# *THE LAW RELATING TO CLINICAL TRIALS IN INDIA: THE PREVAILING DEFICIENCIES AND THE ROAD AHEAD*

**Ms. Gayathri N. M**

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# Preface

Clinical trials stand at the crux of medical advancement, serving as the vital link between laboratory research and the availability of new treatments for patients' ailments. In a world increasingly reliant on evidence-based medicine, the importance of rigorous, ethical, and well-regulated clinical trials cannot be overstated. However, the dynamic and multifaceted nature of clinical trials raises complex legal, ethical, and social issues, particularly in a diverse and populous nation like India.

This book, "The Law Relating to Clinical Trials in India: The Prevailing Deficiencies and the Road Ahead," by Ms. Gayathri N. M. and Ms. Nidhi R, provides a comprehensive analysis of India's legal framework governing clinical trials. It assesses the current state of the law, identifies the deficiencies therein, and offers a thought-provoking exploration of the path to rectifying these shortcomings.

The pages within unfold the historical tapestry of clinical trials, setting the stage with an exploration of their evolution both globally and within the Indian context. The book ventures into the intricate lattice of regulations and guidelines that govern clinical trials in India and juxtaposes them against the global standards set by more developed frameworks in the United States and Canada.

Through the chapters, the reader is invited to examine the role of Indian courts in interpreting and applying the laws concerning clinical trials, often acting as bulwarks against unethical practices. The narrative further delves into the comparisons between regulatory systems, thereby drawing lessons from international best practices.

Perhaps most critically, this work does not shy away from discussing the challenges and deficiencies that mar the current Indian clinical trial landscape. It ventures into the depths of the 2019 New Drugs and Clinical Trials Rules (NDCTR), unearthing its flaws and potential. The Covid-19 pandemic and the

resultant vaccine fast approvals present a case study, highlighting the urgency for reform in the face of unprecedented global health challenges.

As we reach the denouement in the concluding chapter, the authors synthesize their findings and articulate a series of well-reasoned suggestions. Their vision for the future of India's clinical trial legal system is one of pragmatism and hope, guided by the twin stars of participant safety and scientific integrity.

The preface serves as an invitation to readers — scholars, practitioners, policymakers, and anyone with an interest in the crossroads of law, medicine, and ethics — to embark on this intellectual journey. The goal is not only to inform but also to inspire action that will shape a more robust, just, and effective framework for clinical trials in India.

In closing, this book aims to contribute meaningfully to the discourse on improving the regulatory environment for clinical trials in India, ensuring that the nation's laws keep pace with scientific progress while safeguarding the rights and welfare of participants.

**Authors:**

Ms. Gayathri N. M.

Ms. Nidhi R

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# LIST OF ABBREVIATIONS

| Abbr. | Abbreviation(s) |
|---|---|
| ADRs | Adverse Drug Reactions |
| AE | Adverse Event |
| AE/ SSAR | Adverse Event/ Serious Suspected Adverse Reaction |
| AIIMS | All India Institute of Medical Sciences |
| AMA | American Medical Association |
| ANVISA | Agencia Nacional de Vigilancia Sanitaria (Brazilian Health Surveillance Agency) |
| AR | Adverse reaction |
| AVR | Audio-Video Recording |
| BMHR | Biomedical and Health Research |
| BRDD | Biologic and Radiopharmaceutical Drugs Directorate |
| CBER | Centre for Biologics Evaluation and Research |
| CDER | Centre for Drug Evaluation and Research |
| CDSCO | Central Drugs Standard Control Organization |
| CDSO | Control of Drug Standards Organization |
| CFR | Code of Federal Regulations |
| CIHR | Canadian Institutes of Health Research |

| | |
|---|---|
| CLA | Central Licensing Authority |
| COHRED | Council on Health Research for Development |
| COVID - 19 | Corona Virus Disease 2019 |
| CROs | Clinical Research Organisations |
| CSIR | Council of Scientific and Industrial Research |
| CT | Computerized Topography |
| CTA | Clinical Trial Application |
| CTD | Common Technical Document |
| CTG | Clinical Trials.gov |
| CTRI | Clinical Trials Registry-India |
| CTs | Clinical Trials |
| CTSI | Clinical Trial Site Information |
| D&C Rules | Drugs & Cosmetics rules |
| DAAA | Drug Administration Amendments Act |
| D&C Act | Drugs & Cosmetics Act |
| DCC | Drug Consultative Committee |
| DCG(I) | Drugs Controller General (India) |
| DCG(I) -CLA | Drugs Controller General (India) - Central Licensing Authority |

| | |
|---|---|
| DGFT | Director General of Foreign Trade |
| DHHS | Department of Health and Human Services |
| DMCs | Data Monitoring Committees |
| DSMBs | Data and Safety Monitoring Boards |
| DTAB | Drugs Technical Advisory Board |
| EC | Ethics Committee |
| EMA | European Medicines Agency |
| EMEA | European Middle East Asia |
| EUA | Emergency Use Authorization |
| FDA | Food and Drug Administration |
| FDAAA | Food and Drug Administration Amendments Act |
| FDARA | FDA Reauthorization Act |
| FDC | Food, Drug, and Cosmetic Act |
| FDR | Food and Drug Regulations |
| FWA | Federal wide Assurance |
| GATT | General Agreement on Tariffs and Trade |
| GCP | Good Clinical Practices |
| GCTs | Global Clinical Trials |

| | |
|---|---|
| GEAC | Genetic Engineering Approval Committee |
| GHTF | Global Harmonization Task Force |
| GMP | Good Manufacturing Practices |
| HC | Health Canada |
| HC-PHAC REB | Health Canada-PublicHealth Agency of CanadaResearch ethics Board |
| HHS | Health and Human Services' |
| HPFB | Health Products and Food Branch |
| HPV | Human Papilloma Virus |
| IB | Investigator's Brochure |
| ICF | International Classification of Functioning, Disability and Health |
| ICH-GCP | International |
| ICMJE | International Committee of Medical Journal Editors |
| ICMR | Indian Council of Medical Research |
| ICT | Information and Communication Technologies |
| IE | Initial Evaluation |
| IEC | Impartial ethics Council |
| INDs | Investigational New Drugs |
| INR | Investigational New Drugs |

| | |
|---|---|
| IRB | Institutional Review Board |
| IRB | Institutional Review Boards |
| ISCTR | International Standards for Clinical Trial Registries |
| ISRCTN | International Standards Randomized Control TrialNumber |
| IT | Information Technology |
| ITA | Investigational Testing Authorization |
| MCI | Mild Cognitive Impairment |
| MoHFW | Ministry of Health and Family Welfare |
| NCEs | New Chemical Entities |
| NDA | New Drug Application |
| NDAC | New Drug Advisory Committees |
| NDCT | New Drugs and Clinical Trials |
| NDCTR | New Drugs and Clinical Trials Rules |
| NDDR | New Drug Discovery Research |
| NDDS | Novel Drug Delivery System |
| NDGA | Nor dihydro guaiaretic acid |
| NFC | No Fault Compensation |
| NGOs | Non-Governmental Organizations |

| | |
|---|---|
| NIH | National Institutes of Health |
| NOL | No Objection Letter |
| NSERC | Natural Sciences and Engineering Research Council ofCanada |
| NSN | Not Satisfactory Notice |
| OCLiP | Office of Clinical Policy |
| OCT | Office of Clinical Trials |
| OHRP | Office for Human Research Protections |
| ORA | Office of Regulatory Affairs |
| PATH | Program for Appropriate Technology in Health |
| PHAC | Public Health Agency of Canada |
| PI | Principal Investigator |
| PIL | Public Interest Litigation |
| PMDA | Pharmaceuticals and Medical Devices Agency |
| PRE | Panel on Research Ethics |
| PSUR | Periodic Safety Update Reports |
| QIs | Qualified Investigator |
| QIU | Qualified Investigator Undertaking |
| R & D | Research and Development |

| | |
|---|---|
| REB | Research Ethics Board |
| REC | Research Ethical Committee |
| RHInnO | Research for Health and Innovation Organizer |
| RTA | Right to Information Act |
| SAE | Serious Adverse Event |
| SSAR | Serious Suspected Adverse Reaction |
| SAM | Swasthya Adhikar Manch |
| SAR | Suspected Adverse Reaction |
| SEC | Subject Expert Committee |
| SOPs | Standard Operating Procedures |
| SSHRC | Social Sciences and Humanities Research Council |
| TCPS | Tri-Council Policy Statement |
| TPD | Therapeutic Products Directorate |
| TRDS | Trial Registration Data Set |
| TRIPS | Trade Related Aspects of Intellectual Property Rights |
| US | United States |
| USFDA | United States Food and Drug Administration |
| WHO | World Health Organization |

| | |
|---|---|
| WMA | World Medical Association |
| WTO | World Trade Organization |

# LIST OF CASES

| | |
|---|---|
| 1 | Cilansetron trial |
| 2 | Cilostazol trial |
| 3 | Genentech Inc v. DCGI |
| 4 | Glaxosmithkline& Merck trial |
| 5 | Glenmark Pharmaceuticals Ltd trial |
| 6 | Jananeethi v. Union of India |
| 7 | Mepacrine trial |
| 8 | M/s Cadila Healthcare Ltd& others |
| 9 | NDGA trial |
| 10 | Oxford AstraZeneca Trial |
| 11 | People's hospital case |
| 12 | Ragaglitazar Trial |
| 13 | Risperidone trial |
| 14 | SAM Case |
| 15 | Seroquel XR trial |
| 16 | Streptokinase trial |
| 17 | Theravance trial |
| 18 | Tonapofylline trial |

# CHAPTER 1
# Introduction & Historical Evolution

## Introduction

The struggle against illnesses has been a constant and evolving task since the dawn of human civilisation. Clinical research has led to the discovery of new treatments and equipment, which has aided in the fight against mankind's disease. Biomedical processes are done to produce potential, sustainable and safer medications, as well as the system of therapeutic processes as needed for existing treatments, due to the constant demand for novel therapeutic agents. As a result, clinical trials constitute a crucial attachment as made between the pre-clinical identification of a new findings and its application in Clinical trials (CTs)[1].

CTs, also called in another name as clinical studies, are intended in assisting in determining how to safely and effectively administer a novel medication to individuals. This procedure is a well-designed innovation work that aims to find novel ways to prevent, detect, diagnose, or treat an ailment or condition while also attempting for the betterment of a patient's well-being[2].

India is quickly establishing itself as a global centre for CTs. This is because of the "India Advantage", which comprises vast numbers of physically ailing people, highly dedicated and competent paramedical and clinical professionals, sophisticatedly equipped hospitals, and strong set up of IT. Pharmaceutical companies along with CROs have been approaching doctors and medical institutions with requests to perform CTs in India in increasing numbers over the years. As a result, it's critical that clinicians who are the primary investigators in these trials are well-versed in all elements of clinical research[3].

India is now the world's fourth-largest pharmaceutical producer. Approximately 6,000 recognized producers and 60,000 different medicine brands are currently available in

[1] Mohammed Imran et al., Clinical Research Regulation in India-History, Development, initiatives, Challenges and Controversies: Still Long Way to Go, 5 JOURNAL P. B. S. 2–9 (2013).
[2] Tarun Garg et al., Opportunities And Growth Of Conduct Clinical Trials In India, 8 INT. J. P. S. R. R. 028 (2011).
[3] Subramani Poongothai et al., Whyare Clinical Trials Necessary in India?, 5 PERSPECT. C. R. 55-56 (2014).

the Indian market. Surprisingly, most patients use two or more drugs at the same time, whether prescribed or not, growing up the chances of a drug-and-drug interaction and ADRs. As a result, there is a need to enhance India's CT infrastructure in order to avoid this situation and protect patients from any hazardous consequences produced by new or existing drugs[4].

These facts as stated above are the fundamental motivation to build up the present thesis that attempts to the locate the gaps present in India's CT Law. Furthermore, the study aims to furnish recommendations of improvements in the regulation framework that are existing after New Clinical Trial Rules, 2019 incorporated to address the existing concerns of laws of CTs in India.

## 1.1 Background

### 1.1.1 Concept and Types of Clinical Trial

Clinical trials are the most reliable method of evaluating a novel treatment, which is why they must be conducted. It is the testing of medicines, drugs or any kind of treatment, in order to assess its effectiveness.[5] Clinical trials are necessary because they enable patients access to improved treatments in the future, despite the fact that there are many current medicines accessible. Scientists and clinicians all over the world are still trying to figure out which treatments are the safest and most effective for their patients. CT connects the pre-clinical discovery of new drugs and their public utility.[6]

Treatment processes, preventative checks, screening trials, and trials to upgrade quality of life are the four primary categories of CTs. Clinical researchers can also gain access to potentially life-saving treatments for people with critical illnesses through these trials[7].

These types can be used in a variety of ways:

Treatment Trials: They are used to validate new treatments, pharmacological combinations, and surgical or radiation therapy techniques.

[4] Royal Patel et al., Present era of drug safety in India: An overview, 2 JOURNAL P. D. R. 3-4 (2021).
[5] LILYSRIVASTAVA, LAW AND MEDICINE 163-194 (2013 ed., Universal Law Publishing house) (2013).
[6] NANDITA ADHIKANI, LAW AND MEDICINE 356-384 (4th ed., Central Law Publications) (2015).
[7] Pikee Saxena and Rohit Saxena, Clinical Trials: Changing Regulations in India, 39 INDIAN J. C. M. 197–202 (2014).

Preventive Trials: They are used to develop safer and better medical processes to prevent diseases in people who are availing such treatments initially or to keep an illness from reoccurring. Medicines, vitamins, vaccinations, minerals, and lifestyle changes are examples of these techniques.

Diagnostic Trials: These are studies that are carried out to develop improved clinical observations or processes for locating a specific ailment or health status. Screening Trials: Determine the most effective method for detecting specific physical dysfunctionality or health issues.

Quality of Life (also known as Supportive Care Trial): They investigate ways to enhance provisions and quality of life for those who have a chronic suffering.

### 1.1.2 General Drug Development Procedure and Clinical Trial Process

Clinical Trial is an integral part of recognized drug development Process that is performed through the following stages[8]:

(1) Researchers find, isolate, and analyse thousands of compounds in the lab to see if they have the potential to become future therapeutics. (2) After a compositional molecule is found in the lab, it undergoes extensive pre-lab test procedure (in the lab and/or tested on animal samples) to determine its biological, compositional, and toxicologic features. These pre-clinical studies provide pharmacy professionals with an early indication of whether a chemical has pharmacological functions. (3) If the pre-clinical investigation outcomes fit the desired criteria, the molecule may be chosen into a clinical trial process, which entails numerous 'phases' of research, beginning with minor tests in healthy human subjects and proceeding further to medication evaluation in persons with the condition. (4) Only compositional ingredients that meet strict requirements as non-damaging and potent are permitted for the next stage in each phase. (5) When clinical trials show that the substance under investigation is safe and effective as a curative, the company requests to the legal authorities for marketing approval (permission to sell).

Clinical studies are divided into four stages following a Pre-Clinical Trial[9].

[8] Pooja Agarwal and Priyanka B, Regulations Governing Clinical Trials In India, Europe And USA- A Comparative Study, 5 INT. J. D. R. A. 30-39 (2017).
[9] Tarun Garg et al., supra note 2.

A Pre-Clinical Trial is a type of study that is carried out in vitro (test tube/lab processes) procedures and trials using animals. A wide range of medication of the drug that is tested are supplied to animal samples or an in-vitro substrate from where primary efficacy, toxicity, and functional information are collected. The process assists pharmaceutical companies in determining if it is viable to progress with future research[10].

Phase I: This phase focuses on gathering data to examine a drug's safety (pharmacovigilance), pharmacokinetics, resistance, and pharmacodynamics. The first step of human testing commonly mentioned as phase I trials. A small (20-80) sample of healthy volunteers is usually chosen.

These studies are frequently carried out in an inpatient Centre with provisions for the participants to be watched by skilled full-time staff. The individual under this scanning is given medicine and kept under constant surveillance for numerous half-lives of the substance. Dose-level, also known as dose escalation, investigations are usually included in the process to measure the optimal dosage for curing an illness.[11] In most cases, the dose range that is examined is a part that causes injury in animal testing.

The most crucial phase is the second. During this phase, clinical efficacy is confirmed together with the rates of adverse reactions in the patient group. Also, the most appropriate dose schedule is decided, and a complete pharmacological detail for the most effective medication routine is finalized. Trials conducted in Phase II are undertaken on larger volunteer samples and patients in order to discover how beneficial a treatment is. Together to this, it continues Phase I safety tests over bulk volunteers and patients (20-300).

Circumstances where any approach of a novel pharmaceutical process fails, it usually happens at the time Phase II trials are done, in case the pharmaceutical sample is found to be ineffective or to have harmful side effects. Phase II studies are classified as two groups: Phase II A and Phase II B. Phase II A focuses on identifying dosing needs, whereas Phase II B focuses on determining the power of the tested medication, that is the potency of the medicine to cure an ailment.

[10] S. B. Thorat et al., Clinical Trial: A Review, 1 ARTICLE 019, 101-102 (2010).
[11] 11SHAUN D PATTISON, MEDICAL LAW AND ETHICS(South Asian ed., Sweet & Maxwell) (2017).

Phase III: Determine appropriate intake routine, measure of dosage, viability of medicine in patients, treatment certainty, and the frequently occurring adverse responses of the substance by comparing it to accessible and established treatments.

These tests are randomized controlled multicenter trials with large samples of patients (about 300–3,000 or even more accounting on the disease/medical state under scanning) with the goal of providing the ultimate assessment of the drug's efficacy in contrast to existing 'gold standard' medical system.

Phase III trials are high priced processes, lengthy, and challenging to plan and carry out, especially in therapy for long term medical diseases, due to their scale and comparatively long duration.

Phase IV: During this phase, abnormalities associated with long-term therapy, drug potency in long-term usages, other novel processes, a validation of misuse or over intake risk, dosage reactions, and interaction with other agents are all revealed. After a medicine has been cleared for sale, phase IV trials are incorporate to monitor its safety (pharmacovigilance) and give ongoing methodical help.

### 1.1.3 Benefits and Risks in Participation in Clinical Trials

India's engagement in worldwide CTs has a number of benefits for Indians, including[12]: (1) For an illness that can't be treated with a conventional medicines or protocol, participating could provide the access to an effective treatment before it's offered to the general public, as well as advanced biomedical development with lifesaving promises and assurance of your health results. (2) Through global clinical development programmes, medical experts and students can upgrade their capacity by doing research fitting with the international norms. (3) Indian health care units are compensated for enrolling in scientific case analyses that benefit all of the hospital's clients; for example, Pfizer has provided each of the clinical sites that are testing its osteoporosis treatment with a $100,000 bone density check-up equipment. (4) Emergence of the Indian health-care system to the field of worldwide scientific practice in order to promote evidence-based clinical medical care by improving record-keeping and patient communication. (5) Incentives would support India's regulatory agencies to clarify the system, improve resource availability, and boost skill

[12] Tarun Garg et al., supra note 2.

levels. (6) Systematic trial participation also allows medical professionals to be on the upgrade of new technology and scientific breakthroughs, which broadens their horizons in terms of medical innovation and stimulates scientific thinking. (7) Clinical research employs site workers, study monitors, and associated services, resulting in a positive cost centric impact on the entire town. (8) Drugs and systems used in clinical studies are easy to avail free of charge to participants. Sufferers who cannot afford the curatives or recovery system they require should agree in joining in a clinical trial to gain access to the medical methods that may be of use to them. (9) Some patients have no other options for treatment and are on the verge of permanent disability or death. In such circumstances, taking part in a clinical study may provide individuals with hope or opportunities that they would not otherwise have. (10) Many medications, gadgets, and therapies have been tested on white males in the past and proved to be safe and effective. Women, minorities, and children have had fewer trials designed and conducted. Humanity benefits from involvement in a trial that expands the practice of decent medicine for one of these underserved groups.

CTs that are conducted in India, on the other hand, may pose the following risks[13]:

(1) Unpleasant reactions or outcomes may occur, and they may sustain a short time or may cause damage for the rest of your life. (2) Patients have no idea if they're getting the experimental drug or treatment, a previously verified medical options or treatment processes, or even a placebo (a dummy relieving process). As a result, such a treatment is availed as an alternate of the regular treatment that isn't currently available to the general public, there is usually a 50 percent scope to be recovered. (3) The treatment that is availed may have no good effect, either because the clients aren't receiving the treatment being studied or because they aren't receiving it properly. (4) The amount of time and attention demanded of the participants is a critical factor. Test time, distance to reach the clinic, hospital stays, or intricate dosing may be required. (5) Better doesn't always imply new.

### 1.1.4 Evolution of Clinical Law/ Regulation Frameworks in India

During British rule, when the majority of pharmaceuticals were imported from abroad, India implemented a system of drug regulation. Many unprincipled outside producers

[13] Id

invaded the Indian medical sector pushing counterfeit and contaminated medications in the early twentieth century[14].

To control the widespread 'Gigantic Quinine Fraud,' India's central authority established a Unit of Drug Inquiry led by Sir Ram Nath Chopra, mentioned alternately as the 'Chopra Committee,'. The propositions of this regulatory unit were later tabled as 'The Drug Bill,' which was updated afterwards to the Drugs and Cosmetics Act 1940 (D and C Act) and Drugs and Cosmetic Rules of 1945(D & C Rules).

The CDSCO and the controller's division under its authority, the DCGI, were founded later. The CDSCO serves a section of the Ministry of Health and Family Welfare of India, led by the DCGI. To carry out its activities, there are four zonal centres, sub-zonal units in three areas, and seven airport/port chambers, as well as six medical test units.

In the D and C, in 1962, the government expanded the regulating powers to include cosmetics, and the Act was renamed the Drugs and Cosmetics Act 1940. The mentioned law is organised into Explanatory Sections, Rules, and Schedules, and it is updated on a regular basis to commit the safety, potency, and standard of drugs. It is a law that governs the import, production, supply, and public availability of pharmaceuticals and cosmetics.

This Act establishes a DTAB and a DCC for the Modern Scientific System of Medicine and the Indian Traditional System of Medicine, respectively.[15]Furthermore, it provides for the establishment of a Central Drug Laboratory at the Central Research Institute, Kasauli, to test medical chemicals.

The Rule 122 A to E norms given in the D and C Act, Schedules Y of the Drugs and Cosmetics Act and its subsequent rules (that is changed in 2005), the Good Clinical Procedure (GCP) rules stated by CDSCO in 2001. Then, the ICMR's Ethical Guidelines for Biomedical Research on Human Subjects[16].

The Indian Patents Act of 1970 only allowed for 'process' patents at the time. It covered non-chemical product patents as well as chemical process patents such as

[14] Mohammed Imran et al., supranote 1.
[15] VIJAY MALIK, LAW RELATING TO DRUGS AND COSMETICS 1559-1600 (EBC Books) (2016).
[16] Id

pharmaceuticals, agrochemicals, and food goods. Its provisions allowed Indian companies to imitate still-patented medications by slightly modifying a manufacturing process, leading in a burgeoning generic industry in India. As a result, western companies were hesitant to launch new inventive items in Indian markets.

India fully complied with TRIPS in 2005. From its initiation, the government has attempted to alter the regulation set up and laws in order to facilitate clinical trials as conducted in India. Pharmaceutical companies have been advised to boost their clinical experimental operations as a result of these developments[17].

