www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i8.03

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

'Clinical Trial' or 'Critical Trial' – A Scientific Affront on Human Rights

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Abstract
Change is the law of life, Law always supports changes for development and prosperity. Science is the inevitable tool for achieving progress in human civilization. The relationship of science and law is as old as the creation, the modern tendencies of human life and human attitudes Vis-a-Vis the technical development often lead to miscalculations and over enthusiastic estimations.
The fact is that both science and Law are the two sides of human life and they always move hand in hand for happy human life. Genetical Engineering, Cloning, Stem cell therapy and Clinical Trials etc., have been few of modern perplexities.
Traditionally Clinical Trials are associated more with serving the humanity, as a trend to understand disease patterns and seeking solutions for the dreadful diseases in the terms of better diagnostics. But in the recent times through Clinical Trials on humans, have created great alarm as it has been directly impacting on Human Rights philosophy.
This write-up intends to sketch a general sweep on the issues of Clinical Trials which have consumed many lives in the process of the Experiments and procedures by the scientific researches and the pharmaceutical sector.
Key Words: *Clinical Trials, The Drug Controller General of India (DCGI), Drugs Technical Advisory Board (DTAB), The Central Ethical Committee of ICMR on Human Research.*

"'Science in itself' is nothing, for it exists only in the human beings who are its bearers. 'Science for its own sake' usually means nothing more than science for the sake of the people who happen to be pursuing it."
Rudolf Virchow

Introduction

India has been continuing to be the cynosure of all civilizations, creatures, preachers, practitioners and wonders. India's pride and reputation as giver of knowledge even at the cost of self-destruction, is mysterious qualitative attitude inviting perdition from outside world. Law and Science in our country were embraced spiritually exposing the scientific propositions of Indian science which always permitted scientific inventions to touch human body for relief and alleviation of pain, and creatures hardly were sacrificed for predictions and practical experiments. Modern Indian scientific knowledge appears to have lost its

virginity at the altar of global scientific thought. There is no much difference between a human and a pig now a days in pharma-world, and for experimentation in drug-invention, small creatures like rat and rabbit are not preferred, for human is abundantly available and accessible at inexpensive tariff. Clinical trial, once an individual labour of intellectuality has flourished into 'favored and flavored industry'. Thanks to the western knowledge – Indian soil is proved to be the best place for such flouring industry!

Let us rejoice at the fact that human beings lost their lives to be crowned as 'Martyrs of Clinical Trials'. The number of deaths in India resulting from clinical trials has increased to an unendurable figure of 2,868 during the period 2005-2012.[1]

If on the one hand this figure relating to number of deaths resulting from clinical trials is fearful, on the other hand the decline in the number of clinical trials and approval given for conducting such trials in last few months is equally shocking. Till April 2013, only 12 (twelve) clinical trials have been approved by the authority as compared to almost a three digit figure in last year.[2]

Of course, it is important to note that it is not just the multinational companies that are conducting clinical trials, but Indian firms, too, have started conducting trials. Indian firms not only focus on clinical trials for developing new drugs, but are also open to innovation for discovering new drugs. India offers huge patient pools to CROs because the country has a large urban population; also, the disease prevalence rate is too high.

India alone accounts for one-fifth of the global burden of disease. Since India has a large population divided into multiple ethnic groups, it is home to all types of diseases. Due to high level of poverty and low capacity to pay for healthcare, the country has a wide variety of treatments for the native population. The native people suffer from various diseases but do not seek treatment because of financial reasons. Also, since the government is unable to provide healthcare services to all of them, it leads to market failure. In such case, while India can offer these vulnerable populations for CTs, on the other side, CROs can offer drug or medical testing services under clinical trials at zero cost.

However, one should not forget that most of the big CROs are keen to relocate to India because clinical research is 60 per cent cheaper than in the US or UK. Russia, Argentina and China are also cost-efficient locations but India, in addition, can provide a large patient pool for trials. In India, CTs are inexpensive because labour and other professional costs are relatively low. Also, Patent law is now very flexible and favorable to drug producers. Foreign companies can collaborate with domestic firms and easily enter the Indian pharmaceutical industry. Collaboration with domestic companies also reduces the cost of drug testing because they can readily utilize Indian laboratories, hospitals and other infrastructure.[3]

We fail to balance the interests in between the need and greed, nature vs. nurture. Law and Science are moving as disjunctive species.

Whether 'Human Rights' are exempted in this drugged world, is an astonishing food for thought, Humans are exploited and victimized with no compensation or 'mocking money'.

What are Clinical Trials?

