CONTAMINATION WITH CYTOTOXIC DRUGS IN THE WORKPLACE
ESOP PILOT STUDY

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BACKGROUND

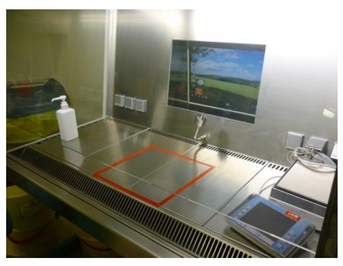
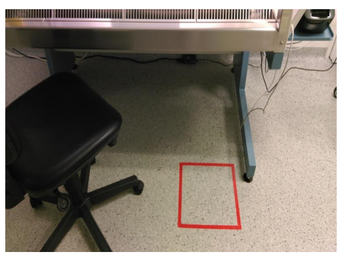
Evaluation of environmental contaminations with cytotoxic drugs in the hospital is one of the fundamental requirements to ensure the safety of all healthcare professionals. Several reports and publications on surface contaminations in pharmacies and hospitals have been reported in the last years. However, knowledge levels on surface contamination with anti-neoplastic drugs in European hospitals in the areas where these drugs are handled, is still limited. No multicentre, non-commercial studies in different European hospitals have been conducted so far.

OBJECTIVES

- To obtain an overview of the current contamination levels of cytotoxic drugs in the workplace in European hospitals (**PART I**)
- To measure the level of environmental contamination with cytotoxic drugs circulating within a facility, known as the hospital medication system - process flow of drug (**PART II**)
- To evaluate the impact of changes to practice designed to protect those who work in the areas where the cytotoxic drugs are handled (**PART III**)

MATERIALS AND METHODS

An evaluation of surface contamination in preparation and administration areas (PART I), and after implementation of cleaning recommendations (PART II). Wipe samples were taken from 10 comparable surfaces (5 in preparation areas and 5 in administration areas), in each of the participating hospitals. Each sample was analyzed for the presence of following 12 cytotoxic drugs using LC-MS/MS: *5-fluorouracil, cyclophosphamide, ifosfamide, gemcitabin, etoposide, methotrexate, paclitaxel, docetaxel, topotecan, irinotecan, doxorubicin and epirubicin*.

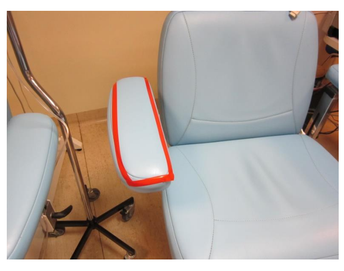
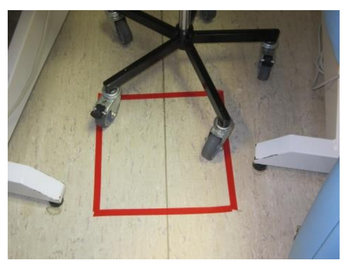




Wipe sampling surfaces in the **PHARMACY**: *work surface of BSC/Isolator, floor under the BSC/Isolator, checking counter (clean area), checking counter (storage area), refrigerator door*

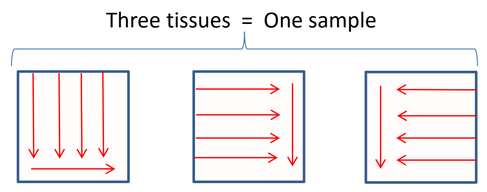
Wipe samples were taken at the end of a working day, before general cleaning.

In each hospital, the investigated surface was wiped by designated pharmacist, according to established procedures.




Wipe sampling surfaces on the **WARD:** *checking counter (nurse station), lid of cytotoxic waste container, armrest of patient chair, floor around the infusion stand, phone*

