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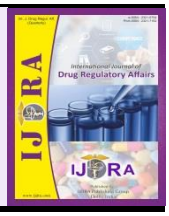

Review Article

Comparative study of updated Clinical Trial Regulations in India with respect to Australia, Europe, Japan and US

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Abstract

The national regulatory authorities, such as the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), Central Drugs Standard Control Organization and the Australian Therapeutic Goods Administration (TGA), approve every drug that is prescribed for patients around the world. The process of approval undertaken by pharmaceutical companies for drug candidates consists of a series of phases to ensure the product is safe and effective at treating the disease.

In this paper, we will compare the clinical trial regulations of India with respect to Australia, Europe, Japan & USA in order to determine the safety and efficacy of pharmaceutical products like drugs, biologics and medical devices in different geographical regions and to confirm the clinical trials studies follow strict scientific standards.

Keywords: Clinical Trials, Post Marketing Surveillance, FDA, CDSCO, EMA, TGA, MHWF, Regulatory Framework, Institutional Review Board, CTX Application, Investigational New Drug Application

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1. Introduction

Any investigation or research that involves one or more human subjects, undertaken to assess/evaluate the safety or effectiveness of an investigational medicinal product. (1)

A clinical trial, also known as a clinical research study, is a protocol to evaluate the effects and efficacy of experimental medical treatments or behavioural interventions on health outcomes. The purpose of a clinical trial is to determine if a new treatment or test or a potential drug or medical device works and is safe. (2)

Clinical trials explore how a treatment reacts in the human body and are designed to ensure a drug is tolerated and effective before it is licensed by regulatory authorities and made available for use by doctors. Studies vary in their primary goal or endpoint, the number of patients involved, and the specifics of the study design. However, all clinical studies confirm to a strict set of criteria to protect the patients involved and to ensure rigorous evaluation of the drug.

For safety purposes, clinical trials start with small groups of patients to find out whether a new approach causes any harm. In later phases of clinical trials, researchers learn more about the new approach's risks and benefits. (3)

1.1 Clinical Trial Phases

Phase 0 Clinical Trial

A phase 0 trial is the first trial where a proposed drug is used on a very small number of human volunteers. Phase 0 trials are the first clinical trials done among people. They aim to learn how a drug is processed in the body and how it affects the body. (4)

Phase I Clinical Trial

Phase I studies of a new drug are usually the first that involve people. The main reason for doing phase I studies is to find the highest dose of the new treatment that can be given safely without serious side effects. These studies also help to decide on the best way to give the new treatment. (5)

Phase II Clinical Trial

Phase II studies test the efficacy of a drug or device. Phase 2 trials are usually randomized, controlled studies evaluating the safety and efficacy of a drug for a particular condition and involve participants selected

using narrow criteria, to allow close monitoring of a relatively homogenous patient population. One of the main goals of phase 2 trials is to determine an appropriate dose and treatment regimen that can be tested in phase 3 trials. (6)

Phase III clinical trial

Treatments that have been shown to work in phase II studies usually must succeed in one more phase of testing before they are approved for general use. Phase III clinical trials compare the safety and effectiveness of the new treatment against the current standard treatment. (5,7)

Phase IV Clinical Trial: (Post Marketing Surveillance)

Phase IV trials, otherwise known as post-marketing surveillance, occur after the experimental drug has been approved and marketed. This stage offers manufacturers further insight into the medication's comparison against other treatments currently on the market. Phase IV trials also serve to highlight the long-term benefits of the treatment in a much larger patient population size. (8)

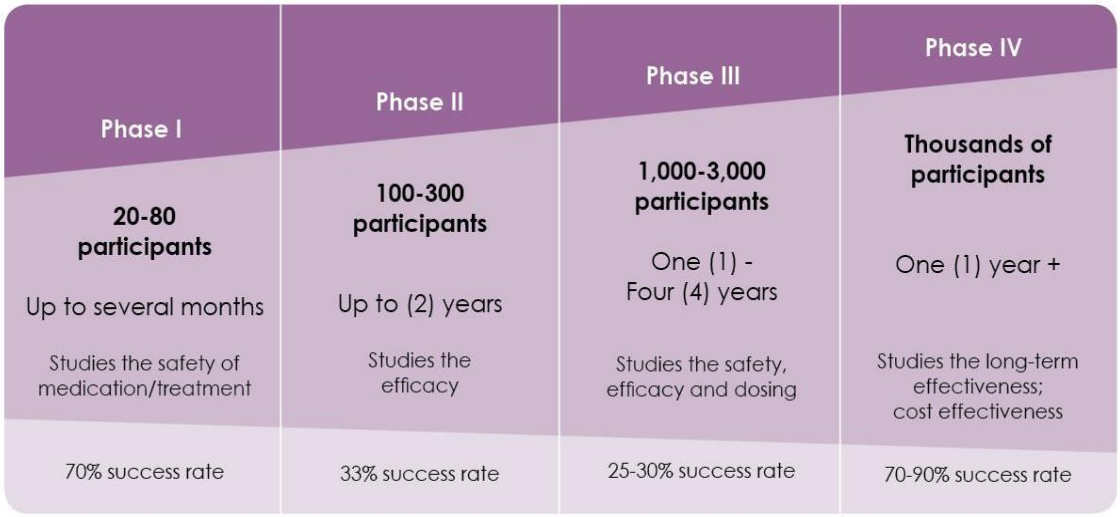

Figure 1. Clinical Trial Phases

1.2 Regulatory framework in India

As per CDSCO, Clinical Trial means a systematic study of any new drug in human subject to generate data for discovering and verifying the clinical, pharmacological (including pharmacodynamics and pharmacokinetic), and adverse effects with the objective of determining safety and efficacy of the new drug. (9)

In India, the Central Drugs Standard Control Organization (CDSCO) which comes under the Ministry of Health and Family Welfare (MHWF) (10) is the main body which works on development of regulatory procedures and standards for drugs, cosmetics, diagnostics and devices. It lays down regulatory guidance by amending acts and rules; and regulates new drug approval process. Its main objective is to standardize clinical research and bring safer drugs to the Indian market.

