

Rapport de veille n° 59

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

1^{er} janvier 2023 – 28 février 2023

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)**

E Silva L.S., Machado C.D.S.B., Linden R., Antunes M.V., da Silva L.C., Wayhs C.A.Y., Capp E., Ness S.L.R.

Residual contamination in antineoplastic drug packaging.

Journal of oncology pharmacy practice, 19 janvier 2023

Résumé : *INTRODUCTION: The handling of antineoplastic drugs should follow strict supervision and safety rules to minimize the occupational exposure risks to professionals involved. The external surface contamination of drug vials is recognized as a health risk. So, our goal was to determine if there is residual contamination on the vials and containers surface of the antineoplastic drugs doxorubicin (DOX) and cyclophosphamide (CP). METHODS: A cross-sectional study was conducted. Samples were collected using a uniform sampling procedure on the inner surfaces of the packages/boxes and the outer surfaces of the vials. The analyzes were executed by high-performance liquid chromatography/mass spectrometry (UHPLC-MS/MS). RESULTS: A total of 209 samples were analyzed, 66 of CP and 143 of DOX. CP levels were detected in nine samples (13.63%), three were below the lower limit of quantification (LLQ) and the other six had contamination levels ranging from 1.24 to 28.04 ng/filter. DOX levels were detected in 36 samples (25.17%), two were below the LLQ and the others had levels between 1.32 and 664.84 ng/filter. The majority of samples with residual contamination were in vials (80.0%), however, boxes also showed contamination. CONCLUSIONS: The results revealed the presence of residual contamination in the vials and packages of CP and DOX drugs. Although the residues found in each sample are small, special care should be taken in the handling and disposal of the antineoplastic drugs. The use of personal protective equipment is fundamental while handling the vials and packaging of cytotoxic drugs.*

<https://doi.org/10.1177/10781552231151693>

Saint-Lorant G., Vasseur M., Allorge D., Beauval N., Simon N., Odou P.

Four-year follow-up of surface contamination by antineoplastic drugs in a compounding unit.

Occupational and environmental medicine, 30 janvier 2023

Résumé : *OBJECTIVES: This study aimed to monitor the contamination by antineoplastic drugs on work surfaces in a compounding unit 4 years after its implementation. METHODS: This descriptive study was done in a unit performing on average 45 000 preparations per year. Surface sampling points (N=23) were monitored monthly in the frame of routine activity from the opening of an anticancer drug compounding unit. Contamination with nine antineoplastic drugs (cyclophosphamide, ifosfamide, dacarbazine, 5-fluorouracil, methotrexate, gemcitabine, cytarabine, irinotecan and doxorubicin) was assessed on wipes with a local liquid chromatography coupled with a tandem mass spectrometer analysis. The contamination rate (CR, %) was prospectively monitored every month during the entire study period. The occurrence of critical incidents was also registered. The effect of each safety measure implemented during this period was also analysed. RESULTS: Based on the 1104 samples collected between March 2016 and March 2020, the CR was 18.5%. If three different critical incidents among a vial breakage that occurred were individually considered, this CR was slightly lower than that in the literature. Eight months after opening and taking different corrective actions, the overall CR dropped from 42.39% to 11.52% ($p<0.001$). Contamination was limited to the area that includes the compounding room and, more precisely, the welder and the QC-Prep(+) sampling points. CONCLUSIONS: From the beginning of the*

study and from month to month, surface contamination was limited to the nearest sampling points to the compounding unit. This 4-year monitoring study allowed us to determine the intravenous conventional antineoplastic drugs and sampling points to be focused on.

<https://doi.org/10.1136/oemed-2022-108623>

Delafoy C., Benoist H., Vasseur M., Breuil C., Divanon F., Odou P., Simon N., Saint-Lorant G.
Perception, knowledge, practices and training regarding the risk of exposure to antineoplastic drugs in three French compounding units.

Journal of Oncology Pharmacy Practice, 14 février 2023

Résumé : *INTRODUCTION: Healthcare workers are exposed to hazardous drugs such as antineoplastic drugs, which have potential carcinogenic, mutagenic and teratogenic effects. Protective measures must be taken after appropriate staff training to handle antineoplastic drugs in a safe way. The objective was to assess perception, knowledge, practices and training regarding the risk of exposure of healthcare workers in three French compounding units. METHODS: This descriptive study was based on a questionnaire made of 33 questions divided into five sections related to the handling of antineoplastic drugs: perception of the risks, knowledge of the risks, protection practices, specific training and general questions. RESULTS: Among the 39 participants, over half considered their overall risk of exposure to antineoplastic drugs not being very low. Inhalation was known to 69.2% of them as possible route of contamination. The breakroom was identified by 28.9% of them as a place of contamination. The procedure in case of accidental exposure to antineoplastic drugs was known by 69.2%, but only half could explain it. Only 38.5% said they changed their gloves every 30 min as recommended. Barely half said that they had been trained specifically for the handling of antineoplastic drugs during an initial training. Over half wished to be informed, trained and aware of the proper handling of antineoplastic drugs. CONCLUSION: Although some of these results are encouraging, specifically when compared to the other settings where antineoplastic drugs are handled, there is still room for improvement. Efforts to build an adapted and impactful training program must pursue.*

