Conducting Feasibilities in Clinical Trials: An Investment to Ensure a Good Study

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Abstract

Conducting clinical trial feasibility is one of the first steps in clinical trial conduct. This process includes assessing internal and environmental capacity, alignment of the clinical trial in terms of study design, dose of investigational product, comparator, patient type, with the local environment and assessing potential of conducting clinical trial in a specific country. A robust feasibility also ensures a realistic assessment and capability to conduct the clinical trial. For local affiliates of pharmaceutical organizations, and contract research organizations, this is a precursor to study placement and influences the decision of study placement. This article provides details on different types of feasibilities, information which is to be included and relevance of each. The article also aims to provide practical hands-on suggestions to make feasibilities more realistic and informative.

Key words: Investigator, Patient recruitment, Site, Program, Country capability, Clinical operations

What is clinical trial feasibility?

In general terms, clinical trial feasibility is a process of evaluating the possibility of conducting a particular clinical program / trial in a particular geographical region with the overall objective of optimum project completion in terms of timelines, targets and cost.

Significance of clinical trial feasibility

About 25% of many investigational new drug (IND) applications include critical data from outside the US. 1 The number of foreign investigators conducting research under FDA IND has increased several folds in the last few years. 2 In spite of the fact that the US and most Western European countries remain the important centers for conducting clinical trials, ~35% of delay in studies is due to patient recruitment, nearly one-fifth investigators do not enroll any patients and about one- third enroll only 5% of evaluable patients. In most programs, only one-third consistently enroll patients. 2 These challenges have prompted most sponsors to conduct clinical trials in developing countries of Asia, Latin America, Central and Eastern Europe, Middle East and Africa. 1, 2

As the pressure on the biopharmaceutical industry increases, more clinical trial activities are expected to be conducted in these areas, in the next few years. 2 While there are clear advantages in conducting clinical trials in these areas such as increased recruitment potential, lower costs, there are challenges such as variability in clinical practice, regulations, ethical processes and local guidelines. Global data in recent times has shown a much longer clinical trial cycle time in terms of patient recruitment rates, time from first patient first visit (FPFV) to last patient last visit (LPLV) and total recruitment. 4

Clinical trial feasibilities actually help in identifying these challenges before-hand and help in taking a decision on how to work efficiently with different countries and sites with their respective challenges. In the absence of a clear organized networking of clinical trial centers, feasibilities help in identifying region-specific or even institution-specific practices which can have an impact on overall study completion.

Finally, feasibilities, especially in terms of number of sites and patients would be a scorecard for future performance. From the study team’s point of view, feasibilities would help in:

- Finding whether the disease under study is relevant to the patient population
- Is the study design in its current form, comparators, and subjects’ visits acceptable?
- What are the anticipated Regulatory and Ethical challenges?
- What are the general timelines for study approval and site start-up?
- What is the overall commitment of potential partners–country offices, CROs, sites towards completion of the program?

At a global or regional level, feasibilities are often managed by the global study teams but the actual execution is done by the country offices (sponsor) or contract research organizations (CRO) as the case may be. Feasibilities form
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the basis of a robust relation between various team members.

Types of feasibilities:

There can be three broad types of feasibilities:

a) Program level: this relates to the entire program of studies planned e.g. a program on antibacterial in a variety of infections
b) Study level: this is very specific to a particular study e.g., an antibacterial in skin and soft tissue infections
c) Site or Investigator level: this is most specific related to conducting the study in a particular hospital / clinic

a) Program level: Program level feasibilities are broad based. They are mainly aimed towards finding prevalence of particular diseases or conditions in a particular region and hence include clinical and epidemiological information

- Ethical and Regulatory: Program feasibilities aim towards finding overall time for clinical trial approval, particular regulatory requirements which can affect decision related to placing of the study etc.
- Medical: Disease frequency, prevalence of program-specific patient population, nature of existing treatment patterns or guidelines, presence of alternative drugs and treatments.

The broad objective of program level feasibilities is to identify which regions can be considered for the more-specific study level feasibilities.

b) Study level: Study level feasibilities are more customized towards assessing whether a particular clinical study can be conducted in a country or region.

- Clinical aspects: This relates to the epidemiological data on the study specific population (more specific in terms of stage of disease, protocol based definition of study disease and population), availability of standard care (in terms of background therapy and comparators), specific agreement with inclusion and exclusion criteria and acceptance of study specific procedures in line with existing medical practices.
- Regulatory: This is one of the most important pieces of information in a study level feasibility. This would include the overall approval timelines to get the study ongoing, understanding specific regulatory requirements (e.g., translated protocol, export of biological materials, special requirements in case of biological samples etc)
- Technical: The usage of technology in clinical trials has increased significantly in recent times. This includes e-CRFs, tools for randomization, clinical supplies shipments, etc. Feasibilities can assess prior experience of usage of tools, any problems which are anticipated and exploring possible options to overcome these challenges

• Operational: As clinical trials are becoming more global, some countries (e.g., Eastern and Central Europe, Korea, Taiwan, India etc) have emerged as major destinations for clinical trials across therapeutic areas. This increases the chance of studies with similar patient population being conducted in the same country and actually competing with each other for recruitment affecting overall study and country performance. It is necessary to identify such a risk. Similarly assessing a general estimate of sites and numbers of patients helps in resource allocation and study planning. From a recruitment point of view, identifying recruitment strategies and exploring various options also helps in planning of the study.

c) Site or Investigator level: This is actually the micro-feasibility – deciding whether to work with an investigator or not and identifying challenges and probable solutions. Given the challenges above, selecting the right site is of paramount importance. While country offices have greater responsibility in this case, study teams provide overall oversight and guidance. It consists of the following

