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## **Hygienic guidance values for wipe sampling of antineoplastic drugs in Swedish hospitals**

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## Abstract

The use of antineoplastic drugs in the health care steadily increases. Health care workers can be occupationally exposed to antineoplastic drugs classified as carcinogenic or teratogenic. Monitoring of surface contamination is a common way to assess occupational exposure to antineoplastic drugs, since wipe sampling is used as a surrogate measure of dermal exposure. Since no occupational limits for antineoplastic drugs in work environments exist, 'hygienic guidance values (HGV)' should be used instead. HGVs are practicable, achievable levels, not health based, and can be calculated from exposure data from representative workplaces with good occupational hygiene practice. So far, guidance values for surface monitoring of antineoplastic drugs only exist for pharmacies where antineoplastic drugs are prepared. The objective was to propose HGVs for surface monitoring of cyclophosphamide (CP) and ifosfamide (IF) in Swedish hospitals where antineoplastic drugs are administered to patients. In total, 17 workplaces located at six hospitals in Sweden were surveyed by wipe sampling. Wipe samples were collected, worked-up, and then analyzed with liquid chromatography tandem mass spectrometry. Surface contamination of CP and IF was found on 80% and 73% of the sampled surfaces, thus indicating that there is potential for health care workers to be exposed to CP and IF via the skin. The median surface load of CP was  $3.3 \text{ pg cm}^{-2}$  (range  $<0.05\text{-}10800 \text{ pg cm}^{-2}$ ). The corresponding value for IF was  $4.2 \text{ pg cm}^{-2}$  (range  $<0.13\text{-}95000 \text{ pg cm}^{-2}$ ). The highest surface loads were found on the floors. The proposed HGVs were set at 90th percentile values, and can be applicable to hospital workplaces where patients are treated with CP or IF. Surface monitoring combined with HGVs is useful tool for health care workers to regularly benchmark their own surface loads which could

control and reduce the occupational exposure to CP and IF in hospital workplaces. Thus, the occupational safety of the health care workers will be increased.

### **Environmental impact**

Although several studies have shown the occurrence of widespread surface contamination of antineoplastic drugs in hospital work environments, no other study has focused on providing hygienic guidance values for wipe sampling in hospitals workplaces. In our study 17 wards located at six hospitals in Sweden were surface monitored by wipe sampling and hygienic guidance values for cyclophosphamide and ifosfamide were calculated. The introduction of hygienic guidance values will be useful for health care workers since they will be able benchmark their own surface loads of antineoplastic drugs. Thus, our research can contribute to reduced surface loads of antineoplastic drugs in hospital work environments, and thereby reduce the occupational exposure and increase the safety of the health care workers.

## **Introduction**

Antineoplastic drugs are frequently handled in the medical care of e.g. cancer patients and the annual used amounts steadily increases. For instance, during a decennium the number of registered antineoplastic drugs for use in Sweden has almost doubled from 44 to 77.<sup>1,2</sup>

Antineoplastic drugs can have carcinogenic, mutagenic or teratogenic properties. To protect the health care workers use of adequate personal protective equipment (PPE) e.g. gowns and disposable gloves, effective safety equipment e.g. biological safety cabinets, and devices for safe handling e.g. closed-system devices, disposable sheets, waste boxes, are required. However, studies have shown that health care workers, such as pharmacy personnel, nurses, assistant nurses and cleaners still can be occupationally exposed to antineoplastic drugs during preparation and administration of antineoplastic drugs, nursing of treated patients or cleaning despite of use of adequate PPE and safety equipment and devices for safe handling.<sup>3-7</sup> Reproductive effects on nurses exposed to antineoplastic drugs have also been shown.<sup>8,9</sup>

Absorption of antineoplastic drugs are thought to primary occur through the skin.<sup>6,10-11</sup> However, antineoplastic drugs can also be taken up via inhalation or orally by e.g. hand-to-mouth-contact. A large number of different antineoplastic drugs are used in the anticancer therapy and it is therefore not realistic to monitor all. Cyclophosphamide (CP) and ifosfamide (IF) are two commonly used antineoplastic drugs in Swedish hospitals and for which sensitive analytical methods are available.<sup>12-14</sup> The International Agency for Research on Cancer (IARC) has classified CP as carcinogenic to humans and IF as

probably carcinogenic to humans.<sup>15-17</sup> Thus, CP and IF were used as indicator substances for surface contamination of antineoplastic drugs.