The Drug Controller General of India (DCGI) (11) is responsible for giving regulatory permissions for the conduct of clinical trials and is responsible for approval of marketing licenses for drugs in India. Along with the DCGI office, there are other governmental bodies involved in the pharmaceutical regulations of the new drugs. (12)

1.3 Regulatory framework in US

According to the National Institutes of Health (NIH), a clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of those interventions on health-related biomedical or behavioural outcomes. (13)

Food & Drug Administration (FDA) (14) is the regulatory authority that regulates clinical investigations of medical products in the United States (US). USFDA plays an important role in reviewing and authorizing Investigational New drug applications (INDs) (15) to conduct clinical trials using investigational drug or biological products in humans. Federal Food, Drug, and Cosmetic Act (FD&C Act) (June 25, 1938) is the main regulatory law for conducting clinical trials in US. (16)

1.4 Regulatory framework in EU (European Union)

As per DIRECTIVE 2001/20/EC of EU (European Union), any investigation in human subjects intended to discover or verify the clinical, pharmacological and other pharmacodynamics effects of one or more investigational medicinal product, and to identify any adverse reactions to one or more investigational medicinal product and to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product with the object of ascertaining its (their) safety and efficacy. (17) Clinical trial in EU (European Union) regulated under the Clinical Trial Regulation (Regulation (EU) No 536/2014 which repeal the earlier Clinical Trials Directive 2001/20/EC. (18)

1.5 Regulatory framework in Australia

As per TGA, Clinical trial (synonyms: clinical study, intervention study) is a planned study in humans of an intervention (including a medicine, treatment or diagnostic procedure) with the object of investigating

safety or efficacy and designed to achieve at least one of the following:

- the discovery or verification of clinical, pharmacological and other pharmacodynamics effects
- the identification of adverse reactions or adverse effects
- the study of absorption, distribution, metabolism and excretion. (19)

Therapeutic Goods Administration (TGA) is the regulatory body in Australia. To conduct a clinical trial in Australia, the trial must have an Australian sponsor. The main governing laws for conducting clinical trials in Australia are following:

- Therapeutic Goods Act 1989 (20)
- Therapeutic Goods Regulations 1990 (21)

1.6 Regulatory Framework in Japan

Clinical trials in Japan are regulated under the Pharmaceutical Affairs Law.

Pharmaceuticals and Medical Devices Agency (PMDA) is the regulatory agency within the Ministry of Health, Labor and Welfare (MHLW) which regulate the clinical trials in Japan. (22)

2. Clinical Trials study in various countries

The study is based on guidelines and approval process for the clinical trials in various countries.

1. CDSCO for India (23)

2. USFDA for USA (24)

3. EMA for European Union (25)

4. TGA for Australia (26)

5. PMDA & MHLW for Japan (27)

2.1 India

Central Drugs Standard Control Organization (CDSCO) is the regulatory authority responsible for clinical trial oversight, approval and inspections in India. (23) Drugs Controller General of India (DCGI) heads CDSCO is responsible for granting permission for clinical trials to be conducted and for regulating the sale and importation of drugs for use in clinical trials. The DCGI is commonly referred to as the Central Licensing Authority in the Indian regulations. (28) CDSCO functions under the Directorate General of Health Services (DGHS), which is part of the Ministry of Health and Family Welfare (MOHFW). (29) Drugs Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC) advise the DCGI. (30)

Timeline of Review

DCGI constitutes one or more of these expert committees or group of experts to evaluate scientific and technical drug-related issues, the committee/group may submit its recommendations within 60 days from the date of the request. (28)

Upon receipt of a clinical trial application, the DCGI has 90 calendar days to evaluate the application for drugs developed outside India and 30 days for drugs discovered, researched, and manufactured in India. If the DCGI does not respond within 30 days to applications for drugs developed in India, the sponsor (applicant) may conclude that permission to conduct the trial has been granted. (31)

