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Review Article

CURRENT REGULATIONS FOR CLINICAL TRIALS**Devakar Rohit Chandrakant*, V. Lavanya**Department Of Regulatory Affairs, Princeton College Of Pharmacy, Pocharam, Hyderabad,
Telangana 500088.**Abstract:**

Clinical trials (CTs) are conducted to explore new methods of intervention that are better than the existing ones and can also be easily tolerated by patients. CTs are conducted in accordance with the regulatory guidelines recommended for the same by the drug regulatory authority of the country where they have to be conducted. In USA, CTs are regulated by USFDA as per their 21 code of federal regulations part 312 (CFR) of Federal Food, Drug, and Cosmetic act. In EU, they are regulated by European Commission and EMA as per their CT directive 2001/20/EC of the European Parliament and of the council of 4 April 2001 and GCP directive 2005/28/EC of 8 April 2005. In India, they are regulated by CDSCO (Schedule Y of the Drug and Cosmetics Rules, 1945) and ICMR (Ethical Guidelines for Biomedical Research on Human Subjects), respectively. In Singapore, CTs are regulated by HSA as per the Medicines Act and Medicines (Clinical Trials) Regulations Chapter 176, sections 18 and 74. The role of these authorities is to ensure the quality, safety, and effectiveness of all medicines in their respective countries. In this work, clinical trial regulations in USA, EU, India, and Singapore were compared on the basis of parameters such as regulatory bodies involved, regulations for CTs, clinical trial application format, application fee, approval time, the various forms required, role and responsibilities of IRB/IEC, record retention time, and GCP guidelines. The success rate of CTs in USA and Europe is higher in comparison to India, and Singapore which may be due to well-trained investigators, fast regulatory approval process and volunteer participation by the subjects. Some case studies related to the clinical trials conducted in these countries have also been incorporated.

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INTRODUCTION:

Clinical trials are prospective biomedical or behavioral research studies on human participants 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 dosage, 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 the therapy is 'safe' or effective, only that the trial may be conducted.

Depending on product type and development stage, investigators initially enroll volunteers or patients into small pilot studies, and subsequently conduct progressively larger scale comparative studies. Clinical trials can vary in size and cost, and they can involve a single research center or multiple centers, in one country or in multiple countries. Clinical study design aims to ensure the scientific validity and reproducibility of the results.

Costs for clinical trials can range into the billions of dollars per approved drug.² The sponsor may be a governmental organization or a pharmaceutical, biotechnology or medical device company. Certain functions necessary to the trial, such as monitoring and lab work, may be managed by an outsourced partner, such as a contract research organization or a central laboratory. Only 10 percent of all drugs started in human clinical trials become approved drugs.³

Trials of drugs

Some clinical trials involve healthy subjects with no pre-existing medical conditions. Other clinical trials pertain to people with specific health conditions who are willing to try an experimental treatment. Pilot experiments are conducted to gain insights for design of the clinical trial to follow.

There are two goals to testing medical treatments: to learn whether they work well enough, called "efficacy" or "effectiveness"; and to learn whether they are safe enough, called "safety". Neither is an absolute criterion; both safety and efficacy are evaluated relative to how the treatment is intended to be used, what other treatments are available, and the severity of the disease or condition. The benefits must outweigh the risks.^{4,5} For example, many drugs to treat cancer have severe side effects that would not be acceptable for an over-the-counter pain medication, yet the cancer drugs have been approved since they are used under a physician's care and are used for a life-threatening condition.⁶

In the US, the elderly constitute 14% of the population, while they consume over one-third of drugs.⁷ People over 55 (or a similar cutoff age) are often excluded from trials because their greater health issues and drug use complicate data interpretation, and because they have different physiological capacity than younger people. Children and people with unrelated medical conditions are also frequently excluded.⁸ Pregnant women are often excluded due to potential risks to the fetus.

The sponsor designs the trial in coordination with a panel of expert clinical investigators, including what alternative or existing treatments to compare to the new drug and what type(s) of patients might benefit. If the sponsor cannot obtain enough test subjects at one location investigators at other locations are recruited to join the study.

During the trial, investigators recruit subjects with the predetermined characteristics, administer the treatment(s) and collect data on the subjects' health for a defined time period. Data include measurements such as vital signs, concentration of the study drug in the blood or tissues, changes to symptoms, and whether improvement or worsening of the condition targeted by the study drug occurs. The researchers send the data to the trial sponsor, who then analyzes the pooled data using statistical tests.