Furthermore, for a variety of reasons, major pharmaceutical corporations have outsourced their initiatives to India: 1) operational costs are practically halved; 2) Provision of a large number of capable, skilled, English-speaking staff; and 3) Abundant number of patients available for treatment; 4) subjects are of various ethnicities; 5) a wide age range availability of subjects (About 64 percent of physically ailing persons in India are between the ages of 15 and 64); 6) Unmet medical needs are huge in count - the significant spread of acute and chronic diseases, as well as lifestyle-based problems growing rapidly; 7) there are medical care units and laboratories with cutting-edge technology, and so on.

Furthermore, India's favourable regulatory environment, poverty, limited understanding about clinical experiments, illiteracy, and an ill implemented healthcare system made it an appealing destination for clinical trials outsourcing. In India, unethical clinical trials were the result of insufficient GCP knowledge among associated segments and a poor management provision.

Investigators were able to enrol bulk number of patients despite not furnishing sufficient information to them on clinical researches. In fact, the vast majority of ailing people included in such research were ignorant and needy, were paid inequitably, and gave their informed permission insufficiently.

It doesn't help that most Indians regard their doctors as gods, and as a result, patients follow doctors' orders. As a result, most firms were able to benefit from the poor and ignorant by putting them as a volunteer in clinical studies. Furthermore, drug industry

[17] Kalindi Naik, Clinical Trials in India: History, Current Regulations, and Future Considerations, THE SCHOOL OF HEALTH SCIENCES EASTERN MICHIGAN UNIVERSITY, Michigan, 2-3 (2017).

found it easier to acquire trial approval in India due to the country's weak compliance environment.

Over the years, NGOs and press campaigners in the country have addressed a slew of issues in response to these unlawful drug testing. Meanwhile, India's Supreme Court highlighted substantial concerns about clinical trials in 2013, highlighting flaws in the present regulatory framework and barring the licensure on new trials unless laws and processes were modified.

This caused India's regulatory agency, the CDSCO, to close gaps in the execution and licensing of clinical studies in order to defend Indian citizens' rights and well-being. As a result of this pressure, India's CT industry has reduced its operations. While several administrative concerns arose in India, and CT clearances were halted, businesses moved part of their operations to other Asian countries.

On March 19, 2019, the central government issued a New Drugs and Clinical Trials Rules (NDCTR) prescribed within Indian Gazette. Keeping up with the newest rules is critical for the smooth running of clinical trials and the application of sound ethical principles throughout the study[18].

These rules replace the Part XA along with most of Schedule Y as primarily included in Drugs and Cosmetics Rules 1945. The amended rules of CTs address some uncovered aspects in the previous regulations like the compensation aspects, it also aims at the timely review of CT application, tries to bring transparency in the system, covers post-trial aspect too[19].

To assist such research at the site, an effective Ethics Committee (EC) is established, which can meet the major goal of the ICH-GCP criteria.

In Chapter III stated in the gazette, the EC for CTs, Bio-availability, and Bio-equivalence Study discusses modifications to the EC constitution and ethical member training. According to the rule, at least 50% people of the committee must be non-

[18] Shivaprakash G and Pallavi LC, New Drugs and Clinical Trial Rules 2019, What is New?Our Views from Ethical Perspective, 67 JOURNAL A. P. I. 75-76 (2019).
[19] Swati Jadhav and Ravindra Ghooi, New Drug and Clinical Trial Rules 2019- Two Steps Forward and One Back, 12 INDIAN J. P. P. 209-214 (2019).

affiliated, and all EC members must complete mandatory training on a regular basis to remain on the committee.

Chapter IV explains the EC for Biomedical and Health Research that mentions a separate EC for research that is basic, applied, operational, or clinical (Biomedical and health research). The institutes/organizations should each have their own EC, which should be registered with the central government's Ministry of Health and Family Welfare.

The National Ethical Guidelines for Biomedical and Health Research covering Human Participants should also be followed in the functioning and proceedings of such an EC. Chapter V of the guideline, Clinical Experiments, Bio-availability, and Bio-equivalence Study of New Drugs and Investigational New Drugs, it is clarified as how to perform research studies at a location without an ethical commission.

Newer rules in Chapter VI place a greater emphasis on SAE and remuneration. It has drastically reduced the time it takes to complete the long regulatory process involved in SAE. The independent expert committee has sixty days' time counted from the date they received the SAE report to make a recommendation to the Central Licensing Authority on the purpose of the SAE and the amount of promise money to be paid.

Previously, death as an SAE took 105 days, and there was no clear schedule for SAEs other than death. It has also established a deadline for the CLA to make decisions. In Chapter X, Import or Manufacture of New Medicine for Sale or Distribution, it is stated that if a person or pharmaceutical firm plans to sell a new drug as permitted and marketed in the list of countries indicated from time to time in regulation 104, local clinical studies are waived.

### 1.3 Clinical Trial Rules of United States of America

New pharmaceuticals were accepted for submission and processed with a pre-market safety evaluation in 1938 under the rule of US Food, Drug, and Cosmetic Act as enacted from the mentioned year. FDA authorities put strict rules on the assessment of both pre-clinical and clinical test data for new medications as a result of this. The newly allotted management permitted drug inspectors to formally prevent or

postpone the commercialization of a new drug by seeking further data, despite the fact that the statute did not define the types of tests that were requisite for approval[20].

The act also let the officials in minimal negotiating choice with the pharmaceutical sector and medical profession over systematic investigation and certification criteria. In reaction to a widely spread drug disaster in 1961, the FDA launched the 1962 Drug Amendments, which indicated clearly that the FDA would be depended on lab experimentation and that new drug grants would be based on "substantial evidence" of a drug's usefulness [i.e. the influence of a medical dose in a clinical study setting].

The AMA Council on Drugs, the United States Pharmacopeia, and the National Formulary are gradually taking on obligation for testing requirements that were previously specified as voluntary by the FDA. The FDA has monitored substantial changes to the wide legal compulsions that new drugs be approved based on "adequate and properly controlled" trials done after 1962 since 1962.

The FDAAA, Title VIII, enacted the duty in 2007 where Clinical study results should be furnished to the appropriate clinical trial register in the United States. In addition, the DHHS released a last rule in 2016 providing the details of some unclear FDAAA reporting obligations and regulations; it took effect on January 18, 2017[21].

One of the most notable distinctive features in the final rule is the extending of the results disclosing provision to trials of unapproved pharmaceuticals (original guidelines contained in the FDAAA related records of approved drugs only). Relevant CTs, which are diagnostic and therapeutic trials with one or more parts not available in trials of phase 1 and contain an FDA-regulated drug specimen, are now required to provide summary results.

Furthermore, one or more of the below mentioned requirements must be attained: (i) at least one trial facility must be located in the United States; (ii) the drug under qualifying test must be manufactured in the United States; and (iii) the trial must have an FDA investigational new drug number. The sponsor or primary investigator

[20] Suzanne White Junod, FDA and Clinical Drug Trials: A Short History, U.S. FOOD AND DRUG ADMINISTRATION, Available Online at https://www.fda.gov/media/110437/download (Last visited Feb. 05, 2022).

[21] Jan Borysowski et al., Legal Regulations, Ethical Guidelines and Recent Policies to Increase Transparency of Clinical Trials, 86 BRITISH J. C. P. 679–686 (2020).

submits summary results, which include number of people who took part in the clinical test, baseline features, outcome measures, statistical analysis, and adverse events; these are checked by the concerned staff before being posted.

It's worth noting that in the United States, the requirement to publish summary results applies not only to drug studies, but also to medical device trials with a primary goal leaving away the eligibility study. This is a significant distinction between the United States and the European Union.

There are negative cases revealing that results reporting standards are not always followed. According to a recent analysis, several previous evaluations may have exaggerated the level of noncompliance. In addition, several research found that the FDAAA resulted in a much higher percentage of trials being registered and published in journals when compared to earlier trials.

### 1.4 Clinical Trial Rules of Canada

The FDR form the sole federal norm concerning clinical research in Canada, and they are controlled by the Food and Drugs Act.3A CTA that is alternately called an ITA is a request to Health Canada to conduct a research approach with a new medication or equipment (I, II, or III Phases of drug studies). Normally, the CTA is requested for approval by the pharmaceutical business (or called as 'sponsor') or the investigator (or called as 'sponsor-investigator')[22].

Health Canada will evaluate the appeal for health defects within a time of 30 days, and if it is cleared, a NOL will be dispatched. The FDR must get permission from Health Canada as well as the local REB's ethics committee before the study can commence. The sponsor is ultimately responsible for the trial's overall conduct; however, the local PI must guarantee that the study is carried out according to protocol and that all requirements are observed.

Canada has adopted two national guidelines and policies: one is an international record and the other is a Canadian one. The two bodies are, namely, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use–Guidance for Good Clinical Practice (ICH E6) and the TCPS2: Ethical Conduct for

[22] Josmar K. Alas et al., Regulatory Framework for Conducting Clinical Research in Canada, 44 THE C. J. N. S. 2 (2017).

Human Research (2014). Ethics review conformity is required for sections receiving public funds from any of the three national funding organisations, according to the TCPS2 (2014), a Canadian document.

Not only do the ethics rules apply to initiatives supported by the agencies, but they also are valid to all inspections involving human participants, bio-banks, or genetic ingredients. Furthermore, PIs must follow provincial and territorial laws controlling access to, disclosure of, use of, and modification of personal health information.

The research community has also widely deployed a precise format of ethical study conduct guidelines. In summary, such a framework needs the fulfilment of multiple processes before a PI can carry out a clinical research activity.

In terms of legislation, the FDR as specified in the F & D Act are the only federal regulations that govern clinical research in Canada. 3A CTA or an ITA is a request to Health Canada to conduct a treatment test with a medical product or equipment (I, II, or III Phases of drug studies).

The ethical constraints applicable to all experimental approaches that involve human candidates, bio-repositories, or genetic constituents, not simply those financially secured by the suitable operational bodies. Local and territorial rules controlling availability, grant of, use, and altering of patient records must also be followed by PIs. The FDR (Part C, Division 5) regulates the application of medicines in human clinical studies and lays out the steps for selling or importing a medical product for that purpose. The norm includes the sponsor's responsibilities during the analytical methods, such as adhering to best GCP. The FDR is also the only federal healthcare law that specifies the function and membership qualifications for a research ethics unit. Unlike several other jurisdictions that have established guidelines to regulate REB activities, Canada lacks a unified government research ethics framework.

## 1.5 Literature Review

1) Lily Srivastava, (2013)[23] discussed the concept of clinical trials beginning from its pre-history. The international guidelines i.e. The Nuremberg Code, its basic principles, the declaration of Helsinki are covered in a structured format by the author. Schedule Y of the Drugs and Cosmetics Rule 1945 which laid the

[23] LILY SRIVASTAVA, supranote 5.

provisions related to the conducting of clinical trials till 2019, is discussed by the author. The schedule Y is now replaced with the New Clinical Trials Rules, 2019. The author has given a clear understanding of the concepts of controlled clinical trials like pre-clinical testing, selection of subjects, selection of variables, etc. in a nutshell. The author has also described the phases of clinical trials into 5, which begin with phase O (pre- clinical studies) and end with Phase IV, which is the study done after the marketing of the drugs. The author has given a picture of the practical aspects of lab based medical analysis by discussing the cases of clinical trials in India and the US and the interpretation of the courts in related matters of compensation in clinical trials.

2) Nandita Adhikani, (2015)[24]has discussed a chapter 'Experiments of Human Beings', under which the concept of clinical trials is discussed. The ethical concepts, the ethics committee of the clinical trials are covered by the author giving us an overview of the system of trials. The author in the chapter has classified the clinical trials as low and high risk and states the consequences. The author also discusses the sponsor of clinical trials, which can be a commercial company or a clinical investigator. The author in the book gives insights into the US National Clinical trials Registry. The concepts of approval, responsibilities of sponsors, investigators discussed by the author give an idea about the actual working of the system. The essentials of the consent of the trial subjects and their role in the conducting of clinical trials are very well put by the author. The author also gives remarks about the clinical trials of today and compares them to that of what was conducted for decades. The author has covered most of the aspects of the clinical trials by giving the readers an overview of the procedure in the country and its importance of it.

3) Vijay Malik, (2016)[25]has discussed various definitions related to clinical trials, protocols, ethical principles, which are followed in the clinical trial process. The author has also explained the process of clinical trial precisely and in easily understandable manner. The responsibilities of investigators and the compensation related aspects are also discussed by the author herein. The phases

[24] NANDITA ADHIKANI, supra note 6.
[25] VIJAY MALIK, supra note 15.

as well as the obligations on the part of the investigators are also discussed by the author.

4) Shaun D Pattison, (2017)[26]discusses about the history of clinical research in different countries. The author talks about the role and validity of consent in clinical research. He talks about the need and the duty of participation in these kinds of research. He also emphasises on the 'vulnerable' participants in clinical research. The author in the book discusses various shams in the clinical trials, like the placebo treatment etc and also about the lack of consent obtained from the participants, who lack the capacity to consent for such kind of trials. The Ethics committee and the regulations are briefly discussed here.

5) Shivaprakash and Pallavi, (2019)[27]discuss the New Clinical Trial rules which were published in 2019. The important changes that are brought in by the new rules are discussed. The ethical perspective of the changes in the roles, responsibilities of the stakeholders has been discussed by in the article. There is a critical analysis of the rules for the functioning of the ethics committee. The new rules have come up with the GCP training and inclusion of 50 % of non-affiliated members in the committee to ensure fair and unbiased decision-making. The new rules also shorten the time for dealing with compensation for serious adverse events and bring it to 60 days on receiving the report. The authors are in favour of waiver of local clinical trials for import or manufacture of the new drug if it comes within Rule 104. According to them, this waiver avoids exposure to the study risks and upholds the interest of the participants. The article is concluded stating that the new rules gives a clear understanding of the roles of ECs and help in the functioning of the clinical trials system.

6) Swati Jadhav and Ravindra Ghooi (2019),[28]appreciate the new changes brought in the New Clinical trial rules, at the same time pointed out some discrepancies which have arisen. It is stated that the ethical guidelines governing clinical trials have not shown many changes in recent times, whereas the regulations relating to clinical trials have undergone major changes in recent times. The Schedule Y is discussed and it's called a historical document, which served for around 30 years

[26] SHAUN D PATTISON, supranote 11.
[27] Shivaprakash G and Pallavi LC, supra note 18.
[28] Swati Jadhav and Ravindra Ghooi, supra note 19.

and which is scrapped down on the introduction of the new rules. Schedule Y had a major role in the development of clinical trials, there were 2 major amendments made to it. The amendment brought the schedule Y on par with the ICH-GCP. There was also the introduction of new rules in 2013 wherein the ethics committee was empowered and the recording of the consent process was mandated. The authors highlighted the main positive changes in the new rules are the logical arrangement of the new rules in the form of chapters, framing of timelines, exemption of fees for molecules assisted by the state or central government, post-trial access, etc. Some of the discrepancies pointed out by the authors are: the duplication of rules i.e. The new rules are numbered similar to that of the Drugs and Cosmetics Rules so there can be confusion. The other is the contradiction in rule 6 and rule 25 (ii) of the new rules, some conflicting rules of that of the EC. The authors have concluded that the drawbacks of the new rules have to be amended soon.

7) Amar Jesani and Sandhya Srinivasan (2019)[29]is about the plight of clinical trials in India in the year 2005 when there was an amendment made to facilitate private business interests. But this resulted in ethical violations and serious adverse events such as deaths. Then in 2013, Supreme Court strengthened the regulations and laid down criteria for approval of the trials. But according to the authors, the new rules of clinical trials don't help to operate the criteria laid down by the Supreme Court. The authors have criticized that the Ethics Committee gives supremacy to the Good Clinical Practices and New Rules and looks like will undermine the ICMR guidelines. They have also criticized the concept of waiver, where if a drug is approved in some developed countries, recognized by India, it can waive the Clinical trials in India. The criticism is based on the fact that there is no reciprocal recognition given by the other countries for a drug that is approved in India and also no criteria is laid down for waiver. The authors have also thrown light on the provision of 'no fault' compensation, which was part of the proposed draft rules and which did not find its place in the new rules. They have also highlighted the transparency issue, in the new rules there is no mandate for the researchers and sponsors to

[29] Amar Jesani and Sandhya Srnivasan, New Drugs and Clinical Trials Rules, 2019: The market trumps ethics and participant rights, 4 IND. J. M. E. 89-91(2019).

make public the primary and secondary outcomes within the time stipulated. The article ends by stating that the new rules have both good and bad sides.

8) Sangeeta Kumari, et al. (2020)[30]studied if the clinical trials running in India registered with the CTG of the U.S is registered with the CTRI that included India as a location, when there is a mandate to register the trials from the period starting from 15 June 2009. The algorithms were matched with the CTG and CTRI. The result of the research was that 3664 US records that listed India as a location, did not have a CTRI ID, which shows that they were not registered with CTRI. The article proves that the Indian law was violated and between 50 and 300 trials that were registered with CTG, were not registered in CTRI.

9) V. Vennu and P. Saini (2020),[31]studied India as the hub for companies conducting clinical trials. But they have also pointed the non-compliances of the regulations, use of unethical trials, etc. have adversely affected the clinical trial industry. The authors have discussed the concept of clinical trials from its historical evolution. The various phases and types of clinical trials are also discussed in the article. The ethical aspects relating to clinical trials in-depth and the need for ethical trials in the country are also discussed. In the article, the various clinical trials conducted, which have been discussed stating the unethical aspects which ruled in it. The recent regulatory changes in India and the impact of the New Clinical trials rules are discussed in the article. According to the authors, the new rules have the potential to raise the ethical standards of the trials and speed up the process of clinical trials. They put forward that the new rules also ease the registration renewal process. The article also states that the new rules have a more practical consideration of the aspect of compensation in the event of injury or death. It is concluded that the new regulations will uphold the interest of stakeholders who aims to expand the clinical trials in India.

[30] Sangeeta Kumari, et al., Hidden duplicates: 10s or 100s of Indian trials, registered with ClinicalTrials.gov, have not been registered in India, as required by law, 15 PLOS O. e0234925 (2020).
[31] V. Vennu and P. P. Saini, India's Clinical Trial Regulatory Changes, Indian Researcher?s Awareness of Recently Changed Regulations, and the Impact of the New Drugs and Clinical Trial Rules: A Review, 82 INDIAN J. P. 726 (2020).

10) Nusrat Shafiq et al., (2020)[32] studied to determine if recent legal modifications in India compel Ethics Committees to maintain an eye on existing clinical trials. The discussed subject covered on-site monitoring in this systematic investigation. The Ethics Committee of a tertiary care, expert driven, and research segments in India that narrates on-site monitoring experiences of clinical trials in the article. They discovered a slew of flaws in the areas of informed consent, risky events, protection, and reimbursement that would have gone undetected if the documents had been reviewed off-site. Surprisingly, on-site monitoring set up by medical study sponsors failed to discover several flaws. According to the analysis team, the data lead to the proposal of on-site monitoring of ongoing clinical examination as a critical task for Indian Ethics Committees.
11) Mark Yarborough, (2021)[33] reviews a variety of evidences in this article to illustrate that a large number of ethically compromised studies from a variety of key medical endeavours are gaining REC clearances. Many of the trials are early phase trials with benefits that may not be justified when contrasted to their hazards, while many others are later phase trials with societal value that may be lacking. The evidence covers topics such as methodologically insufficient preclinical studies that cannot support the outcomes that REC members must consider to attain the prospects for potential advantages in averting the risks in early phase research, as well as sponsorship bias that can lead to improperly constructed, operated, analysed, and reported later phase trials. The findings shows that REC practises need to be reinforced if they are to qualify their gate keeping role effectively. The essay also looks at how RECs might improve their gate-keeping role.
12) Nisha Venugopal and Gayatri Saberwal, (2021)[34]contrasted the WHO's key registries (17 public registries) with that of Clinical Trials.gov practised in United

[32] Nusrat Shafiq et al., On-Site Monitoring of Clinical Trials by an Ethics Committee in India: A Road Less Travelled, 17 RES. E. 45-54 (2020).
[33] Mark Yarborough,Do we really know how many clinical trials are conducted ethically? Why research ethics committee review practices need to be strengthened and initial steps we could take to strengthen them, 47 J. M. E. 572-579 (2021).
[34] Nisha Venugopal and Gayatri Saberwal,A Comparative Analysis OfImportant Public Clinical Trial Registries, And A Proposal For An Interim Ideal One, 16PLoS O. (2021)

States to look at how the ISCTR were implemented, with the goal of establishing features of an interim ideal registry. Quality, Content, and Validity, Technical Capacity, Accessibility, Unambiguous Identification, Administration and Norms, the TRDS, Partner Registries, and Data Interchange Standards are the nine categories divided into. The 18 submissions' websites were assessed for 14 aspects that related to one or more of ISCTR's nine sections, and levels were assigned for their variants of these aspects. The nature of the content; the number and field types for doing the search; data download procedures; the audit trail system; the patterns of health condition; the documentation available on a registry website; and so, on are among the features that have been evaluated. Based on a scoring rationale created for each unique aspect assessed, the registries got scores for their particular version of a given feature. The authors believe that the initiative is the first to quantify the highly disparate quality of primary registries' compliance with the ISCTR, based on their facts and expertise.

### 1.6 Research Problem

The researcher in this study analyses the legal challenges and deficiencies in the system of Clinical trials in India. The regulations and guidelines governing Clinical trials in the country are not comprehensive. The researcher compares the regulations and practices of Clinical trials in India with that of the U.S and Canada, which have a full-fledged regulatory system in determining the challenges faced in India.

### 1.7 Research Objectives

a. To study clinical trials and their regulatory framework in India.
b. To examine the legal challenges and difficulties faced in the implementation of fair Clinical Trials in India.
c. To compare the scenario of Clinical Trials in India with that of the U.S & Canada.
d. To suggest measures & actions for a better regulatory framework of law regarding Clinical Trials.

### 1.8 Research Questions

a. What are Clinical Trials and how effectively clinical trials are conducted in India?

b. How were the Clinical Trial Regulations before and after 2013?
c. How effective are the New Drugs and Clinical Trials Rules, 2019?
d. What are the legal challenges/ difficulties faced in conducting the Clinical Trials in India?

## 1.9 Hypothesis

The New Drugs and Clinical Trials Rules 2019 are not comprehensive.

## 1.10 Scope and Limitations of the Study

The study analyses the concept of Clinical Trial, its Regulations & prevailing deficiencies within India. The regulations of the U.S and Canada are taken for comparison of the scenario of India.

## 1.11 Research Methodology

The research is based on the doctrinal method. The information for the study is gathered from textbooks, journals, reports, websites, research papers, etc.

## 1.12 Scheme of Chapterisation

**Chapter 1 - Introduction & Historical evolution**:

The chapter covers the meaning and introduction to Clinical trials in India. The evolution of CTs i.e. When and how it evolved in India is discussed in detail in the chapter and also the plight of Clinical trials before 2013 is also discussed. A brief introduction of CTs in U.S and Canada is also covered.

**Chapter 2 - The law governing Clinical trials in India: An Assessment**

The chapter deals with the regulations governing the CTs in India. In India the enactment is the D&C Act, 1940 and the recent rules on this is the New Drugs & Clinical Trial Rules,2019. The New rules replaces the Part XA & Schedule Y of the D&C Rules,1945. Apart from these rules, the ICMR guidelines, GCP guidelines etc are also taken into account in the process of CTs, which are discussed in detail.

**Chapter 3 - The Role of courts in Application & Interpretation of laws relating to Legal Trials: An assessment.**

The chapter discusses the cases of Clinical trial violations in India and how the court and the concerned authorities have dealt the matter. The violations are related to unethical trials due to lack of informed consent, unfair compensation etc.