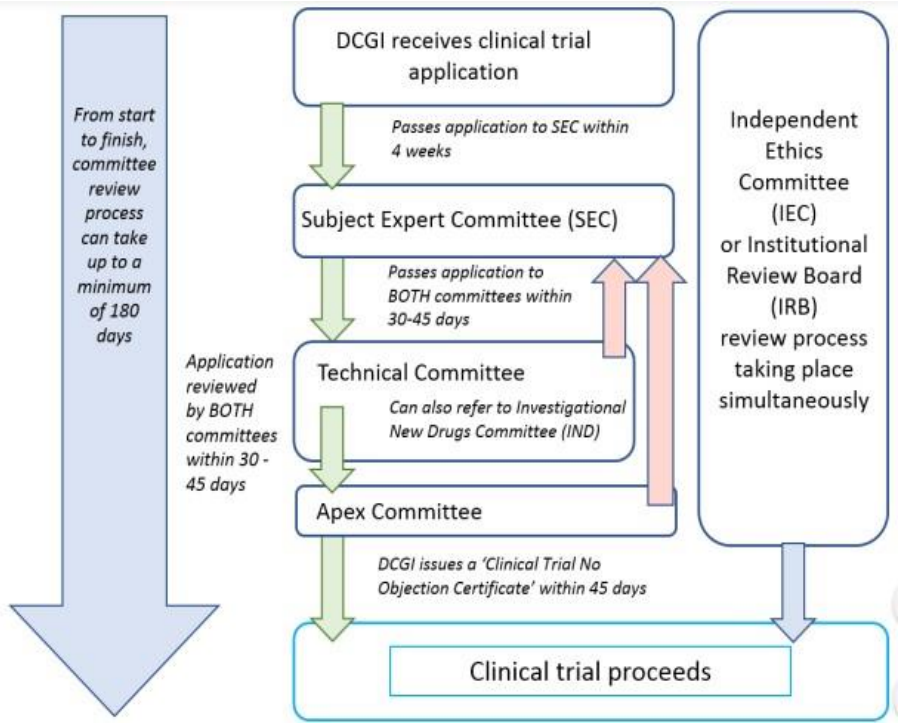

Figure 2. Flow chart for Clinical trial approval process in India

The DCGI, with the approval of the Central Government, may waive the requirement to conduct a local trial for a new drug already approved outside India. The waiver will be considered for applications submitted to conduct a trial with a new drug already approved in certain countries, as specified in periodic orders.

The DCGI plans to issue periodic orders to specify the countries that may be eligible for this waiver. For countries that do not meet the waiver eligibility requirements, that these applications shall be approved by the DCGI within 90 working days from the date of application receipt. Once the sponsor (applicant) obtains approval, he/she must inform CDSCO prior to initiating the clinical trial via Form **CT-4 (Annexure 1).** (32)

The DCGI's permission to initiate a clinical trial granted via either Form CT-06 or as an automatic approval via Form CT-4A shall remain valid for two years from the date of its issue, unless extended by the DCGI. (33)

CDSCO's review and approval process operates as a three-tiered system. The Subject Expert Committee (SEC) or IND committees initially evaluate clinical trial applications and new drugs. At the second level, the SEC's/IND's recommendations are reviewed by the Technical Committee (TC), which consists of experts from various therapeutic areas. At the third level, the Apex Committee conducts the final review and approves the application based on the TC's recommendations. Upon receipt of the Apex Committee's approval, the DCGI then issues final approval to the sponsor (applicant). (34)

2.2 USA

Food & Drug Administration (FDA) is the regulatory authority that regulates clinical investigations of medical products in the United States (US) and this is commonly called as USFDA. (35)

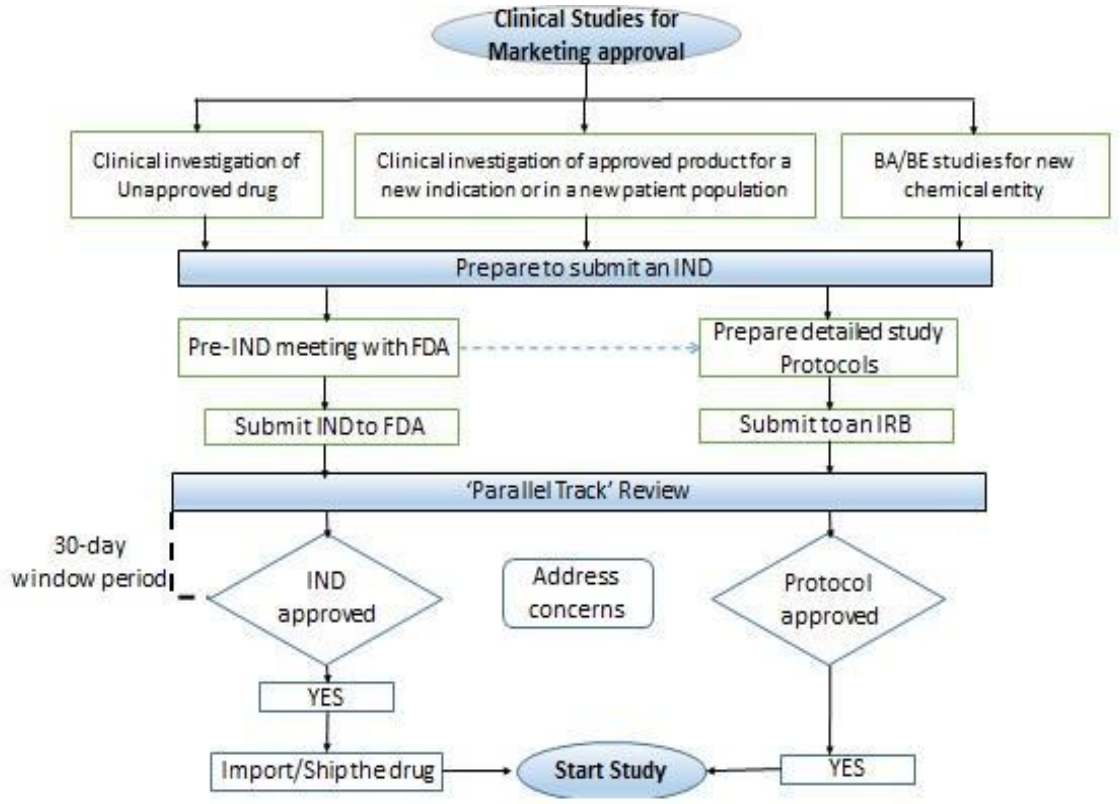

Figure 3. Flowchart of clinical Trial Approval process in US

USFDA plays an important role in reviewing and authorizing investigational new drug applications (INDs) to conduct clinical trials using investigational drug or biological products in humans. Regulatory requirements relating to compliance with federally funded or sponsored human subjects research protections, known as the Common Rule, which the Department of Health & Human Services (HHS) implements in subpart A of 45CFR46. (36) Several centers are responsible for pharmaceutical and biological product regulation are:

- Center for Drug Evaluation and Research (CDER) (37)
- Center for Biologics Evaluation and Research (CBER) (38)
- Additionally, the Office of Good Clinical Practice (OGCP) plays a pivotal role in the FDA's oversight of good clinical practice and human subject protection issues stemming from clinical research. (39)
- HHS' Office for Human Research Protections (OHRP) guides the agency's efforts to safeguard the rights, welfare, and well-being of human research subjects for studies conducted

or supported by HHS. OHRP also provides oversight to all federal agencies engaged in human subject research. (40)

Timeline of Review

Institutional Review Board (IRB) review of clinical investigation may be conducted in parallel with the Food & Drug Administration's (FDA) review of the investigational new drug application (IND). However, EC approval must be obtained prior to the sponsor being permitted to initiate the clinical trial. (36,41)

USFDA IND Review and Authorization

The FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) review teams will evaluate all initial INDs for drugs and therapeutic biological products respectively. Within 30 calendar days of receipt of the original IND, the CDER/CBER team will contact the sponsor when a clinical hold is being imposed. A clinical hold is an order the FDA issues to delay or suspend a clinical investigation. If the team determines there may be grounds for imposing a clinical hold, an attempt will be made to discuss and resolve any issues with the sponsor prior to issuing the clinical hold order. An IND automatically goes into effect in 30 days, unless the FDA notifies the sponsor that the IND is subject to a clinical hold or the FDA has notified the sponsor earlier that the trial may begin. (42,43)

2.3 Europe

The conduct of clinical trials in the EU is currently governed by the Clinical Trials Directive. The Clinical Trials Regulation however, will replace the Directive. Its aim is to ensure a greater level of harmonization of the rules of conducting clinical trials throughout the EU. The goal of the Clinical Trial Regulation is to create an environment that is favourable for conducting clinical trials in the EU, with the highest standards of safety for participants and increased transparency of trial information.

Regulatory Authority

The European Medicines Agency (EMA)

The European Medicines Agency (EMA) is a European Union agency for the evaluation of medicinal products. Prior to 2004, it was known as the European Agency for the Evaluation of Medicinal Products (EMEA). The EU is currently the source of about one-third of the new drugs brought onto the world market each year.

Timeline of Review

The reporting Member State shall submit, through the EU portal the final assessment report including its conclusion to the sponsor and to the other Member States concerned within 45 days from the validation date.

The reporting Member State may also extend the period up-to 50 days for clinical trials involving an advanced therapy investigational medicinal product or a medicinal product for the purpose of consulting with experts.

For clinical trials involving more than one Member State, the assessment process shall include three phases:

a) An initial assessment phase performed by the reporting Member State within 26 days from the validation date

b) A coordinated review phase performed within 12 days from the end of the initial assessment phase involving all Member States concerned

c) A consolidation phase performed by the reporting Member State within 7 days from the end of coordinated review phase. (44)

2.4 Australia

Regulatory Authority

Therapeutic Goods Administration (TGA) is the regulatory authority responsible for clinical trial approvals, oversight and inspections in Australia at the national level. The TGA grants exemptions for the supply of unapproved therapeutic goods to be used in clinical trials for experimental purposes in humans in accordance with the provisions in the TG Act (Therapeutic Goods Act) and the TGR (Therapeutic Goods Regulations). (45)

There are two regulatory schemes for supplying unapproved therapeutic goods in clinical investigations:

- CTN Scheme (46)
- CTX Scheme (47)

TGA is part of the Health Products Regulation Group (HPRG) within the Australian Department of Health. (26) The TGA regulates the supply, import, export, manufacturing and advertising of therapeutic goods-prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices, blood and blood products. The TGA manages the Australian Register of Therapeutic Goods (ARTG) for all therapeutic goods for human use, and it grants exemptions from the ARTG for unapproved therapeutic goods to be used in clinical trials. (48)

Clinical Trial Review Process

The sponsor is responsible for the overall decision as to whether the CTN or CTX scheme should be used. Consulting the EC responsible for protocol approval may assist the sponsor in making the decision. Some class IV biologicals must be conducted under the CTX scheme. The main difference between the CTN and CTX schemes is the TGA's level of involvement in reviewing data about the therapeutic goods before the clinical trial commences. TGA can request certain information or documents from the sponsor about therapeutic goods exempt under the CTN scheme or approved under the CTX scheme relating to the supply, handling, monitoring, and the results of the supply of the goods. (49)