Examples of clinical trial goals include assessing the safety and relative effectiveness of a medication or device:

- On a specific kind of patient
- At varying dosages
- For a new indication
- Evaluation for improved efficacy in treating a condition as compared to the standard therapy for that condition
- Evaluation of the study drug or device relative to two or more already approved/common interventions for that condition

While most clinical trials test one alternative to the novel intervention, some expand to three or four and may include a placebo.

Except for small, single-location trials, the design and objectives are specified in a document called a clinical trial protocol. The protocol is the trial's "operating manual" and ensures all researchers perform the trial in the same way on similar subjects and that the data is comparable across all subjects.

As a trial is designed to test hypotheses and rigorously monitor and assess outcomes, it can be seen as an application of the scientific method, specifically the experimental step.

The most common clinical trials evaluate new pharmaceutical products, medical devices, biologics, psychological therapies, or other interventions. Clinical

trials may be required before a national regulatory authority⁹ approves marketing of the innovation.

Trials of devices

Similarly to drugs, manufacturers of medical devices in the United States are required to conduct clinical trials for premarket approval.¹⁰ Device trials may compare a new device to an established therapy, or may compare similar devices to each other. An example of the former in the field of vascular surgery is the Open versus Endovascular Repair (OVER trial) for the treatment of abdominal aortic aneurysm, which compared the older open aortic repair technique to the newer endovascular aneurysm repair device.¹¹ An example of the latter are clinical trials on mechanical devices used in the management of adult female urinary incontinence.¹²

Trials of procedures

Similarly to drugs, medical or surgical procedures may be subjected to clinical trials,¹³ such as case-controlled studies for surgical interventions.¹⁴

Types

Clinical trials are classified by the research objective created by the investigators.¹⁵

- In an observational study, the investigators observe the subjects and measure their outcomes. The researchers do not actively manage the study.¹⁶
- In an interventional study, the investigators give the research subjects an experimental drug, surgical procedure, use of a medical device, diagnostic or other intervention to compare the treated subjects with those receiving no treatment or the standard treatment. Then the researchers assess how the subjects' health changes.¹⁶

Trials are classified by their purpose. After approval for human research is granted to

the trial sponsor, the U.S. Food and Drug Administration (FDA) organizes and monitors the results of trials according to type:¹⁵

- Prevention trials look for ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include drugs, vitamins or other micronutrients, vaccines, or lifestyle changes.
- Screening trials test for ways to identify certain diseases or health conditions.
- Diagnostic trials are conducted to find better tests or procedures for diagnosing a particular disease or condition.
- Treatment trials test experimental drugs, new combinations of drugs, or new approaches to surgery or radiation therapy.
- Quality of life trials (supportive care trials) evaluate how to improve comfort and quality of care for people with a chronic illness.
- Genetic trials are conducted to assess the prediction accuracy of genetic disorders making a person more or less likely to develop a disease.
- Epidemiological trials have the goal of identifying the general causes, patterns or control of diseases in large numbers of people.

Clinical trials are conducted typically in four phases, with each phase using different numbers of subjects and having a different purpose to construct focus on identifying a specific effect.¹⁵

Phases

Clinical trials involving new drugs are commonly classified into five phases. Each phase of the drug approval process is treated as a separate clinical trial. The drug development process will normally

- Compassionate use trials or expanded access trials provide partially tested, unapproved therapeutics to a small number of patients who have no other realistic options. Usually, this involves a disease for which no effective therapy has been approved, or a patient who has already failed all standard treatments and whose health is too compromised to qualify for participation in randomized clinical trials.¹⁷ Usually, case-by-case approval must be granted by both the FDA and the pharmaceutical company for such exceptions.
- Fixed trials consider existing data only during the trial's design, do not modify the trial after it begins, and do not assess the results until the study is completed.
- Adaptive clinical trials use existing data to design the trial, and then use interim results to modify the trial as it proceeds. Modifications include dosage, sample size, drug undergoing trial, patient selection criteria and "cocktail" mix.¹⁸ Adaptive trials often employ a Bayesian experimental design to assess the trial's progress. In some cases, trials have become an ongoing process that regularly adds and drops therapies and patient groups as more information is gained.¹⁹ The aim is to more quickly identify drugs that have a therapeutic effect and to zero in on patient populations for whom the drug is appropriate.^{20,21}

proceed through phases I–IV over many years, frequently involving a decade or longer. 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.¹⁵ Phase IV trials are performed after the newly approved drug, diagnostic or device is marketed, providing assessment about risks, benefits, or best uses.¹⁵

