External contamination of antineoplastic drugs vials on the Canadian market

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Background

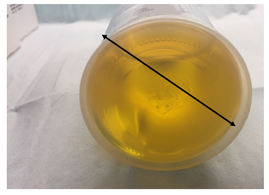
- Antineoplastic drugs traces can be measured on healthcare centers' surfaces.
- The exterior of vials is contaminated with drug traces; this contributes to the exposure of workers.
- Workers that are occupationaly exposed to antineoplastic drugs and other hazardous drugs are at risk of adverse health effects.

Objectives

- The aim of the study was to determinate the contamination of the exterior of antineoplastic drug vials on the Canadian market.

Methods

- Period: between January and March 2018
- One wholesaler and four different oncology pharmacies in Quebec were targeted.
- Nine molecules were measured: cyclophosphamide, docetaxel, fluorouracil, gemcitabine, ifosfamide, irinotecan, methotrexate, paclitaxel and vinorelbine
- One wipe was used to sample the external surface of five vials from the same manufacturer, dose and batch.
- For each vial, the external surface, the septum and the bottom were sampled with each side of a wipe.
- Analysis were performed by UPLC-MS-MS by the INSPQ.



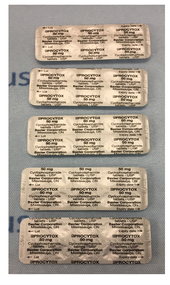


Table 1. Limits of detection and quantification

Antineoplastic drug	Limit of detection (ng/cm²)	Limit of quantification (ng/cm²)
Cyclophosphamide	0.0010	0.0033
Docetaxel	0.30	0.30
5-Fluorouracile	0.0400	0.1400
Gemcitabine	0.001	0.001
Ifosfamide	0.004	0.0055
Irinotecan	0.0030	0.006
Methotrexate	0.0020	0.0060
Paclitaxel	0.04	0.1200
Vinorelbine	0.01	0.0120

Results

Table 2. Contamination measured on the exterior of vials

Drug, drug dose or concentration, manufacturer	Concentration (ng/cm²)
Cyclophosphamide, 2000 mg, Baxter®	**0.024**
Cyclophosphamide[1], 50 mg, Baxter®	**0.020**
Docetaxel, 10 mg/mL, Sandoz®	<LOD
Gemcitabine[2], 1 g, Accord®	**0.14**
Gemcitabine, 1 g, Pfizer®	**2.0**
5-Fluorouracile, 50 mg/mL, Sandoz®	**0.090**
5-Fluorouracile, 50 mg/mL, Accord®	**0.050**
Ifosfamide, 3g, Baxter®	<LOD
Ifosfamide, 3g, Baxter®	<LOD
Irinotecan[2] , 20 mg/mL, Accord®	**0.0030**
Irinotecan[2], 20 mg/mL, Accord®	**0.038**
Irinotecan, 20 mg/mL, Pfizer®	**0.029**
Methotrexate, 25 mg/mL, Hospira®	**0.0078**
Methotrexate[2], 25 mg/mL, Hospira®	**0.017**
Methotrexate, 10 mg/mL, Hospira®	**0.015**
Methotrexate[2], 25 mg/mL, Novopharm®	**0.0030**
Methotrexate, 25 mg/mL Novopharm®	<LOD
Methotrexate, 25 mg/mL Accord®	**0.018**
Paclitaxel, 6 mg/mL Biolyse®	**0.060**
Paclitaxel, 6 mg/mL Sandoz®	<LOD
Vinorelbine, 10 mg/mL Pfizer®	<LOD

[1] Blister packaging; [2]Plastic cover on vials; LOD : Limit of detection

- 21 samples (100 vials and 5 blisters)
- 9 different manufacturers
- External contamination was found on 15 samples (71.4%)
- Extreme values : <LOD—272 ng/cm² for gemcitabine vials

- Sixteen (76.2%) samples were cross contaminated with other antineoplastic drugs
- Amaximum value of 0.20 ng/cm² of 5-fluorouracile was measured on an gemcitabine vial

Table 3. Cross contamination of vials with other drugs

Drug measured	Drug vial sampled	Concentration (ng/cm²)
5-Fluorouracile	Irinotecan	0.19
Gemcitabine	Docetaxel	0.0049
	5-Fluorouracile	0.0035
	5-Fluorouracile	0.021
	Irinotecan	0.011
	Irinotecan	0.20
	Irinotecan	0.17
	Methotrexate	0.0029
	Methotrexate	0.063
	Paclitaxel	0.013
	Vinorelbine	0.0023
Irinotecan	Methotrexate	0.003
Methotrexate	Cyclophosphamide	0.046
	Gemcitabine	0.0079
	Irinotecan	0.003
	Vinorelbine	0.003

Discussion / Conclusion

- 50% of the containers were contaminated with at least one antineoplastic drug
- Vials were sampled after their receipt, thus any contamination measured at this step came from the manufacturing process or the wholesaler storage.
- Shipment receipt is one important entry point of environemental contamination with antineoplastic drugs in healthcare settings.
- Manufacturers and wholesalers shouls ensure that vials are cleaned before they are shipped.
- Gloves must be worn by healthcare workers receiving hazardous drugs.
- Vials should also be cleaned upon receipt.

References: *NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016. 42. ; Fleury-Souverain S, Nussbaumer S, Mattiuzzo M, et al. Determination of the external contamination and cross-contamination by cytotoxic drugs on the surfaces of vials available on the Swiss market. Journal of Oncology Pharmacy Practice 2014; 20: 100–111. ; Favier B, Gilles L, Ardiet C, et al. External contamination of vials containing cytotoxic agents supplied by pharmaceutical manufacturers. Journal of Oncology Pharmacy Practice 2003; 9: 15–20.*

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