

Wipe Sample Monitoring on Workplace Contamination with Antineoplastic Drugs in Pharmacies

Heinemann A¹, Eickmann U¹, Kiffmeyer TK², Tuerk J², Stuetzer H³, Hahn M³, Hadtstein C⁴

⁽¹⁾ Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege, BGW, Cologne, Germany

⁽²⁾ Institute of Energy and Environmental Technology, IUTA e.V., Duisburg, Germany

⁽³⁾ Institute of Medical Statistics, Informatics & Epidemiology, IMSIE, Cologne, Germany

⁽⁴⁾ Institute of Applied Pharmacy, IfAP e.V., Cologne, Germany

Introduction and Aims:

Antineoplastic drug applications for the treatment of cancer patients are prepared in some 800 German pharmacies. These drugs have carcinogenic, mutagenic and/or adverse developmental or reproductive properties and effective safety measures are therefore required to protect the employees.

The BGW therefore launched a large-scale study (MEWIP*) in order to determine the contamination level and to investigate the suitability and effects of wipe sample monitoring at regular intervals. Further aims were to investigate the causes of contamination, its spread and the development of strategies for minimizing exposure. In terms of the study, the BGW expected monitoring to promote readiness for taking appropriate measures to improve working conditions and occupational safety. The German ordinance on the handling of hazardous substances (GefStoffV) also stipulates measurements of such workplaces.

For the purpose of the study, wipe samples in 130 German pharmacies (hospitals and public pharmacies) were taken from three sampling locations from early 2006 until the end of 2007.

Methods:

Three selected sampling areas (floor in front of the safety cabinet, most intensively used work top, fridge door including handle) were repeatedly monitored by wipe sampling. The samples were analysed for their amount of 5-Fluorouracil (5-FU), Cyclophosphamide (CP), Gemcitabine (Gem), Me-



Fig. 1: Preparation area



Fig. 2: Sampling areas (floor, work top, fridge door)

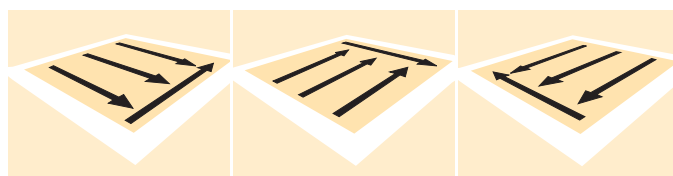


Fig. 3: Wiping directions

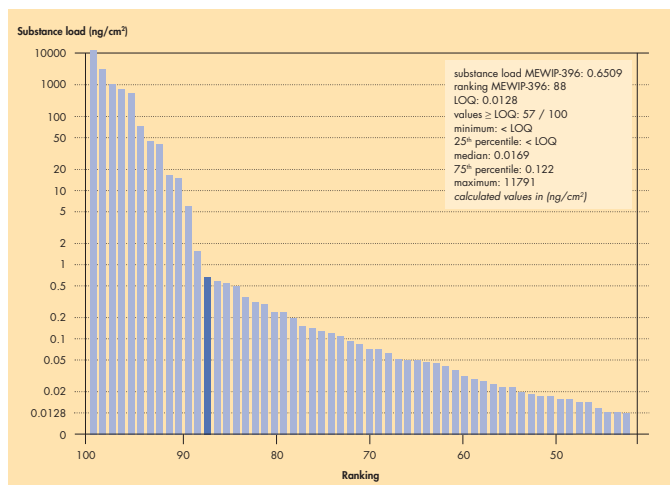


Fig. 4: Report for participants

thotrexate (MTX), Etoposide (Eto), Ifosfamide (IF), Docetaxel (Doc) and Paclitaxel (Pac). In addition, the working conditions were recorded by a detailed questionnaire on working procedures (e.g. type and amounts handled, hazards and spillage, cleaning procedures, waste management, protective equipment, education of personnel, training). The participating pharmacies were split into two study groups: 55 pharmacies performed quarterly wipe sampling and were informed about the analytical results throughout the study (group A), while in the remaining 75 sites, samples were taken only at the start and end of the study and the analyses values were not reported until the project had finished (group B). Samples were taken under strict, standardised conditions and the results were made anonymous (Fig. 4). Each sampling surface was wiped clean with three cloths which had been soaked in a solvent especially adapted for this purpose (Fig. 2, 3). Once the samples had been processed, they were analysed by means of tandem mass spectrometry (LC-MS/MS). A total of 1,272 wipe samples were taken resulting in 10,176 individual values.