**Chapter 4 - Clinical trials in United States, Canada & their comparison with India.**

The U.S and Canada have a full-fledged clinical trial system when compared to India. This chapter discusses on the CT system in U.S & Canada in relation to the general regulatory system, review process of CTs, Role of the EC, time period of granting approval, the authorised authority to grant permission for trials, compensation related aspects etc. A comparison of CT system of India, U.S & Canada is done on these heads.

**Chapter 5 - Challenges & deficiencies in the law of clinical trials: The way forward**

This chapter covers the challenges and deficiencies in the system of CTs and the deficiencies in the NDCT Rules 2019, which needs to be improvised. The NDCT Rules have covered some of the prevailing deficiencies with respect to CTs. There are still some flaws in those rules i.e.; duplication of rules, lack of transparency, no provision of no-fault compensation etc.

**Chapter 6 - Conclusion & Suggestions**

This chapter summarizes briefly the system of CTs discussed in the other chapters and suggest measures which will help to overcome the existing flaws, deficiencies and challenges in the system of CT in India.

## 1.13 Conclusion

CTs are a crucial instrument for advancing human well-being in the search for innovative treatments for the diseases and health issues that plague humanity. However, due to its subjection to the business motivation of pharmaceutical corporations rather than the fundamental motive, the use and usage of this technology is severely perverted.

There's also a demand to acknowledge the power dynamics that exist between territories, within countries, between various socio-economic groups, and between medical persons and sufferers, all of which have shaped how the CTs sector has

expanded in the developing world. All of the restrictions that may be put in place to protect the ethical conduct of clinical studies are undermined by these power connections.

Because of its readily available resources and infrastructure, medical companies believe India to be a better option for CTs than other countries around the world. However, non-compliance with laws and reports of unethical experiments have had a negative impact on India's growing CT business.

Understanding Indian researchers' notions of new medications and CT standards, as well as their impact, is critical for determining if trials are done in accordance with the new rules and regulations.

CTs must be liberated from their submissive role in generating money invested in the healthcare business. This necessitates the Indian Ministries in withdrawing from the TRIPS protocols and replacing it with a patent process that is formatted to challenge not only our benefit seeking national interests, but also the model of awareness generation, appropriation, and utilisation enabled by developed countries in defence of the interests of the world's impoverished masses. Building a strong system of public institutions to conduct biomedical analysis in line furnishing the country's public health needs would be critical to such an effort.

This should be fully utilised by a solid manufacturing facility set up in the public sector, as well as the necessary protection options to the private sector in order to secure it from succumbing to the might of multinational corporations from the developed world. India should make an effort to liberalise the sharing of insight/method developed in its labs with other developing countries and develop its clinical trial platforms to permit the major foreign investors, such as, USA and Canada, ensuring security and benefit of its own ethical and infrastructural interests.

# CHAPTER 2

# The Law Governing Clinical Trials in India: An Assessment

## 2.1 Introduction

Clinical research is presently regarded as one amongst the most fastest growing fields in medical care systems. In India's pharmaceutical sector, this is one of the fastest expanding specialities. Over the last few decades, India has conducted a considerable number of CTs, and the global CTs based in India is growing higher in number although in slower and irregular manner.

CTs were formerly favoured in Latin America and Eastern Europe, such as Russia, Czech Republic, Romania, Poland, Slovenia, Croatia, Hungary, and others, but India is now being viewed as a global hub for these trials.

International life sciences businesses recognised India as a viable venue for conducting CTs as recently as 2010. The country is the world's most populous democracy, with a vast patient population that is not just diversified, but also easily accessible in urban areas, typically treatment-naive, and eager to engage in CTs.

Sponsors' interest in India dwindled drastically as start-up deadlines grew longer and data quality became increasingly suspect. The number of CT applications approved hit 500 in 2010, which turned out to be a high point. In 2014, the number fell to 150, and by mid-December 2015, it had decreased to 81.

To renew interest in India as a trial site, Indian regulatory officials have made a concentrated effort over the last two years to reform the study licensing procedure and revise the laws dictating how trials are conducted. Although revisions are still being made, many of the issues that sponsors saw as roadblocks have either been resolved or greatly minimised. And, as a result, trial activity has begun to ramp up, with the rate of approvals rising up in 2015. The evolution of worldwide as well as Indian CT norms is described in detail in this chapter. The last part of the chapter examines the NDCT Rules,2019, as well as a critical examination of the significant modifications that have been implemented.

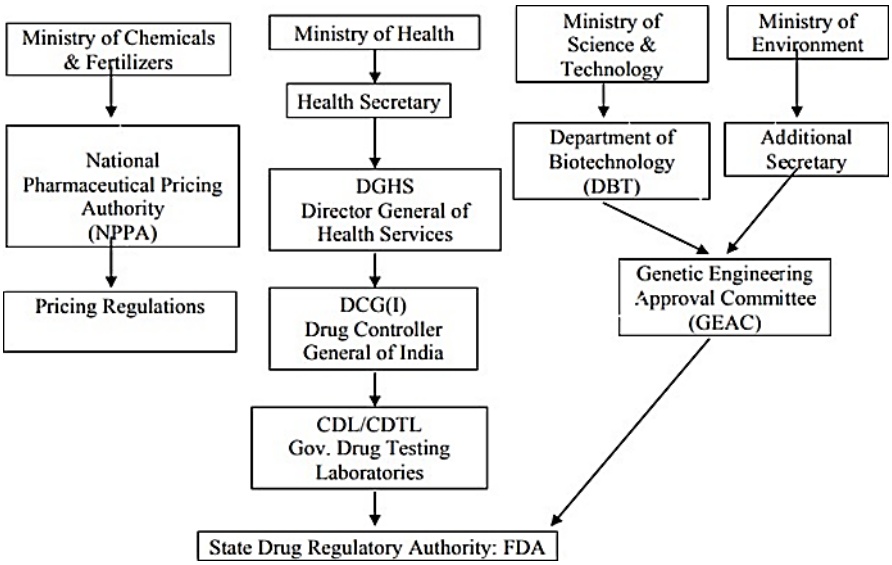


**Figure 2.1:** India's Drug Development Regulatory Units

## 2.1 India's Drug Development Regulatory Framework

The Ministry of Health and Family Welfare's CDSCO is the major authority in charge of developing regulatory procedures and standards for diagnostics, medications, cosmetics, and accessories. It establishes regulatory guidance by changing acts and regulations, and it oversees the approval of new drugs.[35]

The **CDSCO**, which reports directly to the Ministry of Health (MoH) and regulates drug development and use in India, is made up of several agencies. The organisational structure, on the other hand, is a streamlined version of what was previously in place. The reorganization's purpose was to define roles and duties while eliminating gaps and overlaps. Biologics, non-biologics, medical devices, and diagnostics are all divided into various units within the New Drug Evaluation Division. Both the ICMR and the CSIR, which serve as advisory organisations for research policy and implementation guidelines, collaborate closely with these units.[36]

[35] Hitt Sharma and Sameer Parekh, Clinical Trials Regulations in India, 1 PHARMACEUTICAL. R.A., 1-e118 (2012).

[36] 36Pharm-Olam Report, Reconsidering India as a Clinical Trial Location Revised Regulations Warrant a Fresh Look, PHARM-OLAM,

The following are the roles of India's key Clinical Trial Regulatory Units[37]:

Health and Family Welfare Ministry: This segment is operated by Government for monitoring, whose primary focus is on healthcare. Several bodies are under the administrative supervision of this unit. Here are a few examples:

- Central Drugs Standards Control Organization
- Drug Controller General of India
- Medical Council of India
- Pharmacy Council of India
- Hospital Services Consultancy Corporation Limited

This administration unit functions by prescribing the medical parameters in order to ensure the health benefits, potency as well as the quality of the following products:

- Drugs
- Diagnostics
- Cosmetics
- Accessories

Additionally, this monitoring unit side-by-side controls the following activities of CT

- Market approval processes of new drugs
- Clinical trials standards

This agency is also in charge of overseeing medicine imports. Furthermore, it is this regulatory organisation that will approve the drug manufacturing licence.

CDSO: It is branch of the Ministry of Health and Family Welfare, and it is the country's main regulating office for pharmaceuticals and medical equipment. The CDSCO fulfils a comparable function as done by the EMA in the European Union, FDA in the United States, and the PMDA in Japan.

The DCGI is the regulatory agency in charge of all medicines and medical devices in India. As a result, the DCGI receives advice from DTAB and DCC[38].

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https://cdn2.hubspot.net/hubfs/4238150/PharmOlam_March2018/PDF/pharm-olam_india_clinical_trials_white_paper_1.pdf?t=1524594556831 (Last visited Mar. 12, 2022).

[37]Pooja Agarwal and Priyanka B, supra note 8.

As a result, the entire management unit has been separated into region-based offices to carry out the following responsibilities:

- Pre-licensing tests
- Post-licensing inspections
- Post-market proceedings
- Recalls (as applicable)

India's Drug Controller General (DCGI): This unit is in charge of granting regulatory authorization for the conduct of clinical studies as well as the approval of drug marketing licences in India. Other governmental entities are involved in the pharmacological regulations of new pharmaceuticals, in addition to the DCGI office.

The process for obtaining marketing approval varies depending on the type of drug that is being approved. It is classified into three groups: a) discovery of a new active drug ingredients that have previously been endorsed/sold in other countries; b) newly discovered therapeutic substances that have not yet been approved/marketed in other countries; and c) newly discovered drug types in India.

The DCGI reviews a petition once it is lodged; the time it takes for clearance is governed by the trial's guideline status in other countries. To expedite the authorization for research officially approved by regulatory bodies in other countries, the DCGI office has divided all applications into two major types: A and B.

Clinical studies in Category A have had their protocols authorised by EMEA or regulatory agencies in the Canada, United States, South Africa, Switzerland, the United Kingdom, Australia, Germany, or Japan. Permission is granted for such investigations in exchange for those countries' protocol approval.

An expert committee reviews category B clinical trial applications in accordance with the standard approval process. This period does not account for any delays caused by incomplete applications or the time it takes for the sponsor to respond to regulatory authority questions. The application is accompanied by a summary of material in the form of an Investigators' Brochure, which includes thorough pharmacology, toxicology, and clinical experience data, if applicable.

[38] Hitt Sharma and Sameer Parekh, supra note 35.

On a case-by-case basis, the DCGI may seek advice from other independent government organisations, such as the ICMR or the Department of Biotechnology (for biotech products), lengthening the assessment time-frame. To get a test licence to import trial supplies, DCGI permission is also required.

After the DCGI has approved a CT, the DGFT must approve the export of specimens of blood. Parallel submissions to the ECs of potential sites, which are mainly hospitals and/or clinics, can be made in addition to the application to the DCGI office. ECs, which generally adhere to the ICH-GCP principles and Schedule Y of the 1945 D&C Act.

In the last few years, the norms associated with the CT approval criteria, as described above, have been revised in numerous parts to ensure human well-being. The growth in unethical actions that came out of the cracks in these regulations is one of the main causes for these adjustments.

The most recent changes to CT rules, which will be described later in this chapter, occurred in 2019. The New Rules have replaced Schedule Y of the CT Protocol and given the EC more responsibility, as explained later.

## 2.3 Significant Global Development of Clinical Trial Regulations Associated with India's Drug Development Framework

In the modern era of drug development system, these legal protocols are the major stages to ensure safety and compatibility to the global care service procedure:

The Nuremberg Code (1947)[39]: The law formalised the need for medical experimentation on humans to be conducted within generally well-defined limitations in order to comply with medical ethics. Human studies are acceptable for they generate leads for the greater benefit of the public that cannot be attained by other research options or means. The following is the legal framework for this rule: (1) The human subject on whom the research will be conducted should agree freely which is most essential. That is, the person involved must have legal scope to agree; they must be free to exert their choices without the use of pressure, fraud, overreaching,

[39] Subhash C. Mandal and Moitreyee Mandal, Evolution of clinical trial regulation in India, CONFERENCE: 2ND INTERNATIONAL& 4TH NATIONAL CONFERENCE OF INDIAN SOCIETY FOR RATIONAL PHARMACOTHERAPEUTICS at: Kolkata (2012) (Last visited Mar. 19, 2022).

deception, duress, or any other form of coercion; and they must have enough knowledge and reasoning of the components of the concern at hand to make an informed decision. (2) The study should not be haphazard or needless in form, and it should be targeted to provide beneficial results for mankind that cannot be achieved through other techniques or means of research. (3) The investigation has to be structured on animal testing and based on the understanding of health problems. (4) The experiment should be conducted without causing undesired physical or mental suffering or injury. (5) Leaving the trials in which the experimental physicians are also participants, no such procedure should be conducted if any presumption of occurrence of risk or bodily damage is there. (6) The element of risk incurred should never exceed the level of humanitarian urgency of the concern that the experiment will address. (7) Adequate precautions and facilities must be taken to safeguard the experimental subject from any risk of bodily damage, disability, or death. (8) The study should only be carried out by people who are technically certified. Those who conduct the experiment or engage in it should be required to employ the maximum degree of awareness and care at all times. (9) While performing the experiment, if the human subject faces a physical or mental situation in which he considers that continuing the experiment is untenable, the test should be terminated. (10) At the time the experiment is performed, the lead scientist must be willing to call a halt at the circumstances if he has valid logic to consider, in the exertion of the good understanding, superior capacity, and well decided judgement as required of him, that proceeding the study will cause in harm, impairment, or death to the experimental human volunteer.

The WMA has published a series of guidelines to clinicians around the world who undertake biomedical research using human subjects, judging on the purpose and demand of performing tests on humans to aid knowledge enhancement. This is in addition to any ethical, administrative, or penal obligations imposed by the country in which the analysis is carried out.

The fundamental concept of the Declaration are as follows: Only scientifically qualified individuals should conduct biomedical research on human volunteers under the direction of a capable medical doctor who is formally recognized. The study must be based on well-conducted laboratory and animal experiments and follow well-established scientific concepts.

Before any research can be carried out, it needs certified by a distinctly formed independent committee. Biomedical research involving human members is only considered appropriate when the goal's importance is proportional to the inherent dangers to the participants. A careful processes of the project's foreseeable hazards in relation to the tangible results to the subjects or others should precede any such endeavour.

The research subjects' rights must be maintained, and if the hazards are found to take

greater advantages, the research must be discontinued by the doctors. It is critical to have the subject's full informed consent (preferably in writing) for any research involving human volunteers.

The overall study approach must always consist a mention of ethical considerations. In terms of clinical research, the Helsinki Declaration emphasises that a practitioner must possess freedom to use a new diagnostic or therapeutic tool while serving a sick person if it has the potential to save the patient's life or reduce suffering, in his or her judgement. The research approach's benefits and drawbacks in comparison to the finest accessible methodology must also be thoroughly assessed.

Only seek medical procedures if the effective diagnostic/therapeutic value to clients justifies it. Volunteers - either healthy persons or sufferers whose study design is unrelated to their condition - should be employed in non-therapeutic biomedical research on humans, according to the agreement.

## 2.4 Guidelines for GCP: Role and Guidelines

Guidelines for GCP for Pharmaceutical Product Experiments: With the purpose of developing universally valid guidelines for the patterns of such biomedical processes on human subjects, the WHO released Guidelines for GCP for Trials on Pharmaceutical Products[40]. They are based on legislation that have been passed in a variety of wealthy countries in the past.

These guidelines will surely range in substance and priority, but in terms of the needs to be satisfied and the standards to follow in order to preserve the ethical and scientific bonding of clinical trials, they will all be uniform. They have, in fact, developed a

[40] Bushra Shamim, Good Clinical Practice (GCP): A Review, 2 PHARMATUTOR 20-29 (2014).

formal mechanism for the exchange of clinical data generated inside the participating countries.

A new document called GCP was published in 2005. It is planned as a source and informational support to help in understanding and building of GCP and includes protocols, such as the ICH-GCP: Condensed Guideline.

- outlining the clinical investigation process as it applies to health and medical items, as well as defining and clarifying each of the actions that are common to most trials, as well as the individuals who are usually in charge of executing them out;
- tying each of the said actions to one or more of the GCP theories discussed in this Handbook;
- outlining each GCP concept and giving recommendations on how to use and apply each principle on a regular basis;
- alerting the consumer to particular international legal order or other references for more extensive explanation on how to conform with GCP.

The ICH-GCP are as follows[41]:

(1) Medical studies should adhere to the Statement of Helsinki's ethical standards, as well as GCP and any legal requirements. (2) Before beginning a study, major hazards and impediments should be measured against the expected gains to each trial member and community as a whole. A medical lab trial should only be arranged and completed if the expected benefits outweigh the risk. (3) The most notable factors are the trial participants' rights, safety, and health conditions, which should take good care over the interests of study and humanity. (4) For an experimental item, the non-clinical and clinical evidence should be adequate to justify the clinical trial plan. (5) CTs should be conducted according to a methodology that is both systematic and well-documented. (6) The methods used in a study should have been authorised by an IRB and confirmed by an IEC. (7) Medical treatment and conclusion as taken on behalf of human volunteers should always be overseen by a recognised medical expert or, when needed, by a certified dentist. (8) Each person involved in a trial should be qualified to

[41] Subhash C. Mandal and Moitreyee Mandal, supra note 39.

do his or her position based on his or her education, training, and experience. (9) Before participating in a research trial, each patient should offer their free and informed consent. (10) Facts collected from CTs should be collected, handled, and stored in such a way that precise responses, understanding, and certification can be achieved. (11) Materials that may identify individuals must be kept confidential in line with the proper legal need for secrecy and security. (12) When making, transporting, and storing investigational materials, all applicable rules must be followed GMP. They must be utilised in accordance with the clearance process. (13) Practises must be developed to ensure the quality of each aspect of the trial.

## 2.5 ICMR: Role and Guidelines

The ICMR is a non-profit organisation dedicated to The Union Health Minister chairs the governing body of this institution, which is funded by the Indian government. This regulatory agency is also receiving assistance from the scientific advisory board. ICMR receives scientific and technical assistance from a number of notable professionals in biomedical sciences.

This regulatory authority is responsible for promoting biomedical research in the country and is the highest functioning unit for the following operations[42]:

- Development of biomedical studies
- Intercommunication of biomedical research
- Publications of biomedical research

The ICMR is a regulatory authority that has developed rules for numerous elements of national health. The ICMR has issued guidelines for the treatment of diseases such as malaria, cancer, type 2 diabetes, and retinoblastoma.

The first document, titled "Policy Statement on Ethical Considerations Involved in Research on Human Subjects," was created in 1980, and detailed ethical guidelines were created in 2000, re-revised in 2006, and the most recent version, "National Ethical

[42] Pooja Agarwal and Priyanka B, supra note 8.

Guidelines for Biomedical and Health Research Involving Human Participants," was released in 2017[43].

The recommendations include a wide range of themes, and it is hoped that they would assist biomedical researchers, members of ECs, institutions, and sponsors in carrying out their duties while respecting ethical ideals in research.

The rules are divided into 12 sections, each concentrating on a distinct topic of study and the ethical criteria that go along with it. The first six sections are more generic in nature, including subjects that are relevant to all kinds of biomedical and researches on physical problems. The six sections at the end are more focused on the types of study that researchers conduct. The following are the highlights of each part:

The Principles of Essentiality: This principle emphasises the need of using humans as test subjects. It must be confirmed by the proper authorities, and it must be concluded that it is for the advancement of human knowledge and prosperity.

1. The Principles of Essentiality: This principle emphasises the need of using humans as test subjects. It must be confirmed by the proper authorities, and it must be concluded that it is for the advancement of human knowledge and prosperity.
2. Voluntariness, Informed Consent, and Community Agreement Principles: This concept pertains to the research subjects. The subjects must be told about the study's impact, danger, and repercussions well in advance. The research subjects have the free willed choice to deny taking part in the study.
3. Non-Exploitation Principles: Normally, study volunteers are compensated for their time. The research subjects should be adequately compensated in the form of insurance or other ways. This approach ensures that the trial subjects are given immediate compensation and rehabilitative measures.
4. Privacy and Confidentiality Principles: This concept ensures that the trial participants' personal information is kept private. There are some exceptions in the case of acceptable scientific or legal grounds, but only after confirming that the participant is not inconvenienced as a result of their participation in the study.

[43] Roli Mathur, Handbook On National Ethical Guidelines For Biomedical And Health Research Involving Human Participants, I. C. M. R (2018).

5. Precaution and Risk Minimization Principles: This principle states that adequate care should be taken throughout the study process to ensure that participants and those impacted by it are exposed to the bare minimum of hazards.
6. Professional Competence Principles: The notion that research must be undertaken by a person with competence and qualifications in the field of study, as well as integrity and impartiality, should be respected, and researchers should be trained to bear ethical considerations in mind.
7. Accountability and Transparency Principles: In research studies, the principles of fairness, honesty, impartiality, and transparency should be upheld.
8. Maximization of the Public Interest and Distributive Justice Principles: Trials are held in order to improve people's quality of life. All groups, including the creamy and non-creamy layer classes, as well as the research projects themselves, should benefit.
9. Institutional Arrangements Principles: The investigator and anyone participating in the research will be committed to affirm that all procedures are done in accordance with the principle of transparency.
10. Public Domain Principles: The research is published in the public domain in order to make the results available to the researcher through publications.
11. Totality of Responsibility Principles: This principle states that professional and moral responsibility in adhering to the principles and guidelines is required. It could be related to the study or experiment, the money for the research, the institution where the research is carried out, groups, individuals, sponsors, those who benefit, and so forth.
12. Compliance Principles: It is the general and positive responsibility of anybody conducting, associated with, or connected with human subject research to guarantee that the latter, as well as the spirit of the rules applicable to that area of study, is observed or completed.

## 2.6 India's Clinical Trial Regulations Before New Drugs and Clinical Trials Rules, 2019

There was a huge in flow of unauthorised foreign drug makers in the Indian market with fraudulent contaminated drugs in the early twentieth century. To deal with the adversity, the government instituted a drug inquiry commission, whose recommendations were presented to the legislature as The Drug Bill, which became the D&C Act of 1940 and the D&C Rules of 1945. They form the foundational laws that

govern the importation, manufacturing, exposure, and sale of medicinal components and cosmetics in India.[44]
GSR 944(E) dated September 21, 1988, inserted CT criteria and procedures for the import and production of innovative pharmaceuticals to the D&C Rules as Schedule Y, which was later amended by GSR 588 (E) dated June 2, 1989[45].
This initiative compelled the pharmaceutical sector to complete Phase III tests in order to validate novel drugs for marketing in India. Novel chemicals must also be registered as drugs, according to the law. However, in relation to the standards of other countries/organizations, it was regarded inadequately rigorous.

India took part in the Uruguay phase of GATT discussions, ended on the event of a settlement involving 75 countries and the European Members, culminating in the WTO being established in 1995. The WTO attached signatory nations to comply with "TRIPS" laws in order to unify their intellectual property rights.[46]

This meant that governments had to recognise the preservation of patent rights in the case of pharmaceuticals. Article 33 of the 'Intellectual Property Rights' contract stipulates that patent are protected for a term of 20 years from the date of entry. Beginning in 1995, the least progressed countries were given a ten-year window to align their patent regimes with TRIPS obligations, with the stated purpose of allowing "them to create a sound and robust technological base." The Doha Round of TRIPS and Public Health Negotiations in 2001 increased this period until 2016.
India is fully TRIPS compliant in January 2005, recognising product patents for the first time. The 'Patents (Amendment) Act 2005' established product patents for all industrial sectors.
In order to bring in global pharmaceutical businesses, the patent bill for pharmaceutical products was altered in 2005 and the process was broadened, in order to improve the TRIPS competent “product” patent system. Consequently, western firms have no anxiety about marketing new pharmaceuticals to Indian markets; the amendments to India’s Patent Bill bar Indian companies from copying patented drugs by making tiny adjustments to the production process.
A number of scholars have pointed out that this legislation has flaws, such as:

[44] Kalindi Naik, supra note 17.
[45] Subhash C. Mandal and Moitreyee Mandal, supra note 39.
[46] Vikas Bajpai, Rise of Clinical Trials Industry in India: An Analysis, INT. S. R. N. (2013).