A large number of studies have demonstrated presence of antineoplastic drug contamination on many different types of surfaces in work environments in e.g. hospital workplaces where antineoplastic drugs were administered to patients and where chemotherapy treated were patients nursed.<sup>5,6,11,18-20</sup> Thus, health care workers might be dermal exposed to antineoplastic drugs and their associated risks during administration and nursing of treated patients. Skin absorption seems to be an important exposure route for occupational exposure to antineoplastic drugs.<sup>6,10-11</sup> It is therefore important to use adequate safety equipment and devices to control the exposure during handling of antineoplastic drugs and thereby minimize the risk of leakage of antineoplastic drugs to the work environment. If the exposure is not adequately controlled antineoplastic drugs could leak to the work environment and cause dermal exposure. No or low levels of antineoplastic drugs in the work environment indicate that the exposure of antineoplastic drugs is controlled and no or low occupational exposure occurs. It is therefore important to aim for as low levels of surface contamination of antineoplastic drugs as possible in the work environments.

Monitoring of surface contamination of antineoplastic drugs is a well-established, simple and frequently used method to assess the surface loads in work environments.<sup>6,12-14,21-27</sup> Surface monitoring of antineoplastic drug contamination can be used as a surrogate for dermal exposure, and can thereby indicate occupational exposure to antineoplastic drugs. Normally, monitoring is performed on surfaces such as work areas, handles and floors, which give a measure about the contamination levels of surfaces the health care

workers might have skin contact with during their work, but surface monitoring also indicate how widespread the antineoplastic drug contamination is in the work environment. High levels of antineoplastic drugs on different surface areas in the work environment indicates that the handling of antineoplastic drugs is not adequately controlled, and this implies an increased risk of health care workers to become dermally exposed.

No occupational exposure limits (OELs) for antineoplastic drugs in work environments exist or is likely to be established in the near future.<sup>28</sup> In theory, antineoplastic drugs classified as carcinogenic to humans should not be present in work environments.<sup>28,29</sup> However, in practice, this is not a realistic goal although use of adequate safety equipment and devices controlling exposure. Thus, the contamination levels of antineoplastic drugs in work environment should be as low as possible, since these also then indicate that the dermal exposure is low. Therefore, other limits should be used instead. For a number of chemical agents guidance values for biological monitoring have been established and used.<sup>30-33</sup> The guidance values are not toxicological or health based, but are instead practicable, achievable levels generally set at the 90th percentile of available monitoring results collected from representative workplaces with good occupational hygiene practice<sup>a</sup>.<sup>30,31,33</sup> If a measured value exceeds the guidance values it does not necessarily mean that ill health will occur, but it does mean that the exposure is not adequately controlled.<sup>33</sup> Comparable 'hygienic guidance values (HGVs)' based on the same criteria and set at the 90th percentile could be used for surface monitoring of antineoplastic drugs.<sup>34</sup>

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<sup>a</sup> Workplaces protecting and promoting the health and safety of workers through preventive actions such as work performed according to legislation and safety guidelines, use of exposure control and adequate PPE.

So far, HGVs for antineoplastic drugs have only been proposed for German pharmacies.<sup>28,34</sup> No HGVs for surface contamination of antineoplastic drugs have been proposed for hospital workplaces such as outpatient wards and wards.

The objective of the paper is to propose HGVs for surface monitoring of CP and IF in Swedish hospitals. The HGVs will be based on data from studies monitoring surface loads of CP and IF in hospital workplaces. By calculating of 90th percentile values for the surface load data from work areas, other surfaces, floors and handles HGVs could be achieved. By introducing HGVs collection of wipe samples will be a useful tool for the health care workers and they will be able benchmark their own surface loads as a surrogate of dermal exposure, and thereby check so the exposure is adequately controlled. If surface monitoring is performed regularly this might result in reduced dermal exposure as well as reduced surface loads of antineoplastic drugs in time, and thereby increased occupational safety for the health care workers.