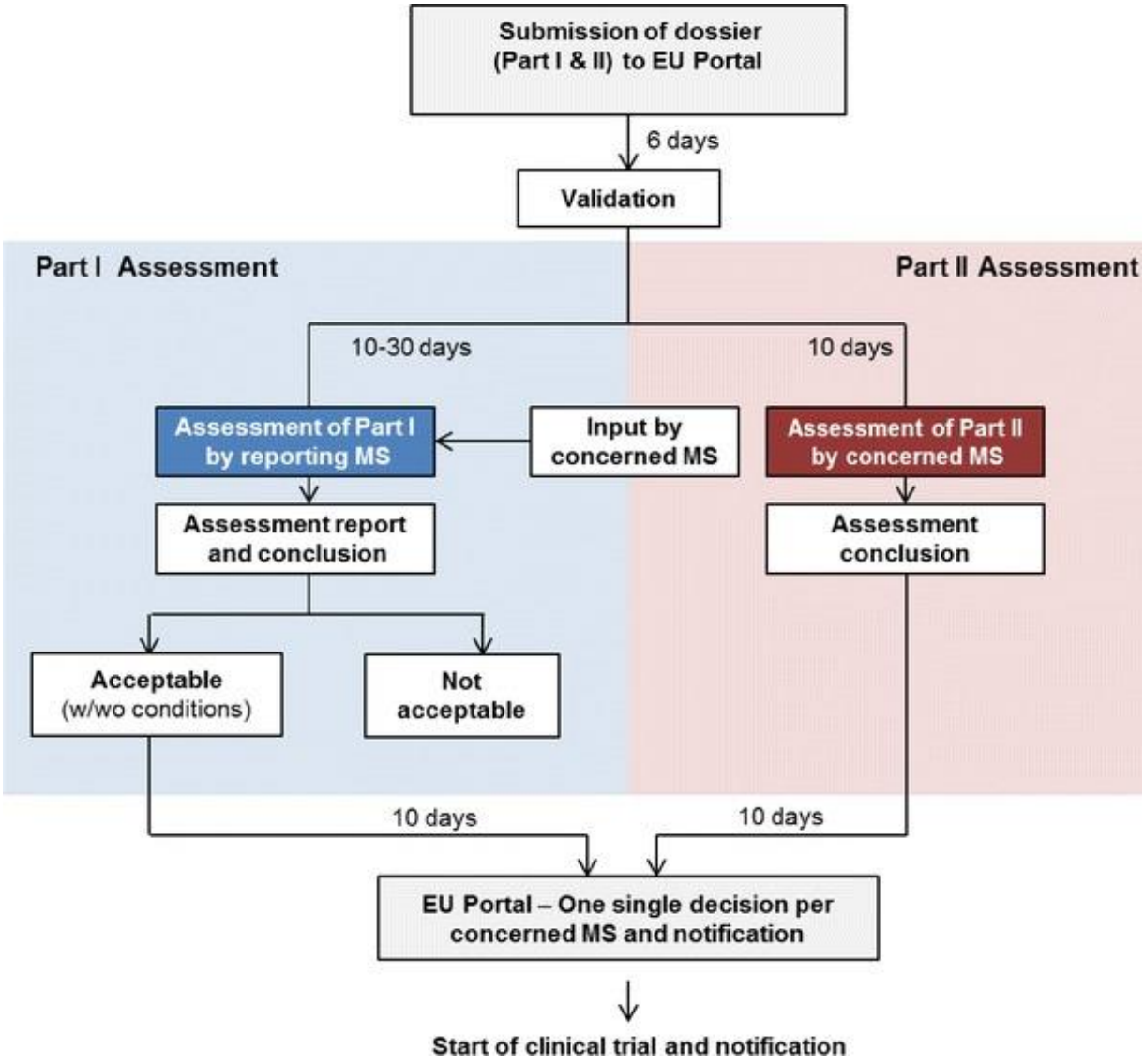

Figure 4. Flowchart of Clinical Trial Approval process in EU

TGA Approval

CTN Scheme

Under the CTN scheme, the TGA is notified of a clinical trial. The sponsor may submit the CTN form simultaneously while obtaining the necessary endorsements. It is the responsibility of the sponsor to ensure that all relevant approvals are in place before supplying the therapeutic goods in the clinical trial. TGA's target time to process online CTNs is five to seven working days. The TGA may request additional information if the trial raises any concern. CTN trials can commence when the trial has been reported to the TGA and the appropriate notification fee paid. (46)

CTX scheme

The CTX scheme application procedure is currently undergoing review by the TGA. The data requirements for a CTX application will be available in the TGA website archive while the TGA develops new guidance. (47)

The CTX scheme consists of a two-part process.

- Part 1, the regulatory approval part, constitutes the formal CTX application, which the sponsor completes and submits directly to the TGA and the TGA reviews relevant, but limited, scientific data, and its primary responsibility is to review the safety of the product.
- Part 2 requires the sponsor to notify the TGA when a trial commences and alert the TGA to new sites in ongoing CTX trials. (50)

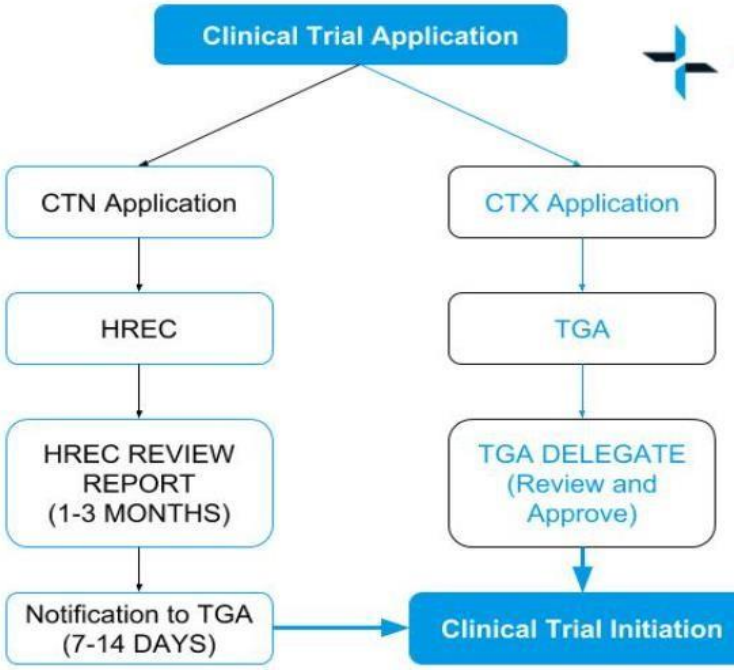

Figure 5. Flowchart of Clinical Trial Approval process in Australia

2.5 Japan

Japan is the world's second-largest single-country pharmaceutical market, accounting for approximately 10 percent of global drug sales and expanding quickly. (51)

