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Development of clinical trials in regulatory point of view in India

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ABSTRACT
The journey moves from dietary therapy – legumes and lemons – to drugs. After basic approach of clinical trial was described in 18th century, the efforts were made to refine the design and statistical aspects. Clinical trials hold enormous potential for benefiting patients, improving therapeutic regimens and ensuring advancement in medical practice that is evidence based. Unfortunately, the data and reports of various trials are often difficult to find and in some cases do not even exist as many trials abandoned or are not published due to "negative" or equivocal results. In India, in spite of all the present pitfalls, the country is certainly gearing up to attract more and more researchers from around the world to conduct their clinical trial studies. Laws are being amended to facilitate the entry of global clinical trials and the regulatory system is being polished. The current situation improves by massive and concerted efforts are on to train research professionals and increase the base of investigators and supporting staff. India is already off the starting blocks and gearing up for an inundation of clinical research trials and this will ensure the timely conduct and completion of the clinical trials and at the same time generate high quality data for international submission. India is poised to offer the global pharmaceutical industry high quality and cost effective contract services (a proven track record for some of these services and an enthusiasm to expand into services at the higher end of the value chain.) to support drug discovery, clinical trial conduct, data management and manufacturing. An increasing number of international pharmaceutical companies will seek to establish outsourcing arrangements in variety of forms after uphold international intellectual property laws with high ethical standards. The primary driver for outsourcing will change from cost saving to the quest for high quality and speed as the sector matures. India's more ambitious pharmaceutical companies to fulfill their aspirations of becoming players in global pharmaceutical industry through a thriving contract Skills developed by Indian workforce.
Keywords: clinical trials, regulatory, dietary therapy, legumes, drugs, human testing, Harmonisation.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

These are experiments or observations done in clinical research. Such prospective biomedical or behavioral research studies on human participants are designed to answer specific questions about biomedical or behavioral interventions, including new treatments (such as novel vaccines, drugs, dietary choices, dietary supplements, and medical devices) and known interventions that warrant further study and comparison. Clinical trials generate data on safety and efficacy.[1] They are conducted only after they have received health authority/ethics committee approval in the country

where approval of the therapy is sought. These authorities are responsible for vetting the risk/benefit ratio of the trial – their approval does not mean that the therapy is 'safe' or effective, only that the trial may be conducted.

