

A review on essentials perspectives for clinical trial

Rishikant Tripathi^{1*}, Pushpendra Kannoja², Anil kumar¹, Emdad Hossain¹, Upendra Kumar¹

¹Pharmacy College, Itaura, PO Chandeshwar, Azamgarh 276128, Uttar Pradesh, India;

²College of Pharmacy, IPS Academy, Indore 474001, Madhya Pradesh, India

*Corresponding author: rishi.kant2001@gmail.com

ABSTRACT In the latest scenario the global pharmaceutical and biotech industries have been looking at opportunities for cost effective drug development including India to launch new drugs through their own research efforts. This has heightened the importance of developing adequate internal standards to conduct their operations to be able to compete with the globalization demands. Clinical trials are conducted to allow safety and efficacy data to be collected for health interventions for discovery of a new drug. These trials can take place only after satisfactory information has been gathered on the quality of the non-clinical safety and approval from health authority or ethics committee of the concerning country. In planning of a clinical trial, the sponsor or investigator first identifies the medication or device to be tested. Usually, one or more pilot experiments are conducted to gain insights for design of the clinical trial to follow. Clinical trials involving new drugs are commonly classified into four phases. Each phase of the drug approval process is treated as a separate clinical trial. The drug development process will normally proceed through all four phases over many years. If the drug successfully passes through Phases I, II, and III, it will usually be approved by the national regulatory authority for use in the general population. Phase IV are post-approval studies. It is understandable that regulations have to be implemented with due consideration. Central Drugs Standard Control Organization (CDSCO) of India has dedicated for setting of standards for drugs, pharmaceuticals and healthcare devices technologies etc. in India.

Keywords: CDSCO, Clinical trial, Ethical guidelines, FDA, Institutional Review Board

Introduction

Recently all country have seen significant growth in the healthcare sector with international expansion strategies through mergers and acquisitions; bringing in increasing investment in core R&D activities. The global pharma and biotech industry has been looking at opportunities of cost effective drug development and India has emerged as a favorable location for drug development. In addition, India based drug companies have increased their capacity to develop and launch new drugs through their own research efforts. This has heightened the importance of developing adequate internal standards to conduct their operations to be able to compete with the globalization demands. Newer methods of

treatments are in development than ever before and finding better ways to demonstrate their effectiveness. Last few years have also seen an increase in drug safety concerns with some high profile drug withdrawals. This has led to formation of more stringent parameters for safety evaluation of products and therapies by various stakeholders more importantly by the regulatory authorities¹.

Drug development has also witnessed a significant change through new technologies such as genomics, proteomics, bioinformatics systems and new imaging technologies. These new technologies have the potential to provide tools to detect safety problems early, identify patients likely to respond to therapy and lead to new clinical

endpoints. New medical technologies, including bio-engineered tissues, cellular and gene therapies, nanotechnology applications, novel biomaterials and individualized drug therapies are being applied to get better therapeutic outcomes¹.

While there have been advancements in technology, regulations have been trying to keep pace with these changes. Significant changes in the regulatory system are needed to keep abreast with the changing trends in the industry for strengthening the authority with trained scientific and medical reviewers for various aspects of research².

Clinical trials are conducted to allow safety and efficacy data to be collected for health interventions to discover of a new drug. These trials can take place only after satisfactory information has been gathered on the quality of the non-clinical safety and approval from health authority or ethics committee of the concerning country where the trial is taking place³.

Depending on the type of product and the stage of its development, investigators enroll healthy volunteers and/or patients into small pilot studies initially; followed by larger scale studies in patients that often compare the new product with the currently prescribed treatment. As positive safety and efficacy data are gathered, the number of patients is typically increased. Clinical trials can vary in size from a single center in one country to multicenter trials in multiple countries³.

Overview

Clinical trials often involve patients with specific health conditions who then benefit from receiving otherwise unavailable treatments. In early phases, participants are healthy volunteers who receive financial incentives for their inconvenience. During dosing periods, study subjects typically remain on site at the unit for durations of anything from 1 to 30 days, occasionally longer, although is not always required⁴.