Clinical trials are conducted to collect data regarding the safety and efficacy of new drug and device development. There are several steps and stages of approval in the clinical trials process before a drug or device can be sold in the consumer market, if ever. Drug and device testing begins with extensive laboratory research which can involve years of experiments in animals and human cells. If the initial laboratory research is successful, researches send the data to the Food and Drug Administration (FDA) for approval to continue research and testing in humans.

Once approved, human testing of experimental drugs and devices can begin and is typically conducted in four phases. Each phase is considered a separate trial and, after completion of a phase, investigators are required to submit their

data for approval from the FDA before continuing to the next phase. Clinical research is medical research that involves people like you. People volunteer to participate in carefully conducted investigations that ultimately uncover better ways to treat, prevent, diagnose, and understand human disease. Clinical research includes trials that test new treatments and therapies as well as long–term natural history studies, which provide valuable information about how disease and health progress.

Types of clinical trials

There are different types of clinical trials.

- **Natural history studies** provide valuable information about how disease and health progress.
- **Prevention trials** look for better ways to prevent a disease in people who have never had the disease or to prevent the disease from returning. Better approaches may include medicines, vaccines, or lifestyle changes, among other things.
- **Screening trials** test the best way to detect certain diseases or health conditions.
- **Diagnostic trials** determine better tests or procedures for diagnosing a particular disease or condition.
- **Treatment trials** test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
- **Quality of life trials** (or supportive care trials) explore and measure ways to improve the comfort and quality of life of people with a chronic illness.[4]

Human Clinical Trial Phases

Phase I studies assess the safety of a drug or device. This initial phase of testing, which can take several months to complete, usually includes a small number of healthy volunteers (20 to 100), who are generally paid for participating in the study. The study is designed to determine the effects of the drug or device on humans including how it is absorbed, metabolized, and excreted. This phase also investigates the side effects that occur as dosage levels are increased. About 70% of experimental drugs pass this phase of testing.

Phase II studies test the efficacy of a drug or device. This second phase of testing can last from several months to two years, and involves up to several hundred patients. Most phase II studies are randomized trials where one group of patients receives the experimental drug, while a second "control" group receives a standard treatment or placebo. Often these studies are "blinded" which means that neither the patients nor the researchers know who has received the experimental drug. This allows investigators to provide the pharmaceutical company and the FDA with comparative information about the relative safety and effectiveness of the new drug. About one-third of experimental drugs successfully complete both Phase I and Phase II studies.

Phase III studies involve randomized and blind testing in several hundred to several thousand patients. This large-scale testing, which can last several years, provides the pharmaceutical company and the FDA with a more thorough understanding of the effectiveness of the drug or device, the benefits and the range of possible adverse reactions. 70% to 90% of drugs that enter Phase III studies successfully complete this phase of testing. Once Phase III is complete, a pharmaceutical company can request FDA approval for marketing the drug.

Phase IV studies, often called Post Marketing Surveillance Trials, are conducted after a drug or device has been approved for consumer sale. Pharmaceutical companies have several objectives at this stage: (1) to compare a drug with other drugs already in the market; (2) to monitor a drug's long-term effectiveness and impact on a patient's quality of life; and (3) to determine the cost-effectiveness of a drug therapy relative to other traditional and new therapies. Phase IV studies can result in a drug or device being taken off the market or restrictions of use could be placed on the product depending on the findings in the study.[5]

Importance

Clinical trials are part of clinical research and at the heart of all medical advances. Clinical trials look at new ways to prevent, detect, or treat disease. Treatments might be new drugs or new combinations of drugs, new surgical procedures or devices, or new ways to use existing treatments. The goal of clinical trials is to determine if a new test or treatment works and is safe. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses.

People participate in clinical trials for a variety of reasons. Healthy volunteers say they participate to help others and to contribute to moving science forward. Participants with an illness or disease also participate to help others, but also to possibly receive the newest treatment and to have the additional care and attention from the clinical trial staff. Clinical trials offer hope for many people and an opportunity to help researchers find better treatments for others in the future.

The idea for a clinical research study — also known as a clinical trial — often originates in the laboratory. After researchers test new therapies or procedures in the laboratory and in animal studies, the most promising experimental treatments are moved into clinical trials, which are conducted in phases. During a trial, more information is gained about an experimental treatment, its risks, and its effectiveness.

Nature of Clinical Trials

Typically, clinical trials compare a new product or therapy with another that already exists to determine if the new one is as successful as, or better than, the existing one. In some studies, participants may be assigned to receive a **placebo** (an inactive product that resembles the test product, but without its treatment value).