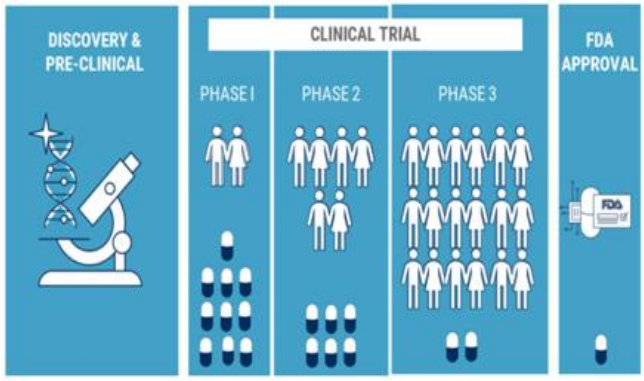


Figure:1 Clinical Trial

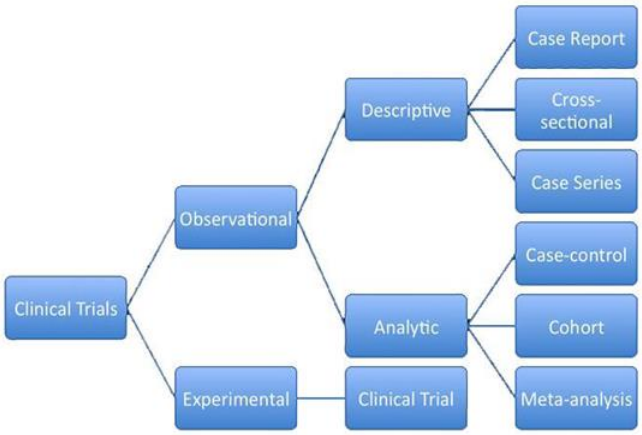


Figure: 2 Types of clinical trials

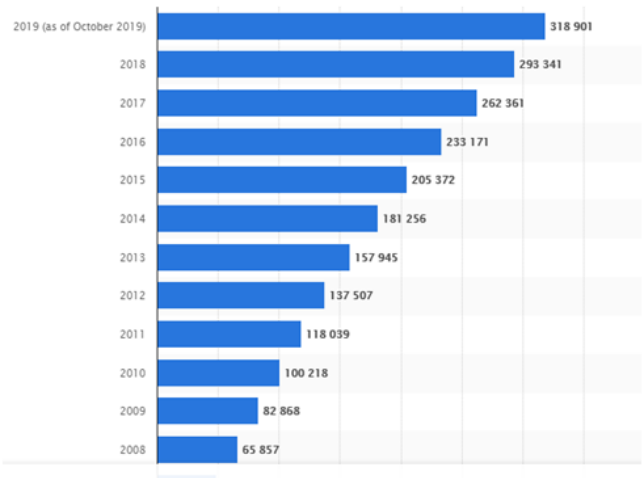


Figure: 3 Year Wise Registered Clinical Trials Around World

Clinical studies are an important part of drug development globally. The number of registered clinical trials has increased significantly in recent years. As of October 2019, there were about 318,901 thousand clinical studies registered globally.

2. Methodology

Clinical Trial

Clinical trial in relation to a new drug or investigational new drug means, any systematic study of such new drug or investigational new drug in human subjects to generate data for discovering or verifying its,

- clinical or;
- pharmacological, including pharmacodynamics, pharmacokinetics or;
- adverse effects,

with the objective of determining the safety, efficacy or tolerance of such new drug or investigational new drug;

Orphan Drug

Orphan drug means a drug intended to treat a condition which affects not more than five lakh persons in India;

Post-trial Access

Post-trial access means making new drug or investigational new drug available to a trial subject after completion of clinical trial through which the said drug has been found beneficial to a trial subject during clinical trial, for such period as considered necessary by the investigator and the Ethics Committee.

New Drug

- A drug, including active pharmaceutical ingredient or phytopharmaceutical drug, which has not been used in the country to any significant extent, except in accordance with the provisions of the Act and the rules made thereunder, as per conditions specified in the labelling thereof and has not been approved as safe and efficacious by the Central Licencing Authority with respect to its claims; or
- A drug approved by the Central Licencing Authority for certain claims and proposed to be marketed with modified or new claims including indication, route of administration, dosage and dosage form; or

The National Regulatory Body

- The Drugs Controller General of India (DCGI) is an official of the CDSCO who is the final regulatory authority for the approval of clinical trials in the country. His ambit, in addition, also extends to inspections of trial sites, inspections of sponsors of clinical research and manufacturing facilities in the country, oversight of the Central Drugs Testing Laboratory (Mumbai) and the Regional Drugs Testing Laboratory as also heading the Indian Pharmacopeia Commission among various other roles, responsibilities and functions.

High patient enrolment rate

India has a huge population base of more than 1 billion, who are genetically, culturally and socio-economically diverse. Indians represent about 15% of the global population. The patient enrolment rate 0.3 patients per month in US as against 3 patients in India and it has a vast pool of heterogeneous population and treatment native patients with a high incidence of diseases common to both the developed and developing world, as a result,

recruitment of patients is generally five to ten times faster in India than it is in the United States.

Spectrum of diseases

It is home to a wide variety of diseases ranging from tropical infections to degenerative diseases (according to IGATE Clinical Research International, India has 40 million asthmatic patients, 34 million diabetic patients, 8–10 million people HIV positive, 8 million epileptic patients, and 3 million cancer patients, So India offers the opportunity to pharma companies to develop drugs for a wide spectrum of diseases, including multidrug-resistant pneumonia, hepatitis B, diabetes, and cancers. Table-4 and Table-5 shows the number of clinical trials in the various fields due to a spectrum of diseases and the status of trial in India in different field respectively.

Human resources and technical skills

Clinical trial execution is a labour -intensive and process driven activity and English-speaking, motivated work forces are well suited to meet the needs of the clinical development sector. In India, the huge and skilled manpower available could revolutionize the clinical trial field. India has 3–4 million scientists, 500 investigators, 572,000 doctors, 43,322 hospitals and dispensaries and about 8.7 lakh beds including both private and public. Many of these scientists are English-speaking and have an excellent technical skill.

Regulatory compliance

In India, responsible for regulatory approvals of clinical trials is Drugs Controller General of India (DCGI) and for advice The DCGI's office depends on external experts and other government agencies. For the export of blood samples to foreign central laboratories, additional permissions are required. All this usually takes about 3months in India. To scrutinize and approve the clinicaltrial before the study begins and also to conduct periodic reviews of the progress of the trial, IEC's is mainly responsible for this work. Studies must first be approved by the local IEC/IRB, and then submitted to the DCGI for additional approval. Bioequivalence studies can be approved by the local ethics committee in India for more than 4 years do not need to go to the DCGI.

