# Rapport de veille n° 58

## *Surveillance biologique de l'exposition professionnelle aux médicaments cytotoxiques. Etude de terrain.*

***1er novembre 2022 – 31 décembre 2022***

***Objectifs :*** Disposer d'une connaissance actualisée du sujet en accompagnement des demandes d'assistance qui découlent de la valorisation de l'étude sur la surveillance biologique de l'exposition aux médicaments cytotoxiques en milieu hospitalier.

*La validation des informations fournies (exactitude, fiabilité, pertinence par rapport aux principes de prévention, etc.) est du ressort des auteurs des articles signalés dans la veille. Les informations ne sont pas le reflet de la position de l'INRS.*

*Les liens mentionnés dans le bulletin donnent accès aux documents sous réserve d'un abonnement à la ressource.*

- ***Articles de périodique (PREPRINT)***

Delafoy C., Benoist H., Patin A., Vasseur M., Guillouet S., Eveno C., Guilloit J.M., Odou P., Simon N., Saint-Lorant G.
**Knowledge and practices about safe handling regarding the risk of exposure to antineoplastic drugs for caregivers in compounding units and in operating rooms performing HIPEC/PIPAC.**
Journal of Oncology Pharmacy Practice, 13 décembre 2022

Résumé : *Introduction Ever since the late 1970s, occupational exposure associated with the handling of antineoplastic drugs (ADs) in the healthcare environment has been highlighted and demonstrated. Contamination was detected in both operating rooms (OR) and compounding units (CU), where healthcare workers handle and are exposed to ADs in different ways. In the OR, the risk of exposure is higher and the staff receives less training in handling ADs than in the CU. This study aimed to assess and compare knowledge and practices about the safe handling of ADs by caregivers working in these two locations, namely the CU and OR. Methods Two questionnaires (one each for the OR and CU) were created by two investigator pharmacists and were completed during a personal interview of 20 min. The questions were related to the following topics: training, knowledge about occupational exposure and questions related to protective practices. A scoring system was implemented to assess the knowledge and practices of each participant. Results In total, 38 caregivers working in the OR and 39 in the CU were included in our study. Significantly more CU staff had specific initial training ($p < 0.001$) and ongoing training ($p < 0.001$) in handling ADs. Concerning the knowledge score, OR caregivers had a significantly lower median score for contamination routes ($p < 0.001$), contamination surfaces ($p < 0.001$), existing procedures ($p < 0.001$) and total knowledge ($p < 0.001$) than CU caregivers. Concerning protective handling practices of ADs, the two locations had nonsignificantly different median scores ($p = 0.892$). Conclusion This study suggests that there is still room for improvement in terms of knowledge and protection practices when handling ADs. An appropriate and tailored training program should be developed and provided to all caregivers who handle or come in contact with ADs.*

https://doi.org/10.1177/10781552221144303

- ***Articles de périodique***

**ISOPP Standards for the Safe Handling of Cytotoxics.**
Journal of Oncology Pharmacy Practice, Volume 28, Numéro 73 Suppl, Avril 2022, Page S1-S126

*Résumé : Since the initial release of the International Society of Oncology Pharmacy Practitioners (ISOPP) Standards for the Safe Handling of Cytotoxic Drugs in 2007, much has evolved in oncology pharmacy. Safe handling practices have been refined and new hazardous agents have been discovered and developed for treatment to pose new challenges for workers caring for their patients.*
*As ISOPP continues to serve as a global leader to promote safe handling of hazardous agents, the ISOPP Standards task force was appointed by the society to undertake a comprehensive and evidence-based review of 21 old standards and added eight new standards to focus on additional areas of practice.*

*With the help of many members from across the world, the ISOPP Standards of Practice have been updated for the current state of practice in oncology pharmacy.*

https://doi.org/10.1177/10781552211070933

Acramel A., Fouque J., Blondeel-Gomes S., Matta C., Narayani S., Madar O., Desmaris R., Escalup L., Fouque J.
(Préprint dans Bulletin n° 55)
**Reporting environmental contamination results to healthcare workers could play a crucial role in decreasing the risk of occupational exposure to antineoplastic drugs.**
Frontiers in Public Health, Volume 10, 25 août 2022, Article 989977