Comparing a new product with a placebo can be the fastest and most reliable way to demonstrate the new product's therapeutic effectiveness. However, placebos are not used if a patient would be put at risk — particularly in the study of treatments for serious illnesses — by not having effective therapy. Most of these studies compare new products with an approved therapy. Potential participants are told if placebos will be used in the study before they enter a trial.

Randomization is the process by which two or more alternative treatments are assigned to volunteers by chance rather than by choice. This is done to avoid any bias with investigators assigning volunteers to one group or another. The results of each treatment are compared at specific points during a trial, which may last for years. When one treatment is found superior, the trial is stopped so that the fewest volunteers receive the less beneficial treatment.

In ***single-*** or ***double-blind studies,*** also called single- or double-masked studies, the participants do not know which medicine is being used, so they can describe what happens without bias. "Blind" (or "masked") studies are designed to prevent members of the research team or study participants from influencing the results. This allows scientifically accurate conclusions. In single-blind ("single-masked") studies, only the patient is not told what is being administered. In a double-blind study, only the pharmacist knows; members of the research team are not told which patients are getting which medication, so that their observations will not be biased. If medically necessary, however, it is always possible to find out what the patient is taking.

Risks and benefits

Clinical trials involve risks, just as routine medical care and the activities of daily living. When weighing the risks of research, you can consider two important factors:

1. The degree of harm that could result from participating in the study, and
2. The chance of any harm occurring.

Most clinical studies pose the risk of minor discomfort, which lasts only a short time. However, some study participants experience complications that require medical attention. In rare cases, participants have been seriously injured

or have died of complications resulting from their participation in trials of experimental therapies. The specific risks associated with a research protocol are described in detail in the informed consent document, which participants are asked to sign before participating in research. Also, a member of the research team explains the major risks of participating in a study and will answer any questions you have about the study. Before deciding to participate, carefully consider possible risks and benefits.[6]

Clinic Trials in India

India is one of the major destinations for conducting clinical trials. The Drug Controller General of India (DCGI) is the governing body responsible for all pharmaceutical-research and regulatory issues in India. While conducting clinical trials in India, regulations have come to ensure safety and wellbeing of the study subjects in the trial. The present study was planned to see the number of trials approved by DCGI and their trend over the last 8 years in view of new regulatory guidelines[7]

The Central Drugs Standard Control Organization (CDSCO) is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act. CDSCO has six zonal offices, four sub-zonal offices, 13 port offices and seven laboratories under its control.

Major functions of CDSCO

1. Regulatory control over the import of drugs,
2. approval of new drugs and clinical trials,
3. meetings of Drugs Consultative Committee (DCC) and Drugs Technical Advisory Board (DTAB),
4. Approval of certain licenses as Central License Approving Authority is exercised by the CDSCO head quarters.
5. Their vision is to Protect and Promote public health in India with a mission to safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.

Total 1799 Trials Approved. 2007 had lowest approvals with 3 clinical trials & 2010 being highest with 500 trial approvals. Mean ± SD Approval of 224.88 ± 172.46 with Median rate of 206 per year was observed. Trend of Trials approved by DCGI shows sharp peak around 2008-2010 which follows sharp fall around 2013[8].

The new drug as defined under the Drugs and Cosmetic Rules 1945 (DCR), and subsequent amendments include:

i. A new chemical entity (NCE)
ii. A drug which has been approved for a certain indication, by a certain route, in a certain dosage regimen, but which is now proposed to be used for another indication, by another route, or in another dosage regimen.
iii. A combination of two or more drugs which, although approved individually, are proposed to be combined for the first time in a fixed dose combination (FDC). Drugs Controller General (India) (DCGI) is equivalent to the US Food and Drug Administration (FDA) and European Medicines Agency (EMEA). The DCGI is the official governing body responsible for all pharmaceutical research and regulatory issues in India described in the Drugs and Cosmetics Rules, 2005 (DCR). Clinical trials are regulated per Schedule Y of the DCR

In 2005, India became fully compliant to TRIPS. Since then the policymakers have been trying to make changes in the policy framework and regulatory environment in order to promote clinical trials in India. These changes are known to have encouraged the international Clinical Research Organizations (CROs) to expand their clinical research. Recently, pharmaceutical companies that are involved in clinical trials are being trailed by a growing concern over the clinical research ethics followed in India. Global pharmaceutical companies are outsourcing their

projects to India for several reasons: enhancing profit, cutting the cost of drug development and speeding regulatory approval, and, fostering a less hostile environment among the world's impoverished ill. Clinical trials are more than 50 per cent cheaper in India compared to developed countries[9].