The reporting of adverse events from clinical trials has become clearer and unambiguous after the latest amendment (20th January 2005) to the Schedule Y of Drugs and Cosmetic Act 1945 and the implementation of the GATT has opened a new opportunities for India to concentrate on the clinical trial market. India has implemented product patents since 2005, which will encourage multinational companies to import technology into India to develop new products. These developments will open up increased opportunities for the clinical trials of biotech, medicinal, and indigenous like Ayurvedic products. India represents an embracing international IP protection legislation, with important consequences to both its local industry as well as its positioning in the global pharmaceutical industry. This legislation enabled the growth of a domestic generic pharmaceutical industry. India is committed to recognize and enforce product patents in all fields of technology including pharmaceuticals after signatory to the WTO Trade- Related Intellectual Property Rights (TRIPS) agreement in 1995

ICH-GCP Compliance

The Drug Control General India (DCGI) has implemented conformity to ICH (High level of International Conference on Harmonisation of technical requirements forregistration of pharmaceuticals for human use) GCP (Good Clinical Practice)/ GLP (good laboratory practice) guidelines. Generally, most competent authorities (CAs), including the FDA (US Food and Drug Administration), will find the standards of Indian clinical trials acceptable

Cost advantage

The amount of analytical work completed in India, most sponsors will enjoy a 30–50% cost advantage over a similar trial in the US or Europe, depending on the number of patients and investigators. Investigator and site fees are approximately one-half of those in the United States. Further costs to the sponsor for providing trial-related medication, investigations, and hospitalization could be as low as 30% of those inAmerica. Because of the concentration of sites in the major cities and comparatively less costly fares and tariffs that's why Domestic travel costs for monitoring sites are lower and Support services such as printing, translation, and local courier fees are also less expensive. A 2004 study by Rabo India Finance found that in India, phase I trials cost less than half of similar trials in the United States; Phase II and III trials cost less than 60% of their American equivalents.

Reliable data quality

Indian research/data generation capabilities are of international standards and Indian data is accepted by all major medical conferences and journals because of its reliable data quality that's why Clinical trial data has been accepted by international regulatory authorities for pivotal studies. Generally, sponsors have been satisfied with the quality of clinical data provided by clinical trial sites in India in spite of the relatively nascent clinical development environments.

Clinical data management

Access to a large resource pool with IT and business process skills in a low-cost labour environment provide the basis for cost-effective data management services by large numbers of IT-literate biomedical graduates. India ideally positioned for the widespread adoption of EDC technologies to prevalent high-speed Internet connectivity and absence of the biases stemming from the use of legacy systems.

Infrastructure

At present, India can offer a considerably good and suitable infrastructure for conducting clinical trials. For example, a specialty oncology centre (Tata Memorial Hospital in Mumbai) is very well suited to participate in global clinical development. The centre is equipped with state-of-the-art facilities, including spiral CT scanner, gamma cameras, linear accelerator, and bone marrow transplant facilities. Each year 25,000 cancer patients visit this hospital, 1000 patients attend out-patient clinics every day, 441 inpatient beds, 10,000 major operations are performed and about 5000 radiotherapy and chemotherapy treatments are delivered each year.

Economic environment

The present day economic environment in India is quite favourable for foreign direct investments (over US$2 billion a year). According to the recent reports, clinical research outsourcing is, perhaps, seeing the fastest growth for example, Pfizer had announced a doubling of its R&D spend in India, bringing the cumulative investment on clinical research in India to around $13 million and Novartis, Astra Zeneca, Eli Lilly and GSK, were also committed to making India a destination for their clinical research activities. India 20-fold increased the bio statistical and clinical trial logistics services.

Manufacturing

According to Kotak Securities, as far as manufacturing was concerned, things looked pretty good for India. The country ranked second only to the US in terms of the annual number of global Drug Master Filings (DMFs).

Speed

For almost all drug companies, speed is of essence. To develop a new drug, it takes 10-15 Years and the 20-yearclock on a drug patent starts ticking when a new compound is discovered. The faster a drug is developed, the longer its patent protects it. Conducting Phase III trials can save companies between two and five years in getting their drugs to market in India.