Results:

Sixteen percent, i.e. 1,699 readings, are positive. In 61% of the 1,272 wipe samples, at least one of the eight substances was established. In conformity with the stated consumption quantities, 5-Fluorouracil, Cyclophosphamide und Gemcitabine were found more frequently and in higher concentrations than the other analysed cytostatics. The floors in front of the workbench were the most contaminated position, followed by the work surfaces and the

Project phases	Period												Partner(s)
	2005			2006				2007					
	II	III	IV	I	II	III	IV	I	II	III	IV		
Year													
Quarter													
Phase 1: Contact pharmacies, 1st questionnaire													IUTA (BGW, IMSIE, IFAP)
Phase 2: Evaluation 1st questionnaire													IUTA, IFAP (BGW, IMSIE)
Phase 3: Prepare and develop the study design													BGW, IUTA, IMSIE
Phase 4: Kick-off events													BGW (IUTA, IMSIE, IFAP)
Phase 5: 2nd questionnaire, interview, monitoring													IUTA, IFAP (BGW, IMSIE)
Phase 6: Evaluation, feedback to the pharmacies													IUTA, IMSIE (BGW)
Phase 7: Develop handling instructions													BGW, IUTA
Phase 8: Final report, closing event, publications (to 7/08)													BGW, IUTA, IMSIE, IFAP

Fig. 5: Project work plan and time schedule

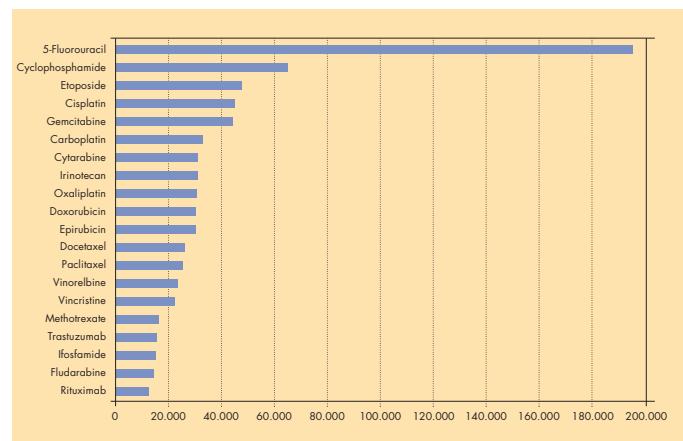


Fig. 6: Number of preparations by substance per 100 pharmacies in 2005

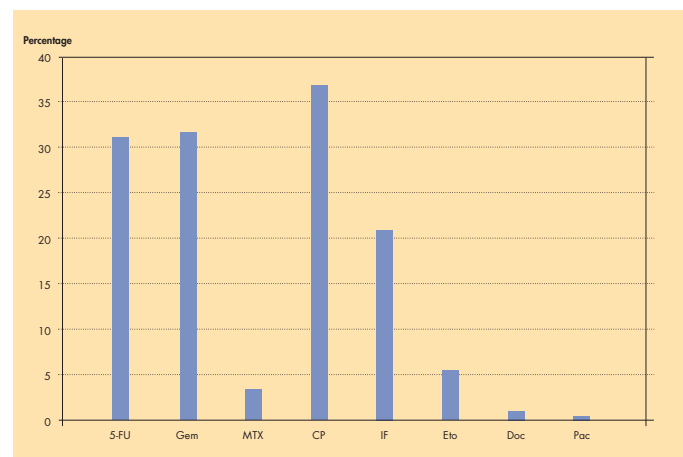


Fig. 7: Percentage of positive wipe samples by substance

refrigerator doors. The measured concentrations were similar to those found in other studies and ranged from below the limit of quantification (LOQ) through to a peak value of 1,888 ng/cm² for Gemcitabine. It is notable, that the 9 highest values were found in two pharmacies only (Fig. 8).