Résumé : *OBJECTIVES: The risk of chronic exposure to antineoplastic agents in hospitals, mainly by skin contact with contaminated surfaces, is well established. The aim of this study was to assess indirectly the risk of occupational exposure to antineoplastics drugs at two hospitals by using an environmental monitoring, and to suggest ways of improving the exposure to healthcare workers. METHODS: An observational study of care practices on both sites was carried out. A wipe sampling campaign was then designed to study environmental contamination throughout the chemotherapy process: receipt, storage, compounding, transport, administration, and elimination areas. Samples were analyzed by a validated LC-MS/MS method allowing trace quantification of cyclophosphamide. A guidance 'safe value' of 0.10 ng/cm2 was considered. RESULTS: A total of 293 samples were analyzed, of which 58% were found to be positive. In the compounding units, the drug vials were contaminated before [range = (non-quantifiable [NQ]-0.71) ng/cm2] and after cleaning procedure [(NQ-0.62) ng/cm2], particularly when the flip-off lid was removed during cleaning. The contamination found on manual preparations was operator-dependent: [non-detectable (ND)-3.51] ng/cm2 on infusion bag surfaces; (780.61-24 698.98) ng/cm2 on medication ports. In the case of automated preparations, the average contamination was higher on infusion bag surfaces [(2.43-36.86) ng/cm2] and lower on medication ports [(0.43-7.65) ng/cm2] than manual preparations. Contamination of the analytical control area was also highlighted. In the daily care unit, the contamination was located near the infusion area (armchairs, infusion stands, floor, and patient toilets), and varied somewhat between the two sites, especially on the floor with (0.46-27.32) compared to (ND-0.18) ng/cm2. We did not detect contamination on the transport boxes, on the door handles or in the disposal areas. CONCLUSIONS: The variability of contamination observed between the two sites can be explained in part by the difference in routine practices, especially training of the staff, and cleaning procedures. Findings were communicated to healthcare workers, and news interventions were implemented based on wipe sampling results. This study demonstrated a method for routine environmental monitoring and worker education as a strategy to reduce occupational exposure.*

https://doi.org/10.3389/fpubh.2022.989977

Hon C. Y. & Motiwala N.
**Biological Monitoring via Urine Samples to Assess Healthcare Workers' Exposure to Hazardous Drugs: A Scoping Review.**
Applied Sciences-Basel, Volume 12, Numéro 21, Novembre 2022, Page 1170

Résumé: *Although biological monitoring is beneficial as it assesses all possible routes of exposure, urine sampling of healthcare workers exposed to hazardous drugs is currently not routine. Therefore, a scoping review was performed on this subject matter to understand what is known about exposure and identify*

*knowledge gaps. A literature search was performed on three databases: ProQuest, Web of Science, and PubMed. Articles published between 2005 and 2020 and written in English were included. Overall, this review consisted of 39 full-text articles. The studies varied with respect to design, sample sizes, sample collection times, and drugs examined. Many articles found at least one sample had detectable levels of a hazardous drug. Studies reported urinary drug contamination despite controls being employed. Knowledge gaps included a lack of an exposure limit, lack of a standardized sampling method, and lack of correlation between health effects and urinary contamination levels. Due to differences in sample collection and analysis, a comparison between studies was not possible. Nevertheless, it appears that biological monitoring via urine sampling is meaningful to aid in understanding healthcare workers' exposure to hazardous drugs. This is supported by the fact that most studies reported positive urine samples and that case-control studies had statistically significant findings.*

https://doi.org/10.3390/app122111170

Acramel A., Fouque J., Blondeel-Gomes S., Huguet S., Rezai K., Madar O., Escalup L.
(Préprint dans Bulletin n° 55)

**Application of an Environmental Monitoring to Assess the Practices and Control the Risk of Occupational Exposure to Cyclophosphamide in Two Sites of a French Comprehensive Cancer Center.**

Annals of work exposures and health, Volume 66, Numéro 9, Novembre 2022, Page 1215-1223

