

## Introduction

- Occupational exposure may occur on many levels when handling, compounding or administering a drug considered to be hazardous, from storage to waste management.
- No safe occupational exposure limit exists, so the ALARA « **As Low As Reasonably Achievable** » concept is applied.
- A *National Institute for Occupational Safety and Health* (NIOSH) Alert on Hazardous Drugs was published in 2004 and updated in 2010 and 2012.
- In Quebec, previous multicenter studies of environmental contamination were conducted in 2008-2010 and 2012 involving 25 and 33 Canadian hospitals.

## Objectives

- To describe environmental contamination with cyclophosphamide (CP), ifosfamide (IF) and methotrexate (MTX) in Quebec healthcare centers in 2013.
- To compare the 2013 the results with the 2008-2010 and 2012 results.

## Methods

- Descriptive, comparative study
- Directors of pharmacy departments from hospitals with at least 50 acute care beds were contacted in November 2012 (n=66)
- 12 standardized sampling sites (surface of 600 cm<sup>2</sup>) were analyzed:  
→ 6 sites in pharmacy areas + 6 sites in patient care areas
- Samples collected in February and March 2013 at the end of a day or in the morning before surfaces were cleaned

### Analytical procedure

- Adapted from Larson et al. (2002)<sup>1</sup> and validated by the Institut National de Sant e Publique du Qu ebec
- Samples were analyzed for the presence of the cytotoxic agents by UPLC-MS-MS

**Table I. Limits of detection (LOD) and limits of quantification (LOQ)**

	LOD (pg/cm <sup>2</sup> )	LOQ (pg/cm <sup>2</sup> )
<b>Cyclophosphamide (CP)</b>	1.8	6.0
<b>Ifosfamide (IF)</b>	2.2	7.0
<b>Methotrexate (MTX)</b>	8.0	30

### Comparison

- Personalized report sent to participating centers (figure 1), with a yearly updated local 75<sup>th</sup> percentile value, a comparison with the previous studies results and recommendations for corrective measures
- Comparison of surface contamination between the 2008-2010, 2012 and 2013 studies was made with the 75<sup>th</sup> percentile of CP concentration for the hospitals that participated in all the studies.

**Figure 1. Example of a personalized report.**  
Sites with a level of contamination higher than the overall Quebec 75<sup>th</sup> percentile are highlighted; corrective actions should focus on these sites.

