# Keys to Successful Risk Management in Clinical Trials

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**Effective risk management recognizes variables unique to each clinical trial while embracing consistent documentation practices, stakeholder ownership of responsibility, and best practices informed by experience.**

It is indisputable that already difficult clinical studies are progressively getting tougher — in terms of patient recruitment, regulatory compliance, etc. — as well as longer and more complex. Organizations forged in this fire, rather than burned by it, strive to run high-quality studies, remain vigilant in risk management, and embed processes that prevent data from being lost or adverse events from undermining the study as a whole.

At the heart of this effort is risk management, the exercise of thinking in advance about study risks and implementing mitigation strategies in an attempt to reduce, eliminate, or accept said risks. Risk management is a comprehensive, high-level activity spanning the entirety of the clinical trial life cycle. It demands stakeholders identify critical study processes and calculate risk associated with those processes.

Risk management plans are dynamic, evolving regularly across the industry and within individual studies. Things currently included in every organization's risk plan weren't always considerations (e.g., pandemics) and things previously considered as risks occasionally are phased out.

Note that risk management and risk-based monitoring, often conflated as the same, are distinct activities. Risk-based monitoring incorporates some elements of risk management but is narrowly focused on monitoring your clinical trial.

## ACT EARLY, REVISE OFTEN

Before attempting to identify and prioritize the risks you are trying to avert, the first step in a clinical study is identifying key stakeholders. Capable project managers already understand their key stakeholders based on what the project seeks to accomplish: who will have a direct impact on the clinical study? This is also a key tenet of basic risk management.

The project manager is tasked with assembling not only major voices in the room (medical monitor, data manager, clinical supply staff, safety personnel, etc.), but also supplemental roles (clinical quality assurance, monitors, representatives from sites that may be involved in the study) — people who may not be involved throughout the project life cycle, but whose viewpoints and risk assessments should be noted at the project outset. This effort should not present a significant logistical hurdle, as each member of the clinical study team needs to be in regular communication to run the trial.

The current pandemic and the realities of operations being conducted virtually dictate that not all individuals and teams have to occupy the same room or communicate at the exact same time. Did some team members miss whiteboard discussions of critical data points, critical processes, or clinical supply? Send those people the relevant information and request detailed feedback. Organizations often have codified practices for chasing down and recording such team member input.

Accordingly, each step in the risk management and risk monitoring process adheres to the life sciences adage, "if it isn't documented, it didn't happen." Clear documentation is necessary from the outset of the clinical study process and must be reviewed and updated throughout the study.

Most important, instill the idea that every stakeholder, in a properly conducted study, accepts responsibility for quality and risk management. Each step conducted and documented by each individual should be accompanied by questions (e.g., What is my risk of doing this? Is this a new risk we need

to add to our risk register?). This ownership also enhances compliance documentation, showing regulators you thought about all the things that could go wrong and put contingencies or mitigations in place, when appropriate.

The greatest risk management challenge at the beginning of a study may be the temptation to rush. Instead, move slow to go fast. Building and executing a risk management plan meticulously from the project's start ensures study quality is not compromised and the study team is not unprepared for any foreseeable risks.

While some executives may want to move at an unreasonably fast pace — undermining the system or not allowing it to be as effective as it could be — most of the C-suite understand overall risk and its impact on quality and cost. Failure to create a thorough risk management plan usually comes back to haunt a study.

A good place to start is with relevant regulations and guidance documents from ICH E6, FDA, EMA, MHRA — all of these discuss risk management. Note that FDA, EMA, and MHRA each issued updated guidance documents specific to clinical trial risk management during the COVID-19 pandemic.

## PRIORITIZING STUDY RISKS AND LEARNING FROM EXPERIENCE

Risks should be prioritized according to the golden standard of likelihood, impact, and detectability. This is a well-established method to quantify and score standard risk areas like protocol deviations, subject retention, and data entry timelines.

When crafting an initial risk management plan, you don't want to include every possible risk. Limit your risks — at least the ones that you're following and managing at a given stage — to a few key concerns. If you include too many risks in the initial plan, it may be difficult to follow all of them. Regular review of risks throughout the clinical study keeps this central list, recorded in the trial master file (TMF), up to date.