Résumé : *OBJECTIVES: The risk of chronic exposure to antineoplastic agents in hospitals, mainly by skin contact with contaminated surfaces, is well established. The aim of this study was to assess indirectly the risk of occupational exposure to antineoplastics drugs at two hospitals by using an environmental monitoring, and to suggest ways of improving the exposure to healthcare workers. METHODS: An observational study of care practices on both sites was carried out. A wipe sampling campaign was then designed to study environmental contamination throughout the chemotherapy process: receipt, storage, compounding, transport, administration, and elimination areas. Samples were analyzed by a validated LC-MS/MS method allowing trace quantification of cyclophosphamide. A guidance 'safe value' of 0.10 ng/cm2 was considered. RESULTS: A total of 293 samples were analyzed, of which 58% were found to be positive. In the compounding units, the drug vials were contaminated before [range = (non-quantifiable [NQ]-0.71) ng/cm2] and after cleaning procedure [(NQ-0.62) ng/cm2], particularly when the flip-off lid was removed during cleaning. The contamination found on manual preparations was operator-dependent: [non-detectable (ND)-3.51] ng/cm2 on infusion bag surfaces; (780.61-24 698.98) ng/cm2 on medication ports. In the case of automated preparations, the average contamination was higher on infusion bag surfaces [(2.43-36.86) ng/cm2] and lower on medication ports [(0.43-7.65) ng/cm2] than manual preparations. Contamination of the analytical control area was also highlighted. In the daily care unit, the contamination was located near the infusion area (armchairs, infusion stands, floor, and patient toilets), and varied somewhat between the two sites, especially on the floor with (0.46-27.32) compared to (ND-0.18) ng/cm2. We did not detect contamination on the transport boxes, on the door handles or in the disposal areas. CONCLUSIONS: The variability of contamination observed between the two sites can be explained in part by the difference in routine practices, especially training of the staff, and cleaning procedures. Findings were communicated to healthcare workers, and news interventions were implemented based on wipe sampling results. This study demonstrated a method for routine environmental monitoring and worker education as a strategy to reduce occupational exposure.*

https://doi.org/10.1093/annweh/wxac035

Dugheri S., Mucci N., Bucaletti E., Squillaci D., Cappelli G., Trevisani L., Bonari A., Cecchi M., Mini E., Ghiori A., Tognoni D., Berti N., Alderighi F., Vigni N.L., Orlandi I., Arcangeli G.
**Monitoring surface contamination for thirty antineoplastic drugs: a new proposal for surface exposure levels (SELs).**
Medycyna Pracy, Volume 73, Numéro 5, Novembre 2022, Page 383-396

Résumé : *BACKGROUND: Chemotherapy drugs are widely used to treat cancer, but their active compounds represent a danger for workers who could be exposed to them. However, they aren't yet included in directive CE No. 1272/2008 and the European Biosafety Network has only recommended a limit value of 100 pg/cm(2) for surface contamination. Thus, it is crucial to assess surface contaminations in healthcare environments. Currently, the technique of choice is surface wipe test combined with liquid chromatography tandem mass spectrometry to achieve high sensibility. MATERIAL AND METHODS: A campaign involving Careggi University Hospital (Florence, Italy) was performed from January 2020 to December 2021, collecting 1449 wipe samples between administration units, preparation unit, and personnel gloves. From the obtained data, the 90th percentile was calculated for 30 antiblastic drugs and proposed as surface exposure levels (SELs); while from data concerning personnel glove contamination, weekly contamination was estimated. RESULTS: In the 2-year period only 417 wipe samples were found positive (28.8%), the majority of which regard samples coming from administration unit bathrooms. The proposed SELs are almost all <100 pg/cm(2), except for few drugs which produce higher contamination on bathroom surfaces. Also, the estimation of pharmacy personnel's glove contamination highlighted very low results (ng/week). CONCLUSIONS: Deeply established protocols and procedures for safe handling of ADs allow for obtaining excellent cleaning results and thus a safer work environment, however, the risk of cytostatic contaminations cannot be avoided in healthcare workplaces, and thus a harmonization of classification and labeling of chemotherapy drugs throughout the European Union should be done.*

https://doi.org/10.13075/mp.5893.01288

Demircan Yildirim F., Ekmekci I.
(Préprint dans Bulletin n° 56)
**Design of analytical method validation protocol evaluating environmental monitoring of and contamination on surfaces based on cleaning validation procedures: a multi component RP-UHPLC method.**
Journal of Chromatographic Science, Volume 60, Numéro 10, Novembre-Décembre 2022, Page 926-936