In planning a clinical trial, the sponsor or investigator first identifies the medication or device to be tested. Usually, one or more pilot experiments are conducted to gain

insights for design of the clinical trial to follow. In medical jargon, effectiveness is how well a treatment works in practice and efficacy is how well it works in a clinical trial. In the U.S., the elderly comprise only 14% of the population but they consume over one-third of drugs³. Despite this, they are often excluded from trials because their more frequent health issues and drug use produces unreliable data. Women, children, and people with unrelated medical conditions are also frequently excluded⁵.

In coordination with a panel of expert investigators, the sponsor decides what to compare the new agent with (one or more existing treatments or a placebo), and what kind of patients might benefit from the medication or device. If the sponsor cannot obtain enough patients with this specific disease or condition at one location, then investigators at other locations who can obtain the same kind of patients to receive the treatment would be recruited into the study³.

During the clinical trial, the investigators: recruit patients with the predetermined characteristics, administer the treatment(s), and collect data on the patients' health for a defined time period. These patients are voluntaries and they are not paid for participating in clinical trials. These data include measurements like vital signs, concentration of the study drug in the blood, and whether the patient's health improves or not. The researchers send the data to the trial sponsor who then analyzes the pooled data using statistical tests³.

Some examples of what a clinical trial may be designed to do:

- Assess the safety and effectiveness of a new medication or device on a specific kind of patient (e.g., patients who have been diagnosed with Alzheimer's disease)
- Assess the safety and effectiveness of a different dose of a medication than is commonly used (e.g., 10 mg dose instead of 5 mg dose)
- Assess the safety and effectiveness of an already marketed medication or device for a new indication, i.e. a disease for which the drug is not specifically approved

- Assess whether the new medication or device is more effective for the patient's condition than the already used, standard medication or device
- Compare the effectiveness in patients with a specific disease of two or more already approved or common interventions for that disease (e.g., Device A vs. Device B, Therapy A vs. Therapy B)

It is to be noted that while most clinical trials compare two medications or devices, some trials compare three or four medications, doses of medications or devices against each other. Except for very small trials limited to a single location, the clinical trial design and objectives are written into a document called a clinical trial protocol. The protocol is the 'operating manual' for the clinical trial, and ensures that researchers in different locations all perform the trial in the same way on patients with the same characteristics. A protocol is always used in multicenter trials. The clinical trial is designed to test hypotheses and rigorously monitor and assess what happens, it can be seen as the application of the scientific method to understanding human or animal biology³.

The most commonly performed clinical trials evaluate new drugs, medical devices (like a new catheter), biologics, psychological therapies, or other interventions. Clinical trials may be required before the national regulatory authority approves marketing of the drug or device, or a new dose of the drug, for use on patients³.

Beginning in the 1980s, harmonization of clinical trial protocols was shown as feasible across countries of the European Union. At the same time, coordination between Europe, Japan and the United States led to a joint regulatory-industry initiative on international harmonization named after 1990 as the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Currently, most clinical trial programs follow ICH guidelines, aimed to ensure good quality, safe and effective medicines in the most efficient and cost-effective manner.

These activities are pursued in the interest of the consumer and public health, to prevent unnecessary duplication of clinical trials in humans and to minimize the use of animal testing without compromising the regulatory obligations of safety and effectiveness⁶.

Types

The U.S. National Institutes of Health (NIH) organizes trials into five (5) different types⁷:

- *Prevention trials*: look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vitamins, vaccines, minerals, or lifestyle changes.
- *Screening trials*: test the best way to detect certain diseases or health conditions.
- *Diagnostic trials*: conducted to find better tests or procedures for diagnosing a particular disease or condition.
- *Treatment trials*: test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
- *Quality of life trials*: explore ways to improve comfort and the quality of life for individuals with a chronic illness.