The regulator of clinical trials in Japan is the Ministry of Health, Labour and Welfare (MHLW). The sponsoring, preparation, management and execution of clinical trials for the purpose of applying for product approvals in Japan must be in accordance with MHLW's Ordinance on Standards of Implementation of Clinical Studies on Drugs (Ministerial Ordinance No. 28 of March 27, 1997), MHLW's Ordinance on Standards of Implementation of Clinical Studies on Medical Devices (Ministerial Ordinance No. 36 of March 23, 2005), and MHLW's Ordinance on Standards of Implementation of Clinical Studies on Regenerative Medicine Products (Ministerial Ordinance No. 89 of July 30, 2014) (Good Clinical Practices or GCP). In addition, investigations on the compliance with GCP are carried out by the Pharmaceuticals and Medical Devices Agency (Article 14-2(1) of the Act of Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act). (52)

The clinical trials environment in Japan has changed dramatically over the last eight years. Changes in the Pharmaceutical Affairs Law (PAL) (53) have allowed the acceptance of foreign clinical data and fulfilled the growth of the clinical trial sector in the country. There is an increased need for businesses involved in clinical trials to take heed of the rapidly changing environment to capitalize on its growth. (52)

Pharmaceutical administration in Japan is governed primarily by the Pharmaceutical Affairs Law (PAL; Law No. 145 issued in 1960) that controls clinical research, manufacturing, marketing, labeling, and safety of drugs, diagnostic and medical devices. (54)

Preparation for conducting a clinical trial starts with the sponsor requesting a clinical trial consultation under the interview advice or face-to-face advice system. The sponsor may request a prior consultation with the PMDA to organize consultation items so that the clinical trial consultation proceeds smoothly. (55)

Regulatory Authority

Pharmaceuticals and Medical Devices Agency (PMDA) is the regulatory agency within the Ministry of Health, Labor and Welfare (MHLW). (56) The Pharmaceuticals and Medical Devices Agency (PMDA) is the government organization in Japan in charge of reviewing drugs and medical devices, overseeing post-market safety, and providing relief for adverse health effects. The current PMDA was established in 2004 by incorporating the Pharmaceuticals and Medical Devices Evaluation Center of the National Institute of Health Sciences (PMDEC), (57) the Organization for Pharmaceutical Safety and Research (OPSR/KIKO), and part of the Japan Association for the Advancement of Medical Equipment (JAAME).

Ministry of Health, Labor and Welfare (MHLW)

- MHLW conducts scientific reviews of marketing authorization and clinical trial applications of pharmaceuticals and medical devices, monitoring of their post-marketing safety and providing relief compensation for sufferers from adverse drug reactions and infections by pharmaceuticals or biological products. (58)
- The consultation process of PMDA takes about 3 months.
- Notifications for drugs with new active

ingredients or new routes of administration and new combination drugs must be submitted at least 31 days before the planned start date of the trial stated in the contract with the medical institution performing the clinical study.

For other categories of drugs other than above must be submitted at least 2 weeks before the planned date of the trial. (59)

