

Methotrexate residues on the outer surface of medicine vials: from contamination assessment to the testing of two decontamination procedures

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CONTEXT

Methotrexate (MTX) is a cytotoxic drug used intramuscularly in the treatment of ectopic pregnancies. During working hours, each medical prescription leads to the preparation of a syringe of a MTX dose based on the patient's weight at the Pharmaceutical Technology Department (PTD). Outside working hours, the syringe is prepared in the Obstetric Emergency Department by trained nurses using a Closed System Drug-Transfer Device (CSTD). In this context, an assessment of MTX surface contamination was carried out and revealed residual contamination (RC) on the surface of the vials stored in this care unit.

MATERIALS AND METHODS



Standardised sampling by wiping vial surface (Table 1) **right after the delivery to the PTD:**

- with a desorption solvent-soaked compress
- before of after vial decontamination

2 successive steps **decontamination**

- o Sterile Surfanios IP PAE AniosTM Detergent-Disinfectant
- o 70% ethanol

2 methods assessed: use of a sterile compress (S3)
or a single-use wipe (S4)



B : on the FOC
C : on the septum
under the FOC

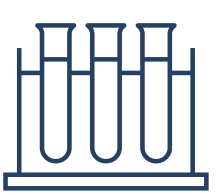
A : side contour
and under the vial

FOC = flip-off cover

Figure 1. Vial surface sampling areas

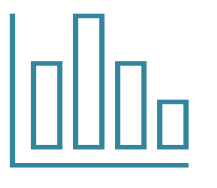
Vials series		n
Before decontamination		
S1	3 areas A, B and C sampled separately (Figure 1)	30
S2	Whole vial with flip-off cover	10
After decontamination		
S3	Whole vial after sterile-compress decontamination	10
S4	Whole vial after single-use-wipe decontamination	10

Table 1. Description of the sampled and analysed vials series



Samples analysis using ultra-high performance liquid chromatography-mass spectrometry/mass spectrometry (UHPLC-MS/MS)

- Limit of detection (LOD) = 1 pg of MTX/vial
- Limit of quantification (LOQ) = 2.5 pg of MTX/vial



Data analysis:

- RC quantification (median [Q1 ; Q3]) in pg/vial or pg/cm²
- Comparison using the Kruskal-Wallis test followed by Dunn's post-hoc test.

Quantity < LOD: included using the value LOD / $\sqrt{2}$
Quantity between LOD and LOQ: converted to LOQ / $\sqrt{2}$

DISCUSSION - CONCLUSION

External contamination of MTX vials was consistently detected before decontamination at a higher rate than reported in the literature (100% vs. 15.1% [1]), probably due to the greater sensitivity of our analytical method. This residual contamination observed on the vials suggests that the industrial decontamination process after the flip-off cap placement is only partially effective.

Both procedures tested significantly reduce the residual amount of MTX, with no significant difference between them, whether a sterile compress or a single-use wipe was used. This vial decontamination by the PTD, before delivery to the Obstetric Emergency Department, will help reduce occupational exposure for nursing staff when handling the vials outside working hours.

