

One Year After the Opening of a Cleanroom : What Is the Level of Chemical Contamination and How Should It Be Interpreted?

C. Leblond ¹, D. Goulley ^{1,2}, C. Pernot ¹

¹ Pharmaceutical technology unit, Dijon University Hospital, 14 rue Paul Gaffarel, 21000 Dijon, France; ² Faculty of Health Sciences, 9 Boulevard Jeanne d'Arc, 21000 Dijon, France

Introduction

A new cleanroom was commissioned within the pharmaceutical technology unit, equipped with 4 new isolators:

- 2 dedicated to **Cytotoxic Preparations (CP)**,
- 1 dedicated to **Immunotherapy Preparations (IP)**
- 1 dedicated to **non-CP / non-IP Preparations**

One year after the opening of this cleanroom, an **environmental chemical monitoring campaign** was conducted in accordance with French Good Preparation Practices.

Objectives

1. What is the level of **environmental chemical contamination** ?
2. Is there any **cross-contamination** between the different isolators ?
3. Is the **cleaning protocol** using an **alkaline cleaning solution** effective ?



Materials and Methods



Standardized **self-sampling kits** (Centre Léon Bérard / Lyon Sud University Hospital)

- **20 hazardous drugs**
- Quantitative **analysis** by HPLC-MS/MS

6 surface samples collected :

- 4 isolators
- 2 workbenches (drug picking / preparation packaging)



Results

Development of an **analytical score** (1 to 100) → **three-level critically scale** :

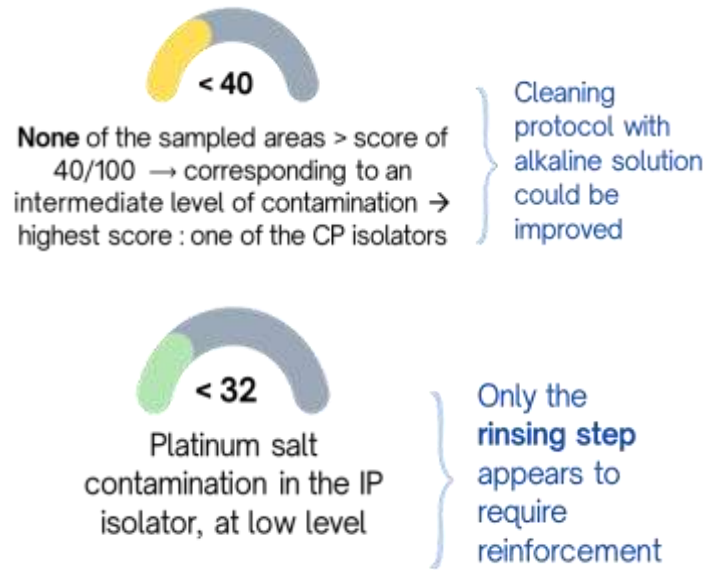
	1	2	3	4	5	6	7	8	9	10
1	1	2	3	4	5	6	7	8	9	10
2	2	4	6	8	10	12	14	16	18	20
3	3	6	9	12	15	18	21	24	27	30
4	4	8	12	16	20	24	28	32	36	40
5	5	10	15	20	25	30	35	40	45	50
6	6	12	18	24	30	36	42	48	54	60
7	7	14	21	28	35	42	49	56	63	70
8	8	16	24	32	40	48	56	64	72	80
9	9	18	27	36	45	54	63	72	81	90
10	10	20	30	40	50	60	70	80	90	100

Incorporating :

- **Environmental chemical monitoring results**
 - Number of quantifiable compounds
 - Quantification thresholds, using the Limit Of Quantification (LOQ)
- **Environment**
 - Preparation area (airtight/non-airtight)
 - Cleaning procedures (frequency of decontamination)
 - Isolator usage frequency (daily/non-daily)
- **Type of preparations**
 - Solution / Powder
 - Non hazardous / Irritant, harmful or toxic / Cancerogenic, mutagenic or reprotoxic

Low
Intermediate
High

	BM1 isolator : non- IP/non-CP	BM2 isolator : IP	BM3 isolator : CP	BM4 isolator : CP	Drug picking workbench	Preparation packaging workbench
Number of quantifiable compounds	0	1	2	3	0	1
Nature of the quantifiable compounds	/	Platinum salts	Platinum salts, Fluorouracil	Platinum salts, Cyclophosphamide, Methotrexate	/	Platinum salts
Quantification thresholds	/	< 10 × the method's LOQ	< 10 × the method's LOQ	< 10 × the method's LOQ	/	< 10 × the method's LOQ
Score (using the critically scale)	6	8	24	32	16	32



Conclusion

All tested surfaces show **contamination levels < LOQ**, indicating low chemical contamination in the cleanroom a year after installation. Cross-contamination is **limited to platinum salts** (IP isolator). The cleaning protocol appears effective, though the **rinsing step seems to require reinforcement**. The development of this analytical tool provides valuable support for **tailoring corrective actions** according to the contamination level observed. This tool will also facilitate the implementation of a **risk-based environmental monitoring plan** for future sampling campaigns and help **assess the effectiveness of corrective measures** over time.

Perspectives

- Enhance **decontamination of vials before transfer** into the isolators
- Increase **cleaning frequency** of storage bins
- Segregate storage of medicinal products