(1) insufficient protections were put in place to protect the concerns of trial subjects.
(2) The investigator's flexibility was hampered by a number of ineffectual techniques.

Schedule Y that was updated in 2005 per GSR 32 (E) put to effect from 20.01.2005 to abolish limits and boost clinical studies while protecting trial subjects' benefits.
The nature and characterization of CTs have been clarified and simplified in the new version. Human subjects' rights are also secured by rules like following GCP, constituting an EC, and establishing parameters for papers like informed consent, declared on papers, EC acceptance, ADR reporting, and the investigator's undertaking, among others. Stability Testing of New Drugs was included as a new criterion. The following are the key aspects of the revised Schedule Y:

- Informed consent is based on the concept that the test patient must give freely given, aware, written consent. When a subject is incapable to give informed permission (for example, if they are incapacitated, a juvenile, or have a severe mental illness or handicap), legally permissible agents can do so on their account. The entire procedure of gaining consent should be videotaped, it was urged.
- Responsibilities of the interrogator: This entails establishing quality control process to verify that the clinical trial is carried out and that output is processed, archived, and presented in accordance with the protocol and GCP Guidelines, as well as all applicable regulatory requirements. At the appropriate intervals, file a progress update on the CT to the Licensing Authority.

If studies are early ended for whatever basis, including an insufficient financial interest in continuing the novel drug application, a summary of the process should be produced within three months. Occurrence of any SAE during a CT should be brought to the notice of the Licensing Authority and other investigators, who are part of the study, as soon as possible, generally within a period of 14 days.[47]

The researcher must ensure on whether the study is conducted in accordance with the protocol and GCP Guidelines. Keeping track of level of operating procedures is crucial. Any adverse effects that arise during or after a subject's involvement in a trial should

[47] V. Vennu and P. P. Saini, supra note 31

be treated appropriately by the investigator. All grave and unforeseen abnormalities must be documented to the Sponsor within 24 hours of onset, and to the EC within 7 working days, if the study protocol has been approved.

- EC: This statement describes thoroughly about the constitution of the EC, that is composed in the following way:
- Basic Medical Scholars, one pharmacologist specifically
- Legal Professionals
- Medical Staff
- NGO Staff/Social Scientist
- Ethicist/Human Theorists/Theologian or similar person
- Common individual from the community

The EC's responsibilities, which include conducting meetings and keeping minutes, are also outlined in Schedule Y. Before approving any trial protocol, assess the risk/benefit ratio. Examine and approve/disapprove studies according to a set of guidelines, as well as oversee any trial and, if required, amend the study protocol. The previous limit on the number of subjects and locations has been lifted, providing the scientist more leeway and incentivizing studies. The proposed amendment helps clinical studies in India by allowing phase II, III, and IV trials to proceed simultaneously.

Regulatory trials in India have been required to be registered in the CTRI from June 15, 2009. If the responsible individual or organisation fails to do so, the licensing authority has the authority to issue a warning letter, reject the trial results, or bar the investigator or sponsor from participating in future trials for a definite period of time[48].

Since 2008-09, CDSCO has worked with a variety of managements to develop a logical plan for CT legal regimes, such as the United States FDA, WHO, ANVISA Brazil, Health Canada, and South Africa. Since then, several changes, revisions, and a road plan have been made to improve the review regime[49].

- Application of the CTD format for life forms and the deployment of the CTD format for novel drugs.

[48] Sangeeta Kumari, et al., supra note 30.
[49] Hitt Sharma and Sameer Parekh, supra note 35.

- Creating a legislative framework that allows phase 0 (micro dosage) and phase 1 trials to be undertaken phase by phase in the nation.
- CTs must be filed with the clinical trial registration since June 2009.
- Twelve NDAC were formed to review submissions for clinical trial authorization and novel drug clearances.
- A draught announcement for the certification of clinical scientists was published in January 2011.
- Draft criteria for disclosing SAEs were released in May 2011.
- November 2010 Clinical Trial Inspection Guidance
- The EC will be required to register.
- Drafter proposals for increasing the Ethics Committee's, Investigator's, and Sponsor's responsibilities to secure that trial participants who incur trial- related damage or death receive financial recompense as well as healthcare.
- On the internet, GHTF-compliant Schedule M III instrument regulations have been published.
- The concept of a drug will be separated for medical devices, and the rules will be altered. There is a framework for foreign inquiries in Rule24-A. (5). Since 2011, frequent abroad inspections have been done in several nations where drug imports occur.
- On November 10, 2008, GSR 780(E) was issued, notifying Good Laboratories Practices, which have been in force since November 1, 2010.

Many loopholes persisted in India's CT rules despite many amendments between 2005 and 2015. Many human rights violations performed by researchers can be traced back to India's failure to enforce its ethical norms. Scientific misconduct, such as the manipulation of informed permission, experimental data, or personal qualities, was also widely documented, even in the popular press. This prompted for further amendments of Clinical Trial Processes conducted in India thereby New 2019 Clinical Trial Rules have come to play[50].

## 2.7 India's NDCTR, 2019

The NDCTR for 2019 has been introduced by India's MoHFW. The new rules include clauses to promote scientific work as well as more challenging topics such as orphan

[50] V. Vennu and P. P. Saini, supra note 31.

medications, post-trial access, and pre- and post-submission briefings. The updated qualifying guidelines tend to better India's CT ethical and quality norms, benefiting both patients and industry[51].

There are thirteen chapters (107 regulations) and eight schedules in the proposed update. The new rules are applicable to all prescribed therapies, investigational novel medicines for human use, bio-equivalence, CTs and bio-availability studies, and EC. The new rules, which take effect immediately, will replace Part XA and Schedule Y of the D&C Rules, 1945. Schedule Y, animal health treatments, and existing limitations will all stay in force[52].

Following a series of media allegations of misconduct, the CDSCO office implemented stricter guidelines for performing clinical studies in 2013. Many new legislations have been passed, many of which have caused anxiety and uncertainty among sponsors undertaking worldwide clinical trials in India. The CDSCO modified its standards on CTs and novel medicines, releasing the NDCTR, 2019, to alleviate India's paucity of scientific practice.

**2.7.1 Significant New Definitions Included in 2019 New Clinical Trial Rules**

Clinical Trial: Each and every detailed analysis of a therapeutic agent or interventional fresh medicinal substance in study participants to gather facts for finding or verifying its[53]:

(i) pharmacological, including pharmacodynamics and pharmacokinetics; (ii) medical; or (iii) ill outcomes, with the view to ascertaining the safeness, potency, or sensitivity of these new compositions or interventional new drug.

Academic Trial: Any examiner, analytic, or science programme conducts a clinical trial of a therapeutic agent that has already been approved for a specific argument for a possible treatment, new method of taking the prescribed dosage, new prescription, or new kind of dosage, with the findings expected to be used only for analyzing and not for getting consent from the Central Licensing Authority or any country's legal body for branding or business ventures.

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[51] Shivaprakash G and Pallavi L. C., supra note 18.

[52] K. Bangarurajan, Regulations and Guidelines Specific to Ethics Schedule Y and CDSCO- GCP, CDSA, https://www.kem.edu/wp-content/uploads/2019/12/Regulations_Dr.Bangaruranjan-Well- drfine-Drug-ministry.pdf (Last visited Mar. 18, 2022).

[53] ISCR Report, New Drugs and Clinical Trial Rules, 2019, ISCR (2019), https://www.rgcb.res.in/documents/New%20drugs%20and%20clinical%20trial%20rules%202019.pdf (Last visited Mar. 22, 2022).

Orphan Drug: An orphan treatment is one strategy for treating a disease that affects fewer than 500,000 persons in India.
Post-trial access is defined in the New Rules for 2019 as the process of making a new drug available to a trial candidate after the completion of a CT in which the drug was discovered to be beneficial to the trial candidate during the CT.

### 2.7.2 Impact of Replacement of Schedule Y

Following the ratification of the 2005 modification to Schedule Y, India observed a progressive addition in the number of clinical studies. The practise of running trials without informed consent and failing to notify patients about the potential risks associated with the trials was exposed in 2012. The year 2012 was marked by a massive crackdown on any unethical practises that were masked behind the rapid growth of CTs.
According to the Indian Health Ministry, 668 CT participants died across the country in 2010. The relatives of the killed and affected participants, on the other hand, were not given a reasonable compensation, which the Health Ministry of India deemed to be the worst-case situation. The government then tightened the CT regulations via Gazette notification G.S.R.53(E) dated 30 January 2013[54].
As a result, a growing number of pharmaceutical companies have begun to perform clinical studies outside of India. Following the release of the new CT rule in 2013, the US NIH announced the postponement of 30 CT and also ceased recruiting subjects in some other trials in India.
In 2015, the Indian government fractured several of these laws after noticing a decline in clinical research. The Indian regulators were compelled to adjust the new standards due to a decrease in the clinical trials amount.
The incompetence of these two rules is eliminated in the 2019 Clinical Trial Rule making it more organized and conducive[55].

### 2.7.3 Role of EC

Per the revised standards, the ECs must compose 50% of non-affiliated people with the organisation and should at least consist of one single representative from outside.

[54] K. Bangarurajan, supra note 52.
[55] Akhilesh Dubey et al., New Drugs and Clinical Trials Rules, 2019: Towards Fast-track Accessibility of New Drugs to the Indian Population, 53 INT. J. P. E. R. S451 (2019).

There is a requirement to attend the training and development programmes as determined by the CLA by the members of ECs.
In addition, every update in the membership or structure of a registered EC must be reported in writing to CLA within 30 days. Before taking on any new CTs for evaluation, To rightly connect with the new rules, ECs will have to undergo breakup (and subsequent re-registration).
The EC should have the following responsibilities[56]:

(1) EC shall examine and authorise a CT, BA/BE study stages, and other relevant documentation, as well as manage CT performance, in accordance with the standards as required, GCP Guidelines, and other statutory standards, to protect the safety, interests, and advantages of trial subjects.
(2) Based on (2.a) regular study activity data prepared by the investigators, (2.b) tracking and audit reports done within the segment as prepared by the sponsor, or (2.c) by visiting the research sites, the EC shall evaluate the CTs for which it has given authorisation at suitable intervals.
(3) In the process of rejection or making a change in the protocol, reasons have to be given to be made available to the CLA.
(4) The EC have the responsibility of reviewing the records of any subject's significant adverse event (SAE) during any trial and report it to CLA.
(5) The EC have the power to ask to halt or suspend the CT at any time during the trial, if it thinks that the trial will cause any kind of threat to the rights, safety, or well- being of the trial participants.
(6) Any officer authorised by the CLA may conduct the site visit, go through any official log, or any official communications related to CT, with or without issuing a formal alert note; provide data in response to any doubt highlighted by such authorised person belonging to CT; and ascertain adherence with the format of these guidelines and other associated regulations.
(7) To preserve the rights of CT or BA/BE subjects, EC must adhere to additional standards or restrictions not specified in the Act, which may be established by the CLA with the Central Government's consent.

EC should be responsible for the following:

[56] Neelu Singh et al., New drugs and clinical trials rules 2019: Changes in responsibilities of the ethics committee, 11 PERSPECT. C. R. 37 (2020).

i. In connection with the study/trial method that has been inspected and allowed, EC is accountable for ensuring the benefits, protection, and well-being of all human candidates enrolling in the trial.
ii. The EC should take special care to secure the benefits, convenience, and health status of all vulnerable study participants, such as members of hierarchical groups (e.g., convicts, members from armed forces, and concerned staff and candidates who are studying medicine, nursing, and study institutions under pharmacy), patients with incurable health problems, jobless or deprived people, patients in emergency situations, ethnic minority groups, homeless people, and nomadic communities.
iii. The EC have to note down and keep a record of its works.
iv. EC should observe the trials continuously, for which they examined the protocols. This assessment could be centred on periodic experiment status reports from the investigators, supervision and within the segment audit reports from the sponsor, or a visit to the trial sites.
v. If an EC decides to withdraw a trial proposal's approval, it must explain the rationale of such a conduct and notify the investigator and the CLA as soon as possible.

**2.7.4 Compensation Rules**

The terms 'Nominee' and 'Legal Heir' are defined in the NDCTR as follows: When a participant in a CT die, the funding source is legally obligated to compensate the legal heir through monetary means, it is discussed in the Chapter VI, Rule 39(1)). There is no mention of the method of determining the legal heirs. In the ICF, the nominee's name and association must be included. (Table 3, Third Schedule, NDCTR)[57].

There appears to be some ambiguity on the mode through which the legal heirs should be found and whether it is the inspector's responsibility to do so. Previously, the nominee, whose identity was provided by the ICF participant, was compensated Without involving the sponsor or the investigator, the legal heirs might file a claim with the nominee and receive their part. The sponsor is in this case bound to ensure that the payment is made to the rightful heirs under the new standards.

For no fault of their own, the site and the sponsor are likely to become embroiled in legal wrangling due to the confusion between heir and nominee. The government

[57] Swati Jadhav and Ravindra Ghooi, supra note 19.

would be at significant gain to alter the rule as soon as possible and return to paying benefits to the nominee as it ever was.

### 2.7.5 Post Marketing Studies

The guidelines specify the actual post-marketing need, as are divided into three categories in the Fifth Schedule. These include: (1) a post-marketing Phase IV trial;
(2) a post-marketing surveillance study; and (3) post-marketing surveillance via periodic safety update reports[58].
The post-marketing studies must be completed in accordance with rules 77 and 82. Medications as brought from outside for the purpose of sales and marketing are covered by Rule 77, while drugs manufactured for sales and marketing are covered by Rule 82.
In sub-rule (iv), both of these rules employ the same wording, hence 77 (iv) and 82(iv) both states.' The applicant must provide reports of applicable safety options as part of evaluation processes during post-marketing phase, as given in the Fifth Schedule;' The necessity for PSUR becomes apparent, but it is unclear when the medical business is expected to do the Phase IV study or the Post Marketing Survey. Sponsors, investigators, and EC members will benefit from clarification on these problems.

## 2.8 Conclusion

CT protocols have been formed after a lot of tribulations all around the world, including in India, and the legislation is continually changing. Because of the enormous pool of patients available, as well as a large English-speaking and IT-savvy workforce, India has natural advantages for conducting CTs.
Indian legal segments are engaging with international bodies to maintain the CT technique and regulatory framework up to date. With the assistance and expertise of international regulatory organizations, India's regulatory system has become more robust, efficient, and successful.
With the growth of global CT market and increasing opportunities for India to gain its prospects by permitting foreign investors, the country's legal system in this area has been evolved accordingly. India's ICMR guidelines that forms the baseline of ethical

[58] Parveen Jain and Rahul Chauhan, India’s New Drugs and Clinical Trials Rules: An Industry Perspective, 7 REGULATORY F. (2019).

framework to follow during clinical trial process has been updated multiple times to keep pace with the global drug analysis procedure.

These modifications are intended for the purpose to suitably align the social, cultural, legal, political and environment aspects with the process. All these aspects have an integral connectivity with CT as they are to involve human participants for the purpose of the medical analysis.

Hence, the latest ICMR updates incorporate certain significant Social and Behavioural aspects within ICMR compliances, such as, policies of informed consent, ethical committee role and duties, clinical trial operational framework and part of possible mis-conducts. As a major reform, such changes are intended to blend expectedly with the advancements and approaches of clinical trial processes currently that are being followed.

Another remarkable guideline of equal importance is GCP that ensures protection of human participants and ethical principles in the scientific framework of clinical trials. Like ICMR guidelines, GCP guidelines are changed meeting the practical requirements of CTs. Basically, updated ICH-GCP are more concerned to secure human rights of the volunteers.

However, these laws are still not ideal if we see the practical complexities of CTs. Due to its enslavement to the business motivation of pharmaceutical multinationals rather than the fundamental objective, the application and practise of CT Rules in India has been considerably altered. It is incorrect to say that CT can only accomplish human well-being provided enough monetary incentives are built in for researchers and medication producers, because such infrastructural format has singularly damaged the trust and reliance of patients.

Furthermore, it is necessary to acknowledge the interconnections that exist between India and its foreign investors, as well as between different socio-economic groups and physicians and patients. Throughout the reform timeline of India's CT Regulation System, an appropriate balance is continually pursued, according to the chapter. Unfortunately, despite significant advancements, the legal system appears to be undermining India's ethical environment for Clinical Trial Procedures.

The Government implemented the NDCTR with a number of considerations in mind. The most important of these challenges include integrating the clinical analysis entities in India, attracting more businesses on international clinical tests to India, and boosting Indian indigenous drug making processes. Overall, the new protocols are

expected to boost the country's ethical and quality requirements for clinical trials, benefiting both consumers and industry.

The 2019 clinical trial guideline updates have trimmed out Part XA and the rules under Schedule Y in the D&C Rules, and ECs are given new responsibilities. The earlier procedure that the 2019 NDCTR have reworked for, was made up of numerous stopgap measures. As a result, this update of a dedicated, better organized set of rules for conducting experimental assessment on new drugs. Therefore, the CTs are expected to deliver more transparency and order to the regulatory demands for conducting CTs in this country.

Even then, certain problems remain to be attended precisely. The laxity in the process to establish a method for compensating trial subjects in the case of death or harm, for example, could be seen as the loose end of the guideline indicating its limitation to move beyond its authority and into the sphere of the courts.

# CHAPTER 3

# The Role of Courts in Application & Interpretation of Laws Relating to Clinical Trials: An Assessment

## 3.1 Introduction

CTs are very much a necessity for finding of a new drug, technology, or tending approach; without them, protection and efficacy in humans, cannot be determined.
There are legal and ethical regulations connected to CTs, which have been created at both the international and national levels, with one of their main goals being to give protection to CT participants.
Despite the availability of a variety of ethical norms as well as legal requirements, CTs have been conducted unethically and illegally in India and other nations where clinical trials are legitimately conducted.
Due to restrictions such as huge investments, human rights recognition, high access to education, free press to investigate any untoward incidents, strong legal and judicial systems, strong economy and per capita income, and overall strong integral IRB's and health agencies, drug trials were and are becoming exceedingly challenging in advanced nations[59].
Drug trials have progressively been moved to identify the poor and gullible masses of these states, and patients have been made guinea pigs without their expertise or formal consent, due to a lack of human rights bodies and recognition, corrupt and inefficient health controllers and practitioners, deprivation, and illiteracy in poor and developing countries[60].
Major ethical issues of India that are exposed to risk of human participant's health and security are: (1) Informed consent process and documentation; (2) Awareness about safety and compensation rights; (3) Academic/Economic limitations; (4) Responsibilities and performance of EC[61];

[59] Khalid Mahmood, Forewarned is Forearmed! Unethical Drug Trials in the Developing Countries, 6 JOURNAL D. U. H. S. K. 79 (2012).
[60] Ankita Chakravarty and Ambedkar Bhavan, Unethical Clinical Trials in India: A Selective Preliminary Overview, 27 EUBIOS J. A. I. B. (2017).
[61] Madhuri Jadhav and Arun Bhatt, Ethics in clinical research in India: A survey of clinical research professionals' perceptions, 4 PERSPECT. C. R. (2013).

CTs conducted in another nation do not need to be retested in India, according to a 2005 change to the D&C Act. It has given India access to the results of international trials as well as the availability of tested medications.

In a landmark bid in 2013 (Public Interest Litigation filed by Swasthya Adhikar Manch, an Indore-based Non-Governmental Organization), the Supreme Court of India derided the use of Indian citizens as "guinea pigs," instructing all State Chief Secretaries to look into all areas of healthcare trials and perform better rules and regulation in this respect.
As a result, a significant number of tests have been halted entirely. Without informed consent, no human person should be exploited as a "guinea pig" in clinical experiments for the benefit of innovation and low-cost drugs. No amount of money, whether promised or forced, can compensate a crippled, deformed, terminally ill individual[62].

### 3.1.1 A Brief Note of SAM Public Interest Litigation

The Supreme Court of India heard the PIL SAM v. Union of India (SAM case) as filed that appealed that the Court should step in to prevent the problem of unlawful and immoral tests that are done in the country on grown-ups, minors, and mentally weak persons[63].
After the Sam Case, the Supreme Court held that the uncontrolled trials by pharmaceuticals have become a threat to the country. After the case, the CDSCO made it mandatory to have an audio-video recording in the stage of informed consent for all CTs.
The audio–video need for informed consent was eventually limited to only 'vulnerable subjects,' however there was no description for vulnerable subjects in the announcement. Furthermore, regulatory organisations agreed that only audio (rather than video) recording of permission would be required to preserve the privacy of participants in anti-HIV or anti-leprosy therapeutic trials.

[62] Mritryunjay Seal, Clinical Trials in India and Role of a Legal Expert in the Ethics Committee, 2018, https://www.latestlaws.com/articles/clinical-trials-in-india-and-role-of-a-legal-expert-in-the-ethics-committee-by-mrityunjoy-seal (last accessed April 05, 2022).
[63] Himani Bhakuni, Informed consent to clinical research in India: A private law remedy, 20 SAGEP. J. 256 (2020).

Clinical research in India is still restricted under the DCA, 1940, as a result of the SAM case. In an updated Schedule Y, however, the necessity to get an AVR of informed consent for vulnerable people has been added. There are some instructions by CDSCO on recording of AVR to deal with the confidentiality and privacy of the participants.

## 3.2 Important Court Judgements on Unethical Clinical Trials

CTs have become more common in India during the last decade, with many multinational drug industries taking advantage of the opportunity. As described in Chapter 2, India's earlier CT standards without specificities to safeguard the security and health safety of human volunteers, which were extensively misused by these firms. A vast set of tests on Indian patients were discovered to have been carried out without observing the required legal and ethical criteria.

### 3.2.1 Mepacrine trial

Thousands of illiterate Indian and Bangladeshi women were subjected to an unapproved multi-country trial in the 1990s, in which the anti-malaria chemical **mepacrine** was used in pellet form as a method of female sterilisation. It caused inflammation and scar tissue growth in the women's uterine cavity, completely closing off the fallopian tubes[64].

While the trials in the West were halted, the substance was provided straight to medical practitioners in India. More than 30,000 women were sterilised in India using this unlawful and unapproved technology, including at least 10,000 in West Bengal alone.

This trial highlights how ethical norms fluctuate depending on where you are in the world. Despite the fact that the trials in the west had been halted, the treatment was provided to medical practitioners without being legally approved for testing, in what was plainly an illegal activity. The medication was banned by the Supreme Court, although it was still available in rural Bengal for up to five years after that.

[64] Ankita Chakravarty and Ambedkar Bhavan, supra note 60.

### 3.2.2 Cilostazol trial

Around 1999, Otsuka conducted **Cilostazol trials** for the therapeutic process of intermittent claudicating as permitted by the DCGI department based on partial, insufficient data that failed to reveal major adverse events[65].

Three distinct randomised medication assessments of cervical screening are arranged in the centres with Indian women in Mumbai, Osmanabad, and Tamil Nadu since 1998. The Mumbai test was supported under the norms of US National Cancer Institute, while the remaining two studies were monetarily aided by the Bill and Melinda Gates Foundation[66].

The aim of these studies was to develop a lesser cost cervical cancer therapy, which can be utilised in public health care. 254 women were adversely affected in the three clinical trials. It was alleged that female participants had no knowledge about the aspects of the trials in which they were to take part. The socio- demographic position was the reason to make women part of it. That was the fundamental ethical question as emerged for these tests: was it valid to deny females of backward socio-economic status access to screening when it was readily available?