Compassionate use trials or *expanded access*: provide partially tested, unapproved therapeutics prior to a small number of patients that have no other realistic options. Usually, this involves a disease for which no effective therapy exists, or a patient that has already attempted and failed all other standard treatments and whose health is so poor that he does not qualify for participation in randomized clinical trials. Usually, case by case approval must be granted by both the FDA and the pharmaceutical company for such exceptions³.

Design

A fundamental distinction in evidence-based medicine is between observational studies and randomized controlled trials. In observational studies, the investigators only observe associations (correlations) between the treatments experienced by participants and their health status or diseases. Currently, some Phase II and most Phase III drug trials are designed as randomized, double blind, and placebo-controlled³.

- Randomized: Each study subject is randomly assigned to receive either the study treatment or a placebo.
- Blind: The subjects involved in the study do not know which study treatment they receive. If the study is double-blind, the researchers also do not know which treatment is being given to any given subject. This 'blinding' is to prevent biases, since if a physician knew which patient was getting the study treatment and which patient was getting the placebo, he/she might be tempted to give the (presumably helpful) study drug to a patient who could more easily benefit from it. A form of double-blind study called a 'double-dummy' design allows additional insurance against bias or placebo effect. In this kind of study, all patients are given both placebo and active doses in alternating periods of time during the study.
- Placebo-controlled: The use of a placebo allows the researchers to isolate the effect of the study treatment.

Active comparator studies

Of note, during the last ten years or so it has become a common practice to conduct 'active comparator' studies. In other words, when a treatment exists that is clearly better than doing nothing for the subject; the alternate treatment would be a standard-of-care therapy. The study would compare the 'test' treatment to standard-of-care therapy³.

Clinical trial protocol

A clinical trial protocol is a document used to gain confirmation of the trial design

by a panel of experts and adherence by all study investigators, even if conducted in various countries. The protocol describes the scientific rationale, objective(s), design, methodology, statistical considerations, and organization of the planned trial. Details of the trial are also provided in other documents referenced in the protocol such as an 'Investigator's Brochure'³.

Every doctor or research center that takes part in the trial uses the same protocol. This ensures that patients are treated identically no matter where or if they are receiving treatment and that information from all the participating centers can be combined and compared⁸.

Design features

Informed consent

An essential component of initiating a clinical trial is to recruit study subjects following procedures using a signed document called "informed consent". It is a legally-defined process of a person being told about key facts involved in a clinical trial before deciding whether or not to participate. To fully describe participation to a candidate subject, the doctors and nurses involved in the trial explain the details of the study using terms the person will understand. Foreign language translation is provided if the participant's native language is not the same as the study protocol⁹.

Placebo groups

Merely giving a treatment can have nonspecific effects, and these are controlled for by the inclusion of a placebo group. Subjects in the treatment and placebo groups are assigned randomly and blinded as to which group they belong³.

Phases

Clinical trials involving new drugs are commonly classified into four phases. Each phase of the drug approval process is treated as a separate clinical trial. The drug-development process will normally proceed through all four phases over many years. If the drug successfully passes through

Phases I, II, and III, it will usually be approved by the national regulatory authority for use in the general population. Phase IV are 'post-approval' studies. Before pharmaceutical companies start clinical trials on a drug, they conduct extensive pre-clinical studies³.

Pre-clinical studies

It involves *in vitro* (test tube or cell culture) and *in vivo* (animal) experiments using wide-ranging doses of the study drug to obtain preliminary efficacy, toxicity and pharmacokinetic information. Such tests assist pharmaceutical companies to decide whether a drug candidate has scientific merit for further development as an investigational new drug³.

Phase 0

Phase 0 is a recent designation for exploratory, first-in-human trials conducted in accordance with the United States Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies¹⁰. Phase 0 trials are also known as human micro dosing studies and are designed to speed up the development of promising drugs or imaging agents by establishing very early on whether the drug or agent behaves in human subjects as was expected from preclinical studies. Distinctive features of Phase 0 trials include the administration of single subtherapeutic doses of the study drug to a small number of subjects (10 to 15) to gather preliminary data on the agent's pharmacokinetics (how the body processes the drug) and pharmacodynamics (how the drug works in the body)³.