## **Material and methods**

### **Investigated hospital workplaces**

The present paper is based on surface load data from two studies that performed surface monitoring of CP and IF in Swedish hospitals (N=6). Surface load data from five hospitals is new, while surface load data from one hospital previously has been published.<sup>14</sup> However, by combining the data from these two studies 90th percentile values to be proposed as HGVs could be calculated.

**New data.** Five different hospitals (A-E) in the south of Sweden were included in this study. All workplaces in the hospitals that handled CP or IF were offered to participate in



the study and all workplaces accepted participation. Hospital A was a minor hospital with only one workplace that handled the requested antineoplastic drugs. Hospital B-D were district hospitals and had three workplaces each where patients were treated with CP or IF. Hospital E was an university hospital with four workplaces that used CP or IF. In total, 14 different workplaces were surveyed in the study and they were specialized in oncology, surgery and hematology. Characteristics of the workplaces can be seen in Table 1.

All workplaces except one received prepared antineoplastic drugs mixtures from nearby hospital pharmacies. The oncology outpatient ward at hospital E had its own preparation unit and it also supplied the oncology ward at the same hospital with antineoplastic drug preparations.

In almost all hospital workplaces antineoplastic drugs were handled according to the ordinance from the Swedish Work Environment Authority and to the local safety guidelines of each hospital.<sup>35</sup> In connection with the exposure measurement in each workplace information about PPE was obtained by a questionnaire. The most workplaces (N=12) used safety equipment, devices for safe handling and PPE. PPE was for instance used when antineoplastic drugs were administrated, when treated patients were nursed or during cleaning activities and their occupational hygienic practices were assessed to be good. However, in two workplaces (surgical outpatient ward in hospital B and hematology outpatient ward in hospital E) no gowns and/or gloves were used by the health care workers, and these two workplaces were assessed not to fulfill the criteria for good occupational hygiene practice. Thus, data from the two workplaces were excluded in the calculations of the HGVs.

The sampling strategy was based on knowledge from previous results with repeated wipe sampling which showed that the variability in surface contamination of CP and IF was rather low, and that a single wipe sample seemed to reflect the contamination levels over time rather well.<sup>14</sup> Furthermore, no correlations were seen between the measured surface contamination and the daily or monthly handled amounts of CP and IF.<sup>14</sup> So, therefore in this study wipe sampling was performed once at each workplace during a two month period. The sampling day was chosen so at least one workplace at the hospital handled CP or IF in connection with the wipe sampling. Surface monitoring was performed on the same categories of surfaces as our previous study.<sup>14</sup> Four different categories of surfaces in the hospital workplaces; work areas, other surfaces, floors and handles were wipe sampled. Work areas, floors and handles are commonly monitored surfaces, while the category other surfaces included several types of surface locations not so commonly monitored e.g. shelves, boxes, control panels. Similar surface locations were sampled in all the workplaces to allow comparison between them.

Wipe sampling was performed according to a standardized sampling protocol and wipe samples were collected with two nonwoven swabs wetted with 1 ml 0.03 M sodium hydroxide each.<sup>12-14</sup> To avoid cross-contamination between the samples a new pair of gloves was used for each collected wipe sample. On work areas and floors a sampling area of 400 cm<sup>2</sup> defined by a plastic frame (20 × 20 cm cut-out interiors) were wiped, and the plastic frame was carefully decontaminated between each wipe sample. Other objects such as handles, balances, control panels of drip counters etc. had self-defined areas, and the entire object was wiped. All objects with self-defined areas except the handles were measured with measuring tape to estimate the size. At each workplace three field blanks

were collected by wetting two wipe swabs with sodium hydroxide and putting them into a bottle. Totally were 42 field blanks collected.

Fifty percentage of the workplaces handled CP during the sampling day while no IF was handled in connection with the wipe sampling. In those workplaces where patients were treated with CP in connection with the sampling day, the chemotherapy treatments were finished before the wipe samples were collected. The number of sampled surfaces varied between 10 and 22 in the workplaces. The total number of collected wipe samples were for the work areas (N=33), other surfaces (N= 47), floors (N=76) and handles (N=50).