The women in these medical inspections were not made aware of the process and its impact, and they had no idea at the time and also, they were kept away in isolation.

If the women had been told throughout the consent procedure that a cervical cancer checking could be minimizing their chances of dying from cancer, they might not have participated in the experiment and instead chose to have their self-chosen check- ups.

Despite moral norms demanding that they be provided all knowledge of risk reward, alternatives, and procedures, this female batch received no notation about the techniques of these experiments.

### 3.2.3 NDGA trial

During the years 1999-2000, the Kerala Regional Cancer Treatment Centre in Trivandrum ran a CT for the medication **NDGA** to treat oral cancer[67]. Patients were not given any clue of their participation in the trial and they had the option to quit. There

[65] V. Vennu and P. P. Saini, supra note 31
[66] Kalindi Naik, supra note 17.
[67] Id.

was death of 2 participants and there was an investigation setup by the media and NGO agitation. But the government gave a decision of halting the trial for 6 months, even though punishment was a necessity in the case. Later on this matter, a confession was made that permission form was not appropriate and the safety of the drug was not checked. Those investigators were stopped from being part of any other CT as main investigators.

### 3.2.4 Cilansetron trial

Solvay Pharmaceuticals tested **Cilansetron**, an unique novel chemical, for the treatment of diarrhoea (2000). Despite the fact that only Phase II trials had been done abroad and the medicine had not been approved anywhere in the globe, the DCGI approved a Phase III trial[68].

Drug studies of pharmaceuticals created beyond India were prohibited at the time under Schedule Y of the D&C Rules, which required Phase II trials to be conducted outside India. The FDA refused to approve Solvay's Cilansetron targeted strategy in April 2005, demanding additional clinical testing. Solvay dropped their NDA in the United States in November 2005.

### 3.2.5. Ragaglitazar trial

In the year 2002, Novo Nordisk ran a significant Phase III clinical trial for the drug **Ragaglitazar**, which could be a treatment for diabetic therapy in many countries. More than 2500 people from all over took part in the trial. On the other side, Indian experts questioned whether the research was acceptable because the drug had not been thoroughly evaluated on animals.
The trial was suspended as its testing on animals did not give desired results. Later it was revealed that there was no connection of drug exposure and cancer.

### 3.2.6 Risperidone trial

In 2003, Johnson & Johnson conducted a clinical trial for **Risperidone**, a medication used to prevent acute mania, in Gujarat, India. The psychiatric patients were asked to quit their current medication and that those therapies were cancelled.[69].

[68] V. Vennu and P. P. Saini, supra note 31.
[69] Kalindi Naik, supra note 17.

The patients were given the drug or the placebo, which is not known. Those received placebo have more chances of danger. A victim also stated that there was no idea that he is made a party of the study system even though consent form was signed, as he was forced by medical workers.
But the company denied all the allegations and stated that informed consent was taken from the participants. But the participants stated that there was no proper information to the participants as to what they were signing.

### 3.2.7 Streptokinase trial

In the legal controversy that erupted on **streptokinase** testing, which were analysing a "clot-busting drug" to apply for the cases of cardiac arrest or diabetes, Shanta Biotechnics (streptokinase) and Biocon (insulin) publicly carried out an unapproved Phase III testing not following the process of informed consent or approval through the GEAC[70].

The methods to follow for these tests was also not evaluated by an ethical review body. Despite Shanta Biotechnics' protestations, the experiments resulted in the deaths of eight persons. ANGO brought an appeal. The trials were found unlawful by India's Supreme Court in March 2004.

### 3.2.8 Theravance trial

Beginning in 2004, Bhopal Memorial Hospital executed therapeutic experiments on sufferers of the 1984 gas tragedy in breach of international ethical rules. More than 14 people who were part of different trials undertaken by Pfizer, AstraZeneca, Sanofi, and others died in it.
A **Theravance** trial examined two antibiotics for treating hospital-generated pneumonia, a second analysis of yet another medication, and a cardiac trial were among these investigations. None of the victims were aware that they were a part of a research study. The victims were handed over Rs. 200 for each visit and the family of these victims were not compensated. Also, the reporting of the death of the participants were also not done in timely manner.

[70] Id.

The illegal activities of the hospital came to the day light, also once such allegation was of choosing gas accident victims as trial participants. Millions of rupees flowed to the hospitals from pharma companies to perform these trials.
As a result, members of the facility's ethics committee who supported the tests were called to account for their actions. Shocking fact came outside that the members of EC were actually the trustees. It was found that one of the representatives was a sub-investigator in a test and there was another, who was evaluating the trial for a family member. Number of distinct improprieties were discovered in the case.
Pharmaceutical companies have always explained this decision by saying that doctors must evaluate whether or not patients fit the requirements for enrolment. Furthermore, neither the hospital ethics committee nor the researchers were prosecuted by the authorities. They just wrote a message to pharmaceutical corporations issuing warnings.

### 3.2.9 Seroquel XR trial

AstraZaneca Plc sponsored big, multi-centred placebo- controlled trials for **Seroquel XR** were recorded on clinical misconduct, according to a 2008 SOMO investigation. The technique is being used by the company to evaluate an antipsychotic medication for the treatment of schizophrenic patients[71].

The medicine was compared to a placebo, which meant that nearly half of the participants all diagnosed schizophrenics went the whole trial without receiving any treatment.
8.3 percent of patients who received the placebo needed to be admitted to the hospital because their diseases worsened. One 25-year-old person took his own life after 173 days of placebo treatment. Nonetheless, Seroquel XR was authorised for the EU market by the Dutch Medicines Evaluation Board. India, Bulgaria, Poland, Russia, and Ukraine also participated in the multi-center trials. While corporations continue to conduct CTs in other locations.

[71] Malia Politzer and Vidya Krishnan, The Dark Underbelly of India's Clinical Trials Business, MINT(Oct 11, 2012, 12:20 AM IST), https://www.livemint.com/Politics/D0gBgwCn3huK72S06p8K5H/The-dark-underbelly-of-Indias- clinical-trials-business.html (Last accessed April 25, 2022).

### 3.2.10 Tonapofylline trial

In 2009, multiple clients at the Maharaja Yashwantrao Public Hospital in Indore were unknowingly joined in a medical trial for **Tonapofylline**, a Biogen Idec drug. People from backward classes and those who were illiterates were chosen for the trials. These participants were assured that the treatments will be taken by the foundation. Some of the individuals in this study went into cardiac arrest and had convulsions.

The exact number of patients who went into cardiac arrest and had convulsions is unknown.

In another incident involving the Maharaja Yashwantrao Public Hospital, a three-day-aged newborn was given an experimental vaccination in 2012. The family accepted a deal which, they couldn't comprehend and were promised the infant would get polio vaccine, so they would have no clue the clinician was offering her an untested vaccine[72].

The records says that she suffered seizures and bronchitis bouts after vaccination was given and further was diagnosed with respiratory and food disorders. But the fact that these problems were due to the vaccine was hidden from the family.

A further breathing problem study was held at the same hospital using an inhaler. There was losing of vision and cataracts as an adverse reaction. The cataracts were corrected by hospital doctors, however participants who were involved in the trial were not aware of the risks in the first place.

In 2005, Dr. Rai learned about his older doctors' questionable practices. He observed that some sufferers visited the hospital frequently and were treated differently. He came to know the fact that the patients were made part of the trial without revealing their participation. Thumbprints were found on consent documents written in English and they chose patients who were illiterate and need of medical care. They broke every basic ethical principle by failing to inform patients about the trials and failing to disclose any adverse events or deaths. 81 patients were adversely affected by the trial. Those doctors who were involved in the unethical trials were punished merely by a nominal fine.

Government did not take any initiative in bringing out the findings of the inquiry to the public on the adverse events and deaths in cases of the trials. The activists were also disappointed with the modest punishment awarded.

[72] Kalindi Naik, supra note 17.

**3.2.11 Glaxosmithkline& Merck trial -** A trial was conducted by the states of Andhra Pradesh and Gujarat in 2009 to create a vaccine to combat cervical cancer induced by HPV. Adolescent girls seen between class of 10 and 14 years were to be made part in the states of Andhra Pradesh and Gujarat[73].
Vaccines were provided by **GlaxoSmithKline and Merck**. PATH created and implemented the initiative, which was funded by the Bill and Melinda Gates Foundation. Unfortunately, the Indian government terminated the initiative in April 2010 after human rights advocates openly denounced PATH's infringement of moral codes. However, 24,000 females had already been immunised by that time. A legislative investigation team found in 2011 that the informed consent process was unsatisfactory.

**3.2.12 SAM Case**
NGO **SwasthyaAdhikar Manch** filed a PIL in 2012, citing a news report by the Economic Offence Wing that discovered major irregularities in clinical trials in Madhya Pradesh. The experiments were said to be conducted on mentally ill patients at Madhya Pradesh's M G M Medical College[74].

The primary investigators, who was also a representative of the ethics board, was sued for violating the procedures of the ICMR. It also drew attention to the insufficient compensation provided to patients who were harmed by drug studies. Proper investigation on trials held in past 5 years was asked in the PIL. It also put forwards for examination of procedures of the current clinical trials. The PIL about suspected illegal clinical studies on minors, grown, and mentally affected people was accepted by the Supreme Court of India.

**3.2.13 M/s Cadila Healthcare Ltd & others**

[73] ECCHR Case Summary, Human Rights Violations in Clinical Trials in India, The case of The HPV Vaccination Project, ECCHR (Feb. 11, 2014), https://www.ecchr.eu/fileadmin/Fallbeschreibungen/Case_Summary Clinical_Trials 2014-02-11.pdf (Last visited April 15, 2022).
[74] Divya Rajagopal ET Bureau, PIL Filed Against Illegal Drug Trials, THE ECONOMICS TIMES INDUSTRY (Feb.06, 2012, 07:54 PM IST), https://economictimes.indiatimes.com/industry/healthcare/biotech/pharmaceuticals/pil-filed-against-illegal-drug-trials/articleshow/11780731.cms?from=mdr (Last visited April 21, 2022).

The MCI - EC realised and instructed the Council to inquire from the DCGI, ICMR, and Medical Council of MP about the action taken on the results of their inquiries at its meeting on 14.2.2012[75].In this regard, Director General of ICMR noted in a report dated 7.3.2012 that the ICMR's role is in capacity creation, establishing up types of norms and criteria for correctly performing Clinical Trials.

The DCGI and the Medical Council of India may take steps to conduct a thorough investigation. As a result, a text was issued to DCGI with a request for an update on the status of any inquiries that had been begun. In a letter dated 15.5.2012, the DCGI stated that a CDSCO team was formed to investigate various forms of medical trials, and it is:

11 tests sponsored by: (1) M/s Cadila Healthcare Ltd. at Ahmedabad; (2) M/s Intas Pharmaceuticals at Ahmedabad, and (3) M/s Emcure Pharmaceuticals located at Pune; were done by Psychiatrists at their private centres with permission from DCGI, which involved 241 subjects participation.There were numerous differences in the clinical studies done by Dr.RaghulamRazdan for patients according to the report.

CDSCO has issued show cause notices to the implicated doctors. CDSCO discovered several inconsistencies in the pattern of clinical studied that were not in conformity with India's GCP criteria for clinical research.

CDSCO has written a letter to the aforementioned pharmaceutical corporations and investigating doctors, advising them to be cautious when conducting trials in order to ensure strict adherence to GCP rules and applicable regulations.

On March 5, 2012, during Lok Sabha discussions, Shri B. Mahtab reiterated his stance that the legal authority for medical studies has to be improved. He claimed that India had become a good model for pharmaceutical corporations running drug studies over time, and that in light of recent occurrences such as the deaths of 49 infants at AIIMS, a more stringent regulatory framework was required[76].

Raahul Dutta, a health activist from Lucknow, has filed a PIL contesting certain elements of the D&C Rules 2011, which were announced by the national govt on November 18, 2012. According to Dutta, the present D&C Act of 1940 does not allow for such policymaking to control CTs and compensate mishaps.

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[75] Mukesh Yadav et al., Compensation Issue in Clinical Trials Recent Indian Scenario, 36, JOURNAL I. A. F. M. (2014).

[76] AshnaAshesh and Zubin Dash, Inadequacies Of Clinical Trial Regulations In India, 5 NUJS L. R. 379 (2012).

On December 19, 2012, the High Court advised the central government to formulate the specific method, scheme, and technique by which gross mismanagement and risks due to drug trials are shrivelled and tested, in response to the claimant's proposal the central government summon out the formal method, schedule, and strategies by which carelessness and risks associated with clinical trials are monitored and inspected.
As a result, the overuse and risks associated with clinical trials must be closely controlled and evaluated. According to the PIL, current legislation is unsuitable to regulate human clinical trials conducted by pharmaceutical corporations in the country.
The government was tasked with creating measures to regulate drug studies and compensate sufferers after Parliamentary Committee research (conducted by the Union Health Ministry).
The High Court has given the central government a month to provide details on the decisions made so far against those undertaking clinical trials in possibly hazardous conditions, seek approval.
According to the PIL, current legislation is ineffective to regulate human clinical practices done by pharmaceutical corporations in the country. Dutta claimed that the government's drafted rule lacks a protocol to figure up the minimum monitory reward for clinical trial failures.

### 3.2.14 Genentech Inc v. DCGI

In 2015, **Genentech Inc. and others**[77]filed a lawsuit against the DCGI, the Department of Biotechnology, the Government of India, and Reliance Life Sciences Private Limited (Reliance Life), challenging, among other things, DCGI's approval of a drug proposed to be launched by Reliance Life under the brand name '**TrastuRel**' (Impugned Drug), claiming it to be biosimilar to the Plaintiff[78].

[77]Genentech Inc And Others vs Drugs Controller General of India - Caveat No.1151/2015.
[78] Khaitan& Co, Delhi High Court permits in-house expert of a contesting party to be a part of Confidentiality Club,LEXOLOGY (June17,2020), https://www.lexology.com/library/detail.aspx?g=68bfa72e-f5db-4f0a-8634-da7cd448cfc3 (Last visited April 11, 2022).

It was alleged that they failed to perform the necessary pre-clinical and clinical tests to confirm the bio similarity of the Appealable Drug with that of the Plaintiffs' Drug, as required by the D&C Act1940, D&C Rules 1945, and Biosimilar Guidelines 2012, and thus the acceptance conferred by DCGI was invalid in law. Reliance Life filed files related to pre-clinical and clinical tests performed by it in connection to the Impugned Drug. To settle the court permitted to file the documents in a sealed cover, which will be inspected by experts and attorneys of the plaintiff.

### 3.2.15 Glenmark Pharmaceuticals Ltd trial

The clinical trial breach case of Malpani Hospital in Jaipur made headlines in 2018. An agent lured 19 men from the villages of Churu and Bikaner by promising them jobs in Jaipur, where they would be responsible for elderly patients at a medical camp[79]. They were in return offered Rs.500 and men between 19 and 35 was targeted and given medications, after which they began to experience dizziness, loss of consciousness, nausea, and difficulty to urinate. People in the Bidasar area of Churu district were reportedly given the drug GRC27864-201 by Malpani Hospital. The drug's maker, **Glenmark**, had its headquarters in Mumbai. Three days later, on April 23, the Swasthya Adhikar Manch, the principal appellant in the lawsuit, lodged a petition with the National Human Rights Commission.

The Office of the DCGI which is segment of the CDSCO, filed a warning to Glenmark Pharmaceutical Limited. According to the DGI's notification, after hearing about the trial in the media, a CDSCO taskforce examined into it and found numerous abnormalities.

According to Malpani Hospital data, just three people were fully recruited in the Phase 2 clinical experiment of GRC 27864 tablets. The CDSCO team determined that the three people's credentials had been falsified on all documents, including their phone numbers, addresses, and consent form authentications, when they checked into their records. The findings is that nearly 25 people were made part of the unethical trial. On May 24, 2018, the National Human Rights Commission filed a warning to the principal secretary working in the Rajasthan government's health department and Jaipur's commissioner of police, urging that they answer to the Churu trials within four weeks.

[79] Health And Caste-Based Harassment, THE CARAVAN (Sep. 11, 2018), https://caravanmagazine.in/health-and-education/churu-drug-trials-four-months-on-dalit-victims-report-severe-damage-to-health-and-caste-based-harassment (April 15, 2022).

According to Sanjay Parikh, a Supreme Court lawyer who is representing the SAM in their PIL, there is no provision to hold pharmaceutical companies responsible for grave negligence by them. He emphasised that if medical studies are to be conducted in India, strict regulation and implementation must be followed in compliance with guaranteed rights, especially in the case of impoverished people's life.

### 3.2.16 Jananeethi v. Union of India

The petitioner had been undertaking field investigations for clinical medication trials in Kerala since June 2009, according to **Jananeethi v. Union of India**, which was filed on January 18, 2021[80]. During the petitioner's investigation, it was discovered that there are serious human rights violations and other harms to clinical trial participants because drug trials are conducted without properly constituted ECs and without the trial participants' prior informed consent, in violation of the D&C Rules.

Physicians were rewarded for enrolling patients in CTs without getting prior consent, according to the petitioner. Participants are subjected to unethical tactics such as being denied access to life-saving medications. The growing number of trial-related injuries and deaths are being denied medical treatment and compensation.

Most clinical drug studies in Kerala, according to the petitioner, are done without a fully constituted Ethics Committee, and there are severe malpractices in the area of getting prior informed consent from trial participants. It was further claimed that this is highly illegal and infringes on persons' fundamental right to life, as guaranteed by Article 21 of the Indian Constitution. As a result, drug companies utilise the poor and illiterate residents of Kerala as "guinea pigs." In response to the appeal, the Kerala High Court granted the petitioner permission to pursue remedies under the RTA, 2005.

### 3.2.17 People's hospital case

A group of doctors and medical rights advocates published a statement on January 14, 2021, urging the Indian government to halt the trial at the **People's Hospital** in Bhopal as they suspected the defendant to have erased all records from the questioned area during trial processing, and prosecute people guilty for violations[81].

[80] Jananeethi v. Union Of India, AIR 2021 SC 273 (2012) (India).

[81] India Correspondent BMJ, India: Doctors Call For Investigation Into Allegations Of Ethical Abuse In Covid-19 Vaccine Trial, BMJ 372 (2021).

### 3.2.18 Oxford AstraZeneca Trial

The Bharat Biotech vaccine is one of two covid- 19 vaccines that India's drug governing agency approved for limited crisis use on 3 January, based on security and antibody evidence rather than quality data.

India has approved the **Oxford AstraZeneca** vaccine after reviewing safety, immunogenicity, and efficacy data from outside India as well as safety and immunogenicity data from India. A trial to see if the Bharat Biotech vaccination is effective has enrolled 25 800 people in 25 locations across 12 cities.

Seven participants in the People's Hospital study contend they were not notified whether they would get a vaccine or a placebo. During a media event on January 10, 2021, respondents described that they were told they would receive a vaccination that would safeguard them from the originated coronavirus and that they would be given Rs750 for the injections.

According to the All-India Drug Action Network, the Forum for Medical Ethics, and the Jan Swasthya Abhiyan (People's Health Movement India), among other groups, trial employees at the location violated the criteria of comprehensive presentation of study goals.

In response to a query opposing Bharat Biotech's licence from the Drugs Controller General of India to conduct a phase II/III treatment test of its Covaxin COVID-19 vaccine on kids ages to 18, the Delhi High Court issued a caution to the Centre on May 20, 2021[82].

A panel of Chief Justice D.N. Patel and Justice Jyoti Singh issued a decree on a lawsuit moved by advocate Sanjeev Kumar against a May 13 order of the Centre allowing authorization to undertake a phase II/III clinical study of Covaxin on 525 normal persons in the age band of 2-18 years.

The appeal contended that the CT of Covaxin on children would very certainly have a negative impact on their mental and physical health. It was stated that the term "volunteer" could not be used for these minor children aged 2 to 18 because they are unable to appreciate the implications of such clinical investigations.

[82] Soibam Rocky Singh, PIL Against Covaxin Trial On 2-18 Age Group: Hc Seeks Centre's Stand, THE HINDU (May 19, 2021, 12:18 IST), https://www.thehindu.com/news/national/pil-against- covaxin-trial-on-2-18-age-group-hc-seeks-centres-stand/article34593271.ece

### 3.3 Conclusion

For the past decade, CTs in India have been in the news. Many foreign pharmaceutical companies have picked the country because of its insufficiently equipped CT legislation and the easy availability of less conscious and poor human subjects for studies. As indicated in the chapter, the country has experienced several examples of CT infractions and illegal procedures as a result of its antiquated legal structure.

People from the poorer parts of society take part in these trials in the hopes of receiving monetary recompense and free medications. Participants, on the other hand, receive substandard care, insufficient remedies and compensation in the event of unfavourable events, insufficient legal protection, minimal government intervention in the event of an emergency, and insufficient consent mechanisms, resulting in the participants' inevitable impoverishment.

These limitations have generated concerns about human safety, particularly in light of PIL filed in the Supreme Court of India by SAM, an Indore-based NGO in 2013, which revealed multiple CT deaths. These cases were all gathered at the trial places. They all pointed to serious unethical conduct on human subjects during the testing phase, which was carried out by sponsors who had obtained a DCGI licence either illegally or under the guise of lax regulations.

Following that, a slew of other legal challenges has surfaced, highlighting many cases of clinical trial volunteers dying, particularly in states like Madhya Pradesh, Andhra Pradesh, and Gujarat. These incidents pushed India's government to establish proper and tighter protection standards in order to prevent deaths resulting from unethical research.

Children, mentally challenged persons, tribal and Dalits who were unable to give free informed permission in the clinical test procedure were deemed to be formally ensured to safeguard their well-being and rights.

Clinical trial violations that occurred between 2000 and 2015 mostly involved violations of ethical guidelines, laws governing clinical trials and medical ethics, and inactive roles by ethical committees, alleging a violation of Articles 21 (Right to health, intellectual property, and access to medicine) and 32 (Right to Constitutional Remedies as a fundamental right) of the Indian Constitution. As a result, new modifications have been enacted in India to make drug analysis more methodical and legally secure.

# Chapter 4

# Clinical trials in United States, Canada & their comparison with India

## 4.1 Introduction

Following the globalisation of clinical trials, Asia, which accounts for a significant share of the global human population (more than half of the world's population), has begun to enter the clinical research arena. Currently, Asia's clinical research market is predicted to grow faster than that of the US and Europe.

By 2008, emerging countries are estimated to account for roughly 30% of the global contract research market enabling clinical research operations, particularly pharmaceutical sector R & D[83]**.** The sudden focus on Asian countries can be linked to multinational pharmaceutical corporations' desire to explore novel possibilities for expanding their company.

The expansion of clinical testing facilities in Asian countries to fulfil rising demand has driven this even further. One of the main motivations for testing drugs in Asia is the higher prevalence of "Western" health complications such as hypertension, dyslipidemia, diabetes mellitus and others, paired with changing eating intake and reduced physical activity.

Singapore, Hong Kong, and Japan are the most sought-after Asian countries, with well-established clinical research infrastructure. Countries like China, Korea, and India, on the other hand, have just recently become active participants in global CTs.

Despite their late emergence, India and China are expected to have a substantial growth prospect in medical trials due to their high disease frequency and treatment-naive patient pools. Because of its enormous biologically diverse population, high end facilities, and highly qualified English-speaking investigators, India is a suitable location for conducting global drug studies.