The limitation of initial risks and the frequency of list updates depend on study size and composition. For example, how many individuals are participating, and what traits define the population? Is this a Phase 1 study, where monthly updates might be appropriate, or a five-year study, where quarterly updates could suffice?

Unforeseen risks are added to the risk register as needed, and the COVID-19 pandemic presents a perfect example. While the pandemic could not have been predicted, an agile risk management plan would be prepared to contend with new challenges. In the case of the pandemic, studies have had to adjust to — among other things — protocol deviations (e.g., patients unable to be physically present at study sites) and unpredictable adverse events (e.g., members of the study population contracting COVID-19). Some risk management measures, such as planning for the shipping of medication to patients or alternate sites, address several scenarios, from pandemic conditions to natural disasters.

Organizations with robust risk management plans in place when the COVID-19 pandemic emerged had a concept, a context, and a platform to quickly implement mitigations for such issues as closed clinical sites and distribution of investigational product.

In addition to contemplating and adding new risks, periodic risk review deprioritizes risks no longer relevant to your study (e.g., a critical enrollment criterion that presents a risk can be discarded once enrollment is complete). Returning to the COVID-19 pandemic example, organizations restarting a study in a few months might identify different severities associated with the virus' risk likelihood and impact.

The TransCelerate Risk Assessment Categorization Tool (RACT), MCC Risk Assessment & Mitigation Management Tool (RAMMT), and similar tools facilitate study team members identifying, documenting, and measuring the risk of a study protocol, as well as devising a risk-monitoring plan. The plan incorporates critical processes, critical data, source data review strategies, and key risk indicators.

Such tools provide a solid foundation on which a company can build its risk management program, as organizations can modify such tools (e.g., how those tools capture information) to meet the needs of their study and match their processes. Note that while no regulations dictate the use of these tools, their use does comprehensively meet regulators' expectations.

For example, a company kicks off risk management by looking at critical data and critical processes: inclusion, exclusion, end points. If the study is examining an imaging agent and a special scan must be performed, everything associated with that scan will be a critical process. If a blood draw is part of the study, all the risks associated with that (e.g., a bleed or bruising) must be considered. This analysis informs a list of all possible risks, which then is narrowed by likelihood, impact, and detectability: Will risk X impact a particular end point, or will it lead to a minor protocol deviation?

To benefit from the sum of these activities, an organization can create a risk library, allowing stakeholders to document their experiences for future reference, simplifying risk management as the organization grows. A risk library includes common risks, though more risks can be added as you identify them and determine how they might affect your study. Thus, it gives the teams a place to start, but should not be construed as comprehensive — each study is different, and teams must remain vigilant in each study's risk considerations.

## CONCLUSIONS

Risk management, like the clinical studies its successful execution insulates, has grown increasingly complicated and become dependent on more job roles and technologies. Just as important as detail-oriented execution are an early start and consistent application of sound principles throughout a clinical study's life cycle — risk management applied retroactively rarely, if ever, leads to positive outcomes. Ultimately, a dedication to quality, fueled by a team focused on the concerns that matter most, is the catalyst driving successful risk management initiatives.

inSeption Group shares this belief with our clients, recognizing that our greatest asset is our people: a knowledgeable, experienced group working in an embedded model where we serve as an extension of the client, not just as another vendor offering a commoditized, faceless process. We mitigate costs through leading with quality and dedicating ourselves to a patient-centric approach.

To learn more about effective risk management at any point in your clinical study, contact the author at **dniccum@inseptiongroup.com** or visit **https://www.inseptiongroup.com/**

## ABOUT THE AUTHOR

Dawn Niccum is Senior Director of Quality Assurance & Compliance at inSeption Group. She brings over 25 years of clinical operations and QA pharmaceutical experience to the role, with expertise in clinical compliance, SOP development, computer system validation, quality document management, training, and safety. Dawn is a Subject Matter Expert member of the TMF Reference Model Group and a current Ambassador of the Metrics Champion Consortium (MCC). She holds a bachelor's degree in nursing and a master's degree in regulatory affairs and quality compliance from Purdue University.

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