Multisite Clinical Trials: What about the Experimental Drug Circuit ? Failure Modes, Effects and Criticality Analysis

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BACKGROUND AND IMPORTANCE

- Multisite coordination of hospitals for clinical trials → Key lever to promote patient recruitment, facilitate access to innovation and enhance the attractiveness of sites
- Requirement for coordination at both clinical research and pharmaceutical levels
- Involvement of multiple hospital pharmacies in the distribution of the experimental product → Differences from usual management → **New risks**

AIM AND OBJECTIVES

The TRINITI project aims to identify, assess, and mitigate the risks associated with the involvement of multiple hospital pharmacies to secure the circuit of the experimental product.

MATERIALS AND METHODS

Establishment of a Multidisciplinary Working Group

- **Coordinating pharmacy** : 1 TRINITI project manager, 1 quality project manager, 2 pharmacists
- **Coordinating clinical research unit**: 1 project manager
- **Pharmacy of a satellite center**: 1 pharmacist

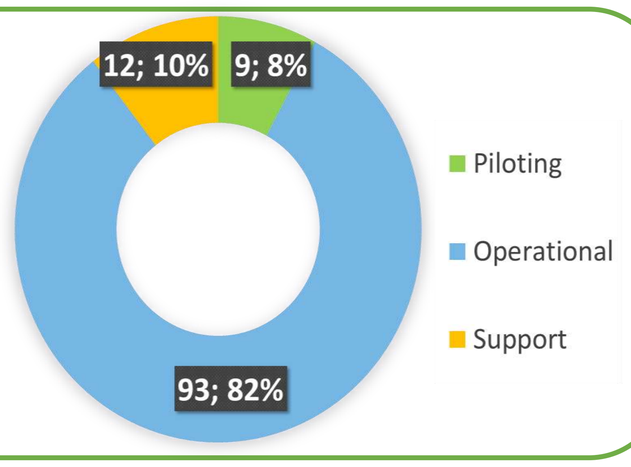
Use of the FMECA method : Failure Mode, Effects and Criticality Analysis (FMECA)

1) **Mapping of device-specific processes and sub-processes**
2) **Identification of risks associated with these processes**
3) **Rating of each identified risk in terms of Severity, Frequency, and Detectability→ Criticality**
4) **Risk prioritization**
5) **Existing and/or To-Be-Implemented Preventive Barriers**

RESULTS

Risk identification

- Mapping of device-specific processes and sub-processes
- **56 new subprocesses**
- **114 risks identified**
- **82%** of the risks linked to the operational aspect of the activity



Determination of levels of severity

Five levels of severity

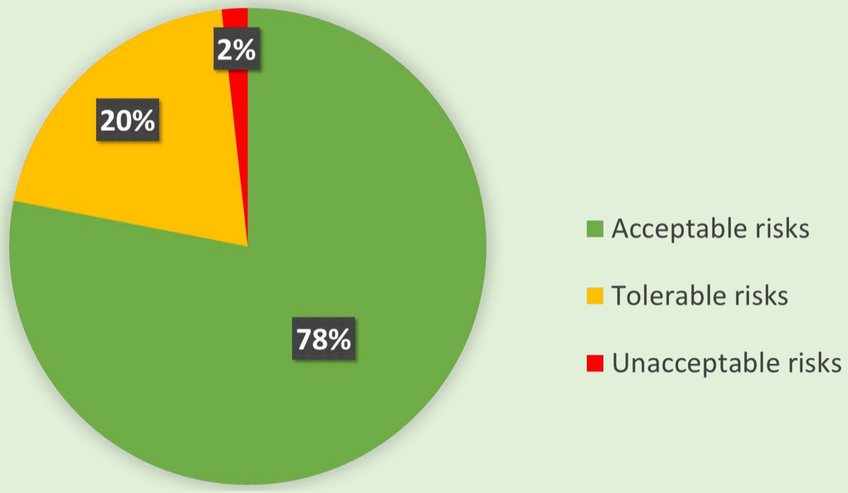
Level	Level title	Activity impact	Clinical trial impact
1	**Minor**	Negligible impact on the execution of the action	No impact
2	**Significant**	Limited mobilization or solely for the management of the incident	Isolated error or lack of traceability
3	**Major**	Moderate mobilization during and after the incident	Protocol design not followed
4	**Critical**	Temporary halt of activity	Study exit, unblinding
5	**Catastrophic**	Extended suspension of activity	Suspension of the trial (halt of inclusions)

Risks with a potential severity of 5

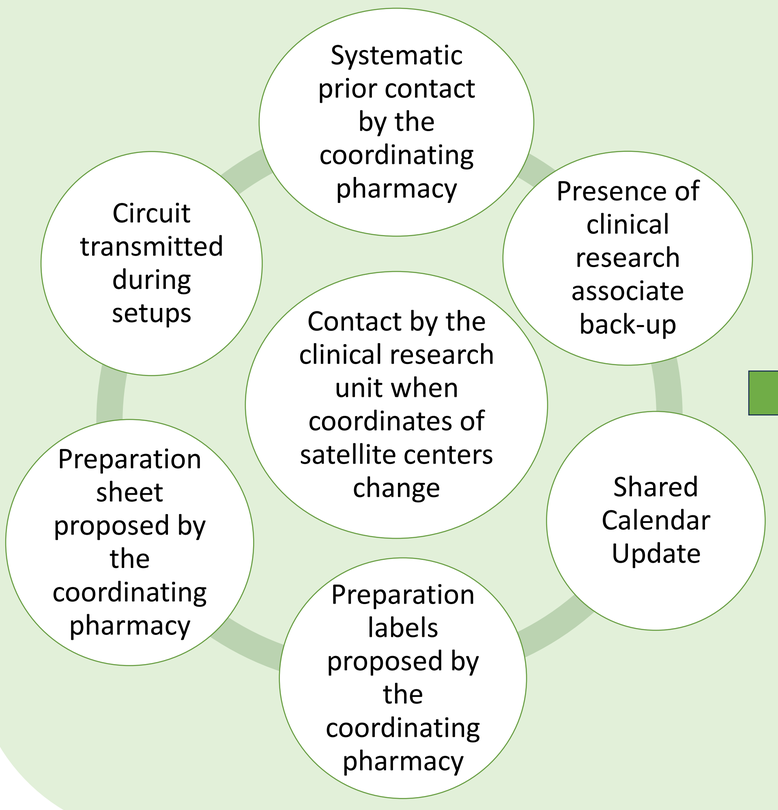
Lack of integration into the quality management system	Regulatory authorization not obtained	Insufficient funds	Insufficient resources
Lack of concordance with the hospital strategy	Lack of feasibility	Lack of prior contact between the promoter and the pharmacies of the satellite centers	Absence of validation of additional costs by the coordinating pharmacy
Lack of validation of additional costs by a pharmacy of a satellite center	Obsolete experimental product preparation sheet	Lack of shared functional forecast planning	No vehicle

83% of these risks with barriers already in place

Analysis of the criticalities obtained



- **Majority acceptable risks (78%)**
- **30% of tolerable risks** related to the preparation of clinical trials in satellite center pharmacies
- **Two unacceptable risks identified** related to the financial viability of the project and the availability of the transport vehicle



29 preventive barriers put in place, including **9 identified during the last meeting**

CONCLUSION AND RELEVANCE

- The most critical steps in the pharmaceutical circuit are identified, facilitating the implementation of preventive measures
- The need to assess residual criticality after implementing these measures
- In continuation of this work, a post-analysis of risks should be conducted based on initial experiences

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