Favorable environment: India offers to the established pharma and biotech industries. These include contract research, R&D alliances, clinical trials, R&D for neglected diseases, in licensing of preclinical as well as early clinical drug candidates, IT applications and data management and herbal heritage and solve the serious problems are Increasing the expenditure on drug development, lengthening time lines for clinical trials, patent regime, changing regulations in pharmaceutical research for development of new drugs.

Higher growth in Asia pacific

Pharmaceutical R&D expenditure in Asia is growing faster than in US and Europe. The Importance of Asia-Pacific market is growing, as pharmaceutical and biotechnology companies continue to explore new geographic opportunities to expand their pipelines of products and create business efficiencies. According to the various estimates, the global contract research market is estimated at US$10 billion in 2004 and about 40 to 50% .

Alliances

India established its strength in developing, manufacturing and marketing generic products for global market. This success is attributed primarily to its strength in the process chemistry, formulation development and manufacturing areas. A number of contract research organizations, pharma companies from developed countries forging R&D alliances with Indian companies because they offer quality and cost-effective services in medicinal chemistry, formulation development, and toxicology areas. These alliances are giving preclinical candidates or clinical candidates with proof of concept in humans.

Established pharma companies

Indian companies have already proven its capabilities in discovering and developing drug candidate molecules and they are highly capable in research and development particularly in drug discovery. There are opportunities to apply modern science to elucidate molecular mechanism of action and to identify active ingredients of those medicines; their molecular mechanism of action and identity of active ingredient(s) may not be known of traditional medicines. The process of reverse pharmacology can be applied to discover new drug candidate molecules from these traditional medicines. To elucidate molecular mechanism of action and to identify active ingredients of these medicines, to apply modern science

3. Results and Discussion

Regulatory Requirements For Clinical Trials In India:

Good research contributes to evidence-based medicine and thus better and improved patient care with the ultimate goal of promoting health. Research, however, is a laborious, time and labour intensive task that can take months or even years to reach fruition. Drug development research, in particular, is long and arduous and bringing a single new drug costs on an average USD 1.78 billion and takes approximately 13.5 years from discovery to the market. Drug development research is primarily funded by the pharmaceutical industry including the process of human testing (Phase I-IV studies). These studies (called clinical trials or regulatory studies) are conducted with the academician as the principal investigator largely in academic centres. The pharmaceutical industry funds or 'sponsors' the studies and ensures compliance with the country's regulatory requirements. Academicians, however, also carry out their own research and these studies are called as 'Investigator initiated studies' (IISs). Here, the academician raises funds for the study through his efforts from various sources including possibly the pharmaceutical industry. In these IISs, he dons the dual mantle of an investigator and 'sponsor' and thus directly becomes responsible for ensuring regulatory compliance.

Anaesthesia as a speciality straddles several diverse disciplines that include various branches of surgery and medicine as well as critical care and pain management among others. The past three decades have also seen remarkable advances in the field of anaesthesia, some of which include pulse oximetry, end-tidal gas monitoring, introduction of propofol and the laryngeal mask airway. Anaesthesiologists are uniquely positioned to carry out translational research given the data-rich environment in which they practice and this research can be used successfully to guide evidence-based practice of the discipline as also public health policy. Regardless of the nature of the research (Regulatory Clinical Trials or IISs), knowledge of the regulatory requirements is an essential imperative for researchers.

The National Regulatory Body(CDSCO):

- The Central Drugs Standard Control Organization (CDSCO) is the National Regulatory Authority in India. Its equivalent counterparts elsewhere include the United States Food and Drug Administration (US FDA), Health Canada and the European Medicines Agency.

- CDSCO is an arm of the Ministry of Health and Family Welfare, Government of India. Its mission is to safeguard and enhance public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.
- The Drugs Controller General of India (DCGI) is an official of the CDSCO who is the final regulatory authority for the approval of clinical trials in the country.
- His ambit, in addition, also extends to inspections of trial sites, inspections of sponsors of clinical research and manufacturing facilities in the country, oversight of the Central Drugs Testing Laboratory (Mumbai) and the Regional Drugs Testing Laboratory as also heading the Indian Pharmacopeia Commission among various other roles, responsibilities and functions.

Department of health research and the Indian council of medical research:

- The Indian Council of Medical Research (ICMR) is the apex body that is responsible for the formulation, coordination and promotion of biomedical research.
- It receives funding from the Ministry of Health and Family Welfare and the Department of Health Research, Government of India.