The reasons for low cost of drug development are cheap human resource, low recruitment cost and lower rate of compensation for any injury sustained or death during the research process. In fact, CROs even recruit patients without any formal assurance of compensation because a large proportion of participants in India are illiterate and lured into trials by offers of free healthcare and financial inducements. However, they are often unaware of the benefits and risks of taking part in a trial, and many may not even be able to distinguish between treatment and research. Also, the concept of informed consent before enrolling in a trial is not very clear[10].

An important ethical question being raised in the debate is: Will the new drugs tested in India actually be of benefit to the local patients, and will these drugs be made available to them at reasonable prices? With 25 per cent of the Indian population living below poverty line, it is unlikely that these drugs will be "affordable". Another important issue in this context is compensation for clinical trial related injury or death. Over the past five years, more than two thousand people have died because of clinical drug trials and amongst them, only a few have received compensation[11].

The Government of India continues to invite multinational companies for conducting clinical trials in order to attract foreign investments for financial and technological gains in this sector. The central ideology of clinical research is that it should be of wider benefit to society. There cannot be two societies—one that takes risks whilst the other reaps the benefits. Will India be able to bridge the gap between two societies, i.e., minimise risk and maximise benefit? Is the clinical trial practice of benefit to public health in general and to the pharmaceutical industry in particular? This study addresses the issues of benefit maximization and risk minimization by reviewing the progress of clinical trials industry in a systematic way. It has attempted to generate an evidence-based assessment to help policymakers shape future policies for development of the clinical trials industry. It also makes an attempt to direct the attention of the Indian policy-making apparatus to the legal and ethical questions being raised by researchers and civil society groups on the process of conducting trials involving human subjects.

Revised clinical trial policy may be just what the doctor ordered for India, which has been losing out as the destination of choice for drug makers globally. CNBC-TV18's Archana Shukla reports that with the policy, which enables quicker approvals and balanced compensation guidelines for both participants and sponsors, India may soon regain its glory days in this area. India accounts for 20 percent of the global disease burden, however less than 1.5 percent of global clinical trials for new therapies in the last 2 years. Policy uncertainties have seen a number of trials moving out of India to countries like Korea and Taiwan. Only 25 global clinical trials have received approval in the country, compared to hundreds that got the green signal every year till 2011.

One big reason for this sharp fall is a lengthy and unpredictable approval process, which ranges anywhere between 6 and 18 months. The new policy also reworks the compensation guidelines which dictate how much patients participating in trials can receive in case of injury or death during the trial period. For one, it proposes segregating compensation for trial-related injury to those caused otherwise and experts say that should help. Suneela Thatte, President, Indian Society of Clinical Research, said "At a certain point if it is determined beyond doubt that this injury had nothing to do with his or her participation in the clinical research then we should not then put the burden of further medical management on the sponsor. So, this is a great point in balancing these guidelines.

The amended guidelines state that if there is injury because of lack of therapeutic benefit compensation has to be given provided there was standard treatment available and denied, which is a fair point.

Conclusion

Clinical trials are absolutely necessary for medical research. Human subjects are required to ensure safe and effective drugs and medical devices. The goal of these trials is to provide the public with innovative and safe products whose benefits outweigh the risks. Informed consent is the most important and potentially the easiest way to minimize exposure to liability for all parties involved in clinical trials. All participants in clinical trials will benefit from full, freely given and informed consent. Researchers must strive to adhere to established standards of conduct and approved protocols for their particular trial. Clearly, as in all medicine, all results, actions and patient interaction must be clearly documented.

Although litigation can be anticipated, clinical trials ultimately serve to advance medicine and develop newer and better medical products and treatments and are invaluable medical research tools. The increased of clinical drug trials by pharmaceutical companies striving to bring more drugs to market is leading to a growing volume of lawsuits being filed by trial participants. The participants who file the suits frequently charge that they were inadequately warned of potential risks of the trials. But despite measures taken, some observers say there has been an increase in the number of cases filed by unhappy participants, or their survivors.

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CHECK UNBRIDLED AND UNREGULATED ENTHUSIASM FOR SCIENTIFIC RESEARCH THROUGH CLINICAL TRIALS FOR FAIRY VICTORY OF GENETIC ENGINEERING AND TRANSGENICS HAS NO RIGHT TO UNFAIR CLINICIAL TRIAL.

When you're taking deaths in clinical trials, mistakes are not an option. It's just an area where we have to have to have absolute, foolproof reporting in place.

Artur Leonard Caplan