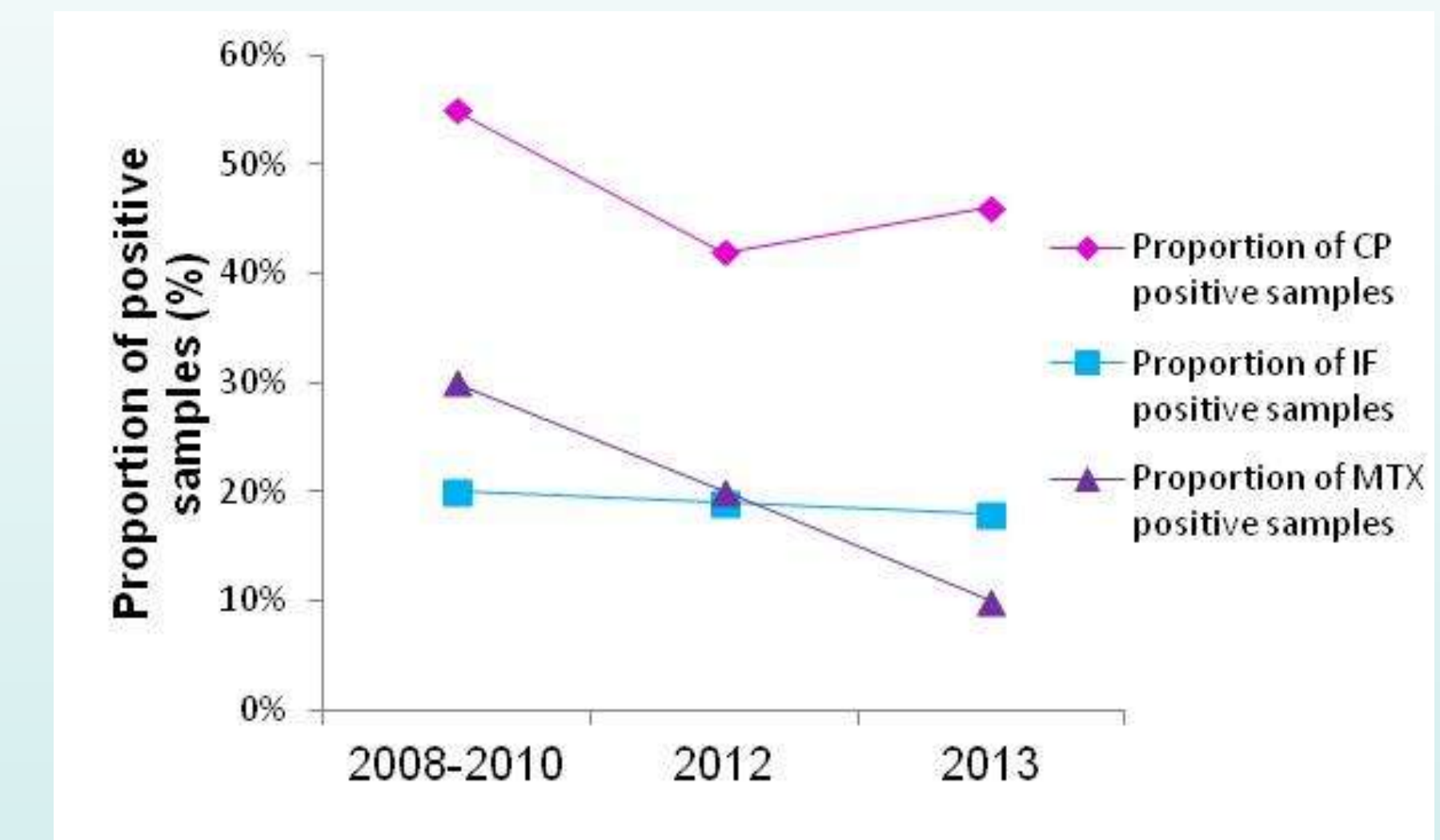
## Results

- 36/66 Quebec hospitals participated in the 2013 study (55% response rate) (422 samples)
- CP:** Median concentration was <LOD ; Highest concentration was 2 100 pg/cm<sup>2</sup> on the storage shelf
- IF:** Median concentration was <LOD ; Highest concentration was 3 800 pg/cm<sup>2</sup> on the arm rest
- MTX:** Median concentration was <LOD ; Highest concentration was 6 100 pg/cm<sup>2</sup> on the front grille inside the hood

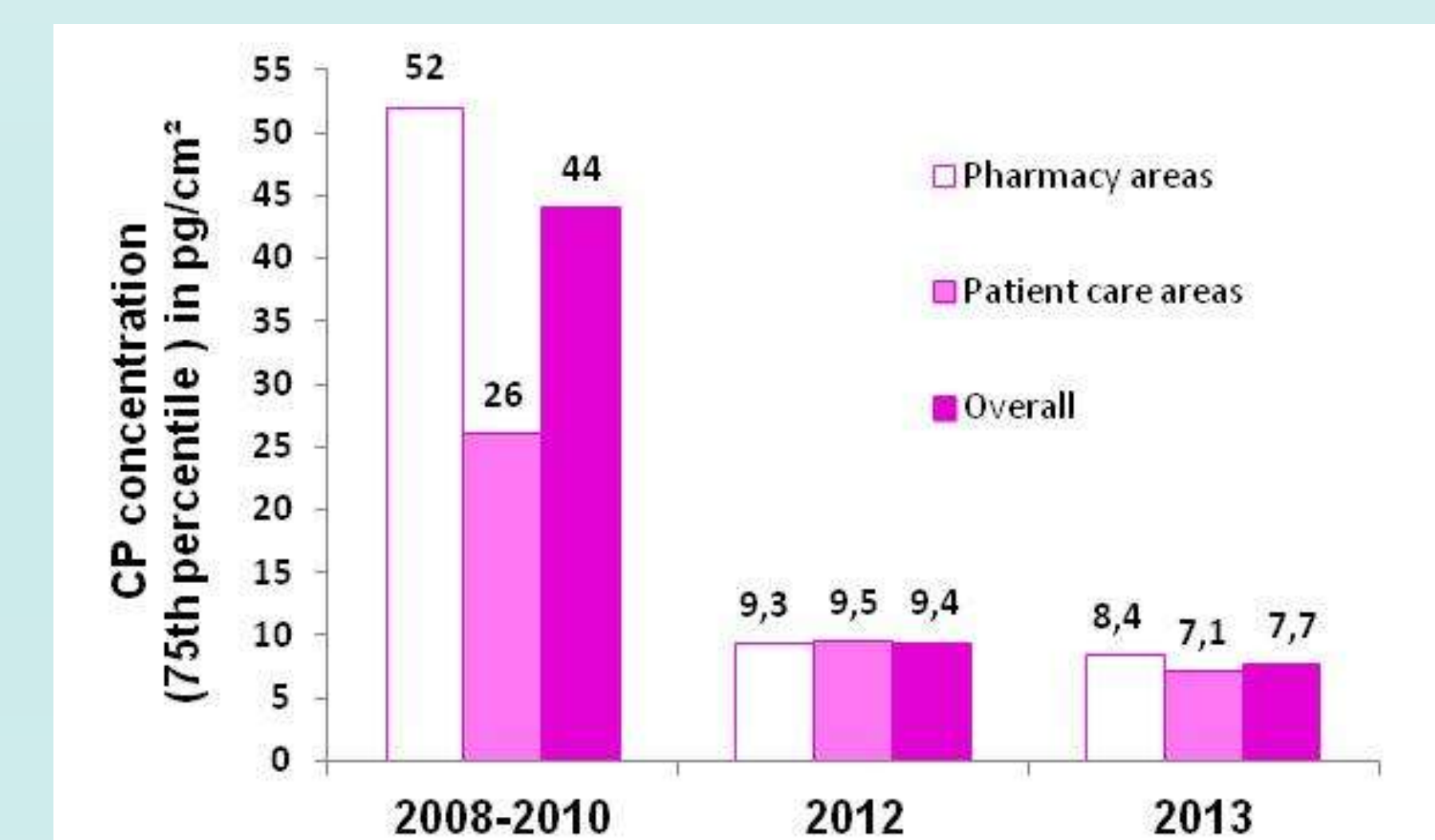
**Table II. Number of CP, IF and MTX positive samples in pharmacy and patient care areas in the 2013 study (n=36 centers)**

