

WHITE PAPER

Risk Management in Clinical Project Management

Dr. Ashok K. Ghone

Introduction

Project Risk is an uncertain event or condition that, if it occurs, will have adverse impact on a project objectives & deliverables. All projects involve risks. In clinical project management, the risks may be like a long delay in IRB/EC approval or regulatory approval or investigational sites not meeting the expectations of recruitment timelines etc. These risks will have impact on quality, timelines and budget which are the important & critical aspects of a clinical project objectives & deliverables and in turn drug development process. Therefore, successful clinical project management requires risk management plan which includes thorough identification, analysis & quantification of risks before and during the projects, as well as development of effective risk response to deliver projects that meet stakeholder demands.

Risk management is a systematic way of identifying potential risks within a project, gauging the probabilities of these risks occurring and assessing the impact, to then develop strategies to manage these risks. This process can be broadly divided into three main processes.

- **Risk Assessment** (identification, analysis & quantification)
- **Risk Response** (Risk mitigation, contingency planning)
- **Risk Monitoring & Control**

Risk Assessment

Risk assessment involves identification, analyzing and quantification with respect to probability and impact of the risk on the project deliverable. Experience & expertise in clinical project management process and the understanding of therapeutic area will help identify various risks that might occur in clinical project life cycle. Some of the risks might be:

- Delay/rejection in Regulatory or EC/IRB approvals or unexpected constraints
- Attrition of key project team member/s
- Investigational sites not meeting recruitment timelines
- Poor retention of the patients on the study
- Investigational site fails to generate quality data on time
- Principal investigator leaving the site in middle of the study
- Non-Availability of IP or other important clinical supplies on time or Shortage of IP /clinical supplies in middle of the study
- Failure of key equipment require for the investigation

To have effective risk management plan to accomplish the project successfully, it is utmost important that all possible risks can be identified before the start and during the project. The dedicated sessions with project management team members will definitely help to identify risks in various areas of clinical project management. Once the risks have been identified, they should be analyzed and quantified further. The risk can be quantified in two dimensions:

- The probability of the risk occurring
- The impact of risk on project deliverables & objectives

The various matrices available for quantification of risks and a simple one as shown below can be considered.

Impact ↑	High	M	H	H
	Medium	L	M	H
	Low	L	L	M
		Low	Medium	High
		Probability →		

If probability of a risk is high, and impact is low, it is towards low severity/priority risk. On the other hand if impact is high, and probability is low, it is towards high severity/priority risk. In Clinical project management, if there is high probability that delay in site initiation in one out of 20 sites due to delay in finalizing clinical trial agreement (CTA) with the site, has low impact on the project timelines, it is considered as low severity risk. Whereas, if there is low probability of delay in regulatory approval but which has high impact on project timelines and budget, it is considered as high severity risk.

This can be further quantified as risk severity index. The risk severity index is the function of probability of risk into impact of risk. The higher risk index warrants active and high priority management of risk to ensure no or minimize adverse impact on project objectives and deliverables.

Risk Index = Risk Probability X Risk Impact

Risk Response

Once the risks have been identified and assessed, the risk responses or risk treatments can be planned to manage the risks. The various risk responses fall into one or more of these four major categories

- **Risk Avoidance** (eliminate, withdraw from or not get involved)
- **Risk Reduction** (optimize - mitigate)
- **Risk Sharing** (transfer - outsource or insure)
- **Risk Retention** (accept and budget)

Risk Avoidance

This includes not performing or involving in an activity that could carry risk. One of the examples in clinical project management could be, not selecting investigational site which will not give quality data because principal investigator and staff are not qualified enough by training, experience and education to perform the clinical study even if the investigational site has a good potential to recruit patients in a short period of time. Another example could be not considering a country for a global clinical trial where there is a high risk of indefinite delay in regulatory approval in spite of the country epidemiology data shows good pool of patients required for the clinical trial and in spite of country having good infrastructure to conduct the clinical trial.

Risk Reduction

Risk reduction or optimization or mitigation involves reducing the severity of the impact on project deliverables or eliminating likelihood of the impact from occurring. For example, in clinical project management sudden attrition of CRA can affect project deliverables. This risk can be anticipated at the start of the project and additional CRA (or as a back-up CRA) can be trained & included in the project team from the beginning with appropriate distribution of FTE fraction across all CRAs. So, even if there is CRA attrition in the middle of the project, the sites and work load can be distributed among rest of the CRAs without having any impact on project quality and timelines. This will also provide good & comfortable amount of time to get new trained CRA on board.

Risk Sharing

Risk sharing is the sharing of potential risks with another party to reduce the burden of impact and also to improve the outcomes. These are the risks that generally have high severity index and have potential to impact quality, schedule and budget of the project significantly.

In a clinical project where patient recruitment & retention is a challenge because of complexity of the study protocol design or stringent eligibility criteria or requirement of specialized patient population, additional support from local site management organization (SMO) will be helpful who will plan strategies based on their experience in the country and

expertise in therapeutic group/indication for patient recruitment & retention to ensure achievement of the required recruitment targets on time.

Risk Retention

This risk response involves accepting the risks, preparing & budgeting for it right from the beginning. The example of this kind of risk response in clinical project management could be selecting additional 1-2 investigational sites in the beginning, considering one of the investigational sites might drop because of issues like clinical trial agreement (CTA) or long delay in EC/IRB approval

All risk responses should include the strategy and action items to address the strategy. The actions should include what needs to be done, who is responsible for it and when is the trigger point for the action to initiate.

Risk Monitoring & Control

Risk monitoring & control is the important step of risk management plan where all possible & potential risks are continually monitored to identify any change in the status, or if they turn into an issue. It is best to hold regular risk reviews to identify risk change, actions outstanding, assess risk probability and impact, remove or close risks that have passed, and identify new emerging risks in life cycle of project.

One of the risk tracking logs as shown below can be used to keep track of the risks on an ongoing basis.

Risk Tracking Log

S. No.	Probability	Impact	Risk Index	Risk Event	Risk Response	Owner	Impact on project aspect (quality/ Schedule/ budget)	Action trigger point (date)	Status	Date Entered	Date to Review
1	2	2	4	20% sites are not meeting the recruitment timelines	Moving ahead with reserved investigational site/s	PM	Project Schedule		Open		

Conclusion

Risk Management is a dynamic process as risks are always changing and new risks are emerging during the clinical research projects. Today, one might assign some risks with a high probability and a high impact. Tomorrow, the probability or the impact might change. Also, some risks might drop completely off the table while others come into play. Therefore it is necessary to always investigate and review – what have been missed? What things could happen that have not been considered yet? This is one of the hardest things to do but one of the most critical things for the success of a clinical project. Risk management is not an event but a process and it is not a complex process if it is managed systematically throughout the life cycle of projects keeping in mind the objectives of the project.