This chapter includes a need-specific comparative analysis of the Clinical Trial Regulatory activities of the United States of America, Canada, and India, taking into account the concerns about adverse effects of drug-related problems that are prevalent

[83] Sandhiya Selvarajan, et al., Clinical trials in India: Where do we stand globally? 4 INT. S. C. R. 160-164 (2013).

and simultaneously ongoing with the advancements of therapeutic availability and progress that are taking place in the country.
The value of this comparison, according to the researcher, arises from the rising alignments of these three nations to collaborate in the commercial drug manufacturing process. This, as well as the obstacles that multinational drug development enterprises face as a result of current regulatory gaps, necessitate a detailed examination, which is what this chapter aims to provide.

## 4.2 Clinical Trial Regulation System of United States of America

The USFDA is a section of the US DHHS entrusted with ensuring that human and veterinary medications are safe, effective, and of top standard. This entity is also in responsibility of advancing the healthcare options in the United States[84].
It is a huge and complicated government agency with a number of centres, departments, and offices in the Washington metropolitan area as well as other regional offices across the country. There are two authorized CT evaluation units in USA. One is CDER. The other one is USFDA's CBER.

### 4.2.1 General Clinical Trial Regulatory System of USA

According to the FDC Act, FDA is the law defining control that oversees drug analysis research of United States' medical commodities that are developed. The FDA's involvement in assessing and allowing INDs applications to perform objective studies in persons using investigational pharmaceuticals or health fluids is addressed in this feature, in agreement with the 21CFR50, FDC Act, and 21CFR312.
The Department of HHS Pre 2018-ComRule and RevComRule, which are implemented in 45CFR46 within subpart A, are also inspected. Finally, if applicable, extra HHS aspects found in 45CFR46 given in subparts B as in the portion of E are detailed utilising acronym 45CFR46-B-E in this category[85].
There are a number of initiatives of FDA and that of HHS' to harmonise their human donors legal parameters. Yet, there are differences due to the entities' specific powers and statutory obligations. As a result, except for being allied with the Department of

[84] Prajapati Vishal et al., A Review On Drug Approval Process For Us, Europe And India, 2 INT. J. D. R. A. 1- 11 (2014).
[85] National Institute of Infectious Diseases Review: USA vs India Clinical Trials, CLINGREGS SURVEY (2021) (Last visited Apr. 03, 2022).

Health and Human Services, the FDA is not a unit under the term of Pre2018-ComRule.
Instead, the authority is controlled by its own class of norms, under FDC Act guidelines and following the 21CFR50 rules.
The two regulatory agencies, namely, CDER and the CBER are working for pharmaceuticals and biologics (CBER). Acting under the US clinical inspection guidelines, the OCLIP also makes the needed medical procedure and human donor practice ensures, restrictions, adding advices.
The RevComRule applies to all publicly financed or promoted human contributor testing that was sanctioned by an EC on or after 21 of January, 2019.
Else, the specified EC scrutiny can be relaxed or declared exempt on or after that date. (Prescribed as per USA-55. Alsounder USA-74, the given RevComRule guideline is recognized as the "2018 Standards".) USA-74 contains the 2018 Requirements Decision Charts that follow the RevComRule.
For OHRP where the Department of Health and Human Services' Office operates, is in charge of overseeing the service's action to preserve the legal protection, livelihood, and well-being of recruited subjects in analytical tests performed or assisted by the unit of HHS. The OHRP often play role here to oversee all central agencies that perform drug potency tests on human respondents under the Pre-2018-ComRule followed by RevComRule terms.
Prior to January 21, 2019, the Pre2018-ComRule conditions applied to research that was certified by an EC, had EC relax the inspection process, or was deemed privileged by the specified law as mentioned in the chapter. Facilities who had their research accepted prior to January 21, 2019 can use the requirements criteria of RevComRule.
The establishment or EC should be reporting and the decision date to transition an investigation on the day the choice was taken. The inquiry must follow the Rev Com Rule starting that day.

### 4.2.2 Clinical Trial Life Cycle of USA

Under 21CFR312 rules, 21CFR56, and terms of USA-42, initiation of a drug study can only be granted when the FDA has reviewed the investigational therapy application (IND) and obtained authorisation from US's organisational ethics committee (EC) (also it is mentioned as the United State's review board (IRB)).

Except if the FDA places a clinical prevention on the IND, there is no need to wait after the 30-day review time[86].

The sponsor may acquire an experimental product after an IND has been received once the review time of 30-days completes, according to 21CFR312 (IP).

a) Clinical Trial Agreement: Rules of 21CFR312 says that includes the terms of US-ICH-GCPs that all research inspectors must have the requisite accreditation, expertise, and competence. The funder must have a formally accepted Investigator's authorization paper, Form FDA 1572, from the research worker(s) prior to the trial's initiation, per the G-1572 FAQs.
   This agreement functions as the investigator's promise to submit relevant details to the advertiser and to follow the FDA's clinical trial rules.

b) Validation of the EC's Assessment and Approval: An EC evaluation of the clinical analysis based on 21CFR312 and 21CFR56 terms, before the sponsoring suggested by Pre2018-ComRule, and the RevComRule can commence the trial, according to the RevComRule 21CFR56, the Pre2018-ComRule, 21CFR312, and.

c) Clinical Trial Registration: FDAAA, FDAMA terms, and 42CFR11 allot clear roles and responsibilities. One authority is an investor and the other is PI, appointed by the funder, to apply digitally preserved under ClinicalTrials.gov databank. According to Fv42CFR11, DAAA, and the terms of USA-26, the PI/promoter is liable to submit formal request 21 calendar days whence the first human contributor is recruited in a drug evaluation study.
   For FDA-approved, authorised, or authorized experimental medications, 42CFR11 elaborate the constitutional standards for providing clinical trial formality and information and findings.
   The NIH issued NIH Trial Info to augment 42CFR11 criteria. Regardless of testing stages, kind of therapy, or whether they are subject to the rule, all NIH-supported grantees and researchers performing clinical trials, whether paid in whole or in part by the NIH, must enroland disclose trial data to ClinicalTrials.gov (USA-78).

d) FDA regulations do not necessitate DSMBs, (also can be called DMCs), except if the study is undertaken in an urgent environment when meeting the informed consent requirement is difficult.
   According to 21CFR50 provision, the FDA needs the organisation of a separate data advisory group to oversee the clinical investigation in this case.

[86] Id.

As the US-ICH-GCPs terms specify, it creates a DSMB to track the clinical trial activity, encompassing safeness norms and noteworthy effectiveness outcomes, and advise the sponsorship on whether to proceed, amend, or discontinue the trial at frequent basis.
Furthermore, as asserted in the Pre2018-ComRule and also under RevComRule terms, the systemic EC must ensure that, when acceptable, the inspection format includes suitable arrangements for measuring the data gathered from the record to plan formulated confidentiality and protection for all study and related prompted and/or monetarily boosted through the Department of Health. Also, HHS works in the same process.
Per the NIH Data Safety Monitoring and USA-72, every NIH-funded drug studies must include a Safeness and Data Handling Plan, and tracking should be proportionate with exposure. DSMBs are also necessary in clinical research active in multiple zones with treatment that could endanger volunteers. The NIH Data Security Management Plan and USA-72 explain HHS/NIH guidelines.

### 4.2.3 Review Process of US Clinical Trial

As stated in 21CFR312, the FDA's foremost goals in thorough checking of an IND are to protect the protection and aspects of the human donors at all stages of this process. Phase 1 proposal reviews are primarily concerned with assessing the experiment's safety, whereas Phase 2 and 3 submitting studies also examine the investigation's technical capacity to deliver results that match the legal requirements for marketing authorisation. An IND can be prepared for one (1) or more rounds of an investigation[87].
According to terms of USA-5 and that given under USA-15, the FDA's Division for CDER work in coordination with CBER for the IND filing approval process for therapeutics and therapeutic biochemicals, respectively.

A sponsor, as mentioned in the 21CFR312, US-ICH-GCPs, and the 21CFR50 terms, is someone who needs to be held accountable for and conducts a clinical trial. An

[87] Maureen Bennett and Jan Murray, Conducting Clinical Trials in the US and Abroad: Navigating the Rising Tide of Regulation and Risk, Squire, Sanders & Dempsey L.L.P., https://www.squirepattonboggs.com/~/media/files/insights/publications/2009/10/conducting-clinical-trials-in-the-us-and-abroad-/files/ssdcentral68696v2draftwhitepaperconductingclinic/fileattachment/ssdcentral68696v2draftw hitepaperconductingclinic.pdf

individual, a pharmaceutical corporation, a public authority, an educational establishment, a private enterprise, or some other entity could be a host.

The inquiry is not generally undertaken by the advertiser unless the supporter is a sponsor-investigator. A sponsor-investigator is someone who organizes and runs a project, and under whose effective authority the investigational product is delivered or furnished, as under the instructions of 21CFR312, 21CFR50, and the US-ICH-GCPs. The word does not include someone who is not an individual.

A sponsor may entrust any or all of his or her tasks to an agreement research institute, complying the terms mentioned under 21CFR312. The US-ICH-GCPs also guides for the provision.

Any trial-related tasks committed to and handled by a CRO. The process should be properly documented, and any commitments not addressed by the documentation would be regarded as not transferred. Furthermore, any CRO that takes any sponsor formalities must adhere to the tight guidelines established in 21CFR312 and will be moderated under the same policy oversight as the sponsor if they do not.

Despite the fact that a sponsor may entrust all of his or her experiment activities and functions to a CRO, the norm states that the promoter is lastly accountable for the test record's consistency and value.

When a clinical halt is put in place, the evaluation teams of CDER with CBER will go through all base INDS and notify the sponsor on 30 days of receipt the INDS. An FDA order that causes a clinical trial to be paused or postponed is known as a clinical hold.

If the team concludes that a clinical hold is necessary, they will work with the sponsor to discuss and address any issues before it finalizes clinical hold order. An INDS is effective 30 days after it is obtained except if the promoter receives FDA alerts that the INDS is pursuant to a clinical hold.

Else the FDA can suggest the sponsor beforehand when the trial can begin. A promoter running a drug evaluation analysis to accompany an upcoming strategic registration may arrange a meeting with the FDA.

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The FDA does not require payment for evaluating investigational new medicine applications. The FDA, on the other hand, has the command to impose and obtain user payment from commercial segments that run businesses on certain therapeutic products and biological commodities as part of the New Drug Application event under the FDC Act, FDARA, and USA-45 (NDA).

The NDA serves as the mechanism throughout which pharmaceutical companies formally seek to the FDA that a novel treatment be licensed for promotion and sales in the country. The information obtained during animal research and human drug evaluating trials for an exploratory novel medication comes under NDA's domain.
The following criteria provide a combined notion of safety notifying systems in accordance with 21CFR312, 42CFR11, USA-38 and the G-IND-Safety: Any unfavourable medical event connected with the usages of pharmaceuticals in humans, whether or not it is recognised a drug-centric activity.
An AR is a term used to describe any AE as occurred by a drug. ARs are a sub element of all putative allergic events for which there is grounds to think the medication is to fault.
SAE/SSAR - An AE/SSAR that ends in extreme cases including death, is life-risk, demanding compulsory hospitalisation for the sufferer or the extension of a continued hospitalisation, results enduring or notable physical damage/incapacity, causes an inherited anomaly/birth deformity, or considerably impedes the individual's opportunity to execute normal life processes.
Any AE that has a strong chance of being triggered by the treatment is classified as a SAR.
Unforeseen Adverse Event/Unexpected Serious Bad Event – A not outlined AE or SAR in the IB, unlabelled at the precision or consequence as has been noted or lack adequate accuracy in terms of risk information should be explained in the common experimental drug development scheme or elsewhere in the implementation if an IB is not required or available.
Life-Harming Unexpected event/Risky circumstance SAR - An AE/SAR is "life-threatening" if it brings a human health in jeopardy right away. It rules out any AE/SAR that could have been fatal if it had occurred in a more extreme condition.

The Department of Health and notably the HHS do not describe or use the terms "adverse event" or "unanticipated difficulties." (Under G-HHS-AEReqs Terms). The Pre2018-ComRule applicable with the RevComRule, on the other hand, define the procedures for assessing and disclosing these cases.

### 4.2.4 Role of Ethics Committee of USA's Clinical Trial System

According to 21CFR56, 21CFR50, and 21CFR312, a decentralised segment to CT ethics review functions in the US. The funder must get the institutional level EC grant validated for those trials to be evaluated. Institutional ECs are also called as institutional review boards (IRBs) in the United States[88].

Under the 21CFR56 guidelines, -ComRule, the RevComRule, the Pre2018, 21CFR312, and the US-ICH-GCPs, the result in a significant of facts analysed by the EC (also known as an IRB) associates to preserving and safeguarding the freedoms and respect of research subjects, as well as guaranteeing their safety all across their ability to participate in a clinical study.

The EC should be formally taking care on doing a full examination of the research design, determining the possible benefits to participation, and guaranteeing that anonymity systems are in place.

According to 21CFR50, 21CFR312 and 21CFR56, all clinical research for drugs and biopharmaceuticals governed by the FDA requires institutional EC authorization.

However, these rules do not encompass the verification of any unspecified bio-specimens in the concept of "human subject." As a consequence, the applications of non-identifiable bio-specimens in studies need not necessitate the use of the Pre2018-ComRule.

In any case, the RevComRule compels federal agencies and departments adopting the policy to re-examine the terms of "identified private information" and "identifiable specimen" opting from either (1) year of the policy's commencement, and at least each four-time period counted annually afterwards.

These aforementioned organisations will collaborate to see if any analytic techniques or procedures may be used to create recognizable private data or recognizable specimens.

Unless an expedient review method is implemented, the prospective trial must be evaluated during scheduled proceedings with a majority of the EC attendees, which has at least one (1) Under the terms of 21CFR56, Pre2018-ComRule condition, and the norms of RevComRule, a participant whose primary interests are non-scientific. The experiment is only considered permitted if the majority of the participants agree.

[88] Prajapati Vishal, et al., supra note 84.

Under 21CFR56 and the Pre2018-ComRule, the EC is obligated to issue in this context at periods sufficient to the risk measure, but no not for once per year, save in the following cases:
Accelerated permission is common in research that presents a low risk or involves only minor changes to formerly cleared research (unless the referee expressly reasserts why arranging a review would provide thorough legal protection of research volunteers)
A condition of exclusion for research is restricted EC review.

Investigation that has evolved to this point includes data evaluation and/or access to note the status of the clinical data from operations - the aspect of medical therapy.
Institutions that undertake or invest in research for a federal office or department must procure an accepted assurance that the investigation will legally bound with the Pre2018-ComRule terms or as the RevComRule as necessities, as well as confirm to the federal unit/agency says the exploration as accepted by an EC stipulated in the confirmation.
A FWA of conformance, as specified by USA-59, is a completing basic by a non-exempt human subject centre of excellence (not an EC) that guarantees to follow Pre2018-ComRule or RevComRule requirements of human subjects' tests that is unavoidable to be performed or financed by HHS.
The OHRP has also validated FWAs for federal wide use, meaning that they can be used in studies by other governmental agencies that have recognised the Federal Principle for the Welfare of Persons.
Institutions undertaking or assisting study work or funded by the federal authorities of non-HHS forms and units hold consultation with the sponsoring office or department to see if the FWA is appropriate for their project.
As per the RevComRule, the institution and the segment of EC must disclose the institution's dependence on the EC's role to decide on research regulation, as well as the accountabilities that each object will assume to enforce consistency with the RevComRule terms applicable on non-exempt investigation (or exclude any studies that partly motivated EC analysis) performed by an EC member that is not controlled by the institution involved in the study.
A legal pact done in between the institution and a chosen EC, a scientific plan, or the execution of an institution-wide guidelines that splits obligations between the preferred institutions and all the designated ECs that are not managed by the institution are all examples of strategies to accomplish conformity.

The EC's records must include such documentation. The G-HHS-Inst-Engagement can assist an institution in determining if a research study is non-exempt. Because of the RevComRule, institutions do not need to amend a current FWA, according to USA-54.
The European Commission's Contribution in CT Authorization in the United States: The FDA requires examine and authorize an IND before a funder can begin a clinical study, and an EC must validate the research plan in accordance with suggested rules[89].
The institutional EC validation of the medical study could take place at some point as the FDA's confirmation of the IND. The EC on its part can approve the sponsor's application before the clinical investigation can commence. Studies that aren't done on-site can be reviewed by an EC. More details can be accessed at G-IRB Review.
All government funded or authorized institutions based in the United States that are participating in multi-centre investigation would have to assign a sole-EC to evaluate the verification for the component of the inspection phases done in the United States in required to conform with the RevComRule.
When a comprehensive evaluation is recommended by law (taking together the tribal norms), or when any federal state agency involved or doing the analysis believes that employing a sole EC not as acceptable, this requirement is waived. The norms of NIH from the portions of NIHNotice16-094 and NIHNotice17-076, say that all institute-backed multi-centre drug studies conducted in the country must be overseen by a one EC if not forbidden by any of US national, primitive, or state law, rules, or governance.
Despite the fact that the provisions do not stipulate an end date for EC consent, the G-IRB ContRev and 21CFR56 both assert that no clinical enquiry can begin unless the based on past review and authorised study is part of the ongoing assessment at ranges adequate to the degree of risk, but no less than annually. The EC must assess by reference at periods appropriate with the level of harm, but no less than one time per year (Under Pre2018-ComRule terms).

## 4.3 Clinical Trial Regulation System of Canada

Local, provincial, and federal policies, guidelines, and suggestions make up Canada's clinical research regulatory regime. To begin, PIs must follow their funders' and

[89] National Institute of Infectious Diseases Review: USA vs India Clinical Trials. ClingRegs Survey. 2021.

financing organisations' guidelines and rules, as well as the rules and regulations of the research and academic facilities with which they are associated[90].
Furthermore, state legislature lays out the procedures for obtaining approval from the REB. The federal government has also signed laws that governs clinical studies.
The research in this field has also widely supported a set of ethical study activity guidelines. In all, such a strategy demands a PI completing a number of processes before beginning a clinical research project.

### 4.3.1 General Clinical Trial Regulatory System of Canada

And according to Canada Food and Drug Administration, the Canada FDR, the G-Canada CT Apps, and mentioned in CAN-29, HC works as the authorized supervisory control body for drug analysis authorization, monitoring, and examinations in Canada. According to the G-Canada CT Apps, the HC authorises drug tests in Canada and oversees the for commercial supply and importing of pharmaceutical products meant for evaluation in accordance with Canada FDR regulations[91].
A "treatment product authorization" is a licence that is sanctioned for the transfer, sale, promotion, production, readiness, protection, packaging, labelling, preservation, or analysis of a medicinal product, according to the Canada FDA; a "medicinal product permit" is a certification that is agreed for the import, selling, promotion, production, planning, restoration, packaging, branding, handling, or validation of a therapeutic product, as per the Canada FDA.
Clinical trials using (Phase I - III): At the time when therapeutic products are not permitted for public consumption in Canada are requested for development and correlating bioavailability evaluations, and Procured drugs where the suggested usage of the medicines for a single or multiple options trying to follow is distinctive. In that cases, norm suggests cues and interventional use; permitted treatment methods; route(s) of management; or dosage exercise routine, according to the G-Canada CTApps (s).
Canada's "Health Portfolio," which consists of five government agencies, is headed by the Minister of Health. Clinical trial procedures are evaluated for participant

[90] Josmar K. Alas et al., Regulatory Framework for Conducting Clinical Research in Canada, 44, THE C. J. N. S. 1-6 (2017).
[91] National Institute of Infectious Diseases Review, supra note 85.

protection and safety, medication value is analysed, facility ethics committee review is ensured, principal investigator abilities are checked, and possible adverse responses are monitored and reviewed, all in compliance with the CAN-31.

The HPFB operational under Department of Health and Human Services' is the national agency responsible for governing, analysing, and supervising targeted therapy quality control, effectiveness, and performance, as well as checking data provided in investigational implementations, as according CAN-23. HC also grants the commercialization or importing of medicines for its use in drug testing.

Two of the nine (9) government departments and one (1) division that make up the HPFB are the TPD. Other one is the BRDD. Medicines, biological medicines, and radiopharmaceuticals for personal use are governed by the TPD and the BRDD, as established by CAN-18 and CAN-17, accordingly.

Per the G-Canada CTApps, the OCT of the TPD and the ORA of the BRDD, among many more units, are actively engaged in the clinical trial verification systems for the applicable pharmaceutical items available in Canada.

The concerned operational authority decides whether a medicine should be classed as a drug, a medical instrument, or a blend of both. If a drug is not conveniently fulfilling one of the statutory categories, other governing sections of HC are invited to join in the committee's proceedings. According to CAN-33, there are no expenses associated with presenting a clinical trial proposal in Canada.

**4.3.2 Clinical Trial Life Cycle of Canada**

Before a clinical study can commence, an IEC together with HC must both authorise it. There is no need to delay after the application receives these clearances. Thus, according CAN-30, the date of trial beginning is identified as the day when the medicinal drug analysis site is ready to recruit participants for the purposes of the Clinical Trial Site Tracking sheet[92].

A clinical study is considered allowed if it has been submitted to HC and then haven't received an opposing appeal within 30 days. Every CTAs of this type are susceptible to a 30-day initial time from the date of acceptance of the completed trial request at the competent Division under HC's HPFB.

While the allocated departments have the option of setting shorter procedural deadlines for bioequivalence trial inspections, such as 7days, the 30-day default

[92] Id.

procedure ensures that the regulatory duty is met. Xenografts, somatic cell treatments, genetic facilities, and prophylactic vaccines, reproductive and genetic processes are all excluded from the Phase I seven-day target plan in clinical studies.

The commencing date is the date where the funder acquired both HC clearance and EC approval from the applicable Directorate (that is, the mentioned date on the No Objection Letter). Furthermore, the initiation date is the date on which the promoter begins implementing the terms, which looks after the screening process prior to check-in.

As per the Canada FDR, the G-Canada CTApps, and the G-Canada Non-eCTD, in each stage, the promoter must maintain the REB Sanction and QIU aspects. This is done for composing the CTSI template in digital form to the proper HC Directorate as done for each trial site.

If a promoter (located in Canada or international) needs to spread a pharmaceutical product into Canada to execute a drug evaluation process, a copy of clinical trial clearance (i.e., the NOL) granted from HC must also have been included in the drug package.

If a funder looks forward to source investigational pharmaceuticals by own without any reference to each trial location, the promoter should altogether permit the acquirer when composing the medical analysis request.

a) Contract for Clinical Trials: The host must sign a deal with all participating parties, notably QIs, research facilities, ECs, and others, before to commencing the trial to comply fully with regulatory standards.

   CAN-28's simple conceptual Clinical Study Agreement (mCTA) can be used by clinical testing places and funders to formally draught phase II and also for phase III research study terms. The mCTA is an available resource to field suggestions for a standardised clinical trial draft arrangement to aid expedite the drafting stages and reduce clinical trial initiation.

b) Certification of the Ethics Committee's Review and Approval: Per the Canada FDR and the G-Canada CTApps, the marketer has to procure institutional EC clearance for collaborating site at each stage before beginning a lab testing.

c) Qualified Investigators: The funder must confirm that a QIU file (CAN-37 or related material that fits the Canada's FDR guidelines) is produced and placed on hold before beginning a clinical study, per the G-Canada CTApps.

According to the Canada-FDR, the documentation confirms the QI role who will execute the clinical trial as based on the best therapeutic interventions and will promptly notify trial respondents and the institutional EC of testing discontinuation and the cause for discontinuation. If the QI needs a system changes it should accordingly be declared through a new CTSI request for HC to validate, and a new QIU record must be retained by the advertiser.

According to the G-Canada CTApps, promoters should enrol their drug evaluation request on one of two (2) recognised public registries that accept international clinical evaluation documentation and are accepted by the WHO:ISRCTN Tracking system together with ClinicalTrials.gov.