No correlation between the number of cytostatic preparations, the amount of substances handled, the day of the last cleaning and the substance load on the surface concerned could be found (for instance Fig. 9). Neither was it possible to verify a correlation with most of the other data describing the work practices. There are no notable differences between hospital pharmacies and dispensaries (Fig. 10). The readings can be used to identify exemplary pharmacies. An explorative significant correlation between the degree of disinfection, type of disinfection and substance load was established. The type of ventilation (circulating air/outgoing air) tends to have an influence, although this cannot be statistically verified. The 90th percentile of the substance loads dropped during the course of the study in group A (Fig. 11).

Conclusions:

Wipe samples are a proper method for a standardised ambient monitoring on workplace contamination with antineoplastic drugs. Values below 0.1 ng/cm² are achievable and can be discussed as "prior art".

The final MEWIP report will be available for download in German from autumn 2008 on the homepage of the BGW.

	Pharmacy	Position	Cycle of Wiping	Type of Pharmacy	Study group	Substance	Substance load (ng/cm ²)
1	„A“	Fridge	1	Hospital pharmacy	A	Gemcitabine	1,888
2	„A“	Work top	4	Hospital pharmacy	A	Gemcitabine	190
3	„A“	Fridge	2	Hospital pharmacy	A	Gemcitabine	109
4	„B“	Floor	2	Hospital pharmacy	A	Gemcitabine	105
5	„B“	Floor	3	Hospital pharmacy	A	Ifosphamide	89
6	„B“	Work top	1	Hospital pharmacy	A	Methotrexate	35
7	„B“	Work top	1	Hospital pharmacy	A	Ifosphamide	31
8	„B“	Floor	1	Hospital pharmacy	A	Ifosphamide	26
9	„B“	Work top	1	Hospital pharmacy	A	5-Fluorouracil	24
10	„C“	Work top	1	Dispensary	B	5-Fluorouracil	18
11	„D“	Fridge	5	Hospital pharmacy	B	Cyclophosphamide	17
12	„E“	Work top	2	Hospital pharmacy	A	Ifosphamide	17
13	„F“	Fridge	4	Dispensary	A	5-Fluorouracil	14
14	„G“	Work top	1	Hospital pharmacy	B	5-Fluorouracil	13
15	„H“	Work top	3	Dispensary	A	5-Fluorouracil	11
16	„I“	Work top	5	Dispensary	A	5-Fluorouracil	11

Fig. 8: Top values by substance load

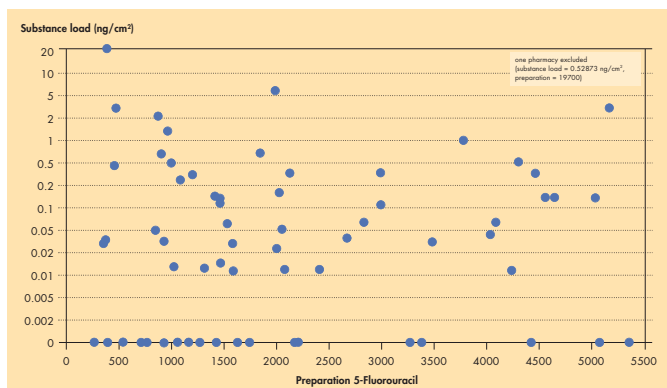


Fig. 9: Correlation between substance load and number of preparations for 5-FU during 2006 (group B)

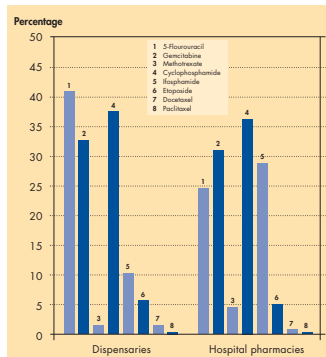


Fig. 10: Percentage of positive wipe samples

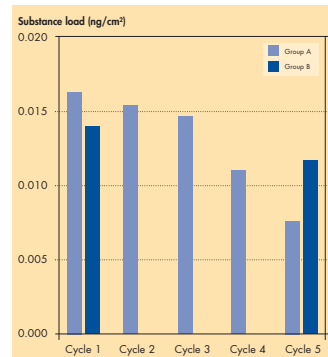


Fig. 11: 90th Percentile over all substances and surfaces