**Older data.** In this study three workplaces (two oncology wards and one oncology outpatient ward) located at an university hospital (F) in the south of Sweden were repeatedly surface monitored.<sup>14</sup> Characteristics of the workplaces in this study can be seen in Table 1. Wipe samples (N=241) from work areas, other surfaces, floors and handles were collected eight times during a nine-month period for analysis of surface loads of CP and IF. The workers in the three workplaces handled antineoplastic drugs according to the ordinance from the Swedish Work Environment Authority and to the local safety guidelines of the hospital.<sup>35</sup> Also information about use of PPE and work practice was obtained in connection with the exposure measurements.<sup>14</sup> Thus, the occupational hygiene practices seemed to be good in the surveyed workplaces.

## **Analysis**

All wipe samples were extracted according to a previously described procedure.<sup>12-14</sup> The analysis of the sampled was blinded and performed with liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) in electrospray ionisation mode. Each sample was injected twice and the mean value was reported. The limit of detection (LOD) for CP and IF was 0.02 ng per wipe sample (0.05 pg cm<sup>-2</sup> for 400 cm<sup>2</sup> area) and 0.05 ng IF per wipe sample (0.13 pg cm<sup>-2</sup> for 400 cm<sup>2</sup> area), respectively.<sup>12,13</sup> No amounts of CP nor IF were quantified in the field blanks.

## **Statistical analysis**

Previous results indicated that the contamination levels in the outpatient wards and wards were in the same range.<sup>14</sup> Based on this knowledge the data from the outpatient wards and the wards were combined in the statistical analysis. For the statistical analysis software PASW Statistic 18 software for Windows (version 18.0.1, SPSS Inc.) was used. P-P plots indicated that data was not normally distributed, and thus median values and ranges are presented. Correlation analysis between the surface loads of CP and IF was performed by using Spearman's rank test for the two datasets, and it showed that the correlations structures of the two datasets were similar (0.62 and 0.64). Calculations of 90th percentile values were made for the HGVs. Values below the LOD were given the value of half the LOD.

## Results

The median annual amounts of CP and IF handled in all the workplaces were 115 g year<sup>-1</sup> and 30 g year<sup>-1</sup>, respectively. All the outpatient wards (N=10) handled CP (in median 139 g year<sup>-1</sup>), but only 50% of the outpatient wards (N=5) handled IF (in median 15 g year<sup>-1</sup>). The outpatient wards had in median eight beds and the frequency of handling CP and IF ranged from daily to monthly. The wards (N=7) handled in median 50 g CP year<sup>-1</sup> and 65 g IF year<sup>-1</sup>, had in median 14 beds and handled CP and IF in a range from weekly to monthly.

Totally 447 wipe samples were collected for CP and IF analysis from 17 Swedish hospitals workplaces. Surface loads of CP were found on 80% of the sampled surfaces. The corresponding value for IF was 73%. In 20% of the wipe samples no antineoplastic drugs were detected.

The detected surface loads of CP and IF ranged between <0.05-10800 pg cm<sup>-2</sup> and <0.13-95000 pg cm<sup>-2</sup>, respectively. The median surface load of CP and IF was 3.3 pg cm<sup>-2</sup> and 4.2 pg cm<sup>-2</sup>, respectively. In Table 2 the number of wipe samples for each location, the median surface loads for each location, ranges, percentage of wipe samples above the LOD and 90th percentile values can be seen. The floors in the patient lavatories were the most contaminated positions with median surface loads of 1100 pg cm<sup>-2</sup> and 260 pg cm<sup>-2</sup> for CP and IF, respectively. The second most contaminated location for CP was found on an elbow rest of a chair (120 pg cm<sup>-2</sup>) used of patients during drug administration, followed by the floors in the treatment room with a median surface load of 30 pg cm<sup>-2</sup>. The second most contaminated location for IF was found on balances located in the utility rooms used for weighing urine from IF treated patients (76 pg cm<sup>-2</sup>). Work areas

with the highest median surface loads were found in the drug rooms ( $0.5 \text{ pg CP cm}^{-2}$ ) and the utility room ( $1.3 \text{ pg IF cm}^{-2}$ ).

In Table 3 HGVs derived from 90th percentile values of surface monitoring data from work areas, other surfaces, floors and handles from 15 workplaces with good occupational hygiene practices are presented. The HGVs can be applicable to hospital workplaces where patients are treated with CP and IF. The highest HGVs for both CP and IF were derived from the floor data.