Key documents in clinical research:

(Drugs and Cosmetics Act (1940) and Drugs and Cosmetics Rules (1945))

- This act first came into being in 1940 and regulates the import, manufacture and distribution of drugs in the country to ensure that drugs and cosmetics sold in the country are safe, effective and conform to essential quality standards.
- It has Chapters, Rules and Schedules[6,7] and is amended at regular intervals to ensure greater safety, efficacy and drug quality.
- The Schedule Y along with rules 122A, 122B, 122D, 122DA, 122DAC and 122E (see below) is the key document that governs clinical research in the country. Per law, it is mandatory that all clinical research that falls under the ambit of Schedule Y complies with the necessary requirements.
- It has 12 appendices, formats for clinical trial protocols, informed consent forms, ethics committee (EC) approval templates and a format for serious adverse event (SAE) reporting.

Ethical Guidelines on Clinical Research In India

The revised ICMR guidelines released in 2006 is called the 'Ethical Guidelines for Biomedical Research on Human Participants' and remains valid as of today, and a revised version is expected in 2017. This guideline covers two broad aspects of clinical research – the general principles that need to be followed and guidance regarding special areas of research (e.g., research in children or herbal research). Researchers are expected to be familiar with both these documents and abide by the requirements in the former and the guidance in the latter.

Clinical trials regulations India:

- What would possibly happen if all the drugs and vaccines are removed altogether from our world? Quite intimidating. Ebola, Aids, Swine flu... all will feed voraciously on the human population. To stop them we need medicines; good and improved medicines. But how could we do that? Significance of Medical Research and Clinical Trials should be seen under this perspective. Drug development is a process that calls for utmost care.
- A clinical trial in simple terms can be defined as a set of practice that helps certify a new drug molecule as safe and efficacious before reaching the market.
- In fact "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes" can be defined as a clinical trial.
- Clinical interventions include drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioral treatments, process-of-care changes, preventive care. To determine the safety and efficacy of drug research on humans is always warranted, but one needs to be cautious and vigilant as to how the players in this field undertakes the process. Adherence to the principles of good clinical practices or GCPs, including adequate human subject protection universally recognized as a critical requirement to the conduct of research involving human subjects. Most countries have adopted good clinical practice principles as laws or regulations. In India, compliance with GCP guidelines issued by the Central Drugs Standard Control Organization or the CDSCO is recommended.
- This article aims to give a brief outline of the Indian scenario regarding Clinical Trial initiation, current regulatory framework and its effectiveness in reality.

7. Drugs and Cosmetic Rules

- New chemical entities cannot be administered to human subjects in a clinical trial without permission from the Drugs Controller General of India. Such permission may be obtained by submitting to the DCGI an application for a clinical trial. The application must include a protocol for the study, a draft of the Informed Consent Document, a list of proposed investigators who have agreed to participate in the study, and background information about the drug in accordance with Schedule Y of the Drugs & Cosmetics Rules.
- It takes almost 12 weeks to obtain permission for a clinical trial for most investigatory drugs. The duration may be longer for drugs with special significance to the healthcare concerns of the country or those that may be considered

controversial since these are liable to be referred to the Indian Council of Medical Research for comments.

8. ICMR

The ICMR guidelines for clinical trials mandates setting up of Ethics Committees or EC's at the institutional levels, for the purpose of scrutinizing and approving a clinical trial before it begins; and to to conduct periodic reviews of the progress of the trial. Ethics Committees are not merely ethics advisors and facilitators of clinical trials. They not only reflect on ethical aspects of research, but also play the role of ethics regulator for the DCGI. Their power to conduct ethics review, including the power to reject trials not conforming to ethical standards laid down in the ICMR's ethical guidelines, flows from the legal requirement wherein the DCGI provides clearance to clinical trials only on the condition that they will be reviewed and certified by an EC. Also, approval by the Ethics Committee is not a necessary precondition for regulatory permission to conduct a clinical trial provided the applicant submits an undertaking that the study will not be initiated at individual sites without prior EC approval.

An example to show the gravity of administrative irregularity in this area is the official statistics published by the Indian Council of Medical Research itself. In 2002, the ICMR conducted a survey of 149 ICMR-supported ongoing clinical research/trials in 71 institutions but interestingly, despite ICMR being the funder, only 36 institutions responded. While all 36 claimed to have institutional ethics committees in place, only 23 had standard operating procedures for their review functions and only 14 claimed that they had trained IEC members in research bioethics. Besides, of the 149 research projects analyzed in this study, only 107 (72%) researchers had furnished IEC clearance certificates. This data alone gives proof that despite the presence of broad guidelines and means of its enforcement, India lacks proper regulatory mechanism to put them in force. Ironically, though the DCGI fully depends on ECs for implementing ethical standards in clinical trials, there is absolutely no direct linkage of any kind between the DCGI and ECs. The DCGI neither cares for the proper functioning of ECs nor assures their competence as these tasks are left to institutions which have a direct interest in trials.

