RISK BASED THINKING AS A SYSTEMATIC APPROACH TO THE PROCESSES OF PHASE 1 CLINICAL TRIALS

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AIM

We aimed to systematically apply risk-based thinking to all phases of processes supporting Phase 1 clinical trials. This project presents the methodology and approach on identifying, assessing, and re-evaluating risks in Phase 1 clinical trial processes involving pediatric patients.

OBJECTIVE

- **Highlight critical points in Phase 1 clinical trial processes**, particularly focusing on potential or effective risks in clinical practices.
- **Reduce critical risks** by implementing programs of mitigation aimed to minimize risks and address potential issues effectively.
- **Prioritize process improvement** by focusing on key areas that can significantly impact safety, efficacy, and efficiency.

METHODOLOGY

- **Every process of the Phase 1 clinical trial Unit was mapped**, and for each phase, possible risk factors were identified
- A customized **web application**, for process mapping was used
- **Risk assessment** was based on:

1. Impact (patient safety, data integrity, and regulatory compliance - GCP)
2. Probability
3. Detectability

- **Risks were monitored** with:

1. "Anomaly Registry" (reporting, assessing, and resolving anomalies identified during the conduct of the clinical trial)
2. Internal and external audits

- **Evaluation and re-evaluation of risks conducted** regularly, annually, or as needed.

PROCESS ANALYSIS AND RESULTS

Each macro process was further detailed into 65 primary processes, with a focus on areas impacting critical trial processes. These primary processes were further analyzed through secondary phases, conducting a comprehensive risk assessment for each phase (Figure 1, Figure 2). This assessment involved evaluating severity, assigning probability numbers, calculating partial risk levels, assigning detection numbers, and determining risk priority numbers. We compared the outcomes against 36 predefined risk areas affecting stakeholders and operational activities, using a 5x5 risk matrix to categorize risks into five levels: Negligible, Low, Moderate, High, and Very High. Evaluation and re-evaluation of risks were conducted regularly, annually, or as needed due to amendments, updated investigator's brochures, or new safety data.

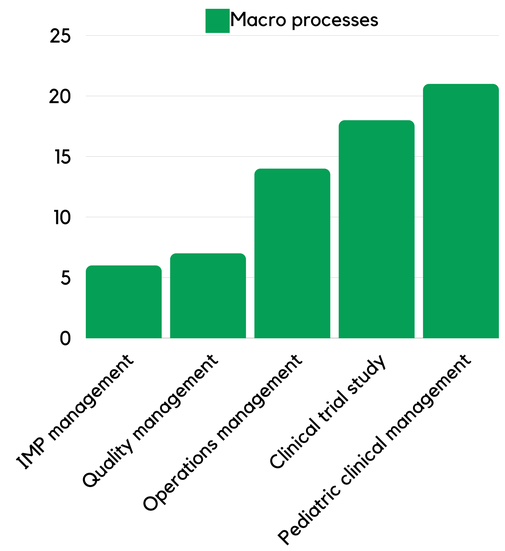


Figure 1 - Macro processes of Phase 1 clinical trials.

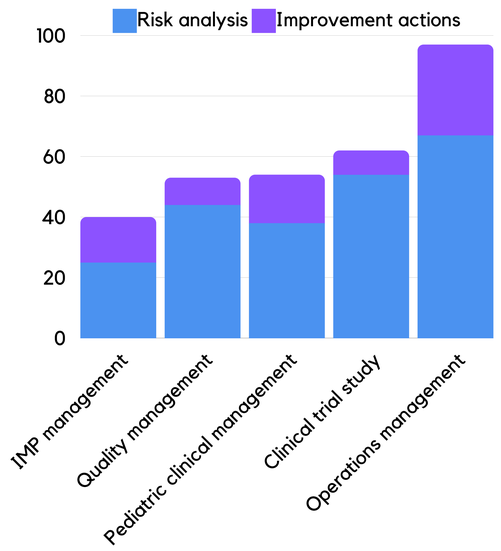


Figure 2 - Risk analysis and improvement actions (triennial 2022-2023-2024).

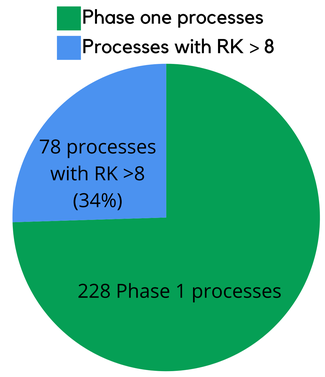
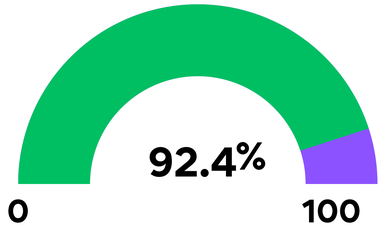


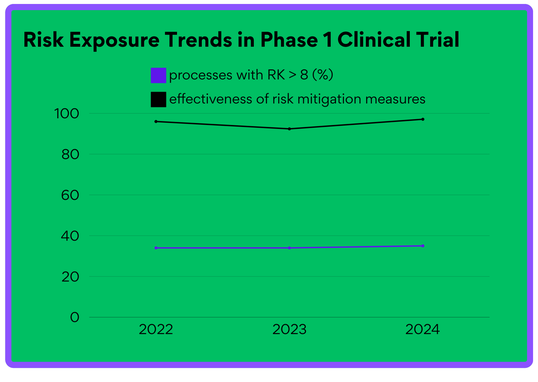
Figure 3 - Processes with risk levels exceeding our threshold (RK > 8).

The assessment identified 78 of 228 processes (34%) with risk levels exceeding our threshold (RK > 8). Improvement actions were implemented for these processes, with each action plan specifying descriptions, responsible parties, monitoring indicators, activity deadlines, and projected risk reductions compared to initial values.

Effectiveness of risk mitigation measures implemented

The effectiveness of the implemented risk mitigation measures was evaluated annually by calculating the risk reduction rate and the number of anomalies detected for specific risks.





DISCUSSION

As a result of the implemented risk mitigation measures, **Phase 1 clinical trials reported fewer adverse events, maintained high data integrity, and completed all regulatory audits** without any major findings.

CONCLUSION

The long-term objective is to verify the robustness of these risk mitigation measures, ensuring they are effective not only in the short term but also capable of supporting the study's evolution over time. This requires a systematic and proactive approach, based on continuous monitoring, periodic assessments, participant feedback, and data analysis. **Only through a constant commitment to improve risk mitigation strategies can we address the complex challenges of Phase 1 clinical trials and ensure reliable and safe outcomes.**