Résumé : *Environmental monitoring of anti-neoplastic drug (AND) residues in workplaces is crucial to limit exposure to workers who handle with them. Although wipe sampling is the most appropriate methodology to evaluate the risk, conflicting results are also reported due to the lack of standardized and validated procedures. In this study, procedures for surface contamination of ANDs in workplaces are presented, with a focus on sampling, sample preparation and instrumentation. The analytical method validation parameters are designed to comply with requirements of The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q7 Good Manufacturing Practice (GMP) for active pharmaceutical ingredients. Additionally, the study provides a simple, specific, rapid and multi-component analytical method to evaluate seven ANDs that are Gefitinib, Imatinib, Dasatinib, Axitinib, Erlotinib, Nilotinib and Sorafenib at very low concentration levels, simultaneously. Quantitative, precise and reproducible results obtained from the study show that environmental monitoring procedure and analytical method validation protocol presented in the study can be used to reduce and monitor occupational exposure risk to ANDs in wokplaces.*

https://doi.org/10.1093/chromsci/bmac071

Fazel S. S., Keefe A., Shareef A., Palmer A. L., Brenner D. R., Nakashima L., Koehoorn M. W., McLeod C. B., Hall A. L. & Peters C. E.
(Préprint dans Bulletin n° 52)
**Barriers and Facilitators for the Safe Handling of Antineoplastic Drugs.**
Journal of Oncology Pharmacy Practice, Volume 28, Numéro 8, Décembre 2022, Page 1709-1721

Résumé : *INTRODUCTION: Antineoplastic drugs are widely used in the treatment of cancer. However, some are known carcinogens and reproductive toxins, and incidental low-level exposure to workers is a health concern. CAREX Canada estimated that approximately 75,000 Canadians are exposed to antineoplastic drugs in workplace settings. While policies and guidelines on safe handling of antineoplastic drugs are available, evidence suggests that compliance is low. In this paper, we identify barriers and facilitators for safe handling of antineoplastic drugs in workplace settings. METHODS: We utilized a unique method to study public policy which involved compiling policy levers, developing a logic model, conducting a literature review, and contextualizing data through a deliberative process with stakeholders to explore in-depth contextual factors and experiences for the safe handling of antineoplastic drugs. RESULTS: The most common barriers identified in the literature were: poor training (46%), poor safety culture (41%), and inconsistent policies (36%). The most common facilitators were: adequate safety training (41%), leadership support (23%), and consistent policies (21%). Several of these factors are intertwined and while this means one barrier can cause other barriers, it also allows healthcare employers to mitigate these barriers by implementing small but meaningful changes in the workplace. CONCLUSION: The combination of barriers and facilitators identified in our review highlight the importance of creating work environments where safety is a priority for the safe handling of antineoplastic drugs. The results of this study will assist policy makers and managers in identifying gaps and enhancing strategies that reduce occupational exposure to antineoplastic drugs.*

https://doi.org/10.1177/10781552211040176

Abu-Alhaija D., Miller E., Bakas T., Shaughnessy E.
**The Development and the Content Validation of the Oncology Nurses Health Behaviors Determinants Scale.**
Seminars in Oncology Nursing, Volume 38, Numéro 6, Décembre 2022, Page 151317

Résumé : *Objective: Chemotherapy exposure is an occupational hazard affecting oncology nurses. The adherence to chemotherapy-handling guidelines is essential to prevent exposure to these drugs. Oncology nurses' health beliefs and the cues in the environment are factors influencing the adherence to these guidelines. There is a lack of instruments with evidence of reliability and validity in the literature that address these factors. The purpose of this article is to describe the development and the content validation of the Oncology Nurses' Health Behaviors' Determinants Scale relative to adherence to chemotherapy-handling guidelines.Data Sources: This study was conducted in two phases: item development, then, content validation using a quantitative cross-sectional design with an exploratory part. A convenience sample of seven experts reviewed the items for relevance, wording, and comprehensiveness. The initial version of the scale that was sent to experts contained 65 items. Conclusion: The Oncology Nurses' Health Behaviors Determinants' Scale has evidence of content validity. Twenty-eight items in the final instrument met the required level of content validity (item content validity index= 0.83). Four additional items were retained due to conceptual significance. Two items were added. The final scale contains 34 items with a*

*total scale content validity index = 0.90.Implications for Nursing Practice: This newly developed instrument could be used to assess the factors that influence chemotherapy exposure among oncology nurses in the light of the Health Belief Model. Following that, interventions can be developed and implemented to foster greater adherence to safe chemotherapy handling guidelines.*

https://doi.org/10.1016/j.soncn.2022.151317