Table 1: Phases of Clinical Trials

Phase	Aim	Notes
Phase 0	Pharmacodynamics and pharmacokinetics in humans	Phase 0 trials are optional first-in-human trials. Single subtherapeutic doses of the study drug or treatment are given to a small number of subjects (typically 10 to 15) to gather preliminary data on the agent's pharmacodynamics (what the drug does to the body) and pharmacokinetics (what the body does to the drugs). ²² For a test drug, the trial documents the absorption, distribution, metabolization, and clearance (excretion) of the drug, and the drug's interactions within the body, to confirm that these appear to be as expected.
Phase I	Screening for safety	Often are first-in-person trials. Testing within a small group of people (typically 20–80) to evaluate safety, determine safe dosage ranges, and identify side effects. ¹⁵
Phase II	Establishing the preliminary efficacy of the drug in a "treatment group", usually against a placebo control group	Phase IIa is specifically designed to assess dosing requirements (how much drug should be given), ^{[29} while a Phase IIb trial is designed to determine efficacy, and studies how well the drug works at the prescribed dose(s), establishing a therapeutic dose range. ^{15,23}
Phase III	Final confirmation of safety and efficacy	Testing with large groups of people (typically 1,000–3,000) to confirm its efficacy, evaluate its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow it to be used

		safely. ¹⁵
Phase IV	Safety studies during sales	Postmarketing studies delineate risks, benefits, and optimal use. As such, they are ongoing during the drug's lifetime of active medical use. ¹⁵

Types and Phases of Clinical Trials

Clinical trials are studies to test new drugs, already approved drugs, devices, or other forms of treatments. Many clinical trials look at new ways to detect, diagnose, or measure the extent of disease. Some even look at ways to prevent diseases from happening. Researchers still use human volunteers to test these methods, and the same rules apply.

Doctors use clinical trials to learn whether a new drug, treatment, or combination works and is safe to use for people. Clinical trials are important in developing new treatments for serious diseases like cancer. All new treatments must go through clinical trials before being approved by the Food and Drug Administration (FDA). Cancer clinical trials can take years to complete. It can take months, if not years, to see if a cancer treatment does what it is meant to do.

Why do we need clinical trials?

Clinical trials show us what works (and what doesn't) in medicine and health care. They are the best way to learn what works in treating diseases like cancer. Clinical trials are designed to answer some important questions:

- Does the new treatment work in people? If it does, doctors will also look at how well it works. Is it better than treatment now being used? If it's not better, is it as good and cause fewer side effects? Or does it work in some people who aren't helped by current treatments?
- Is the new treatment safe? No treatment or procedure – even one

already in common use – is without risk. But do the benefits of the new treatment outweigh the risks?

- Is this treatment better than the standard treatment given for this disease? Clinical trials help show if a new drug or treatment, or a new treatment combination, works better than what is now used.

Answering these questions, while giving as few people as possible an unknown treatment, often requires several clinical trials in different “phases.” Each phase is designed to answer certain questions while keeping the people taking part as safe as possible. Results from these phases show if the new drug or treatment is reasonably safe and effective.

Pre-clinical (or laboratory) studies

Clinical trials are done only after pre-clinical findings suggest that the new drug or treatment is likely to be safe and will work in people.

Pre-clinical studies, also called laboratory studies, include:

- Cell studies: These are often the first tests done on a new treatment. To see if it might work, researchers look for effects of the new treatment on cancer cells that are grown in a lab dish or a test tube. These studies may be done on human cancer cells or animal cancer cells.
- Animal studies: Treatments that look promising in cell studies are tested next on cancers in live animals. This gives researchers an idea of how safe the new treatment is in a living creature.

Pre-clinical studies give a lot of useful information, but not all that is needed. Humans and mice can be very different in the way they absorb, process, and get rid of drugs or treatments. A treatment that works against cancer in a mouse might or might not work in people. There could also be side effects and other problems that didn't show up when the treatment was used in mice but could show up in people. If the pre-clinical studies are completed and the treatment still seems promising, the US Food and Drug Administration (FDA) must give permission before the treatment can be tested people.