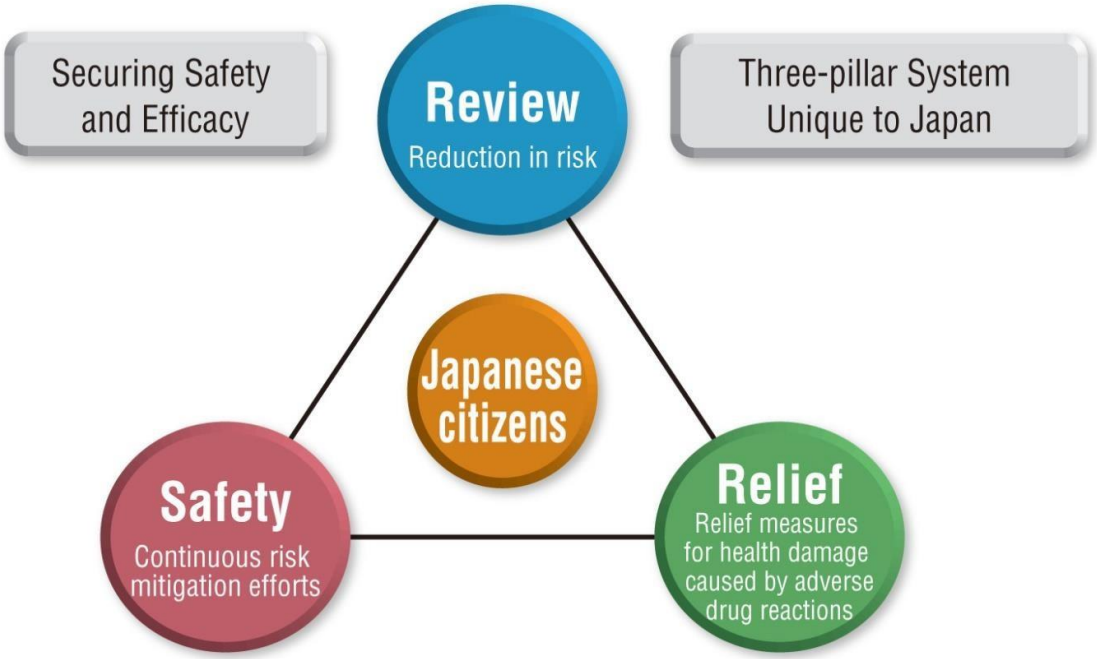

Figure 6. Safety Triangle of PMDA

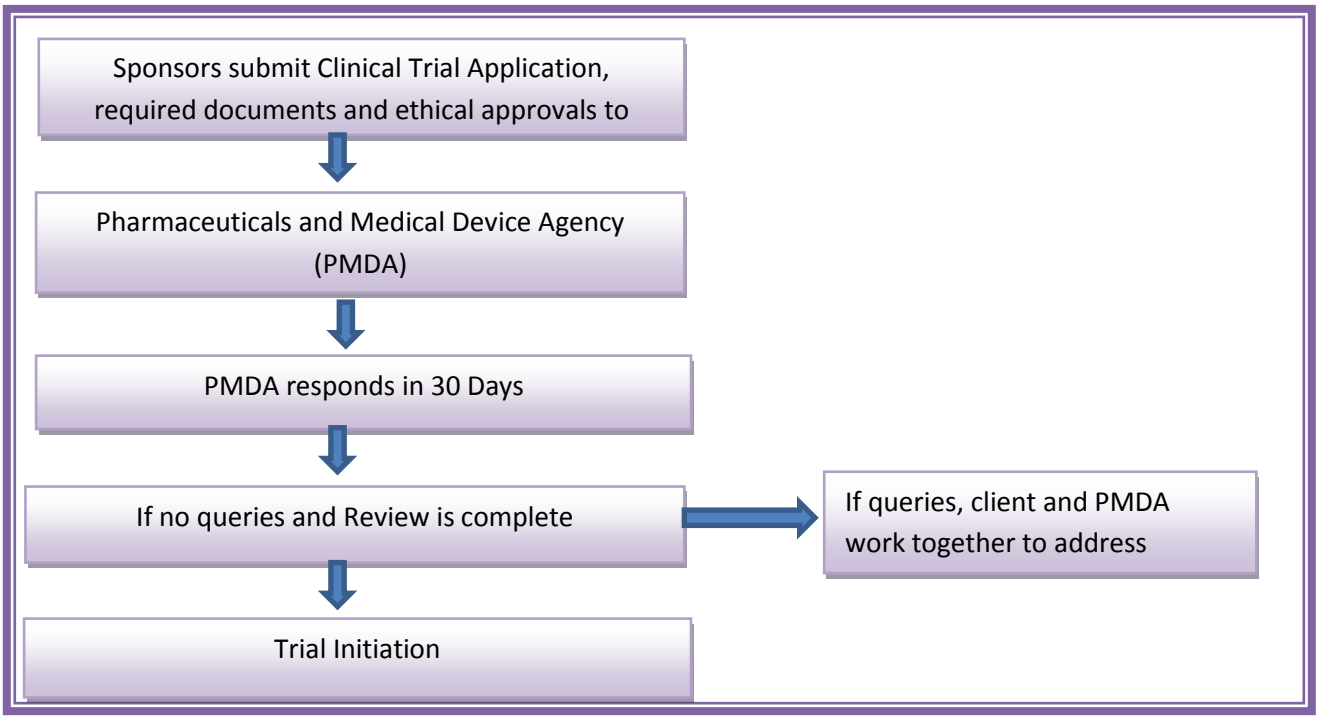

Figure 7. Flowchart of Clinical Trial Approval process in Japan

Table 1. Overview of Clinical Trial Regulation in Different Countries

Features	India	United States (US)	Europe	Australia	Japan
Clinical Trial Definition	As per CDSCO Clinical Trial means a systematic study of any new drug in human subject to generate data for discovering and verifying the clinical, pharmacological (including pharmaco-dynamic and pharmacokinetic), and adverse effects with the objective of determining safety and efficacy of the new drug.	According to the National Institutes of Health (NIH) A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of those interventions on health-related biomedical or behavioural outcomes.	As per Directive 2001/20/EC of EU Any investigation in human subjects intended to discover or verify the clinical, pharmacological and other pharmacodynamics effects of one or more investigational medicinal product, and to identify any adverse reactions to one or more investigational medicinal product and to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product with the object of ascertaining its (their) safety and efficacy.	As per TGA Clinical trial (synonyms: clinical study, intervention study) is a planned study in humans of an intervention (including a medicine, treatment or diagnostic procedure) with the object of investigating safety or efficacy and designed to achieve at least one of the following: - the discovery or verification of clinical, pharmacological or other pharmacodynamic effects - the identification of adverse reactions or adverse effects -the study of absorption, distribution, metabolism or excretion.	There is no specific definition provided by PMDA since PMDA accept the definition provided in ICH-GCP
Regulatory Authority	Central Drugs Standard Control Organisation (CDSCO)	United States Food and Drug Administration (USFDA)	European Medicines Agency (EMA)	Therapeutic Goods Administration (TGA)	Pharmaceuticals and Medical Devices Agency (PMDA) and Ministry of Health, Labour and Welfare of Japan (MHWA)
Regulatory Authority Fees	3,00,000 Rupees for Phase I (human) clinical trials 2,00,000 Rupees for Phase II clinical trials 2,00,000 Rupees for Phase III clinical trials 2,00,000 Rupees for Phase IV clinical trials 50,000 Rupees for reconsideration of application for permission to conduct clinical trial	The Food & Drug Administration (FDA) does not charge any fee to review investigational new drug (IND) submissions.	No specific regulatory fee charged by the EMA. However EMA charge for Marketing authorization application in a specified manner	As per TGR Therapeutic Goods Administration (TGA) Charge for CTX and CTN applications as follows: $380 AUD for medicine, biological, and other therapeutic goods CTN $1,790 AUD for medicine CTX for 30-day evaluation $22,300 AUD for medicine CTX for 50-day evaluation $27,100 AUD for biological CTX	PMDA charge the consultation Fee (JPY) for review of clinical trial application are as following: Consultation Pre-phase I study for drugs: 4,239,400 (Orphan 3,186,100) Consultation Pre-early phase II study for drugs: 1,623,000 (Orphan 1,222,500) Consultation Pre-late phase II study for drugs: 3,028,400 (Orphan 2,274,200) Consultation End of phase II study for drugs: 6,011,500 (Orphan 4,515,700)