## **Discussion**

This study provides HGVs for CP and IF applicable for hospital workplaces administrating CP and IF and nursing treated patients. Moreover, it was also found that contamination of CP and IF was widely spread in hospital workplaces with chemotherapy treatments, and these results indicates that the health care workers potentially can be dermally exposed to CP and IF. Surface loads of CP/IF contamination were more frequently found on the floors (95%/91%) compared with other surfaces (68%/69%), work areas (65%/59%) and handles (53%/35%). The least contaminated surface category was the handles with median surface load of  $0.15 \text{ pg CP sample}^{-1}$ . The corresponding value for IF was not detectable. However, this study provides evidence that health care workers are likely to have hand contact with contaminated surfaces e.g. refrigerator handles (up to  $6.3 \text{ pg sample}^{-1}$ ) and door handles (up to  $160 \text{ pg sample}^{-1}$ ). By estimating the surface area of the door handle (approximately  $77 \text{ cm}^2$ ) the surface load value was calculated to be  $2100 \text{ pg cm}^{-2}$ , which is in the same contamination range as the floor levels. The highest median surface loads of CP ( $17 \text{ ng cm}^{-2}$ ) and IF ( $19 \text{ ng cm}^{-2}$ ) were

found on the floors. This is in agreement with what other studies also has shown.<sup>6,14</sup>

Surface areas related to the patients' excretion of CP and IF in urine have shown to have the highest surface loads. Thus, surfaces in patient lavatories should therefore be considered as contaminated since the surface loads can be very high.

Since the floors had the highest levels of contamination major spillage must occur on this category of surfaces, or the daily cleaning of the floors might not be enough efficient to remove the contamination. An alternative explanation might be that most of the flooring materials in the monitored workplaces were made of plastic and thus porous. It seems like surface contamination of e.g. CP could diffuse into the pores of the plastic flooring material and be accumulated there over time, and then be emitted back to the surface again.<sup>14,36</sup> Antineoplastic drugs are environmentally stable compounds. If the described scenario with accumulation occurs and emission of antineoplastic drugs from different surface materials, then there will be an uncertainty in wipe sampling especially in monitoring of work practice. Therefore, monitoring of e.g. work practice should be performed on work areas instead of floors because work areas are more relevant regarding skin contact. However, these indications should be further studied.

Five of the outpatient wards reported that IF never was handled or administrated to patient. However, levels of surface loads of IF were detected in approximately 15% of the wipe samples from these five outpatient wards. It is possible that patients were sporadically treated with IF in these wards although this was not reported. Another possible explanation might be that antineoplastic drugs were widely spread as diffuse contamination in hospital environments where chemotherapy was give. This is a reason for further investigation of other antineoplastic drugs than CP and IF.

The detected surface loads of CP and IF on e.g. work areas in the two studies were low, but since the drugs are carcinogenic the levels should be as low as possible. In the studies only two antineoplastic drugs were monitored, but today in Sweden 77 different antineoplastic drugs are used in the health care, and of those 13 antineoplastic drugs have classified as carcinogenic to humans (group 1) and 12 antineoplastic drugs classified as probable human carcinogens (group 2A) by IARC.<sup>1,37,38</sup> Thus, it is expected that many of these 77 antineoplastic drugs used in the health care are present as surface contamination in hospital work environments and could potentially cause occupational exposure to the health care workers. Several of these antineoplastic drugs act with similar mechanism e.g. alkylating properties, and can give the same critical effect such as damages in chromosomes 5 and 7 causing cancer.<sup>39,40</sup> Therefore, the goal must be reduce the occupational exposure and in the work environment as much as possible. The contamination levels of antineoplastic drugs must be as low as possible, preferably undetectable levels. But in practice, especially in the wards, this is not a realistic and reachable goal at the moment. A first step in the right direction toward reduced contamination levels is the introduction of HGVs.