A Phase 0 study gives no data on safety or efficacy, being by definition a dose too low to cause any therapeutic effect. Drug development companies carry out Phase 0 studies to rank drug candidates in order to decide which has the best pharmacokinetic parameters in humans to take forward into further development. They enable go/no-go decisions to be based on relevant human models instead of relying on sometimes

inconsistent animal data. Questions have been raised by experts about whether Phase 0 trials are useful, ethically acceptable, feasible, speed up the drug development process or save money, and whether there is room for improvement³.

Phase I

Phase I trials are the first stage of testing in human subjects. Normally, a small (20-100) group of healthy volunteers will be selected. This phase includes trials designed to assess the safety (Pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. These trials are often conducted in an inpatient clinic, where the subject can be observed by full-time staff. The subject who receives the drug is usually observed until several half-lives of the drug have passed. Phase I trials also normally include dose-ranging, also called dose escalation, studies so that the appropriate dose for therapeutic use can be found. The tested range of doses will usually be a fraction of the dose that causes harm in animal testing. Phase I trials most often include healthy volunteers. However, there are some circumstances when real patients are used, such as patients who have terminal cancer or HIV and lack other treatment options³.

There are different kinds of Phase I trial includes Single Ascending Dose (SAD) studies, Multiple Ascending Dose (MAD) studies, Food effect studies³.

Phase II

Once the initial safety of the study drug has been confirmed in Phase I trials, Phase II trials are performed on larger groups (20-300) and are designed to assess how well the drug works, as well as to continue Phase I safety assessments in a larger group of volunteers and patients. When the development process for a new drug fails, this usually occurs during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects. Phase II studies are sometimes divided into Phase

IIA to assess dosing requirements and Phase IIB to study efficacy³.

Phase III

Phase III studies are randomized controlled multicenter trials on large patient groups (300-3,000 or more depending upon the disease/medical condition studied) and are aimed at being the definitive assessment of how effective the drug is, in comparison with current 'gold standard' treatment. Because of their size and comparatively long duration, Phase III trials are the most expensive, time-consuming and difficult trials to design and run, especially in therapies for chronic medical conditions³.

It is common practice that certain Phase III trials will continue while the regulatory submission is pending at the appropriate regulatory agency. This allows patients to continue to receive possibly lifesaving drugs until the drug can be obtained by purchase. Other reasons for performing trials at this stage include attempts to obtain additional safety data, or to support marketing claims for the drug. Studies in this phase are by some companies categorized as 'Phase IIIB studies'¹¹.

Most drugs undergoing Phase III clinical trials can be marketed under FDA norms with proper recommendations and guidelines, but in case of any adverse effects being reported anywhere, the drugs need to be recalled immediately from the market. While most pharmaceutical companies refrain from this practice, it is not abnormal to see many drugs undergoing Phase III clinical trials in the market³.

Phase IV

Phase IV trial is also known as 'Post Marketing Surveillance Trial'. Phase IV trials involve the safety surveillance (Pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold. Phase IV studies may be required by regulatory authorities or may be undertaken by the sponsoring company for competitive (finding a new

market for the drug) or other reasons (for example, the drug may not have been tested for interactions with other drugs, or on certain population groups such as pregnant women, who are unlikely to subject themselves to trials). The safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and longer time period than was possible during the Phase I-III clinical trials. Harmful effects discovered by Phase IV trials may result in a drug being no longer sold, or restricted to certain uses: recent examples involve troglitazone (Rezulin) and rofecoxib (Vioxx).

Length

Clinical trials are only a small part of the research that goes into developing a new treatment. Potential drugs, for example, first have to be discovered, purified, characterized, and tested in labs (in cell and animal studies) before ever undergoing clinical trials. In all, about 1,000 potential drugs are tested before just one reaches the point of being tested in a clinical trial. Some reasons a clinical trial might last several years³.