Sample site (n samples)	Positive samples n (%)		
	Cyclophosphamide	Ifosfamide	Methotrexate
<b>Pharmacy areas</b>			
Shipment reception counter (36)	7 (19)	3 (8)	0 (0)
Storage shelf (36)	14 (39)	14 (39)	3 (8)
Front grille inside the hood (36)	27 (75)	11 (31)	3 (8)
Floor in front of the hood (36)	24 (67)	12 (33)	1(3)
Service hatch or counter for post-preparation validation (36)	13 (36)	7 (19)	0 (0)
Trays used for drug delivery (35)	6 (17)	3 (9)	1 (3)
<b>Total (215)</b>	<b>91 (42)</b>	<b>50 (23)</b>	<b>8 (4)</b>
<b>Patient care areas</b>			
Storage shelf (35)	14 (40)	2 (6)	0 (0)
Counter used for priming or > validation (34)	17 (50)	3 (9)	0 (0)
Arm rest (34)	29 (85)	9 (26)	0 (0)
Patient room counter (35)	18 (51)	5 (14)	0 (0)
Outpatient clinic counter (34)	15 (44)	2 (6)	1 (3)
Exterior surface of hazardous drugs container (35)	14 (40)	4 (11)	2 (6)
<b>Total (207)</b>	<b>107 (52)</b>	<b>25 (12)</b>	<b>3 (1)</b>
<b>Total (422) (pharmacy &amp; patient care areas)</b>	<b>198 (47)</b>	<b>75 (18)</b>	<b>11 (3)</b>

Sampling sites with 50% or more of positive samples are shown. A sample was considered positive if the value was above the LOD.



**Figure 2. Reduction in the proportion of positive samples for hospitals that participated in the 2008-2010, 20112 and 2013 studies (n=21)**



**Figure 3. Cyclophosphamide concentration on surfaces in pharmacy and patient care areas for hospitals that participated in the 2008-2010, 20112 and 2013 studies (n=21)**

The sampling sites with the highest proportion of positive samples remained similar over the years:

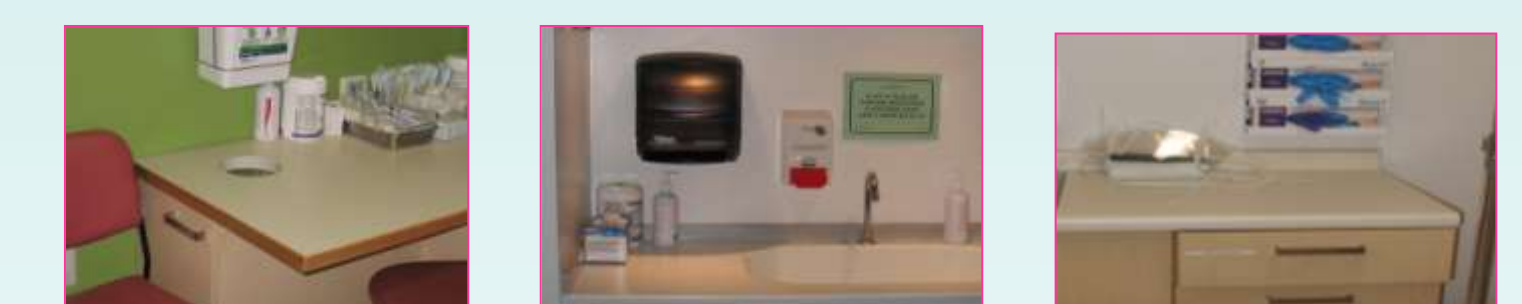
### Pharmacy areas:

- Front grille inside the hood
- Floor in front of the hood



### Patient care areas:

- Arm rest
- Patient room counter
- Counter used for priming



## Discussion / Conclusions

- The 75<sup>th</sup> percentile CP concentrations was reduced over the years: a plateau effect was observed in 2013.
- The 75<sup>th</sup> percentile concentration stayed below the LOD for IF and MTX.
- Biological monitoring will provide useful knowledge about the professional exposure to hazardous drugs and is underway in Quebec.

**References :** 1 - Larson RR, Khazaeli MB, Dillon HK (2002) Monitoring method for surface contamination caused by selected antineoplastic agents. *Am J Health Syst Pharm* 59(3):270-7

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