Today, no OELs exist for antineoplastic drugs in any work environments. So far, only one organisation, the United States Pharmacopeia (USP), has indicated a maximum threshold of  $1 \text{ ng cm}^{-2}$  of CP to limit the risks of uptake in humans.<sup>41</sup> Therefore, HGV could be applicable. In the literature guidance values for biological monitoring were generally set at the 90th percentile and these guidance values were not health based.<sup>30-33</sup> Guidance values based on the 90th percentile have also been used for exposure to carcinogens, which make the method suitable for our purpose.<sup>30</sup> Recently, guidance



values based on 90th percentile values have been proposed for surface monitoring of e.g. CP and IF in German hospitals.<sup>34</sup> Therefore, guidance values based on 90th percentile values could be applied for wipe sampling as a measure of potential dermal exposure to CP and IF. Guidance values can help to assess the occupational exposure and the adequacy of exposure controls.<sup>30,33</sup> According to Cocker et al. guidance values are pragmatic approaches to proposing OELs for e.g. carcinogens where there is a clear need to control exposure but a dose-response relationship or health-based OEL is difficult to establish.<sup>30</sup> HGVs, not health-based but based on good hygienic practice and control of exposure, can help to control and reduce exposure.<sup>30</sup> Another profit with using surface monitoring in combination with HGVs set at 90th percentile is that it can act as a ‘feedback-loop’ to assess exposure and controls.<sup>30</sup> By setting a guidance value at the 90th percentile 90% of the results from workplaces with good control of exposure will be below the guidance value, which means that action is only needed in 10% of the workplaces.<sup>30</sup> Resources required to control exposure are thereby reduced by targeting the action those workplaces exceeding the guidance values.<sup>30</sup> A guidance value will also by the time bring down the exposure levels, if surface monitoring is performed on a regular basis e.g. annually.

Of course, other percentile values than 90th percentile are possible, e.g. 10th percentile value could be used to reach a maximal safety for the health care workers. But in the case of working with antineoplastic drugs the health care workers use both extensive PPE and safety equipment and devices. Therefore, we judged that the current established methodology of using 90th percentile values for guidance values was applicable for surface monitoring of antineoplastic drugs as well. The introduction of HGVs is an

important step in the improvement of exposure control of antineoplastic drugs and to reduce the occupational exposure. HGVs based on 90th percentile values seems to be practically viable and important advantages are e.g. that action only is needed in 10% of the workplaces and that time will bring down the HGVs.

Schierl et al. have proposed guidance values for platinum (as a marker for cis-, carbo-, and oxaliplatin) and 5-fluorouracil in German pharmacies set at the 50th and 75th percentiles due to they found that the current occupational hygiene standard was so high that it was reasonable to set guidance values lower than the 90th percentile.<sup>28</sup> Wipe sampling data below the 50th percentile value demonstrated good work practice while data above the 75th percentile value showed a clear need for optimizing the handling procedures.<sup>28</sup> The German database of antineoplastic drug surface load data was larger than our Swedish database. However, we preferred the concept with one HGV set at 90th percentile value, which will decline over time with regular collection of wipe samples.<sup>30</sup>

The introduction of HGVs seems to be a usable tool to evaluate potential dermal exposure to antineoplastic drugs, especially since the use of antineoplastic drugs steadily increases. The proposed 90th percentile values in this study can be applicable to hospital workplaces working with chemotherapies of CP and IF. The HGVs for surface contamination of antineoplastic drugs can help health care workers to control the occupational exposure by benchmarking their own surface loads of antineoplastic drugs as a surrogate of dermal exposure. Also the work practices and exposure controls can be evaluated. This could lead to reduced occupational exposure as well as reduced surface loads and thereby increased occupational safety for the health care workers. Our proposed HVGs are approximately between 3-357 times lower compared with the

recommended value from USP.<sup>41</sup> Of an occupational point of view it is important to keep the antineoplastic drug exposure as low as practical possible.

Until now HGVs have only been available for pharmacies preparing antineoplastic drugs. The hospital workplaces in this study with surface loads exceeding the HGVs indicated that the antineoplastic drug exposure was not adequately controlled and that the health care workers can be dermally exposed. Workplace improvements regarding the work practice with antineoplastic drugs were needed. These workplaces need to reduce their surface loads of CP and IF and this could e.g. be done by revision of their handling procedures for antineoplastic drugs. Work practice might need to be improved, for example waste contaminated with antineoplastic drugs must be carefully sealed to prevent leakage to the work environment. Use of e.g. a waste sealing system sealing the waste in aerosol-tight bags could prevent this. Also, the handling of urine from chemotherapy treated patients might need to be more closed to prevent spillage of urine, since the concentrations of e.g. CP in the patients' urine are very high during the next days after administration.<sup>42</sup> For instance, we have measured CP concentrations in CP treated patients urine up to 12 days after administration.<sup>42</sup> The handling urine from patients such as measuring the amount of urine by weighing or measuring the volume might be done by the health care workers in e.g. fume cupboards or biological safety cabinets. Hygienic improvements such as changes in the protocol for cleaning by e.g. increased frequency of cleaning could be done. Also more surface locations might need to be included in cleaning protocol. The detergents used for cleaning need to be assessed so their efficiently remove surface contamination of the antineoplastic drugs used in the workplace. The efficiency of different detergents to remove antineoplastic drugs from