Administration

Clinical trials designed by a local investigator and (in the U.S.) federally funded clinical trials are almost always administered by the researcher who designed the study and applied for the grant. Small-scale device studies may be administered by the sponsoring company. Phase III and Phase IV clinical trials of new drugs are usually administered by a contract research organization (CRO) hired by the sponsoring company. A CRO is a company that is contracted to perform all the administrative work on a clinical trial. It recruits participating researchers, trains them, provides them with supplies, coordinates study administration and data collection, sets up meetings, monitors the sites for compliance with the clinical protocol, and ensures that the sponsor receives 'clean' data from every site.

Ethical conduct

Clinical trials are closely supervised by appropriate regulatory authorities. All studies that involve a medical or therapeutic intervention on patients must be approved by a supervising ethics committee before permission is granted to run the trial. The local ethics committee has discretion on how it will supervise non-interventional studies. In the U.S., this body is called the Institutional Review Board (IRB). Most IRBs are located at the local investigator's hospital or institution, but some sponsors allow the use of a central (independent/for profit) IRB for investigators who work at smaller institutions. To be ethical, researchers must obtain the full and informed consent of participating human subjects. One of the IRB's main functions is ensuring that potential patients are adequately informed about the clinical trial. If the patient is unable to consent for him/herself, researchers can seek consent from the patient's legally authorized representative³.

Safety

Responsibility for the safety of the subjects in a clinical trial is shared between the sponsor, the local site investigators (if different from the sponsor), the various IRBs that supervise the study, and (in some cases, if the study involves a marketable drug or device) the regulatory agency for the country where the drug or device will be sold. For safety reasons, many clinical trials of drugs are designed to exclude women of childbearing age, pregnant women, and/or women who become pregnant during the study. In some cases the male partners of these women are also excluded or required to take birth control measures³.

Sponsor

Due to the sizable cost a full series of clinical trials may incur, the burden of paying for all the necessary people and services is usually borne by the sponsor who may be a governmental organization, a pharmaceutical or biotechnology company.

Throughout the clinical trial, the sponsor is responsible for accurately informing the local site investigators of the true historical safety record of the drug, device or other medical treatments to be tested, and of any potential interactions of the study treatment(s) with already approved medical treatments³.

Local site investigators

A physician's first duty is to his/her patients, and if a physician investigator believes that the study treatment may be harming subjects in the study, the investigator can stop participating at any time. On the other hand, investigators often have a financial interest in recruiting subjects and can act unethically in order to obtain and maintain their participation. The local investigators are responsible for conducting the study according to the study protocol and supervising the study staff throughout the duration of the study³.

IRBs

Approval by an IRB, or ethics board, is necessary before all but the most informal medical research can begin. The IRB scrutinizes the study for both medical safety and protection of the patients involved in the study, before it allows the researcher to begin the study. It may require changes in study procedures or in the explanations given to the patient³.

Regulatory agencies

If a clinical trial concerns a new regulated drug or medical device (or an existing drug for a new purpose), the appropriate regulatory agency for each country where the sponsor wishes to sell the drug or device is supposed to review all study data before allowing the drug/device to proceed to the next phase, or to be marketed. However, if the sponsor withholds negative data or misrepresents data it has acquired from clinical trials, the regulatory agency may make the wrong decision. In the U.S., the FDA can audit the files of local site investigators after they have finished participating in a study, to see

if they were correctly following study procedures³.

Accidents

In March 2006 the drug TGN1412 caused catastrophic systemic organ failure in the individuals receiving the drug during its first human clinical trials (Phase I) in Great Britain. Following this, an expert group on phase one clinical trials published a report³.

Economics

Sponsor

The cost of a study depends on many factors, especially the number of sites that are conducting the study, the number of patients required and whether the study treatment is already approved for medical use. Clinical trials follow a standardized process³.

Investigators

Many clinical trials do not involve any money. However, when the sponsor is a private company or a national health agency, investigators are almost always paid to participate³.

