Preliminary Risk Assessment of the Design of Facilities for the Preparation of Advanced Therapy Medicinal Products

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Introduction - Objective

Project **to create premises for the compounding of advanced therapy medicinal products** (ATMP) in our hospital:

- In response to requests from physicians and clinical trial sponsors.

➔ Conducting **a preliminary risk assessment of the ATMP pharmaceutical circuit** within these temporary premises:

- To identify critical steps and, where necessary, to propose improvement measures.

Methods

1 Design of plans for the ATMP unit in vacant premises outside the pharmacy in accordance with:

- Good Preparation Practices
- Guidelines of the French High Council for Biotechnology
- Recommendations of the French Society of Oncological Pharmacy

2 Conducting a Failure Modes, Effects and Criticality Analysis (FMECA):

- By a multidisciplinary working group including pharmacists, technicians, a health executive, and a quality officer,
- Following each step of the circuit for personnel and products, from the reception of the ATMP in the hospital pharmacy to the dispensing of the reconstituted ATMP.

➔ Identification of critical steps by **rating failure modes according to their residual criticality** (Cr):

Cr = occurence (O) × severity (S) × level of control (C)		
low: Cr < 40	moderate: 40 ≤ Cr < 60	high: Cr ≥ 60

Results

Defined areas

- Unpacking
- Storage
- Product entry airlock
- Staff entry and exit airlock
- Preparation room equipped with a hybrid isolator
- Finished product exit airlock
- Release and dispensing
- Waste (room and airlock)

- Identification of **63 failure modes** associated with this circuit,
- **Control measures** considered at each step,
- **No Cr ≥ 40** ⇒ No further action required.

Examples

FAILURE MODE	EFFECTS	S	CAUSES	O	CONTROL MEASURES	C	Cr
Unpacking room							
Inadequate unpacking procedures	Chemical / biological contamination of staff and environment	**3**	Non-compliance with unpacking procedures	**2**	Specific **procedure**. **Training and qualification** of staff. Deconditioning **dry run** of each ATMP. Access restricted to authorized staff.	**3**	**18**
Preparation room – Compounding of ATMP							
Poor cleanliness of preparation enclosure (hybrid isolator)	Cross chemical / biological contamination and loss of ATMP quality. Financial loss	**4**	Non-compliance with preparation enclosure biocleaning procedures	**3**	Compounding procedure for ATMP and isolator biocleaning procedure. **Training and qualification** of staff. **Biocleaning traceability after each compounding**. Checklist validated before compounding.	**3**	**36**
Exit airlock for finished products							
Poor cleanliness of the airlock	Particulate / microbiological contamination of the room and adjacent premises	**3**	Simultaneous opening of entry and exit doors	**2**	Automatic interlocking system preventing simultaneous opening of entry and exit doors. **Annual qualification of the airlock**.	**1**	**6**

Discussion – Conclusion

The FMECA identified the critical steps of the ATMP circuit in the pharmacy, defined appropriate control measures, and validated both facility design and organizational workflow. These findings will support the authorization request to the Regional Health Agency, demonstrating process control, before the initiation of ATMP compounding in our hospital.