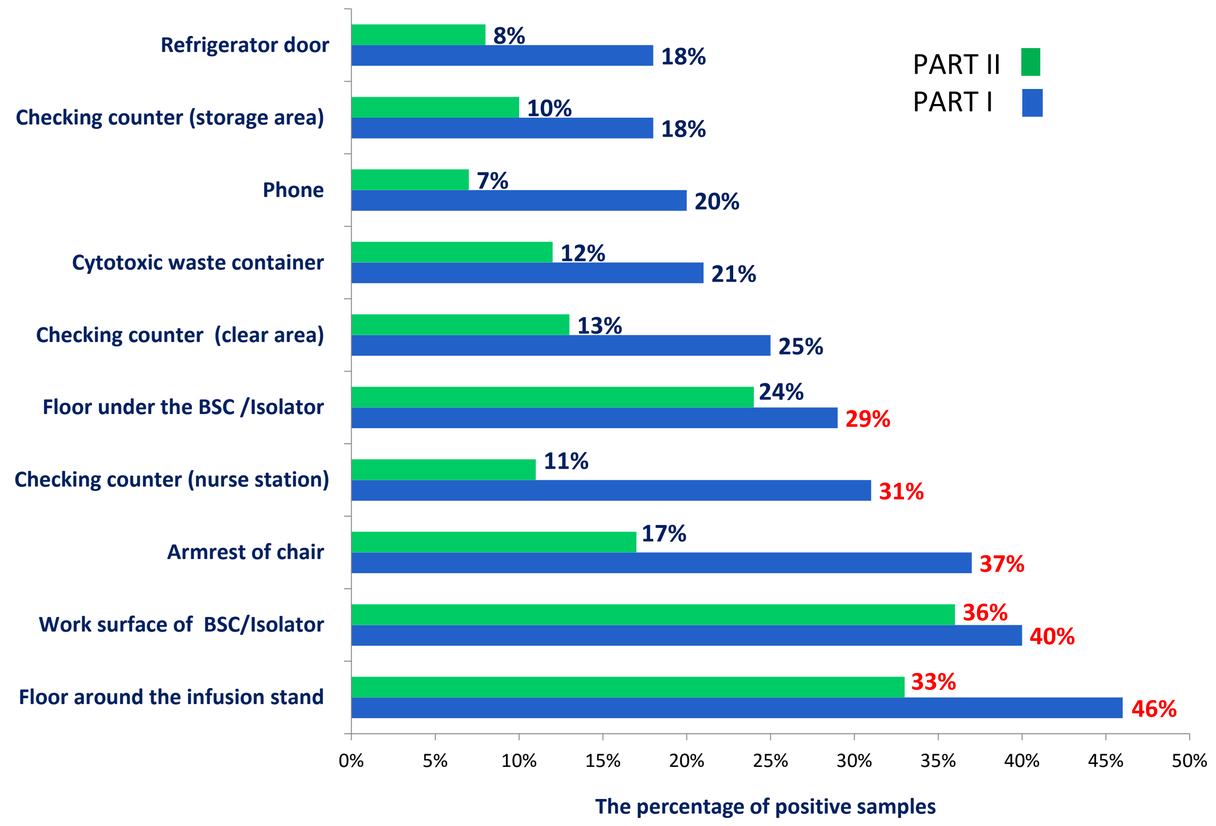


Tuerk J et al. *Int J Environ Anal Chem* **2011**, 91: 1178 - 1190

Evaluation criteria:
90th percentile of load situation
Derived reference value: **0.1 ng/cm²**

RESULTS

The database includes results collected from 15 European hospitals. Out of the 1764 results analyzed in PART I, 505 were positive (29%). In 11 out of 15 hospitals (73%), substances were detected which were not prepared or administrated during the sampling day. After the implementation of the ESOP cleaning recommendations, only 17% of samples were positive (274/1584). Measurable amounts of at least one agent were detected on sampled surfaces in each hospital. Contamination was detected mostly on the work surfaces of BSCs/Isolators, floors (in pharmacies and wards) and the armrests of patient's chairs. The highest number of positive results were recorded for gemcitabin, 5-fluorouracil, cyclophosphamide and paclitaxel. The highest value was recorded for gemcitabin (171 ng/cm²) and 5-fluorouracil (37 ng/cm²) in PART I and PART II, respectively. There was no correlation between contamination and the amounts of prepared drugs.



Range [ng/cm²]	PHARMACY		WARD	
	PART I n = 888	PART II n = 814	PART I n = 876	PART II n = 770
< LOD	655	666	604	644
LOD < 0.1	183	103	208	92
0.1 - 1	32	31	46	30
1.0 - 10.0	14	11	18	4
> 10	4	3	0	0

Fig. 1. Number of analyzed results for all substances in different ranges (PART I and PART II)

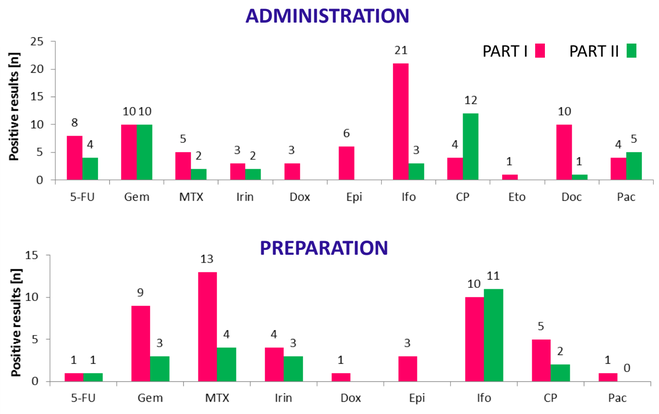


Fig. 2. Number of positive results for substances which were not prepared or administrated in the wipe sampling day (PART I and PART II)

PART I (Pharmacy & Ward)

Min = LOD	5 FU	Gem	MTX	Top	Irino	Dox	Epi	Ifo	CP	Eto	Doc	Pac	All
n	147	147	147	147	147	147	147	147	147	147	147	147	**1764**
Median	0.007	0.003	0	0	0	0	0	0	0	0	0	0	**0**
75th Percentile	0.063	0.024	0	0	0	0	0	0.001	0.020	0	0.002	0.006	**0.001**
90th Percentile	0.284	0.137	0.185	0	0.003	0	0	0.019	0.184	0	0.020	0.038	**0.030**
Max	4.066	170.500	7.458	0.014	14.383	0.036	0.022	6.991	73.162	0.301	1.650	5.775	**170.500**

PART II (Pharmacy & Ward)

Min = LOD	5 FU	Gem	MTX	Top	Irino	Dox	Epi	Ifo	CP	Eto*	Doc	Pac	All
n	144	144	144	144	144	144	144	144	144	n/a	144	144	**1584**
Median	0	0	0	0	0	0	0	0	0	n/a	0	0	**0**
75th Percentile	0.018	0.009	0	0	0	0	0	0	0.026	n/a	0	0	**0**
90th Percentile	0.133	0.072	0	0	0	0	0	0.012	0.131	n/a	0.009	0.066	**0.021**
Max	36.924	11.359	0.046	4.931	0.677	0.082	0.111	14.993	6.932	n/a	0.907	5.122	**36.924**

** n/a: not applicable, because of stability problems during sample storage of some the samples.*

CONCLUSION

The ESOP pilot study provided a brief overview of the local procedures for safe handling of cytotoxic drugs in European hospitals. In PART II of the study, improvements could be seen by the reduction of positive samples, the amount of surface concentration detected and the reduction of the 90th percentile from 0.030 ng/cm² to 0.021 ng/cm². A wipe sampling strategy, together with a clear set of ESOP recommendations based on the results of this pilot study, will be used in the next phase of the ESOP project (PART III).

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