- Clinical aspects: Assessing the investigator’s readiness in terms of standard care (e.g., type of drugs, dosage), actual study population vs. the patient population treated or seen by the potential investigator, readiness and acceptance of background and comparative therapy and familiarity with use of tools and technology is done in investigator level feasibility.
- Site demographics: Site demographics help us in assessing the type of clinical practice (hospital vs. outpatient), prior experience in clinical trials, and availability of study coordinators, pharmacists and nurses. This helps in assessing the ‘competency’ of the investigator/site to conduct the clinical trial, not necessarily in terms of medical knowledge but more in terms of protocol related knowledge, personnel availability etc.
- Recruitment and retention: This is the most important section of the site feasibility. It helps us in finding the recruitment potential, specifically in anticipated subjects per month and in the entire trial. On one hand, it helps in deciding whether we want to explore other sites, on the other it helps in tracking site performance during study conduct. Other information collated includes ethical considerations, presence of competitive studies, prior experience in conducting similar studies etc.
- Ethical aspects: This also helps in site start-up and planning. It includes ethics committee requirements, requirements of translations etc and overall process of ethics clearance.
- Site infrastructure: Most clinical studies have specific requirements related to drug storage, processing of biological samples e.g. refrigerated centrifuge etc.
Hence it is important to assess site’s capabilities related to such requirements, whether it is available at the site or needs to be procured, whether there are team members who have the relevant expertise to conduct these activities and use such tools. Most studies also will have e-CRFs, hence we can assess whether sites have capabilities to use electronic data capture and their familiarity with such tools.

- **Quality**: One more aspect which also needs to be evaluated is whether sites have undergone sponsor independent site audits in the past. Secondly, in the past few years, site inspections have been carried out by the FDA, EMEA and some other regulatory agencies in India and other emerging countries. It may be advisable to check whether the site had undergone any of these and if so, were any concerns raised. This also helps teams in allocating appropriate resources and providing adequate training in the start up period.

**Trial Feasibility as a team approach:**

While the clinical operational teams are overall responsible for conducting clinical trials, by the sheer nature of questions and information desired, it is often essential to collaborate and work closer with other teams to successfully manage a feasibility request. Table 1 provides possible roles of other teams and representatives.

| Clinical Operations | Medical Affairs | Commercial teams |
|---------------------|----------------|-----------------|
| • Specific and general operational issues | • Medical and therapeutic area questions | • Market size, country specific business queries, availability of comparator drugs, exploring possibility of inciting interest from Key Opinion Leaders in trials. |
| • Regulatory and Ethical requirements | • Patient management questions with inputs from potential Investigators | |

Table 1 Roles of specific teams in feasibility

**Clinical Operations**: The clinical operations team can provide valuable inputs into study specific operational aspects based on prior experience including overall startup time, requirement of translated questionnaires, quality and infrastructure. In addition, they can add inputs on overall regulatory requirements including time for approvals, specific requirements such as approvals from other participating countries, contents of the regulatory dossier, and laboratory letters from laboratories located outside India.

**Medical Affairs**: The Medical Affairs team can take responsibility for answering questions on the prevalence of the disease, presenting symptoms and signs of patients, patient management such as diagnosis, standard care, and overall prognosis. While inputs from investigators are a must, Medical Affairs colleagues can also assess relevance and quality of provided information.

**Commercial teams**: In pharmaceutical companies, commercial teams such as Marketing and sales are often a source to provide information on market size of a particular therapeutic area and class of products, availability of comparator or background therapy. In any case, such information may be verified by Medical /Clinical teams appropriately. Finally commercial teams also can provide names of new sites with which Clinical teams may not have any experience. Such suggestions can then be appropriately assessed.

**Practical tips of a good feasibility:**

- **Step 1**: Constitute a team with clear roles and responsibilities and timelines. The task ownership matrix (TOM) can be a general one related to all feasibilities or it may be study specific.
- **Step 2**: Select good clinicians or potential investigators for inputs. It would be preferable to seek opinions from physicians you have either worked or interacted with and who have a sound understanding of the disease under study. For protocol feasibilities, it may be advisable to consider 3-4 potential investigators while for site feasibilities, the number of sites would depend on the country, geographical features, disease under study etc. An average of 8-12 potential investigators may be a good number for site feasibility. The numbers can vary depending on therapeutic area, phase of study, study procedures etc.
- **Step 3**: Collect as much of data that is possible but collate it yourself. It may not be advisable to blindly copy all information that you get. It is essential to review and refine the quality of information, without affecting the integrity. Check the grammar and the English as an unrefined feasibility often can leave an unpleasant impression.
- **Step 4**: Adhere to time at any cost. Requesting for further extensions reflects a poor reflection of team managing feasibility as well as overall working of a country team or CRO.
- **Step 5**: Review, review and review before sending it to the requestor. Be specific in your responses. E.g. In case if specific data is not available, it is advisable to mention so clearly. The start-up time and overall recruitment are reliable indicators for a country’s performance. Be realistic (and never modest) in recruitment targets as well as time for start-up. If you are too unrealistically optimistic, your performance would be worse than what...
is expected and you may not actually achieve your team’s goals. In such cases, teams would have relied on you for completion of certain milestones and you may find yourself in a situation, unable to stand up to those expectations. On the other hand, if you are too modest in terms of number of potential trial subjects or a very long start-up time, you may not be selected for the trial in the first place!

Conclusion:

Conducting clinical trial feasibility is both an art and science. The science comes from the disease area, study design, types of patients etc. The art comes from collation and reliance on the information as well as presenting the real information. The challenge for clinical researchers is to ensure the highest level of quality while doing it. In a true sense, feasibility is an investment to ensure a good study.

Disclaimer:

The author is a full time employee of Pfizer Ltd, India. All opinions expressed herewith are those of the author and do not necessarily reflect that of the organization.

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