Patients

In Phase I drug trials; participants are paid because they give up their time (sometimes away from their homes) and are exposed to unknown risks, without the expectation of any benefit. In most other trials, however, patients are not paid, in order to ensure that their motivation for participating is the hope of getting better or contributing to medical knowledge, without their judgment being skewed by financial considerations³.

Participating in a clinical trial

Phase 0 and Phase I drug trials seek healthy volunteers. Most other clinical trials seek patients who have a specific disease or medical condition³.

Locating trials

Depending on the kind of participants required, sponsors of clinical trials use

various recruitment strategies, including patient databases, newspaper and radio advertisements, flyers, posters in places the patients might go (such as doctor's offices), and personal recruitment of patients by investigators³.

Steps for volunteers

Before participating in a clinical trial, interested volunteers should speak with their doctors, family members, and others who have participated in trials in the past. After locating a trial, volunteers will often have the opportunity to speak or e-mail the clinical trial coordinator for more information and to answer any questions. After receiving consent from their doctors, volunteers then arrange an appointment for a screening visit with the trial coordinator¹².

The problem comes if we as a research community knowingly enroll patients who fundamentally misunderstand the nature of these trials. Given our reliance on having them join in order to further our scientific purposes, moving forward with enrollment in such a context risks being viewed as conflicted and ethically suspect¹³.

All volunteers being considered for a trial are required to undertake a medical screen. There are different requirements for different trials, but typically volunteers will have the following tests³:

- Measurement of the electrical activity of the heart (ECG)
- Measurement of blood pressure, heart rate and temperature
- Blood sampling
- Urine sampling
- Weight and height measurement
- Drugs abuse testing
- Pregnancy testing (females only)

Criticism

Many drugs that are assumed to be effective are probably little better than placebos, but there is no way to know because:

- Negative results are hidden

- Favorable results were published and unfavorable results buried
- The public and the medical profession believed these drugs were potent

Clinical trials are also biased through designs for research that are chosen to yield favorable results for sponsors³.

Regulatory authorities

Over the years regulatory bodies issued numerous guidelines to assist in the development of new drug candidates. Not surprising, cultural characteristics and differing medical practices have led to some degree of disparity among these published guidelines. This is particularly apparent when comparing and contrasting guidelines derived in United States with those from Europe. Unlike guidelines issued in United States, European guidelines tend to be more general in nature and do not provide detailed instruction on such matter as studies design^{1,14}.

Regulatory authorities around the world

- Central Drug Standard Control Organization (CDSCO, India)
- United States food and drug administration (USFDA, USA)
- European Medicine Evaluation Agency (EMA, Europe)
- Medicines And Health Care Regulatory agency (MHRA, UK)
- Therapeutics good administration (TGA, Australia)
- National Pharmaceutical Control Bureau (NPCB, Malaysia)
- State and Food Drug Administration (SFDA, China)
- Medicines and Medical Devices Safety Authority (Medsafe, New Zealand)
- Medicine control council (MCC, South Africa)
- Pharmaceutical and medical devices agency (PMDA, Japan)

Central Drug Standard Control Organization (CDSCO, India)

Central Drugs Standard Control Organization (CDSCO) of India under the

Ministry of Health & Family Welfare, Govt. of India dedicated for setting of standards for drugs, pharmaceuticals and healthcare devices technologies etc. The regulatory authority will have to be equipped with well trained manpower to address the worries associated with application of emerging technologies associated with drug development¹⁵.