Further, ECs do not report to an independent public authority that is responsible for supervising these committees and ensuring their proper and competent functioning. Nor is their expenditure financed by public funds. Thus they are, in reality, either self-sufficient private bodies obliged to the institutions or independent private entities charging for their services. There is no transparency of their functioning and no public scrutiny of their review and regulation of clinical trials. So, despite a substantial period after forming the EC's in India, it still remains an enigma.

9. Informed consent

Is an essential requirement of medical trials, which denotes that the patient undergoing treatment as part of the study should be made aware of the trial being conducted, the drugs being administered on him and its possible side effects. But the country has, at several instances witnessed gross violations of human rights and ethical values while conducting trials on volunteers enrolled in studies. In 1999, without obtaining consent of the patients who were under treatment in the government-run Regional Cancer Centre in Similarly, in 2002, the pharma giant Novo Nordisk conducted multi-centre phase III clinical trials of a diabetes drug even before receiving the results of animal studies. The study report found that the drug, ragaglitazar, caused urinary bladder tumors in rats; and this should have been known before the drug went for phase I trials. In 2003, Mumbai-based Sun Pharmaceutical Industries Ltd. launched a promotional-cum-research programme by getting private doctors to prescribe the anti-cancer drug Letrozole to more than 400 women as a fertility drug for ovulation induction. The company then publicized the doctors' reports to other doctors as "research", using their network of medical representatives. The drug was prescribed despite the fact that it was known to be toxic to embryos.

These are only a few of the numerous shocking human rights violations that have been exposed in the area of clinical trials. These instances throws light on the lacunae in the

Another flaw in the Indian healthcare regulation is the lack of consistency in the licensing procedure. Currently, the interpretation and enforcement procedure varies from one state to another. This variation in procedures creates little accountability, in case an issue arises. At the same time, attempts by the Central government to create a Central Drug Authority is highly appreciable. Such a move gains significance in the context that the US and European drug giants are increasingly outsourcing their clinical testing to the rapidly developing economies like China, India and Africa.

10. Issues and Challenges

Challenge 1: Lack of Public Participation in Clinical Research

The research participants give consent to participate in a clinical study after being fully informed about the study. They are the heart of the clinical research enterprise. Given the stringent regulatory requirements, the number of patients per study is increasing. There is a need to go beyond the bastions, hence the focus is on India. Currently very few eligible patients are aware that they can participate in research studies and recruitment is often difficult and resource-intensive.

Challenge 2: Lack of Awareness and Education about Clinical Research

Awareness may be defined as having the perception or knowledge of an event. In a subject recruitment context, awareness suggests that patients can be recruited for a clinical trial only if they have knowledge of it. Research indicates that lack of awareness of clinical trials is a key reason why potential patients do not participate.

Challenge 3: Lack of an Adequately Trained Workforce

Clinical research requires the expertise of many kinds of investigators, including physicians, dentists, public health

workers, research nurses, raters, psychologists, laboratory technicians, dieticians, computer programmers and others. With the growing need of clinical research participants, there is a shortage of adequately trained workforce.

Challenge 4: Training in Clinical Research

Clinical research training is an important issue given the gap between supply and demand for trained professionals in India. To foster expertise in clinical research, organizations have started training their employees on ICH-GCP Guidelines and Company Policies, then exposing them to hands-on training in their respective departments: clinical operations, data management, regulatory, study drug management or quality assurance. Until recently, there were no structured, formal training courses focusing on clinical research.

Challenge 5: Regulatory Hurdles

All clinical trials in India are carried out under Schedule Y (Appendix 5) of the Drugs and Cosmetics Act of 1940 (Act) and the Drugs and Cosmetics Rule of 1945 (Rule). Both pieces of legislation have been amended several times over the years, the most recent amendments to both were in June 2005. A Sponsor needs to file an Investigational New Drug (IND) with the Central Drugs Standard Control Organization (CDSCO). A clinical trial cannot be initiated until written permission from the chief of CDSCO; the Drugs Controller General India (DCGI) has been issued to the sponsor.