contaminated surfaces has been investigated and it was reported that acid, neutral and alkali detergents easily and efficiently remove e.g. CP from surfaces.<sup>43</sup> To remove the remaining surface contamination of antineoplastic drug and to avoid the introduction of new contamination both work practice need to be re-evaluated and the cleaning need to be improved and more effective reported Sugiura et al (2011).<sup>44</sup> Another preventive measure could be repeated training and education of the health care workers to improve work practice regarding safe handling of antineoplastic drugs.

## **Conclusion**

This study have shown widespread contamination of CP and IF in Swedish hospital workplaces involved in administration of chemotherapy and nursing of chemotherapy treated patients. Highest surface loads were found on the floors in patient lavatories. HGVs set at the 90th percentile value have been proposed. The HGVs should be used in hospital workplaces where CP and IF are administrated to patients and where treated patients are nursed. Surface monitoring combined with the HGVs could reduce the health care workers occupational exposure to antineoplastic drugs, not only exposure to CP and IF, but indirectly for all kinds of antineoplastic drugs handled in the workplace. Thereby, the occupational safety for the health care workers could be increased.

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**Table 1.** Characteristics of surveyed hospital workplaces involved in chemotherapy administration

Hospital	Workplace	Antineoplastic drug				No. of beds <sup>a</sup>	No. of CP treated patients during sampling <sup>b</sup>
		Frequency		Annually amounts (g)			
		CP	IF	CP	IF		
A	Oncology outpatient ward	Weekly	-	115	- <sup>c</sup>	7	3
B	Oncology outpatient ward	Weekly	Weekly	135	77	9	0
	Oncology ward	Monthly	Monthly	23	27	12	0
C	Surgical outpatient ward	Daily	-	183	- <sup>c</sup>	10	2
	Oncology outpatient ward	Weekly	-	142 <sup>d</sup>	- <sup>c</sup>	7	1
	Oncology ward	Weekly	Monthly	- <sup>d</sup>	78	17	0
D	Hematology outpatient ward	Daily	Monthly	182	30	16	2
	Oncology outpatient ward	Monthly	-	14	- <sup>c</sup>	2	0
	Oncology and hematology ward	Weekly	Monthly	180	34	14	1
E	Surgical outpatient ward	Weekly	-	64	- <sup>c</sup>	6	0
	Oncology outpatient ward	Daily	Monthly	673 <sup>d</sup>	176 <sup>d</sup>	19	4
	Oncology ward	Monthly	Monthly	- <sup>d</sup>	- <sup>d</sup>	27	0
	Hematology outpatient ward	Weekly	Monthly	68	35	4	2
F	Hematology ward	Monthly	Monthly	73	65	16	0
	Oncology outpatient ward	Daily	Monthly	620	30	8	- <sup>e</sup>
	Oncology ward	Monthly	Daily	50	420	14-16	- <sup>e</sup>
	Oncology ward	Weekly	Daily	220	1020	12-14	- <sup>e</sup>

<sup>a</sup>Includes beds, stretchers and armchairs<sup>b</sup>No patients were treated with IF in connection with the sampling<sup>c</sup>Not handled in the workplace<sup>d</sup>Total handled amounts in both oncology wards<sup>e</sup>The number of treated patients during wipe sampling is missing

**Table 2.** Levels of antineoplastic drug contamination of CP and IF in the surveyed hospital workplaces (N=17). Median values, range, percentage above LOD and 90th percentile values for different categories of surfaces are shown.