					Pre-application consultations: 6,011,400 (Orphan 4,513,000)
Governing Law for Clinical Trial regulation	Drugs and Cosmetics Act – 1940 (Schedule Y) Drugs And Cosmetics (II Amendment) Rules, 2005 ICMR guidelines DBT guidelines	The federal Food Drug and Cosmetic Act (FD&C) Title 21 is the portion of the Code of Federal Regulations (CFR) that governs food and drugs within the United States for the Food and Drug Administration (FDA) 21 CFR Part 50 - Protection of Human Subjects (Informed Consent) 21 CFR Part 54 - Financial Disclosure by Clinical Investigators 21 CFR Part 56 -Institutional Review Boards 21 CFR Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies 21 CFR Part 312 - Investigational New Drug Application	Clinical trials in EU are governed by two regulations: Clinical Trial Regulation EU No 536/2014 And Directive 2001/20/EC	Clinical trial in Australia are regulated under the following governing laws Therapeutic Goods Act 1989 (TGAct) Therapeutic Goods Regulations 1990 (TGR) Other guidance documents included are: Australian Clinical Trial Handbook: Guidance on Conducting Clinical Trials in Australia Using 'Unapproved' Therapeutic Goods -CTHandbook National Statement on Ethical Conduct in Human Research 2007 - (G-NatlStmt) Access to Unapproved Therapeutic Goods - Clinical Trials in Australia (Archived historical document) - G -UnapprovedTGs) ICH Guideline for Good Clinical Practice, Annotated with TGA Comments (AU-ICH-GCPs)	The main legislation in Japan governing pharmaceuticals and medical devices administration is the PMD Act The handling of clinical trials and government review of clinical trial plans for the purpose of applying for product approvals are governed by Articles 80-2 and 80-3 of the PMD Act and Articles 268 to 280-2 of the PMD Act Enforcement Regulations (Ministerial Ordinance No. 1 of February 1, 1961). The sponsoring, preparation, management and execution of clinical trials for the purpose of applying for product approvals in Japan must be in accordance with MHLW's Ordinance on Standards of Implementation of Clinical Studies on Drugs (Ministerial Ordinance No. 28 of March 27, 1997)
Clinical trial application language	English	English	In all official languages of European Union as well as English	English	Japanese Language

Regulatory authority & ethics committee review may be conducted at the same time	Yes	Yes	Yes	Yes	No
Age of minors	Under 18	Determined at the state level	Vary in different Member States	Under 18	Under 16
Forms Required	Form 44 is required for clinical trial application in India	Form FDA 1572 is required to be signed by the PI, if the study is conducted in US and submitted to IND	Statement of investigator not required by member states	CTN online form accessed via the TGA business services website CTX applications are submitted using paper-based forms: Part 1: The application Part 2: Notification of the conduct of a trial under the CTX scheme	Different forms are required for clinical trial application for Company-sponsored Clinical Trials/Post-marketing Clinical Studies and Investigator-initiated Clinical Trials For eg: Form 3 - Clinical Trial Request Form Form 4 - Clinical Trial Review Request Form Form 5 - Clinical Trial Review Results Notification Form 6 - Protocol Modification Report
Record Retention	Retention of record 3 years after marketing application is approved	Record retention 2 years after marketing application is approved. Record retention 2 years after last shipment and delivery of IMP if marketing application is not approved.	Essential documents record includes CRF excluding medical records	The sponsor retains records for 15 years following the completion of a clinical trial.	10 years and it can be increased up-to 30 years if product contains human plasma derivative

3. Result and discussion

Clinical trials are research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans. These studies also may show which medical approaches work best for certain illnesses or groups of people. The purpose of clinical trial is research, so the studies follow strict scientific standards. These standards protect patients and help produce reliable study results. Clinical trials are one of the final stages of a long and careful research process. The process often begins in a laboratory (lab), where scientists first develop and test new ideas. If an approach seems promising, the next step may involve animal testing. This shows how the approach affects a living body and whether it is harmful. However, an approach that works well in the lab or animals does not always work well in people. Thus, research in humans is needed.

Clinical trials are conducted in different countries by different regulation under the supervision of different regulatory authorities.

The comparison of clinical trials regulation helps to sponsors to find out the easy way for clinical trial application in any country.

The clinical trial regulations of India, US, Europe, Australia and Japan were compared on various aspects like legal framework, clinical trial definition, clinical trial application, application fee, application submission format, approval time, regulatory authority, forms required, regulations. **Table 1** depicts the overview of Clinical trial regulation in different countries**.**

4. Conclusion

It can be concluded that clinical trials in India are less regulated in comparison to USA, EU, Australia and Japan. Fully regulated countries have better established guidelines and regulation in comparison to semi-regulated countries like India. 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 India, neither the fully developed CTs guidelines nor do they follow internationally accepted standards, till now. The success rate of clinical trials is high in US and EU as compared to India.

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Conflict of Interest

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