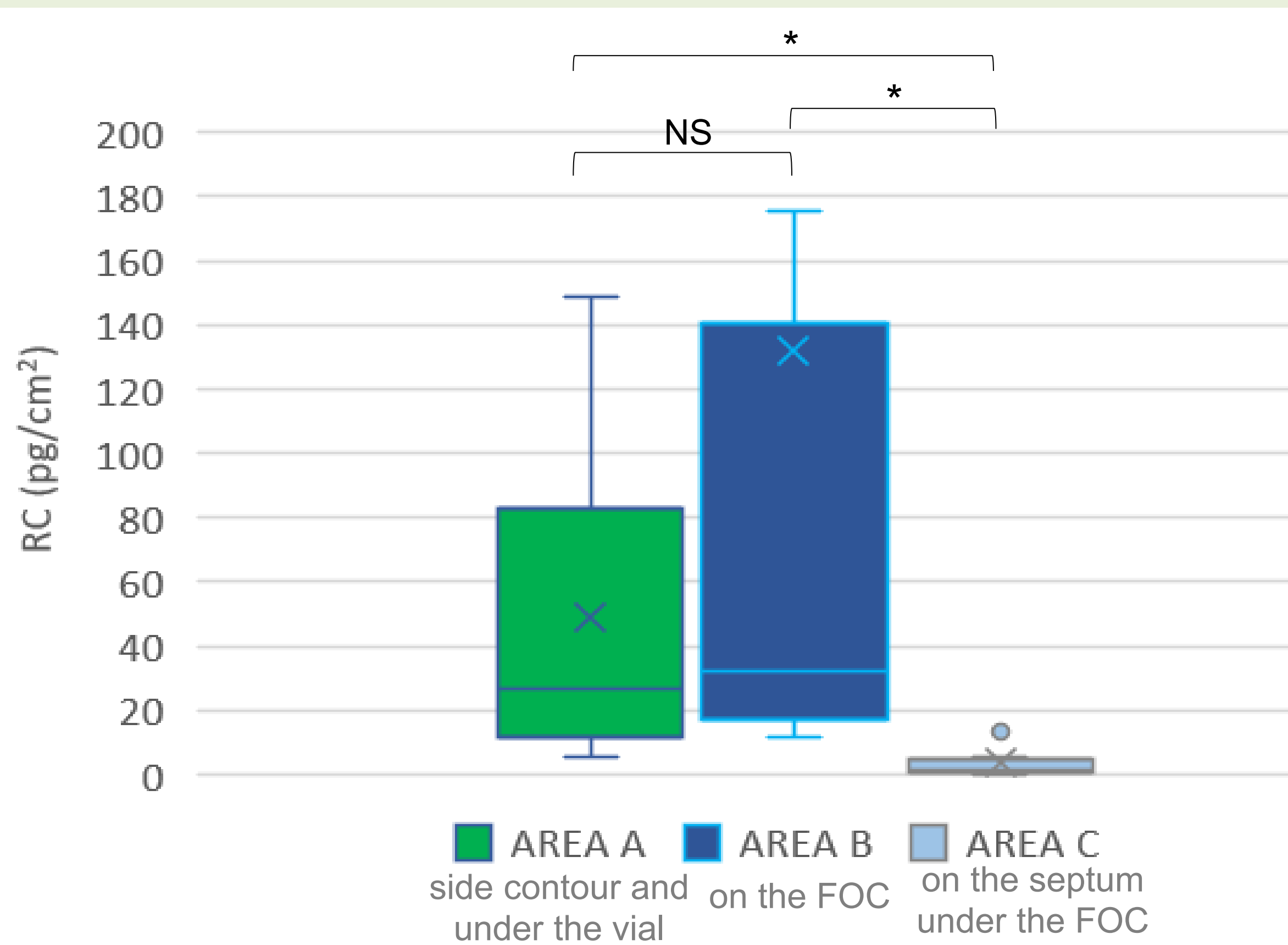
OBJECTIVES

- Assess the **residual MTX contamination** on the outer surface of MTX vials right after their reception in the PTD
- Asses the effectiveness of two **surface decontamination procedures**

RESULTS

→ **Qualitative residual MTX contamination: 100% of samples** before decontamination
80% after decontamination

→ **Quantitative residual MTX contamination** (Figure 2 and Table 2)



*: $p < 0,001$; NS : not significant (Kruskal-Wallis test + Dunn's post-hoc test).
(An outlier from Area B (650 pg/cm²) was removed)

Figure 2. Residual MTX contamination by vial areas (before decontamination, S1)

→ **Quantitatively least contaminated zone: under the FOC**

→ The FOC was therefore kept on for the decontamination tests on whole vials (S3 and S4).

Series	n	Residual MTX contamination median [Q1–Q3], pg/vial
Before decontamination		
S1 + S2	20	367.5 [249.7–1609.9]*
After decontamination		
S3: sterile-compress	10	6.6 [2.6–11.7]
S4: single-use-wipe	10	1.3 [0.8–3.6]

* : $p < 0,001$ → (S1+S2) vs S3 ; (S1+S2) vs S4
NS : not significant → S3 vs S4 (Kruskal-Wallis test + Dunn's post-hoc test).

Table 2. Vial residual MTX contamination before and after decontamination

→ **Effectiveness of decontamination procedures:**
- **98.2% with a compress (S3); 99.6% with a wipe (S4)**

→ No statistically significant difference between the **two decontamination procedures** (S3 vs. S4)

→ **Very low residual MTX concentration after decontamination**
- values close to the method's LOD and LOQ

[1] Hilliquin D, et al. External contamination of commercial containers by antineoplastic agents: a literature review. Eur J Hosp Pharm 2020;27:313–4.