The investigational new drug (IND) application

Before a clinical trial can be started, the research must be approved. An investigational new drug or IND application or request must be filed with the FDA when researchers want to study a drug in humans. The IND application must contain certain information, such as:

- Results from studies so that the FDA can decide whether the treatment is safe for testing in people.
- How the drug is made, who makes it, what's in it, how stable it is, and more.
- Detailed outlines for the planned clinical studies, called study protocols, are reviewed to see if people might be exposed to needless risks.
- Details about the clinical trial team to see if they have the knowledge and skill to run clinical trials.

The research sponsor must commit to getting informed consent from everyone on the clinical trial. They must also commit to having the study reviewed by an institutional review board (IRB) and following all the rules required for studying investigational new drugs

Phases of clinical trials

Clinical trials are usually conducted in phases that build on one another. Each phase is designed to answer certain questions. Knowing the phase of the clinical trial is important because it can give you some idea about how much is known about the treatment being studied. There are benefits and risks to taking part in each phase of a clinical trial.

Although there are clinical trials for devices as well as other diseases and treatments, drugs for cancer patients are used in the examples of clinical trial phases described here.

Phase 0 clinical trials: Exploring if and how a new drug may work

Even though phase 0 studies are done in humans, this type of study isn't like the other phases of clinical trials. The purpose of this phase is to help speed up and streamline the drug approval process. Phase 0 studies may help researchers find out if the drugs do what they're expected to do. This may help save time and money that would have been spent on later phase trials.

Phase 0 studies use only a few small doses of a new drug in a few people. They might test whether the drug reaches the tumor, how the drug acts in the human body, and how cancer cells in the human body respond to the drug. People in these studies might need extra tests such as biopsies, scans, and blood samples as part of the process.

Unlike other phases of clinical trials, there's almost no chance the people in phase 0 trials will benefit. The benefit will be for other people in the future. And because drug doses are low, there's also less risk to those in the trial.

Phase 0 studies aren't widely used, and there are some drugs for which they wouldn't be helpful. Phase 0 studies are very small, often with fewer than 15 people, and the drug is given only for a

short time. They're not a required part of testing a new drug.

Phase I clinical trials: Is the treatment safe?

Phase I studies of a new drug are usually the first that involve people. Phase I studies are done to find the highest dose of the new treatment that can be given safely without causing severe side effects. Although the treatment has been tested in lab and animal studies, the side effects in people can't be known for sure. These studies also help to decide on the best way to give the new treatment.

Key points of phase I clinical trials

- The first few people in the study get a very low dose of the treatment and are watched very closely. If there are only minor side effects, the next few participants get a higher dose. This process continues until doctors find a dose that's most likely to work while having an acceptable level of side effects.
- Phase I trials are also looking at what the drug does to the body and what the body does with the drug.
- Safety is the main concern. The research team keeps a close eye on the people and watches for any severe side effects. Because of the small numbers of people in phase I studies, rare side effects may not be seen until later phases of trials when more people receive the treatment.
- While some people may benefit from being on one, disease response is not the main purpose of a phase I trial,
- Placebos (inactive treatments) are not used in phase I trials.
- Phase I trials usually include a small number of people (up to a few dozen).

- Phase I trials most often include people with different types of cancer.
- These studies are usually done in major cancer centers.

Phase I trials carry the most potential risk. But phase I studies do help some patients. For those with life-threatening illnesses, weighing the potential risks and benefits carefully is key. Sometimes people choose to join phase I trials when all other treatment options have already been tried.

Phase II clinical trials: Does the treatment work?

If a new treatment is found to be safe in phase I clinical trials, a phase II clinical trial is done to see if it works in certain types of cancer. The benefit the doctors look for depends on the goal of the treatment. It may mean the cancer shrinks or disappears. Or it might mean there's a long period of time where the cancer doesn't get any bigger, or there's a longer time before the cancer comes back. In some studies, the benefit may be an improved quality of life. Many clinical trials look to see if people getting the new treatment live longer than most people do without the treatment.

Key points of phase II clinical trials

- A group of 25 to 100 patients with the same type of cancer get the new treatment in a phase II study. They're treated using the dose and method found to be the safest and most effective in phase I studies.
- Usually in a phase II clinical trials, everyone gets the same dose. But some phase II studies randomly assign people to different treatment groups. These groups may get different doses or get the treatment in different ways to see which provides the best balance of safety and response.
- Placebos (inactive treatments) are not used in phase II trials.

- Phase II studies may be done at major cancer centers, community hospitals or even doctors' offices.

Larger numbers of patients get the treatment in phase II trials, so less common side effects may be seen. If enough patients benefit from the treatment, and the side effects aren't too bad, phase III clinical trials are begun.