Challenge 6: Ethical Issues

Ethical issues include incorporating the national and international ethical principles, human subject protection issues and proper functioning of EC. It is responsible for safeguarding the dignity, rights, safety and wellbeing of all trial participants.

11. The Benefits of Participating in Clinical Trials

- If person have a disease that cannot be treated with an existing drug or regimen, participation might provide you with a successful treatment before it becomes available to others and have the opportunity to access cutting edge biomedical innovation which could be life saving and improves health outcomes.
- The global clinical development programs are an opportunity for physicians and medical Students to improve their skills by conducting research in accordance with international standards.
- Indian hospitals receive reimbursements for participating in clinical trials, which will benefit all patients served by that hospital for example; Pfizer has donated a $100,000 bone density testing machine to each of six hospitals testing its osteoporosis drug.
- Enhance the clinical practice of evidence based medicine, through record keeping and better patient communication by exposure of the Indian health care system to the discipline of international clinical research.
- Economic interests will encourage India's regulatory authorities to clarify the rules, expand their resources, and improve skill levels.
- Participating in clinical trials also gives physicians a chance to be on the cutting edge of new technologies and scientific developments that open their eyes to medical innovation and encourages scientific thinking.
- Clinical research creates employment for site personnel, study monitors, and ancillary services, with an economic impact on the whole community.
- The drugs and protocols offered during clinical trials are often provided at no cost to participants. Patients who have trouble affording the drugs or treatment they need may consider enrolling in a clinical trial in order to access the protocols that may help them.
- Some patients have no alternatives for treatment and permanent debilitation or deaths are imminent. In such cases, participation in a clinical trial may give them hope or possibilities that do not exist otherwise.
- Many drugs, devices and therapies have previously been tested on white men, and found safe and useful. Fewer trials have been designed and run for women, minorities, or children. Participation in a trial that broadens the use of a good drug for one of these less tested groups is useful to humanity.

12. The Risks of Participating In Clinical Trials

- There may be unpleasant side effects or outcomes, may last only a short time, or they may affect you for the rest of your life.
- Patients do not know whether they are receiving the experimental drug or treatment, or a previously approved drug or treatment, or even a placebo (a dummy treatment). Therefore, if the reason you decide to participate is because you hope to try a treatment that is not yet publicly available, you usually have, at best, a 50% chance of receiving that treatment.
- The treatment being studied may have no positive effect, either because you aren't really receiving the treatment being studied and the treatment isn't appropriate to help you.
- The long time and attention required of participants involved. It may require hours of testing, miles of travel, hospital stays or complicated dosing.
- New doesn't always mean better

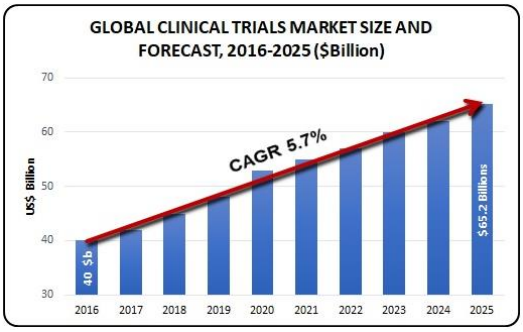


Fig.4. Global share of CTs in India

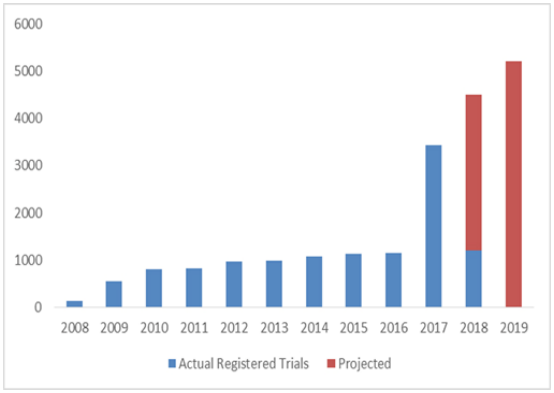
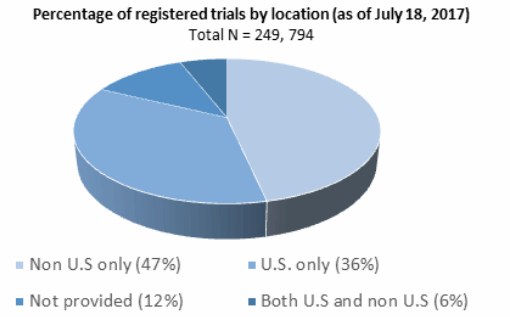