According to HC Notice-CT Reg Disc, clinical testing registration is not necessary at this time. The G-TCPS2 terms establishes the security standard for all ECs formed in Canada's judiciary areas, drug studies have to be maintained in an available to the public record. The purpose suitably connects with WHO visions or the ICMJE before the first trial participant is recruited.

Furthermore, after the completion of registration, researchers should be compliant for keeping the registry up to date with new data, safeness and efficacy reports (as and where applicable), clauses for terminating a trial at early stage, and the zone of findings.

d) Data and Safety Tracking Platform: When actually not needed, a DSMB (also widely recognized as a distinct Data-Monitoring Committee) be founded to measure the ability of a medical trial, along with testing results and crucial efficacy parameters at periods, and notify the facilitator on who should keep going, alter, or cease the experiment.

When the HC Notice-CA-ICH-GCPs is not observed, the ICH guideline applied by HC take priority over other HC instruction. To aid investigators and ECs in assessing if a DSMB is warranted, the G-TCPS2 evaluates the important components:

- The size of the potential research-related damages to participants
- Whether or if the participants' circumstances render them highly sensitive related to the drug trial systems
- Interim data analysis: is it feasible?

- The research's intricacy
- Interest conflicts

### 4.3.3 Review Process of Canadian Clinical Trial

As mentioned in the G-Canada CT Apps and CAN-23, the CTA clearance process is handled by HC's HPFB. Before conducting the experiments, the funder must apply a CTA to the competent HPFB Board. Pharma CTAs are delivered to the TPD, whereas bio-similar and radiopharmaceutical CTAs should be conveyed to the office of BRDD[93].
A host, as per Canada's clinical trial law, is a person, corporation, facility, or agency that performs a drug study. The CA-ICH-GCPs apply to individuals, firms, agencies, or entities that assume charge for the conception, conduct, and/or payment of a clinical investigation.
Under CA-ICH-GCPs terms, a funder may handover some or all of its trial-based tasks and roles to unlike the CRO and/or institutional zones (s). On the other hand, the sponsor is always in charge of the trial record's worth and integrity.
Any trial-based obligations assigned to a CRO needs regularly be documented and recorded. The CRO must be in charge of process validation. When other HC suggestions are conflicting, the ICH guidance applied by HC take priority, as indicated in HC Notice-CA-ICH-GCPs.
According to the Canada FDR and G-Canada CTApps, a promoter could be either external or internal. A senior real scientific professional from a foreign funder must address them in Canada and confirm and seal the request and medical study certification form.
After receiving a CTA, the HPFB board examines the proposal for thoroughness. The Directorate will issue the host an Appeal for Clarification or a Refusal of Screening Notification if any problems are detected. If the Directorate finds the request to be

[93] Therapeutic Product Directorate Report, Overview of Regulation of Clinical Trials in Canada, Vol-2(1), Health Canada, https://admin.ich.org/sites/default/files/inline files/Overview_of_Regulation_of_Clinical_Trials_in_Canadapdf.pdf.

acceptable, the applicant receives an acceptance letter informing them that a 30-day standard approval process has commenced as of the days from the receipt.
As per the G-Canada CT Apps, if a CTA has been presented to HC and has not obtained an opposition in 30 days' timeline, the funder can sell or acquire a drug for use in research.
A NOL is provided if the clinical trial is allowed, as pointed in the G-Canada CT Apps and CAN-23. A declination of CT should be properly acknowledged through a NSN sent as a formal notification. During the testing phase, the concerned board may urge further updates from the host, and the funder has two (2) business days to reply.
HC will not let the advertiser to begin the drug study until each collaborating trial site has regulatory EC clearance (done through the relevant CTSI document), pursuant to the Canada FDR, G-Canada CTApps, and CAN-6. As per the HC Notice-CTSI Application, filled CTSI papers must be delivered to the HC members in advance to the initiation of a clinical trial.
The relevant roles as allotted in legal terms gives a common understanding of Canada's safety disclosure laws:
An extreme case is a degradation of wellness of a clinical testing subject who is tested with a medicine under an uncertainty of whether or not be induced by the drug's distribution.

The ADR is recognized as any unwanted and unexpected effect to a treatment occurred out of the ingestion of any dosage of the medical composition.

Any unintended medical event that carries a risk, is life threatening, presupposes hospital treatment or longer duration of conventional hospital stays, creates enduring or notable mental disorder or lack of capacity, or provokes an inherited anomaly/birth deformity at any dosages is referred to as a SADR. Alternately, it is SAE.
Serious, Unexpected ADR - A significant ADR that is not indicated in terms of its type, severity, or occurrence in the risk awareness data in the investigator's brochure. It may be omitted in drug prescription too.
The G-TCPS2, which formulates the ethical position for all Canadian IECs), means that it is necessary to apprise the EC, a readily viewable tracking system, and other

effective regulatory or consulting entities as soon as new knowledge about the trial's attendees' welfare or permission is noticed during the trial.
Furthermore, researchers must immediately contact all respondents who are affected when new information becomes available that is important to their well-being (including former participants). Scientists and their ethics committees must work together to determine which patients need to be engaged and how they should be briefed.

### 4.3.4 Role of Ethics Committee of Canada's Clinical Trial System

In Canada, the ethical review of investigational proposals is decentralised, and the funder must obtain clearance from each attending study site's IEC. (REBs) are what IECs are called in Canada.) Because various regions in Canada may have higher criteria, the host should inquire with the respective preferred zones for further details[94].
Institutional ECs must follow the requirements in accordance to the Canada FDR, the G-Canada CTApps, and the CA-ICH-GCPs. The institutional ECs should be compliant in adopting the recorded SOPs to fill the detailed evaluation process. The SOPs should have facts that cover the structure of the EC, meeting times, notices, periodicity of assessments, policy failures, presenting to the EC, and maintaining records.

ECs should also make choices during regularly scheduled gatherings with a competence. Only those who are involved in the EC's authentication and analysis are registered to participate, express views, or provide advice.

IECs have the authority to determine whether or not to accept charges for technique assessments. For example, an institutional EC may charge commercial patrons or other for-profit businesses a fee.
In regard to compulsory norms as specified in Canada FDR and given in CA-ICH-GCPs, the G-TCPS2 directs institutional ECs. The G-TCPS2 is an ethical construct by the SSHRC in partnership, the CIHR, and NSERC.
Only NSERC, CIHR terms, and SSHRC-aided establishments, on the other extreme, are expected to adhere to this regulation in order to receive funding. Thus, according

[94] Id.

CAN-14, the SSHRC, CIHR, and NSERC formed the PRE to support the proper behaviour of human subjects' evaluation. The PRE is in charge of creating, analyzing, and putting the G-TCPS2 into practise.
When other HC recommendations are conflicting, the ICH terms are applied HC take priority, as indicated in HC Notice-CA-ICH-GCPs[95].
Facilities that are separately financed by HC or through PHAC should be getting the acceptance from a composite EC encompassing both authorities and adhere to the active laws specified for the event. The HC-PHAC REB is a joint EC that reviews and approves all human research efforts that are done, executed, or somehow under the aegis of respective units.
In addition, if a state fund provided by either of the HC or through PHAC, the HC-PHAC REB should take care and approve the inquiry, even if it has been certified either by EC. CAN-35 contains information on the origin, functions, and structure of the HC-PHAC REB. While assessing medical testing, the combined HC-PHAC REB must adhere to the policy and practices specified in HC's operating policy (CAN-13).
Per the Canada FDR, the G-TCPS2, the G-Canada CTApps, and terms of CA-ICH-GCPs, the foremost purpose of knowledge judged by institutional ECs refers to safeguarding the freedoms and respect of human research subjects, as well as securing their safeness across the whole of their engagement in a medical study.

ECs must also particularly attend in verifying the informed consent and emphasize on the safety of disadvantaged respondents. When other HC instructions are conflicting, the ICH regulation applied by HC take priority, as indicated in HC CA-ICH-GCPs alert.

The G-TCPS2 specifies that all institutional ECs of the state have procedures in place to acquire and answer to observations of incoming knowledge, such as trial data, unforeseen considerations, and diagnosis of early dangers.
ECs must also ensure that all safety and benefit features of the CT design are reviewed objectively, swiftly, and efficiently. They must work for the benefit of potential study subjects and the areas affected by exercising caution and possible benefits, as well as

[95] Josmar K. Alas, et al., supra note 90.

verifying that data protection safeguards are in place. The CA- ICH-GCPs have thorough ethical clearance standards.

The European Commission's Duties in Clinical Trial Authorization in Canada: Per the Canada FDR and terms under CA-ICH-GCPs, certifying power is under HC on a CTA. An institutional ECs must provide security and wellness approval before a funder may begin a drug evaluation processes. Additionally, institutional EC analysis for each medical testing location may happen jointly with the CTA acceptance and confirmation, as specified in the Canada FDR and G-Canada CTApps.

CAN-8 requires the EC that assessed and cleared the scientific study to provide a certification. The filled certification must be kept for a period of 25 years by the clinical trial operator. The testimony should not be sent to HC unless explicitly asked.

According to the G-TCPS2, the scientist must prepare the annual assessment to the EC in need for the EC to evaluate the experiment's ongoing ethical soundness. Per the G-Canada CTApps, if an EC reverses or shuts down any previous approval or acceptable judgement, it must declare its conclusions in writing, clearly stating the trial, the documents reviewed, and the time for the cessation or detention.

## 4.4 Summarized Comparison of Clinical Trial Regulation of USA and Canada with India[96]

**Table 4.1 Summarized Comparison of Clinical Trial Regulation of USA and Canada with India**

| Clinical Trial Process | India | USA | Canada |
|---|---|---|---|
| **Regulatory Authority** | CDSCO | USFDA | HC |

[96] Mohit Hans, Suresh Kumar Gupta, Comparative evaluation of pharmacovigilance regulation of the United States, United Kingdom, Canada, India and the need for global harmonized practices, Vol.- 9(4), Perspectives in Clinical Research, pp-170-174, 2018

| | | | |
|---|---|---|---|
| **Scope of regulatory authority in Clinical Trial Assessment** | Supporting new pharmaceuticals, organizing clinical trials, creating drug regulations, monitoring the quality of imported drugs, offering expert guidance, and managing state licensing bodies that control the manufacturing, sale, and supply of medicines are all takes that the FDA is responsible for. | In compliance with the FDC Act, and 21CFR312, 21CFR50 assessing and authorizing experimental treatment applications (INDs) for drug testing in people utilizing experimental drugs or health fluids; funding and sponsoring trials on human volunteers based on HHS | Examines individual safeness; examines drug efficacy; ensures institutional ethics committee evaluation; confirms primary investigator capabilities; and analyses and examines adverse side effects |
| Regulatory fees | To register a clinical trial proposal, the sponsoring (applicant) must pay a fee to the DCGI | Fee for reviewing experimental treatment applications; ascertain and recover user fees from manufacturing certain human Drugs and biological products as part of the NDA process | There are no costs associated with Submitting a clinical study submission |
| Clinical Trial Phases | 4 | 4 | 4 |
| Sponsor | A human, a firm, or an organisation that is in charge of the start-up, management, or funding of a medical trial. | Individuals or pharmaceutical companies, political agencies, academics, commercial organisations, or other organisations; domestic or international | A clinical study is conducted by a human, corporation, agency, or organisation, which might be domestic or international |

| | | | |
|---|---|---|---|
| Ethics Committee setup | Any institutions/ organizations or individuals operate autonomously and must comply with the 2019-CTRules and the G-ICMR. | Academic review boards are what they're called IRB's | REBs are the acronym for institutional ECs (Varies in zones) |
| Role of Ethics Committee | Preserving and defending all study subjects' rights, protection, and benefit, particularly those in marginalized people; Guarantee that all ethical components of experimental procedures are reviewed by an autonomous, competent, and knowledgeable party; To guarantee ethical terms, monitor permitted clinical trials, biological, and health research projects. | Maintaining and defending research participants' freedoms and respect, as well as assuring their protection during their involvement in a clinical trial; Reviewing informed consent and safeguarding the safety of particular groups of participants who are regarded sensitive; Examine the search strategy, weighing the potential risks and benefits to subjects, and ensuring that anonymity precautions are in place. | Maintaining and safeguard sensitive regarding the participants' dignity and respect, as well as assuring their safety throughout their participation in a clinical experiment; Reviewing informed consent and safeguarding the wellbeing of those persons who are regarded susceptible. |
| Clinical Trial Application Review Time (calendar days) | 90 (for drugs developed outside India); 30 (drugs developed within India) | 30 | 30 |

| | | | |
|---|---|---|---|
| ADR reporting time | 24 hours | 7 days | 15 days (ADR is neither fatal nor life-threatening); 7 days (ADR is fatal and life-threatening) |
| Safety Communication | Via CDSCO pressrelease | Via FDA websiterelease | Via HC website |
| Participants Insurance | Insurance benefitsor a budget line item for potentialtrial-related injury remittance | Not Compulsory | Not Compulsory (Guidance provided by CA-ICH-GCPs) |
| Compensation | In the instance oftrial-related damage, lifelong incapacity, orfatality, money ispaid to targetrespondents and/ortheir legal heir. | Not Compulsory(Sponsor shouldprovide information aboutfatal damage risksto the participants/family/ legal heir) | Not Compulsory (Guidance provided by CA-ICH-GCPs) |
| Informed Consent Document (Before Clinical Trial) | Yes (including compensation details) | Yes (including compensation details) | Yes (including compensation details) |

## 4.5 Conclusion

The chapter as is previously mentioned includes the CT regulatory systems of two major drug manufacturing nations, namely United States of America and Canada. These two nations are particularly chosen for their business interests as attached with India.

The analysis present here, shows the two nations as specific in terms of regulatory framework operation and duties to approve, conduct and monitor clinical trials. The law of both these foreign nations as discussed in this chapters emphasize of eligibility, command and awareness of clinical trial investigators.

Secondly, in both the countries, the CT regulatory system is complex due to the role and authority as assigned under multiple centres (varying in legal protocols region-wise/centre-wise) and their specific guidelines.

Whereas, India's CT legal platform is controlled by fewer number of key players from Central and State Government units added with assigned medical experts to investigate and monitor the clinical trial process.

Both the nations (USA and Canada) and India have specific conditions for CT approval applicable for marketing investigational new drugs. Human testing is formally advised for such clinical trials. Whereas, the laws vary from country to country for medicines that are developed for academic/non-commercial/modified drugs.

EC is decentralized in nature for all these countries differing in norms based on their location and formation type. Roles and responsibilities of the division is primarily focussed to make it accomplished for ensuring the safety advantages and organized procedure of clinical trials. There, India's norms need improvements in terms of organization, efficiency and coordination of the segment. However, the mechanisms to ensure compensation, participant safeguard and ADR reporting are the significant loose ends where none of the nations are thoroughly well defined on fully satisfying measures as to be taken in case of any adverse occurrence. Neither, there is a stricter procedure to minimize the occurrence of adverse incidents.

There are visible legal flaws existing in these laws in varying patterns (some regarding compensation; some in terms of declaration of risks; etc.) to secure the trial participants who suffer injuries. The three countries as discussed in this chapter has policies on paper albeit with vague directions for implementation safeguard the human subjects permitted for clinical trials.

Overall, none of the legal systems is observed as sufficiently formatted as a universal platform of convenient clinical trial management process.

# Chapter 5

# Challenges & Deficiencies in the Law of Clinical Trials: The Way Forward

## 5.1 Introduction

As previously mentioned, India has attracted sufficient worldwide interest as one of the most affordable countries for clinical trials. This is due to India's "India Advantage", which includes a large patient population, highly engaged and productive medical and paramedical staff, state-of-the-art facilities, and robust Information technology assistance[97].

According to Indian government data, the number of applications to conduct clinical trials in India decreased from 480 in 2012 (with 253 approvals) to 207 in 2013 (with 73 approvals). In 2015, the Indian government divided some of the imposed requirements after noticing a decrease in clinical research. The decrease in clinical trials forced Indian policymakers to amend the new laws that regulate clinical trials, and the NDCTR G.S.R.104 (E) was introduced on February 1, 2018[98].

In February, they published a draught guideline to replace Schedules XA and Y of the D&C Act. NDCTR 2019 is a full-fledged guideline. G.S.R.227(E), which applies to "new pharmaceuticals" and "investigational novel medications" for human use, "clinical trial," "bioequivalence study," "bioavailability study," and "ethical Committee," was released on March 19, 2019[99].

According to academic assessments of the aforementioned reforms in India's clinical trials, transparency is needed for any government to sustain public trust. Transparency entails openness, accountability, and communication, allowing others to see what actions are being taken. In India, there is still a lack of transparency in terms of clinical trial rules.

There are no reports of major adverse events linked to clinical trials or specific medications, nor are there any reports of GCP inspections undertaken at clinical trial

[97] Subramani Poongothai et al., supra note 3.
[98] A Nair, Clinical research: Regulatory uncertainty hits drug trials in India, THE P. J. (2015).
[99] Akhilesh Dubey et al., supra note 55.

sites, investigators, sponsors, or ethics committees. The CDSCO does not keep track of the number of inspections it conducts or the results of those inspections.

As a result, the existing legal issues of India's clinical trial system are examined in this chapter.

## 5.2 General Reasons of Clinical Trial Failures

A number of practical considerations may jeopardise the desired outcome of well-conducted clinical studies. Failures can occur due to a lack of performance, safety concerns, or a lack of funding to execute a study, as well as other factors such as poor manufacturing practises, inability to comply regulations, or problems recruiting, enrolling, and keeping patients[100].

### 5.2.1 Inefficacy and Lack of Safety Provisions for Clinical Trials

The inability to establish efficacy has been and continues to be the primary cause of trial failure. Some of the drugs which have the potential to be a boon to patients have not reached the market, due to flaws in CTs like the number of trial subjects are less due to dropouts, rejection of the hypothesis, unreliable trials etc. Safety of the trial is taken care to the utmost in any trials, but any discrepancy is visible, most of the time only in the Phase 3 or 4 or even after these stages. It's not always easy to detect inherent hazards. Clients may have specific concerns about a range of negative outcomes that are not shared by professionals. This can influence which side effects are documented, particularly if the intensity ranges from mild to severe. Sometimes the reason of not working of a particular trial also can be the rushing to phase 3, which sometimes results in the inadequacy of time to plan for the safety-related aspects. A higher educated medical team has been related to a lower risk of mortality and rescue failure, according to study.

[100] David B. Fogel, Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review, 11 CONTEMPORARY C. T. C. 156-164 (2018).

### 5.2.2 Financial Issues

As a result of the enormous financial strain, many trials (in phase 3, but maybe before) are neglected and may not have a clear chance of achieving a favourable outcome. This creates doubt about patient participation.

Patients frequently believe that by taking part in a study, they will participate to the advancement of learning as a result of the study's achievement. Inadequately funded trials are more generally inadequate of the requisite enrolment to achieve statistical validity at a set level of performance[101].

### 5.2.3 Lack of Participant's Eligibility

The participation in the trial is one important aspect in the trial. There are some standards laid down to choose a trial participant in the studies. Inclusion criteria for investigations in a specific field can vary substantially, putting a potential sponsor or scientist in the dark. Inordinately strict inclusion rules can make finding qualified respondents challenging. This is particularly the case in situations where there are only a few people, but it also remains true in general.

Some of the studies, i.e., Oncology studies for instance, they exclude trial participants who underwent Chemotherapy, or the people who have crossed the initial stages of the ailment etc. As technologies screen out more persons, targeted therapy based on particular genetic markers, specifically in oncology, will exacerbate the situation. Excessively stringent eligible participants may result in lengthy selection difficulties and, eventually, a modification in the study design in an endeavour to register more participants. These standards and the selection procedures definitely will impact on the time and cost factor in the trials.

Frequently, assessment methods are provided without a proper definition. Conditions are frequently established with the goal of excluding persons who do not show adequate development toward an outcome, not because their wellness is bad, but that it is outstanding.

### 5.2.4 Issues of Patient Selection and Participation

[101] Akanksha Rani and Vikesh Kumar Shukla, Impact of rules for New Drug and Clinical Trial in India, 8 INT. J. D. R. A. 25-30 (2020).

The willingness of patients to be part of the study is most of the time depends on their belief and assurance that the outcome will have some favourable results on the patients. This being the common thinking, enrolling an adequate number of individuals in a CT has long been a hurdle.

Individuals are paid in some research, primarily to compensate their time and money, but often in the terms of inspiring patient retention. While logic suggests that trials that pay participants should recruit more participants than those that do not, and patients sometimes claim that this is important to themselves, the proof to substantiate this is often equivocal[102].

Even of the same research topic, the added expenses of patient recruitment can be hard to predict and vary greatly.

Clinicians may have an impact on patient attraction and training. Increased involvement in clinical trials is expected if patients are encouraged to trust the procedure. By providing incentives to the trial participants, it has encouraged in obtaining a greater number of participants for the trial, as per the studies.

### 5.2.5 Poor Patient Handling Infrastructure

The willingness of the number of patients to take part in the study comes down when there is a fear in them that they will be controlled of their actions, rather than testing drug or treatment on them. Part of this effect could be explained by patients' lack of understanding of placebos or the specific treatment delivered in the control group. Patients with poor predictions may be apprehensive that they will not receive any care at all.

Patients are frequently given insufficient guidance and do not always comprehend why their involvement is so critical. Additionally, the average public's scientific literacy is inadequate, making it difficult to interpret information about drug testing.

Slow enrolment could be the result of insufficient of manpower and a failure to promote the drug study over day-to-day tasks. It can also occur if the investigator is working on multiple trials at once. If there are counsellors or trainers at trial centres, will be helpful in recruiting and retention of trial participants.

[102] A Nair, supra note 98.

A trial may become underpowered if there are too many dropouts. Clinical trials with insufficient power are difficult. In order to meet the basic enrolment requirement, the funder may raise the amount allocated to the trial or boost the number of centres.
As a result, it is sometimes needed to cancel certain proposed trials in order to redeploy available funds. As a result, the sample size for some endpoints may be limited to detect a meaningful result.
Enrolment speed, for example, is connected to less withdrawals, greater statistical power, and greater confidence in results. Slow enrolment, on the other hand, could suggest a difficulty with the inclusion/exclusion standards.

Another factor which will show some positive impact on the participants enrolment can be advertising of the trials or hiring supporting employees to assist in the process, which will also speed up the process of trial.

Choosing the less expensive option, however, may result in a failure to reach recruitment goals. As a result, more study centres may be required, which may incur additional costs for reviewing, training, protocol changes, and trial implementation. Making smarter decisions can be aided by quantifying these trade-offs.
While some trial candidates may be obliged to shift during the study's duration, the large majority prefer to take part in local studies.
For many years, transportation has been a problem for older participants. Long travel hours, especially in urban areas, can dissuade patients from participating, regardless of their age. In most circumstances, it is desirable to enrol patients from local immediate region to study facilities in metropolitan contexts.

## 5.3 Necessity of Transparent and Well-Monitored Clinical Trial Procedure in India

In recent years, India has been a popular location for clinical studies. Sponsors from Canada, Europe, and the United States may complete their projects quickly and at a lower cost in India. Our trial-conducting criteria have already met international norms, putting India in a position to engage in additional global trials[103].

[103] Subramani Poongothai et al., supra note 3.

India will continue to profit from CTs if regulatory requirements are met and concerned people are properly trained in GCP. It's vital to remember that a medicine can only be utilised if it's been proven through clinical studies.
Despite the fact that there may be problems, the current remedy for clinical trials is worse than the problem. India must improve the trials by enforcing rules and laws to protect the trial as well as participants.
As a result of a 2011 lawsuit challenging the legislative regime and patient safety requirements, India's clinical testing industry faced significant legal difficulties and a complete halt to all medical research activity. As a result, a strict three-tier clinical trial submission process was developed, greatly delaying clearance timelines and rendering India less efficient in clinical trial execution as compared to other developing countries.

