

Carryover contamination in routine HPLC analytical control within a sterile injectable compounding unit : impact on analytical reliability and implementation of a corrective cleaning procedure

F. Kerouredan¹, P. Haristoy¹, T. Morvan¹, J.M. Bernadou¹, A. Berroneau¹, G. Bouguéon^{1,2}

COM26-85399

¹ Pharmaceutical Technology Department, Bordeaux University Hospital, Pessac, France ; ² ARNA laboratory, ChemBioPharm, INSERM U1212, UMR 5320 CNRS, University of Bordeaux, France

CONTEXT

1

Within a sterile injectable compounding unit, **carryover** can **falsely increase measured drug content** and **compromise release**

> 65.000

Sterile preparations produced / year

10.000

HPLC-controlled preparations / year

ANALYTICAL RISK

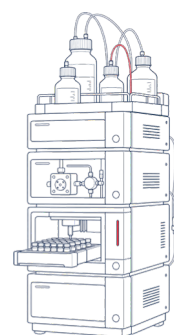
- Generate **false out of specifications results**
- Mask a **preparation with below-specification drug content**

OBJECTIVES

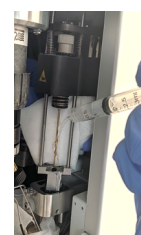
- Characterize recurrent paclitaxel overestimation during mixed-drug sequences
- Evaluate a standardized corrective cleaning procedure

MATERIALS & METHODS

2



12 compounds



HPLC column separative methods or FIA

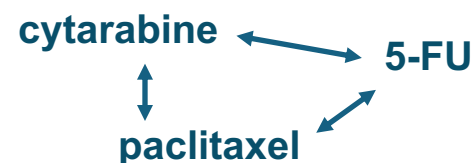
7 months

continuous routine monitoring

85-115%

assay acceptance interval ($\pm 15\%$)

SUCCESSIVE SEQUENCES



CARRYOVER ASSESSMENT

Flagged episode: paclitaxel assay $> 115\%$.

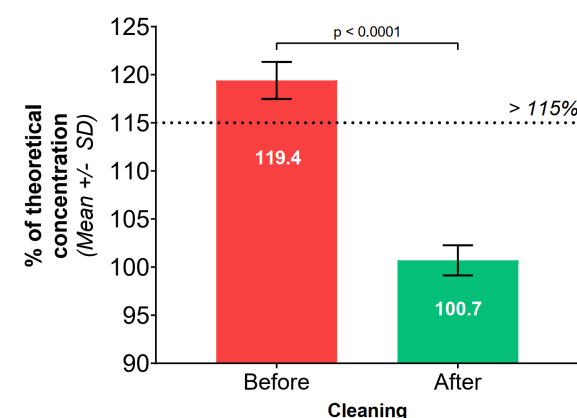
Variables examined:

- Preceding compound in sequence
- Time of occurrence
- Response to cleaning

RESULTS - DETECTION

3

Paclitaxel HPLC-FIA assays

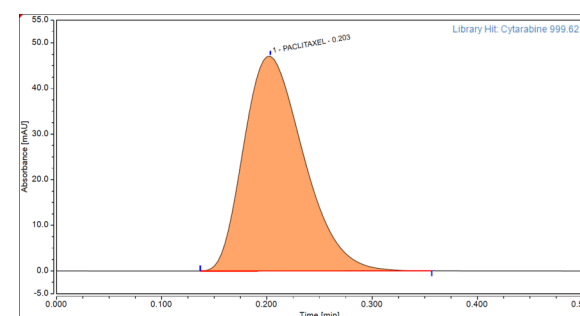


26 carryover episodes

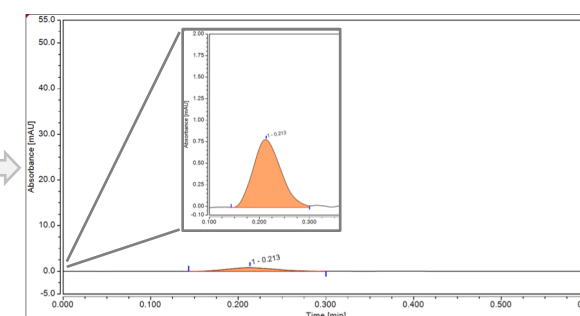
119.4% [115.2 - 122.9]

Carryover episodes were more frequent **later in the day** and **after cytarabine sequences**

Representative water-blank chromatograms



BEFORE CLEANING



AFTER CLEANING

RESULTS - CLEANING

4

1 Manual external cleaning of the injection needle

+

2 Automated external wash H₂O / ACN 50:50 (%v/v)

VERIFICATION

After cleaning: 100.7% [98.5 - 103.8]

< 2 mAU

residual peak height after water injection

100 %

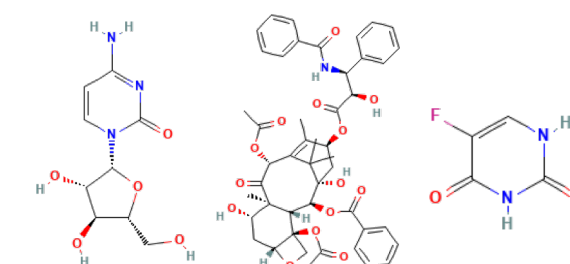
of evaluated checks met the criterion

DISCUSSION & CONCLUSION

5

PROPOSED MECHANISM

Mixed-drug injections
→ accumulation on metallic/polymeric autosampler surfaces
→ desorption into a later injection



CYTARABINE hydrophilic
PACLITAXEL highly lipophilic
5-FU surface crystallization

These contrasting properties may favor **variable adsorption, accumulation or crystallization** on sampler surfaces.

CONCLUSION

A **standardized two-step cleaning procedure** restored paclitaxel assays to the **85-115% compliant results** interval, **improving routine analytical reliability**