Functions undertaken by Central Government are as follows:

- Laying down standards of drugs, cosmetics, diagnostics and devices.
- Laying down regulatory measures, amendments to Acts and Rules.
- To regulate market authorization of new drugs.
- To regulate clinical research in India.
- To approve licenses to manufacture certain categories of drugs as Central License Approving Authority i.e. for Blood Banks, Large Volume Parenterals and Vaccines & Sera.
- To regulate the standards of imported drugs.
- Work relating to the Drugs Technical Advisory Board (DTAB) and Drugs Consultative Committee (DCC).
- Testing of drugs by Central Drugs Labs.
- Publication of Indian Pharmacopoeia.
- Coordinating the activities of the State Drugs Control Organizations to achieve uniform administration of the Act; and policy guidance.
- Guidance on technical matters.
- Participation in the WHO GMP certification scheme.
- Monitoring adverse drug reactions (ADR).
- Conducting training programmes for regulatory officials & Govt. Analysts.
- Distribution of quotas of narcotic drugs for use in medicinal formulations.
- Screening of drug formulations available in Indian market.
- Evaluation/Screening of applications for granting No Objection Certificates for export of unapproved/banned drugs.

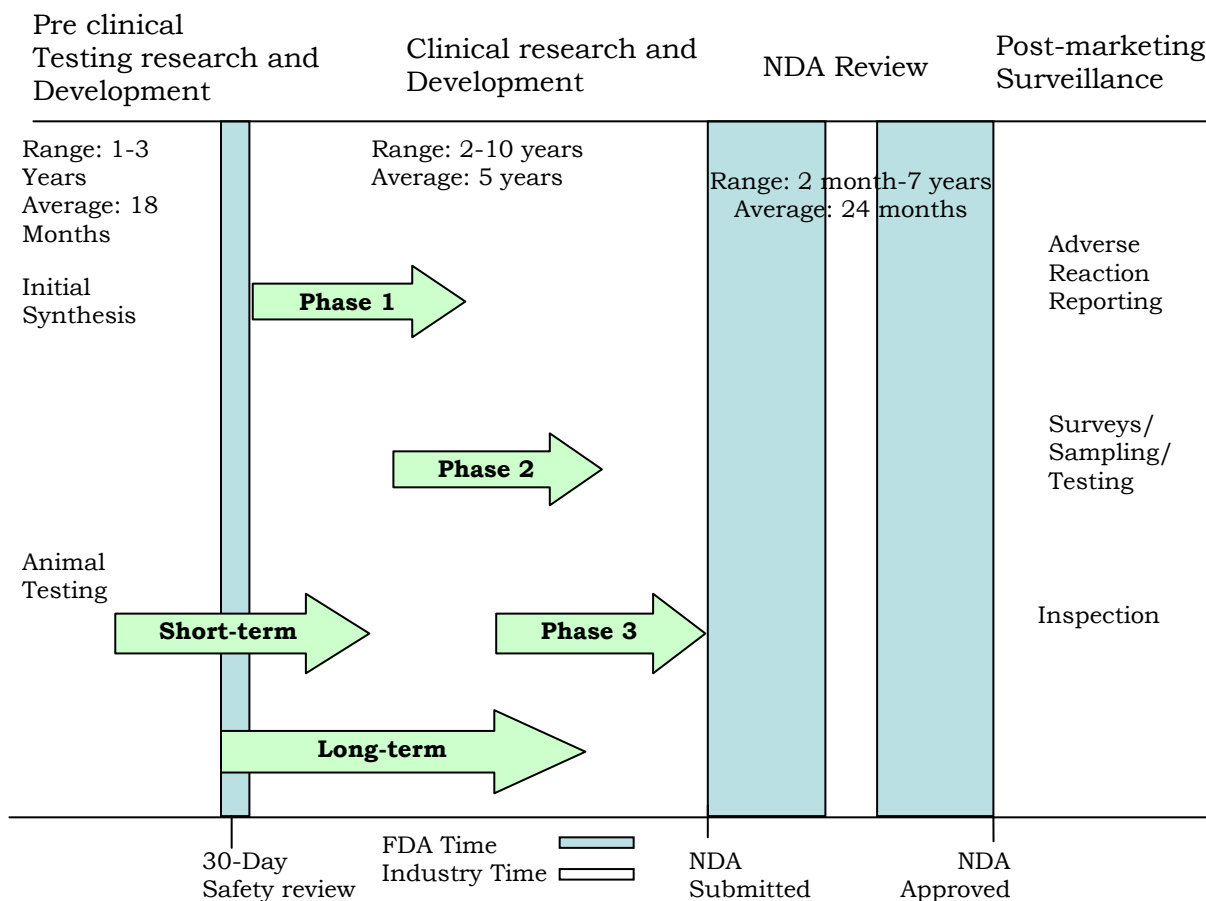


Figure 1: Outlines of different phases of clinical trial

Functions undertaken by State Governments are as follows:

