

Environmental contamination by cyclophosphamide: comparison of manual production in biological safety cabinet and robot-assisted production by APOTECaChemo

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BACKGROUND AND PURPOSE

The use of robotic systems is expected to significantly decrease the working risk of operators to being exposed to cytotoxic substances, as the most critical operations are performed in a closed area under negative pressure. Although

robotic systems are already in use in several international centers, very few systematic studies on workplace contamination, comparing manual and robot-assisted drug preparation, were performed. This study was aimed at

comparing environmental contamination of cyclophosphamide (CP) during one week of drug compounding by manual procedure in a biological safety cabinet (BSC) and the robotic preparation with APOTECaChemo.

Hospital size, number of patients and preparations

Population served	1 125 000
Hospitals served	3
Patients treated with chemo in 2014	2669
IV Chemos compounded in 2014	36963
Chemos compounded with APOTECaChemo in 2014	21530

MATERIAL AND METHOD



Wiped locations (right to left): gloves, chart, tray, table, working area BSC, working area APOTECaChemo

During four consecutive days, similar numbers of infusion bags with cyclophosphamide were prepared with both techniques in a cross-over design. Wipe samples (49 for BSC, 50 for APOTECaChemo) were taken at several locations (gloves, infusion bags, trays, BSC-benches, floor) in the pharmacy and analyzed by GCM-SMS (LOD 0.2 ng/sample). Wipe sampling was performed according to a procedure previously published by Schmaus et al. [1]

RESULTS

BSC	Area	Mon	Tue	Wed	Thu
Sample	cm ²	ng/cm ²	ng/cm ²	ng/cm ²	ng/cm ²
inside BSC BC*	638	nd	0.0007	0.0254	nd
inside BSC AC**	638	0.0010	0.0004	0.0004	-
Cart BC	600	nd	nd	nd	nd
Cart AC	600	nd	0.0003	0.0055	-
Tray BC	522	nd	0.0008	0.0023	0.0019
Tray AC	522	nd	0.0123	0.0010	-
Gloves	600	0.0004	0.0080	0.0967	nd
Gloves	600	0.0006	nd	-	nd
Bag1	414	nd	nd	0.2080	0.0109
Bag2	414	nd	0.0063	1.0200	0.0203
Bag3	414	nd	0.4110	0.3310	0.0016
Bag4	414	nd	2.8990	0.3860	0.0041
Bag5	414	nd	0.1910	0.4520	0.0070
Floor in front of BSC	594	-	-	0.0004	-

nd: below detection limit of 0.2 ng/sample
* BC = before cleaning; ** AC = after cleaning

APOTECaChemo	Area	Mon	Tue	Wed	Thu
Sample	cm ²	ng/cm ²	ng/cm ²	ng/cm ²	ng/cm ²
Loading area BC*	400	0.0013	0.0013	0.0005	nd
Loading area AC*	400	nd	nd	nd	-
Compounding area BC	300	0.0293	0.0747	0.1393	0.1603
Compounding area AC	300	0.0123	0.0090	0.0527	-
Table BC	609	0.0003	0.0004	0.0007	0.0007
Table AF	609	nd	nd	0.0008	-
Gloves	600	0.0007	nd	nd	nd
Gloves	600	nd	nd	nd	nd
Bag1	414	nd	nd	nd	nd
Bag2	414	nd	nd	nd	nd
Bag3	414	nd	0.0019	nd	nd
Bag4	414	nd	nd	nd	nd
Bag5	414	0.0005	0.0094	nd	nd
Floor in front of APOTECaChemo	594	-	-	nd	-

- The detection rate was 70% in BSC versus 15% in APOTECaChemo.
- During manual preparation, contamination with CP was below 0.001 ng/cm² at most locations, but significant on gloves (0.0004–0.0967 ng/cm²) and the majority (70%) of infusion bags (<0.0004–2.89 ng/cm²).
- During robotic preparation, gloves (1 of 8: 0.0007 ng/cm²) and infusion bags (3 of 20: 0.0005, 0.0019, 0.0094 ng/cm²) were considerably less contaminated. Residual contamination was found on the surface under the dosing device in the compounding area (0.0293–0.1603 ng/cm²) inside the robotic system.

CONCLUSION

	BSC				APOTECaChemo			
	n	Mean	Median	Detect. Rate	n	Mean	Median	Detect. Rate
Bags	20	0.2974	0.0090	70	20	0.0006	nd	15
Surfaces	21	0.0029	0.0004	67	22	0.0220	0.0007	68
Gloves	7	0.0151	0.0004	57	8	0.0001	nd	13

Mean and Median are expressed in ng/cm²; Detection rate is in %

- The study confirmed the risk analysis outcomes. The spots more subject to contamination are gloves for BSC and dosing area for APOTECaChemo, respectively. So the recommendation of changing gloves frequently and pay particular attention on the daily cleaning of certain area are fundamental to maintain a low level of contamination.

- Evaluation of the two procedures displays that the overall CP contamination was lower when the production was carried out by the robotic system inside a closed and controlled system. The repeatability of robotic procedures prevent any contamination on the final product and the external surfaces, while the behaviour on the manual compounding is less predictable (inconstant data).
- Compared to other studies on CP contamination, our results are rather low for both procedures. Yoshida et al [2] found median values for CP of 0.093 ng/cm² (BSC), 0.11 ng/cm² (tray), 0.93 ng/cm² (working table) and 0.085 ng/cm² (floor). Also contamination of gloves (median 28 ng/pair) was about 100-fold higher compared to our results. Only after introducing a closed system device (PhaSeal) the contamination has been reduced to levels comparable to our findings.
- to the medications that cannot be automated. The activity covered with APOTECaChemo ranges from 9 to 15%.

References:

[1] G. Schmaus, R. Schierl and S. Funck. 2002. Monitoring surface contamination by antineoplastic drugs using gas chromatography-mass spectrometry and voltammetry. Am J Health Syst Pharm. 59: 956-61.

[2] J. Yoshida, J et al. 2009. Use of a closed system device to reduce occupational contamination and exposure to antineoplastic drugs in the hospital work environment. Ann Occup Hyg 53:153-60.