<https://doi.org/10.1177/10781552231156520>

- **Articles de périodique**

Lema-Atán J.A., Lendoiro E., Paniagua-González L., Cruz A., López-Rivadulla M., de-Castro-Ríos A.
(Préprint dans Bulletin n° 57)

LC-MS-MS Determination of Cytostatic Drugs on Surfaces and in Urine to Assess Occupational Exposure.

Journal of Analytical Toxicology, Volume 46, Numéro 9, novembre 2022, Page e248-e255

Résumé : *The ever-increased usage of cytostatic drugs leads to high risk of exposure among healthcare workers. Moreover, workers are exposed to multiple compounds throughout their lives, leading to cumulative and chronic exposure. Therefore, multianalyte methods are the most suitable for exposure assessment, which minimizes the risks from handling cytostatic drugs and ensures adequate contamination containment. This study describes the development and full validation of two liquid chromatography-tandem mass spectrometry methods for the detection of gemcitabine, dacarbazine,*

methotrexate, irinotecan, cyclophosphamide, doxorubicinol, doxorubicin, epirubicin, etoposide, vinorelbine, docetaxel and paclitaxel in working surfaces and urine samples. The urine method is the first to measure vinorelbine and doxorubicinol. For surfaces, limits of detection (LOD) and limits of quantification (LOQ) were 5-100 pg/cm², and linearity was achieved up to 500 pg/cm². Inaccuracy was between -11.0 and 8.4%. Intra-day, inter-day and total imprecision were <20%, except for etoposide and irinotecan (<22.1%). In urine, LOD and LOQ were 5-250 pg/mL, with a linear range up to 1,000-5,000 pg/mL. Inaccuracy was between -3.8 and 14.9%. Imprecision was <12.4%. Matrix effect was from -58.3 to 1,268.9% and from -66.7 to 1,636% in surface and urine samples, respectively, and extraction efficiency from 10.8 to 75% and 47.1 to 130.4%, respectively. All the analytes showed autosampler (6°C/72 h), freezer (-22°C/2 months) and freeze/thaw (three cycles) stability. The feasibility of the methods was demonstrated by analyzing real working surfaces and patients' urine samples. Contamination with gemcitabine, irinotecan, cyclophosphamide, epirubicin and paclitaxel (5-4,641.9 pg/cm²) was found on biological safety cabinets and outpatients' bathrooms. Analysis of urine from patients under chemotherapy identified the infused drugs at concentrations higher than the upper LOQ. These validated methods will allow a comprehensive evaluation of both environmental and biological contamination in hospital settings and healthcare workers.

<https://doi.org/10.1093/jat/bkac073>

von Grünigen S., Dessane B., Le Pape P., Falaschi L., Geissbühler A. & Bonnabry P.

(Préprint dans Bulletin n° 52)

Development and Evaluation of an E-Learning Module for Low- and Middle-Income Countries on the Safe Handling of Chemotherapy Drugs.

Journal of Cancer Education, Volume 38, Numéro 1, février 2023, Page 285-291

Résumé : *Despite the growing use of chemotherapy drugs in resource-constrained settings, training opportunities on safe handling practices are lacking. This study's objectives were to develop and evaluate an e-learning training module on the safe handling of chemotherapy drugs to strengthen knowledge and practices in low- and middle-income countries (LMICs). The module's curriculum was developed using the Six-Step Approach for Curriculum Development for Medical Education. Asynchronous, self-paced, e-learning lessons within the module were created and uploaded onto a free online platform, Pharm-Ed. The study ran online from January to April 2021. Participant recruitment was done using convenience sampling through various channels (social media, communities of practice). Training module effectiveness was evaluated using knowledge assessments (a pre-test and post-test study design) and participant satisfaction. We developed a comprehensive e-learning module on the safe handling of chemotherapy drugs comprising 11 asynchronous, self-paced, e-learning lessons. Eighty-two participants (68% pharmacists and 17% pharmacy students) from 17 countries completed at least one lesson, with a total of 259 lessons completed. Evaluation of the different lessons showed significant improvements in theoretical knowledge ($p < 0.01$) in all except one lesson and a high degree of participant satisfaction. As the use of anti-cancer drugs in LMICs will continue to increase, this e-learning module is an effective means to address the lack of training opportunities on the safe handling of chemotherapies for healthcare workers in these countries. The module could be integrated into a multi-modal approach aimed at reducing occupational exposure and increasing patient safety in cancer care centers.*

<http://dx.doi.org/10.1007/s13187-021-02113-z>.