- Licensing of drug manufacturing and sales establishments.
- Licensing of drug testing laboratories.
- Approval of drug formulations for manufacture.
- Monitoring of quality of Drugs & Cosmetics, manufactured by respective state units and those marketed in the state.
- Investigation and prosecution in respect of contravention of legal provisions.
- Administrative actions.
- Pre- and post- licensing inspection
- Recall of sub-standard drugs.

Under the Drug and Cosmetics Act, the regulation of manufacture, sale and distribution of drugs is primarily the concern of the State authorities while the central authorities are responsible for approval of new drugs, clinical trials in the country, laying down the standards for drugs, control over the quality of imported drugs, coordination of the activities of State Drug Control Organizations and providing expert advice with a view of bring about the uniformity in the enforcement of the Drugs and Cosmetics Act [16].

U.S. Food and Drug Administration (FDA)

It is an agency of the United States Department of Health and Human Services and is responsible for the safety regulation

of most types of foods, dietary supplements, drugs, vaccines, biological medical products, blood products, medical devices, radiation-emitting devices, veterinary products, and cosmetics¹⁷⁻¹⁸.

Conclusion

Above study was an attempt to compile the knowledge associated with different essential of clinical trial where regulatory authorities have taken important role specifically CDSCO for controlling clinical research in India. Different phases and importance of clinical trial was also discussed.

References

1. Jain N. K. (2005). "*Pharmaceutical Product Development*", Second Edition, CBS Publishers and distributor, New Delhi, pp 457-489.
2. <http://www.iir-events.com/IIR-conf/PTI/EventView.aspx?EventID=95> (Cited March 1, 2010).
3. http://en.wikipedia.org/wiki/Clinical_trial (Cited January 9, 2011).
4. <http://www.rateclinicaltrials.co.uk> (Cited January 10, 2011).
5. Spall H.G.V., A. Toren, A. Kiss, R.A. Fowler (2007). Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *J. Am. Med. Asso.* 297 (11), 1233-40.
6. <http://www.ich.org/cache/compo/276-254-1.html> (Cited January 30, 2009).
7. <http://clinicaltrials.gov/ct2/info/glossary> (Cited January 30, 2009).
8. <http://www.cancer.gov/clinicaltrials/education/how-trials-are-done> (Cited January 9, 2011).
9. <http://clinicaltrials.gov/ct2/info/understand> (Cited January 30, 2009).
10. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm078933.pdf>. (Cited July 18, 2010).
11. http://www.covance.com/periapproval/svc_phase3b.php. (Cited July 28, 2008).
12. http://www.pdtrials.org/en/participate_clinicalresearch_how (Cited December 12, 2009).
13. Kass N.E. (2008). Early phase clinical trials: communicating the uncertainties of 'magnitude of benefit' and 'likelihood of benefit'. *Clin. Trials* 5, 627-629.
14. Gupta S (2010). "*All you need to know about clinical research*", DNA PRESS, Gurgaon, pp. 158-165.
15. <http://www.google.co.in/search?hl=en&q=www.cdsco.nic+.in&meta=&aq=f&oq=w/> (Cited April 3, 2010).
16. <http://images http://www.cdsco.nic.in/html/organisationalchart.htm> (Cited April 3, 2010).
17. <http://www.foodsafety.gov/list.html> (Cited March 29, 2010).
18. http://en.wikipedia.org/wiki/State_Food_and_Drug_Administration.gov (Cited December 1, 2010).