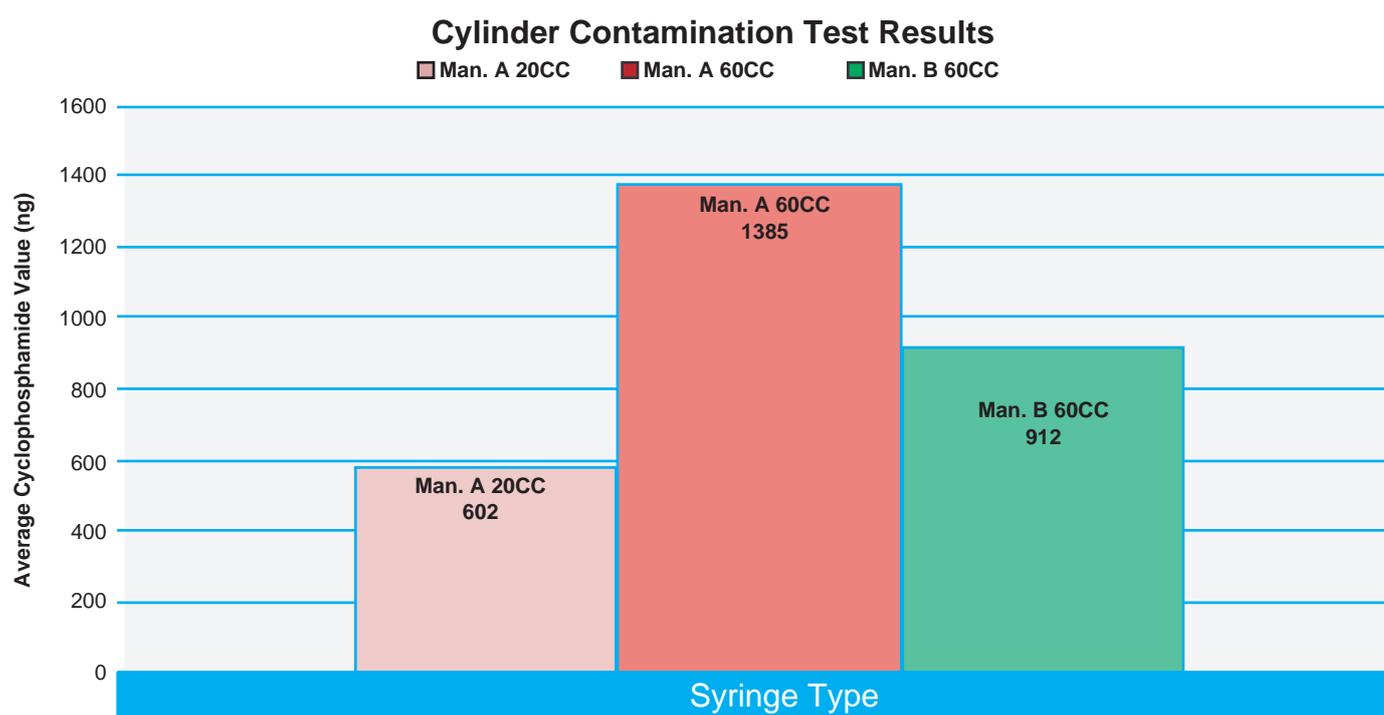
The second test which was performed separately, revealed Cyclophosphamide contamination on all tested syringe barrels (see Table 2 and Figure 4), with greater contamination levels found on the 60cc syringes compared to the 20cc syringes.

Table 2 – Cyclophosphamide Cylinder Contamination Levels (ng)

	Manufacturer A 20cc	Manufacturer A 60cc	Manufacturer B 60cc
Average	602	1385	912
Median	496	1297	964

All the tested syringe cylinders were contaminated with Cyclophosphamide. The values appearing in the table are the detected values divided by 72%, which was the recovery rate.

Figure 4: Cyclophosphamide Cylinder Contamination Levels (ng)



Discussion

Results revealed Cyclophosphamide residuals on the standard syringe plungers and barrels, supporting previous studies that suggest that syringe plunger contamination is an additional route of exposure that may contaminate gloves and work areas during hazardous drug routine preparation and administration at pharmacies and patient bedsides.

These findings may also explain surface contamination, as the contaminated plungers come into contact with healthcare workers' gloves, and consequently, with work surfaces, chairs, tabletops and so forth, despite various precautions such as the use of gloves, safety cabinets and the like. Similarly, aerosols and vapors from the syringe barrels may contribute to air contamination when evaporating into the environment or condensing upon work surfaces.

Furthermore, as standard syringe plungers are used with all but one currently available closed system drug transfer device (CSTD), it is important to alert healthcare workers to the dangers of using these systems that may present a neglected safety concern, which is particularly alarming when considering the unprotected personnel who handle the syringe outside the safety cabinet.

Finally, it is important to note that the contamination levels found on the EQUASHIELD® CSTD's plungers is inconsequential, indicating the effectiveness of a fully enclosed syringe unit. This information may contribute to the development of more effective CSTDs and the enforcement of better policies and regulations concerning the handling of hazardous drugs.

Results indicate that plunger and barrel contamination of common syringes used for drug preparation are a significant source of exposure that requires further investigation and consideration. One possible solution is the use of a fully enclosed syringe such as EQUASHIELD® that has proven to result in significantly lower contamination levels.

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Comparative Study of Syringe Contamination by Hazardous Drugs

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