Fig.5. % of registered trials



Location	Number of Registered Studies and Percentage of Total (as of July 18, 2018)
Non U.S. only	116, 997 (47%)
U.S. only	89, 672 (36%)
Not provided	29, 376 (12%)
Both U.S. and non U.S.	13, 749 (6%)
Total	249, 794

Fig.6

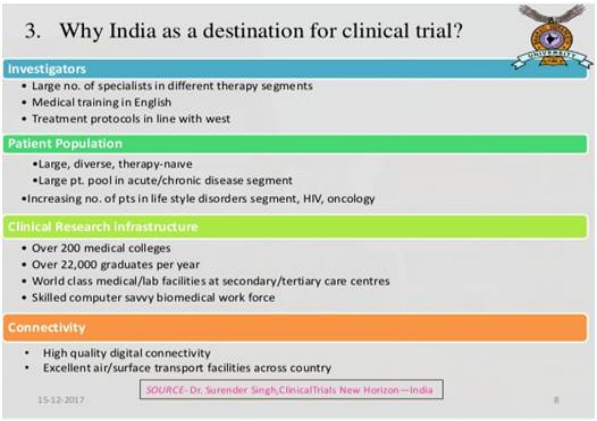


Fig.7

4. Conclusion

Overall, the new rules are comprehensive, well-balanced and will likely improve the ethical and quality standards of clinical trials in the country, which also will further benefit patients and industry. Waiving local clinical trial under these rules will help provide earlier access to drugs for patients in India. The deemed approval for clinical trials in 30 working days for indigenous drugs also will speed up the clinical trial process and encourage local drug development. Provision for accelerated product approval under some conditions, along with provision of pre and post submission with the CDSCO office, would add predictability and confidence in the system. The shortened review timelines would clearly require additional manpower at CDSCO to ensure timely disposal of applications. The government has already planned an expansion of CDSCO strength and it is expected that additional revenue generated through increased application fees will help ensure adequate human resources are available at CDSCO.

In future steps, the CDSCO office may start working on filling some of gaps in areas of Subject Expert Committee (SEC) and post-trial access guidance document. Finally, there could be difficulty in implementing these rules and it will be interesting to watch how the CDSCO office takes on the challenging task of meeting the objectives laid out by these rules.

Without being cynical we would like to end by what we began with that clinical trials are an important tool to further human well-being in the process of finding new solutions to the diseases and health problems afflicting humanity. However, the application and practice of this tool stands greatly distorted due to its subjugation to profit motive of the pharmaceutical multinationals rather than to further its primary motive. It is wrong to assert that human well-being function of clinical trials can only be achieved if there are adequate monetary incentives built in for the researchers and the drug manufacturers for we have seen that such a system has singularly undermined the interests of the patients. Additionally, there is a need to recognize the power relationships that operate between countries, within countries between different social classes, and between the physicians and patients which have defined the manner in which clinical trials industry has grown in the developing world. These power relationships undermine all the regulations that may be put in place to ensure ethical conduct of clinical trials. The solution clearly lies in freeing clinical trials from its subservient role to generating profits for the healthcare industry.

This requires that the Indian government pull India out of the TRIPS agreement and replace it with a patent regimen that is designed not merely to fulfill our narrow national interests but throws a challenge to the model of knowledge generation, its appropriation, and utilization as imposed by the developed countries of the world in defense of the interests of the impoverished masses across the world. Fundamental to such an attempt would be to build a robust network of public institutions for carrying out biomedical research in tune with the public health needs of the country. This should be adequately utilized by an equally robust network of manufacturing facilities in the public sector as also the required support to the private sector to prevent it from capitulating to the might of the multinationals from the developed world. India should make attempts to share the knowledge/technology generated in its labs with other developing countries on liberal terms.

The review concludes that the clinical trial industry in India has great potential to become the most favorable destination

in the world because of low cost of doing business, the availability of skilled professionals, and, the availability of a large and diverse patient pool. Many global CROs relocate their research units to India for drug development activities. Though the CT industry has been taking advantage of the huge financial gains, technological transformation for development of NCE is not happening. Also, the Indian public health industry only partially benefits from CTs. The Government of India needs to establish a policy framework for the Indian CT industry to provide for easy access to affordable drugs developed through adaptive clinical trials in India. There is also a need to create a regulatory environment capable of ensuring the conduct of clinical trials without violation of humanitarian ethics and other social norms.

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