Location		No.	CP				IF			
			Median (pg cm <sup>-2</sup> )	Range	Percentage above LOD (%)	90th percentile	Median (pg cm <sup>-2</sup> )	Range	Percentage above LOD (%)	90th percentile
(a)										
Work areas	Drug room	60	0.5	ND <sup>a</sup> -8.9	67	2.5	0.6	ND-14	57	5.1
	Utility room	34	0.3	ND-37	65	3.2	1.3	ND-720	56	136
	Roller table	4	ND	-	0	-	0.2	ND-0.4	50	0.4
	Office	1	ND	-	0	-	ND	-	0	-
Other surfaces	Control panel of drip counter	30	6.4	ND-170	83	41	36	ND-900	73	250
	Refrigerator shelf/box	29	0.53	ND-3.8	66	2.3	1.4	ND-420	69	23
	Balance	16	2.0	ND-49	81	25	21	1.0-330	100	220
	Control panel of balance	16	3.4	ND-93	69	45	76	1.0-7500	81	930
	Surface of waste bin	9	0.1	ND-38	56	20	ND	ND-0.4	22	ND
	Bottom of transport/storage box	11	ND	ND-20	36	4.7	ND	ND-15	27	4.0
	Table	3	6.0	3.3-17	100	15	0.7	ND-35	67	28
	Desk pad	2	ND	-	0	-	ND	-	0	-
	Elbow-rest	1	120	-	100	-	ND	-	0	-
	Panel of code locking system	1	ND	-	0	-	ND	-	0	-
Floors	Utility room	39	21	ND-110	99	59	16	ND-2700	90	520
	Corridor	37	8.2	ND-240	92	88	10	ND-120	92	78
	Drug room	34	5.9	ND-160	97	32	23	ND-220	88	37
	Treatment room	26	30	ND-220	100	100	8.6	ND-740	88	300
	Patient lavatory	25	1100	5.0-10800	100	4200	260	ND-95000	92	4300
	Office	2	3.2	2.3-4.0	100	3.8	1.0	0.3-1.7	100	1.6
	Patient shower	1	2.1	-	100	-	ND	-	0	-
	Canteen	1	4.2	-	100	-	ND	-	0	-

(b)										
Handles <sup>b</sup>	Refrigerator	20	0.45	ND-6.3	85	2.0	0.53	ND-22	65	3.1
	Door patient lavatory <sup>c</sup>	15	3.3	ND-160	80	24	ND	ND-1.3	33	0.3
	Utility/waste room	7	ND	ND-0.7	14	0.30	ND	-	0	-
	Transport box	6	ND	ND-0.10	17	0.06	ND	-	0	-
	Drug room	2	ND	-	0	-	ND	-	0	-
	Waste box	4	ND	-	0	-	ND	-	0	-
	Flush knob patient toilet	3	6.7	6.2-11	100	10	1.0	0.2-1.2	100	1.2
	Treatment room	1	0.1	-	100	-	ND	-	0	-
	Exit door	1	1.6	-	100	-	ND	-	100	-
	Tap	1	14	-	100	-	ND	-	0	-
	Others (roller table, closet, computer mouse)	5	ND	-	0	-	ND	-	0	-

<sup>a</sup>Not detected

<sup>b</sup>Unit: ng sample<sup>-1</sup>

<sup>c</sup>Both sides

**Table 3.** Number of wipe samples, percentage above LOD, median values and HGVs for different categories of surfaces for hospital workplaces (N=15) with good occupational hygiene practices.

Location	N	% wipe samples > LOD <sup>a</sup>		Median (pg cm <sup>-2</sup> )		HGV (pg cm <sup>-2</sup> )	
		CP	IF	CP	IF	CP	IF
Work areas	95	65	59	0.43	0.81	2.8	24
Other surfaces	112	68	69	1.1	5.0	35	170
Floors	155	95	91	18	23	370	500
Handles <sup>b</sup>	57	53	35	0.15	ND	6.0	1.2

<sup>a</sup>Limit of detection (LOD) for CP: 0.02 ng per wipe sample (0.05 pg cm<sup>-2</sup> for 400 cm<sup>2</sup> area); LOD for IF: 0.05 ng per wipe sample (0.13 pg cm<sup>-2</sup> for 400 cm<sup>2</sup> area)

<sup>b</sup>Unit: ng sample<sup>-1</sup>