Phase III clinical trials: Is it better than what's already available?

Treatments that have been shown to work in phase II clinical trials must succeed in one more phase before they're approved for general use. Phase III clinical trials compare the safety and effectiveness of the new treatment against the current standard treatment.

Because doctors do not yet know which treatment is better, study participants are often picked at random (called **randomized**) to get either the standard treatment or the new treatment. When possible, neither the doctor nor the patient knows which of the treatments the patient is getting. This type of study is called a **double-blind study**. Randomization and blinding are discussed in more detail later.

AIM AND OBJECTIVE:

Aim:

- The goal of clinical research is to develop knowledge that improves human health or increases understanding of human biology. People who take part in clinical research make it possible for this to occur. The path to finding out if a new drug is safe or effective is to test it on patients in clinical trials.
- The purpose of clinical trials is to find ways to more effectively prevent, diagnose, or treat disease. Every medication, vaccine, and procedure that is used in modern medicine was once studied as a part of a clinical trial.
- Clinical trials involve the testing

of intervention in human subjects with the aim of evaluating safety and efficacy of the intervention in humans. Interventions can include drugs, medical devices, procedures and vaccines. Since CTs involves the participation of patients and healthy volunteers as the subjects of the study, so they are highly regulated in all the countries.

The objectives of this work are as follows:

1. To study the regulatory guidelines for conducting CTs in regulated and semi-regulated countries.
2. Comparison of clinical trial regulations in these countries.
3. Regulated countries chosen for this work were USA and EU. Semi-regulated countries chosen were India and Singapore.

CONCLUSION:

Clinical trials are the key tools in new drug evaluation. India has signed the trade related intellectual property rights (TRIPS) agreement as a part of the WTO regulations to gearing up to attract more and more researchers from around the world to conduct clinical trials in India. Recent amendments in the regulatory requirements have shifted the thrust from just safeguarding the subjects to providing them for access for biomedical innovation. India is poised to offer the global pharmaceutical industry high quality & cost effective contract services to support drug discovery.

It can be concluded that regulated countries such as USA and EU have better established guidelines in comparison to semi-regulated countries like India and Singapore. In USA, CTs are highly regulated through their federal agencies. Data related to CTs also is recorded electronically and soon in USA they are

going to enforce eCTD format for submission of IND application, which will eventually speed up approval process. In Europe, CTs are regulated by EMA and EC. There, it is mandatory to submit IMPD application and other CT related data in CTD and eCTD format respectively. In USA and Europe, ICH-GCP guidelines are followed for conduct the CTs. In case of semi-regulated countries such as India and Singapore neither are their guidelines for CTs fully developed and nor do they follow internationally accepted standards, till now. In both countries, CTD format is yet not adopted for submission of clinical trial applications, which leads to delay for getting approval for start the CTs. In these countries, CTs are conducted according to national guidelines. The ICH-GCP guidelines are also not fully.

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REFERENCES:

1. "Clinical Trials" (PDF). Bill and Melinda Gates Foundation. Retrieved 1 January 2014.
2. Dimasi, Joseph A; Grabowski, Henry G; Hansen, Ronald W (2016). "Innovation in the pharmaceutical industry: New estimates of R&D costs". *Journal of Health Economics*. 47: 20–33. doi:10.1016/j.jhealeco.2016.01.012. hdl:10161/12742. PMID 26928437.
3. Emanuel EJ (9 September 2015). "The Solution to Drug Prices". *The New York Times*. Of the drugs started in clinical trials on humans, only 10 percent secure F.D.A. approval. ...
4. FDA Page last updated 25 April 2014 FDA's Drug Review Process: Continued
5. PhRMA. February 2007 Drug Discovery and Development
6. Merck Manual. Last full review/revision October 2013 by Daniel A. Hussar, PhD Overview of Over-the-Counter Drugs
7. Avorn J. (2004). *Powerful Medicines*, pp. 129–33. Alfred A. Knopf.
8. Van Spall HG, Toren A, Kiss A, Fowler RA (March 2007). "Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review". *JAMA*. 297 (11): 1233–40. doi:10.1001/jama.297.11.1233. PMID 17374817.
9. The regulatory authority in the USA is the Food and Drug Administration; in Canada, Health Canada; in the European Union, the European Medicines Agency; and in Japan, the Ministry of Health, Labour and Welfare
10. "Medical Devices, Premarket Clinical Studies for Investigational Device Exemption". US Food and Drug Administration. 17 March 2017. Retrieved 2 October 2017.