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Clinical research: What potential investigators should know

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ABSTRACT

Clinical research trials in India were a very successful industry till recently. The last few years have seen a decline in this industry due to multiple reasons. This loss to the Indian industry has resulted in a gain to clinical research trial industry in China, Russia, Taiwan and some other developed countries.

The reasons for this decline has primarily been due to certain perceptions generated in the public domain by the media and social media as a result of a few poorly conducted trials. The industry needs to make a concerted effort to have better oversight over trials being conducted in India, for safety and ethics. Along with that, it is important to inform the public better about the safety of these trials.

1. Introduction

Clinical research is a science involved in establishing a molecule from its developmental stage to its delivery as a pharmaceutical agent in the market. It involves clinical trials at various stages, Preclinical trial, Phase 0, Phase 1, Phase 2, Phase 3 and Phase 4. It has been estimated that it takes approximately 15 years to convert a small molecule in a laboratory into a lifesaving drug and finally getting an approval to market.

2. Phases of clinical research

- PRE CLINICAL TRIAL: In this phase drugs are tested in non-human subjects (in vitro & in vivo only), to gather data about efficacy, toxicity, and pharmacokinetics. During this phase, the dose is unrestricted and research is conducted by a post graduate level researcher.
- PHASE 0: In this phase a very small sub therapeutic dose of the drug is tested in a small number (about 10) to assess for pharmacokinetics, pharmacodynamics and particularly of human subjects bioavailability and half life.
- PHASE I: In this phase a larger number of healthy volunteers (20–100) are administered sub therapeutic but ascending doses of the drug to assess therapeutic dose range.
- PHASE II: Therapeutic doses of the drug are administered in a larger group of patients (100–300) to assess efficacy and safety of the molecule.
- PHASE III: Usually conducted by both clinical researchers and physicians. In this phase therapeutic doses of the drug is administered to (300–1000) patients for assessing the efficacy, safety, side effects and advertisements.

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- PHASE IV: In this phase physician look out for the long term effects of the drug in the general population of patients i.e. post marketing surveillance.

3. Status of clinical trials In India

India was considered as one of the top centres for leading major worldwide multinational clinical trials in the recent past. There were quite a few reasons for this, which include a vast credulous populace with varied qualities for the quality pool with multiple ailments, along with numerous high level tertiary care facilities. Along with this, lower costs of trials as compared to Western nations, high enrolment rates, greater patient agreeability/maintenance under the ICH (International Conference on Harmonisation) and GCP (Good Clinical Practice), which have been prepared by human services experts (HCPs) and Health care professionals.

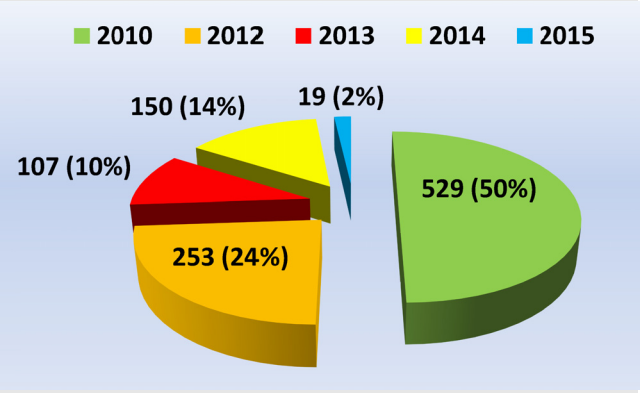
The delay in approvals of clinical trial protocols from regulatory authorities has led to a decline in the Indian Clinical Trial Industry. There are a certain difficulties that the patron organizations are confronted within India, which are leading them to redirect their trials to China and Taiwan. There is a supposed sense of disappointment with the administrative environment in this country. Numerous clinical trials organizations are going to US, European Union, Canada and Malaysia due to faster clearances, which will end up making the trials less expensive over the long run. As of late couple of scholastic NIH trials were likewise put on hold by US NIH. This pattern is a major setback to the Indian Clinical Trial industry. A study by Ice and Sullivan shows that the Clinical Trial business in India is assessed to be worth around USD 500 million, which they project to increase to USD 1 billion by 2016, but industry specialists have evaluated a loss of USD 150–200 million in the previous six months because of changes in the regulations. We need to see if this predicted growth is achievable or not.

Until 2009, the clinical trial industry was doing extremely well in India and this continued to some degree till 2011. Since then, there has been an awakening of the regulatory panels to the way that clinical trials were conducted. From that point on, there has been a sensational drop in effectively conducting worldwide clinical trials outsourced to India. As per some calculations, this drop is nearly 50% in the last 4 years. Meanwhile the global outsourcing of Clinical Trials to China and Russia has expanded significantly in the same period.

India was the second most favoured nation to lead clinical trials outside the US in 2009. However, recent years have witnessed a decrease in number of trials in India (529 in 2010; 253 in 2012; 107 in 2013, 150 in 2014 & 19 in 2015) as compared to developed countries, which are well established in this field. So, in today's scenario, the Indian Clinical Trial Industry once considered a potentially upcoming sector, is undergoing a deep decline of nearly 9.60% in revenues annually. Further decline is predicted because of delay/decreased clinical trial approvals due to the recent amendments in regulations.

The quantity of new medications entering the Indian markets had been progressively decreasing even before the slump in clinical research activities (270 in 2008; 140 in 2011; 44 in 2012; 25 in 2013; 3 in 2015). This requires a relook on the methodology in order to streamline clinical research in Indian setting.

Table 1 – Number of clinical trails in India.



4. Drug regulatory procedure for the clinical trial in India

In India, Drug Controller General (India) (DCGI) is the authority for approving clinical trials and also manufacturing and marketing drugs. DCGI grants approval after appropriate clinical trials are conducted in India with adequate number of trial subjects. In the first place, there are inadequate preparing assets to prepare sufficient number of researchers in order to carry out research activities according to the International Standards.

Act's And Laws Related To Clinical Trials In India

- Drug and cosmetic act 1940.
- Medical council of India act 1956.
- Central Council for Indian medicine act 1970.
- Narcotic Drugs & Psychotropic substances act 1985
- Guidelines for exchange of biological neutral (MOH order) 1997
- Ethical Guidelines for biomedical research on human subjects 2000
- Right to information act-2005

Clinical trials can only be initiated after obtaining written permission from Institutional Ethics Committee (IEC) and Drug Controller General of India (DCGI) as per schedule Y. The application for the start of the clinical trial documents pertaining to chemical, pharmaceutical information, animal pharmacology, toxicology, and clinical pharmacology data. Other documents, which need to be submitted with application are Trial protocol, investigator's brochure, case report form, informed consent form (including preferred languages), patient information sheet and investigator's undertaking, current curriculum vitae & MRC of the investigator, insurance certificate and trial budget.[1] Additional requirements for studies in special population, e.g., children, pregnant women,