Clinical trials are increasingly being conducted in India by multinational pharmaceutical corporations. It's vital to note that we're merely a part of trials that are taking place in other regions of the world. Patients in CTs in India are handled the same way they are being handled in Europe, America, Australia, and other South Asian countries. It is a notable fact that more than 80 % of the trials which are sponsored by foreign countries are multi-trials, which runs to various countries. However, 97% of the trials conducted by Indian Companies and NGOs are locally instituted studies.

Over 53% of the phase 3studies were sponsored by foreign companies, most of which were trials of INDs, NCEs, or GCTs, while 35% were sponsored by Indian companies, most of which were local bridging studies for new drugs.
NGOs funded the remaining 12% of phase 3 trials. Clinical trials for new medications and NCEs are frequently conducted as part of a larger global drug development programme, resulting in multi-country, multi-site GCTs with hundreds of participants in later phases of development (phase 3 and 4).
CTs can be conducted for INDs, NCEs, and novel medications; they can be delayed or concurrent; and they can be funded by for-profit or non-profit organisations. However, the general public's opinion of CTs is uninformed of these finer intricacies, resulting in a divisive debate on the subject.

## 5.4 Need of Ensuring Participant Safety and Well-Being

It is vital to protect the rights, well-being, protection in concept of risk ratios, security, and confidentiality of vulnerable members. Informed Consent is a primary requisite in any ethical research.
Since a result, it is vital that the study be overseen by members of the Institutional or Autonomous EC, as this will provide added safety for the sensitive subjects.
Even if the person is unable to give consent, the principles of voluntariness and informed consent must be followed. Surrogate consents are required for patients who are unable to provide autonomous informed consent due to behavioural or mental disturbances.

Because infants are regarded to have restricted cognitive and emotional capacity, parents must make the decision on their children's part from an ethical and legal position. Where the ailment mostly affects kids under the age of 18, specialized paediatric tests may be required, primarily if they are prone to certain medical problems[104].

There is a need for extra care and caution when it comes to research on Children, to ensure their protection and minimise risk. The study should take place in an environment where the kid and parent can get proper medical and psychological care. The child's permission or acceptance is based on the breadth of the child's cognition; the protocol usually stipulates a minimum age for this.
The recruiting of children, on the other hand, may raise worries that they are being mistreated. As a result, it's vital that the research's primary purpose is to collect data on children's health needs.
Women are denied the opportunity to profit from clinical research when they are barred from participating in a study. It is not necessary to exclude women who are pregnant or planning to become pregnant from research trials. Studies on fertility, birth control etc can be done on them if they are willing to be a part of it. As a result,

[104] Sanil Manavalan and Catherine Sinfield, Conducting Clinical Trials In India: Opportunities And Challenges, Clinical Leader, CLINICAL LEADER - GUESTCOLUMN (Aug. 8, 2017), https://www.clinicalleader.com/doc/conducting-clinical-trials-in-india-opportunities-and-challenges-0001 (Last visited May 11, 2022).

it's crucial to keep track of pregnant subjects during the study. If the subjects become pregnant, they are also tested for reproductive and developmental harm.
The dread of including breastfeeding, pregnant, and child-bearing-age women stemmed from knowledge domain and social worries about latent harm to the embryo, foetus, and neonate. Excluding this group could result in the unreasonable denial of critical diagnostic, preventive, and therapeutic information. When this demographic is excluded from the study, a reasonable justification must be included in the research documentation. Pregnant women as well as feeding mothers are also eligible to take part in the trials, it depends on their informed consent to it. Maximum knowledge and awareness about the chances of risk and the advantages of the study has to be conveyed.
For nursing mothers, informed consent and the procedure of conveying the consent should contain sufficient insight into potential threats to the infant.

Only under rare circumstances, and typically not at all, can prisoners be recruited for study. Prisoners have restricted ability to make decisions or decline due to their constraints, and therefore are not addressed identically to typical respondents. When a study involving inmates is being planned, the investigator and institutional inspection body must first determine if it is even permissible to test offenders.

Only studies that have the opportunity to assist the inmate are normally permitted. The Institutional Ethics Committee should extensively review the informed consent forms, as well as the patient information form. The majority of research undertaken on inmates focuses on health and social concerns with immediate benefits, and is limited to their living situations. Students are also made part of the studies, out of force and they accept to it to do away with harassment. Students and residents may feel forced to contribute, regardless of how well-intentioned the instructor is.
Students feel that failing to do so will harm their academic performance, assessments, and the instructor's. The willing engagement of persons in experimental studies is a basic fundamental of federal regulations on human-subjects research. Inherently, the instructor-student relationship is one of power imbalance.

## 5.5 Need of Fair Consent and Data Security in Clinical Trial

The patients must be made understood that he/she has the option to opt out from the test, that the treatment is an experiment, that if he/she decides to join, he/she will be bound by particular commitments, and that there are both possible benefits and risks to engaging in the investigation[105].

An appropriate consent process guarantees that the norms and ethics of GCP of respect for human dignity free of bigotry and therapeutic misunderstandings are respected in the case of disadvantaged class. All applicable components addressed in the local regulatory norms should be included in the Informed consent document. It is critical that site employees assess the possible susceptible participants' language and literacy ability.

There is a set of professionals, who track safety and effectiveness throughout the trial. The DSMB primary objective is to guarantee safety and quality of care. The DSMB will advise that the study be halted if extremely serious complications are more common in the innovative arm than in the control arm.

This assessment must take into account the risk against benefit ratio. In many circumstances, experimental therapy may create side effects during treatment, such as during chemotherapy for terminal cancer patients. Before discontinuing the experiment, the advantages should be balanced against the potential hazards.

The DSMB's primary job is to ensure passenger care. The DSMB will propose that the study be halted if extremely serious adverse events are more prevalent in the experimental arm than in the control arm.

The assessment must take into account the risk vs. benefit trade-off. In many circumstances, experimental therapy may create side effects during treatment, such as during chemotherapy for terminal cancer patients. Before discontinuing the experiment, the advantages should be balanced against the potential hazards.

[105] David B. Fogel, supra note 100.

## 5.6 Flaws of India's 2019 New Drugs and Clinical Trial Rules

The NDCTR was introduced by the Government in 2019 to concentrate more on the safety of the trial subjects. The data shows the death of the trial subjects were 1442 in the period 2015-18. After portions of the existing D&C Rules, 1945 were rearranged, integrated, and developed, and certain problematic sections were incorporated in the process, the new laws replaced the old[106].

### 5.6.1 Duplication of Rules

There were 169 provisions in the D&C Rules, which were numbered 1 to 169. There are 107 regulations in the NDCTR, numbered as 1 to 107. As a result, there are 107 provisions that are duplicated. Rule 96 of the Drugs and Cosmetics Rules of 1945, for example, deals with the manner of labelling, but the provision 96 of NDCTR talks about permission to give unlicensed new drug in CTs to patients with life-threatening diseases. As a result, while discussing or mentioning them, it's critical to know if a number matches to the D&C Rules or the NDCT Rules.

### 5.6.2 Conflicted Legal Guidelines on Clinical Trial Approvals

The law is contradictory on whether a CT approval can be obtained from another organization if an institute/organization does not have an EC and intends to conduct a clinical study[107].

The Rule 6 of NDCTR puts forwards that approval must be obtained first from EC, followed by registration with EC, before conduction of CTs. "CTs shall be initiated at each site after approval of the CT protocol and other associated papers by the EC of that site, registered with the CLA under regulation 8," says Rule 25(i). From which it can be inferred that the presence of EC is unavoidable for any site.

However, Rule 25 (ii) contradicts this, stating that "where a CT site does not have its own EC, CT at that site may be initiated after obtaining protocol approval from the EC of another trial site; or an independent EC for CT constituted in accordance with the provisions of rule 7."

[106] Swati Jadhav and Ravindra Ghooi, supra note 19.
[107] Id.

Institutional and Independent ECs are no longer in operation; The NDCTR gives no mention about Independent EC, in that way Rule 25(ii) seems contrary.

### 5.6.3 EC Structural Format

ICMR also provides a framework for the constitution of EC. Rule 15 of the NDCTR talks about the compliance to the National Ethical Guidelines for Biomedical and Health Research separately. In respect of CTs, there is different requirement to be complied and constitution of EC is varied from that of other studies. The description is ambiguous and incomplete, leaving the reader with more unanswered questions[108].
Rule 7 asks for a woman member to be part of the EC. When a lady member is mentioned, it raises the issue of whether the physician may be recognized as a lady or merely as a clinician. (Is it feasible for a member of the EC to wear two hats at once?)
The pharmacologist is needed in the unanimity, not the constitution, because the pharmacologist's abilities are unknown. This is clearly stated in the ICMR rules.

### 5.6.4 Role of EC

The EC had the authority to receive, require amendments, or cancel a study proposal under earlier CT rules. When the Institute's EC denied or disapproved a proposition, the investigator's only choice was to file an application for reassessment. If the investigator given ample evidence, the EC may approve the proposal.

For such an aggrieved investigator, the NDCTR has offered an extra method of remedy. "In the event that a CT site's EC rejects the protocol's approval, the details of the same shall be submitted to the CLA prior to seeking approval of another EC for the protocol for conduct of the CT at the same site," as Rule 25 (iii) states.

Investigator has the right to look for a new EC, who would approve the trial and the investigator can continue and carry forward the trial. Furthermore, before addressing another EC, the investigator must report the specifics of the EC decision to the CLA.

[108] S Srinivasan, India's new clinical trial rules weaken safety nets for participants, SCROLL.IN - LAX STANDARDS (Apr. 04, 2019, 02.30 P.M.), https://scroll.in/pulse/918874/new-clinical-trial-rules-weaken-safety-nets-for-trial-participants-to-promote-research (Last visited May 21, 2022).

According to the standard, the CLA's consent is not required. The problem with this law is that it makes people more likely to do their work differently. This rule (Rule 25(iii)) gives an outside EC the superiority in the study because it will now be in charge of it. Under Rule 25(ii), an investigator may consult another EC, but only if his or her home institute lacks a recognized EC. Even though the parent institute's EC has declined the study request, the investigator might advance to that other EC under sub-rule (iii).

### 5.6.5 Issues on Compensation

In United States also the compensation for CT is a matter of argument as there is no provision granted by law. There are various suggestions for a formula, which will provide for a simple compensation[109].

There is a difference between a nominee and a legal heir. A nominee is "a person or entity who is requested or named to act for another, such as an agent or trustee," according to the Legal Dictionary. "An individual selected by law to succeed to the estate of an ancestor who died without a will," says the dictionary. Legal heir is defined as the one to whom the property is inherited by will or law.

Law says that nominee is not the owner of the assets, but is the holder or a trustee. He is just the custodian of the assets. He is remunerated for the same and shall handover the assets to the rightful heirs. In most cases, a legal heir has the right to the deceased's assets. As a result, anyone can name a nominee, but an heir is determined by a will or by law.

The terms ‘nominee’ and ‘legal heirs’ are not commonly interchanged, but the NDCTR uses its interchangeably. In chapter VI, Rule 39(1) talks about the obligation of a sponsor to compensate the legal heir on the death of a trial participant. The method by which the funder or inspector would determine the legal heir of the participant is uncertain. The respondent must include the nominee's name and relationship in the ICF.

As before, if an accident occurs during a trial, the unit is expected to give free medical care for as long as necessary "until it is determined that the harm is not related to the

[109] Id.

clinical research." However, a new questionable language has been added: "as per the investigator's opinion."
This indicates that the test subject's constitutional right to get free healthcare stops once the investigator decides that the impact is irrelevant to the experiment. If the investigator's conclusions are unfavourable, the trial participant has no alternative.
There appears to be a certain ambiguity concerning how legal heirs should be discovered and whether it is the investigator's responsibility to do so. The earlier practice was to compensate the nominee, based on the data given by ICF contributor and the legal heirs could file an appeal and could claim their share without the intervention of facilitator or investigator. Under existing regulations, the sponsor is accountable for maintaining that payment is made to the legitimate heir. For no fault of their own, the site and the sponsor are likely to become embroiled in legal wrangling due to the confusion between heir and nominee.

### 5.6.6 Safety and Well-Being of Participants

Earlier to 2019, the Supreme Court criticised existing clinical trial guidelines and demanded that clinical study authorization be based on safety profile and performance standards. It looked at three things: the participants' risk vs. value, development vs. conventional remedies, and the country's unfilled health costs. The core of these demands, on the other hand, appears to have been disregarded, as the NDCTR has made little effort to put the Supreme Court's vision into practise[110].
A SAE under the NDCTR is a medical happening which leads to a participant's hospitalisation, death, or permanent disability during a clinical trial. There have been a variety of occurrences resulting to trial injuries in recent Covishield and Covaxin immunisation trials, including SAE. These incidents have revealed how regulatory procedures have allowed for the flippant management of such injuries.

Under the NDCTR's decision-making procedures, the disparity between the powers afforded to trial funders and those accorded to volunteers is particularly obvious. This is of relevance on the payment of the loss. Any unforeseen event maybe it the death or injury to the trial subject, Under Rule 41 compensation can be claimed by the

[110] S Srinivasan, supra note 108.

participant or the legal heirs. occurrence. This rule focuses on the injury's trial-relatedness.

The Ethics Guidance of the NDCTR and the ICMR, on the other end, aren't clear on how to close the loop with the individual. That is, decisions on the experiment of the injury/death do not need to be explicitly communicated to the affected subject with justifications. This, added to the fact that neither the respondents nor their advocates are permitted to engage in any level of judgement, demonstrates how the NDCTR lacks proper participatory rights.

Furthermore, the new standards provide that member of a medical experiment's ethics board or sponsors can appeal to a ruling of DCGI. But in the aspect, the right of the trial participant is very far, they have no right to counsel for any recompense in the event of any injury or death, being a part of the CT investigation process.

As previously stated, the consideration for the participant's death or injury must be paid if it occurs as a result of any of the occurrences enumerated in Rule 41 of the NDCTR. The final decision is made by the CLA or an impartial committee constituted by the CLA. The committee comes to a decision following the advice of the EC.

As a result, the EC is primarily responsible for drafting a conclusion on the trial-relatedness of the incidence and assessing reimbursement based on the primary investigator's findings and the components mentioned in Schedule VII. The lack of a chance to challenge the EC's decision raises the likelihood of incorrect results and helps the students to rely solely on legal channels.

Furthermore, participants will be given with free medical care if they sustain an injury throughout the trial. The length of free medical care provided to study participants is solely regulated by the investigator's "opinion." When establishing such a viewpoint, there are no norms to apply. This is particularly troubling because it is on this assumption that the trial person's legal commitment to undergo free healthcare ceases, leaving the subjects with little redress against the investigator's findings.

### 5.6.7 Unclear Post-Marketing Terms

The guidelines specify the requirements for post-marketing research, which are divided into three categories in Schedule V**.** They are Post Marketing Phase IV trial,

Post marketing assessment inspections & post marketing inspections via time-to-time status update reports[111].

Post-marketing investigations must be done in compliance with regulations 77 and 82, according to the time schedule. Rule 77 applies to pharmaceuticals acquired for the intention of marketing and advertising, while Rule 82 applies to drugs created for product marketing. In sub-rule (iv), both of these rules employ the same wording, hence 77 (iv) and 82(iv) both states.
"The applicant shall provide PSUR as defined in the Fifth Schedule as post marketing surveillance;" The importance of PSUR seems clear, but it's uncertain when such company will conduct the Phase IV or Post Marketing Analysis. Clarify on these issues will assist funders, investigators, and EC members.

**5.6.8 Elimination of NFC**

The legal successor of a trial respondent who died or experienced permanent disability within 15 days of hearing the EC's judgement was entitled to interim reimbursement of 60% of compensation packages, according to a clause of the February 2018 Draft Rules[112].
The WHO took issue with this provision in the plan, with Soumya Swaminathan, the Deputy Director general active at the same time and the head researcher, writing to Union Health Secretary Preeti Sudan, stating that "CT sponsors will leave India if the guidelines are adopted as they are now."
As a result, the administration has withdrawn the nearly NFC clause that civil society had demanded. NFC can be viewed as a pragmatic compromise between the sponsor's restricted responsibility and the participant's limited internal relief. However, the same was deleted in the process of relaxing the process of conduction of CT in India.
If NFC had been in place, it would have partially alleviated the problem of erroneous compensation or trial-related decisions. As a result, the government's action has tipped the scales against the participants, especially given the lack of a right to appeal and a right to be heard in the above-mentioned compensation proceedings.

[111] Swati Jadhav and Ravindra Ghooi, supra note 19.
[112] S Srinivasan, supra note 108.

### 5.6.9 Doubtful Waiver

Local trials of a new medicine will be exempted to meet faster accessibility if "the new drug is approved and commercialised in countries designated by the CLA" and "no series of challenges harmful effects have been documented," according to the plan.

The rapid authorization granted under Schedule 2(2)(ii)(A) sets a low bar for obtaining CLA approval. This is apparent in the way the Law allows any medicine to be approved after only finishing Phase II trials, with the proviso that the experiments demonstrate extraordinary efficacy.

Because of its clear connection to drug safety, the requirement of remarkable efficacy must be respected. The association between effectiveness and safety can be as easy as collecting data on safety precautions such as hospital care, side effects, problems, and SAE in a larger public to identify and quantify the quality of inferior efficacy. However, the guidelines are silent on what defines extraordinary efficacy or how to determine it.

Even more intriguing is the fact that Phase II trials primarily confirm immunogenicity results. As a result, requiring only Phase II eligibility jeopardises the drug's efficacy before it is administered to a greater population.The clinical efficacy statistics for the drug are only developed in Phase III trials, when the medication is tested on a larger public. As a result, requiring extraordinary performance in only Phase II trials is ridiculous. The untimely clearance of Covaxin, which was authorized without any efficacy data, exemplifies this carelessness[113].

It is important to note that immunogenicity does not imply efficiency. These estimations would be dependent on other previously done drug testing or known/expected host defence that could be successful. The use of estimations to determine utility can be ascribed to the NDCTR's failure to set a standard for showing remarkable efficacy. As a result, immunogenicity cannot assure the drug's stability without demonstrating remarkable efficacy.

[113] Suneha Kasal and Swini Khara, Reviewing the New Drugs and Clinical Trials Rules, 2019: Lessons from the COVID-19 Pandemic, NAT. L. S. I. R. (2021), https://nlsir.com/reviewing-the-new-drugs-and- clinical-trials-rules-2019-lessons-from-the-covid-19-pandemic/ (Last visited May 05, 2022).

The fact that CDSCO found a way around this clause can be traced to a confusion in the Rules about what comprises "remarkable efficacy," necessitating a review of the standards for remarkable efficacy. As a result, it's critical to strengthen the fast approval procedure to determine that simply passing Phase II studies isn't enough to get a medication approved, and that the condition of demonstrating remarkable efficacy is rigorously implemented.

This could be accomplished by establishing a 'remarkable' level or unambiguous boundary. This also leads inevitably to our point about the importance of accountability, because there isn't enough verifiable information sphere on how the regulator combined effectiveness and immunogenicity data. Due of a lack of public evidence, it's unclear whether the NDCTR standards were met in order to meet the 'remarkable' threshold.

The CLA has the authority to define procedures for post-licensure research under the rapid clearance clause. This research is utilised to collect data from a broader group of people in order to validate the clinical advantages. This NDCTR requirement is actually a well-considered provision because it assures that a drug's ongoing approval is subject to restrictions. This phrase, however, should not have been confined to post-licensure research or drug testing, but should have been broad enough to encompass other contingent needs for emergent situation pharmaceuticals.

These contingent conditions are important to account for any further adjustments. Changes to the approval's applicability duration and particular requirements for withdrawal and process improvement, as well as storage, usage, supplying, circulation, and other relevant instructions, are examples of these circumstances.

The generosity with which such exemptions are granted in the midst of more clear information of the particular drug's safety is concerning. Local trials are critical for determining the impact of medications on diverse persons, particularly in a place like India with such cultural minorities.

Drug trials should not be skipped even while developing orphan medications to address rare disorders. These medications are less certain to be properly investigated because they are designed for a limited number of patients and the drug companies has little motivation in them under typical economic environment. Clinical trial

exemptions, despite what the guidelines say, will not reduce the exorbitant cost of pharmaceuticals.

#### 5.6.10 Lack of Transparency

Transparency has certainly not increased for research subjects. There's no indication of study results or data being publicly disclosed or accessible to them. For example, material from rotavirus clinical studies, which formed the basis for India's public health choices to introduce the rotavirus vaccine, is not public information[114].

The new rules have made a change in the period from 180 days to 90 days for DCGI to look into and decide on the application of an investigational drug for the ones made out of the country and 30 days for the ones made in India. This is excellent news for the clinical testing enterprise, but it presents health and safety concerns being compromised in the interest of efficiency.

The rules also give kind of relaxation to the Investigators by providing a condition that where no communication on the part of DCGI is acquired within 30 days, it is presumed that the permission to conduct CT is given. This can lead to corruption and it amounts to the authority failing to fulfil the responsibility of approving the CT.

### 5.7 Covid-19 Vaccine Fast Approval: A Case Where 2019 NDCTR Flaws Were Exposed

The regulation for the conducting and testing of vaccines for Covid-19 would be the NDCTR 2019, which deals with clinical trials. The NDCTR provides for the rules for developing any drug.

Under the definition of the NDCT Rules, all potential COVID-19 vaccines will be deemed "new drugs." As an outcome, these rules can control the acquisition, production, and sale and distribution of all vaccines used in clinical trials[115].

The Rules would need the DCGI, to get initial necessary permits.

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[114] S Srinivasan, supra note 108.

[115] Abanti Bose, Law regarding emergency use authorization of vaccines in India, iPLEADERS (Dec. 06, 2021), https://blog.ipleaders.in/law-regarding-emergency-use-authorization-of-vaccines-in-india/ (Last visited May 17, 2022).

It is important to note that the emergency use authorization or any other term like EUA is nowhere mentioned in the NDCTR, despite the fact that these terms have found their way into the legislation of countries like the United States, the United Kingdom, and other developed countries.

Covishield is approved by the SEC of CDSCO for 'restricted emergency use'. Covaxin is for 'restricted use in an emergency scenario in the public interest as an abundant precaution in CT mode'. The usage of these phrases is nowhere found in the NDCTR nor D&C Act or D&C Rules. This creates ambiguity and makes it suspicious for the people to understand and rely on the safety and effectiveness of these COVID-19 drugs.

Despite this, India's regulatory structure provides provisions for a "unique case." These regulations include a provision for an "expedited approval process" that is dependent on the circumstances. These provisions are in line with the present pandemic situation's requirements. It goes on to say that the 'product' (medicine, vaccination) must have a "meaningful therapeutic benefit" in such a case.

The Rules provide that a new medicine or vaccination can be approved if it is needed to treat life-threatening diseases such as the COVID-19 pandemic that is now afflicting the world, providing that the new drug or vaccine demonstrates "remarkable efficacy" during Phase 2 human trials. However, according to the IE Report, this approval will only be granted for a limited time and will have a one-year validity period[116].

There is only provision in the NDCT Rules where there can be anexpedited process for the drug approval or rapid approval. It calls for an "accelerated approval process for a new drug for a disease or condition, taking into account the severity, rarity, or prevalence of the disease or condition, as well as the availability or lack of alternative treatments, provided that the product is of meaningful therapeutic benefit over the existing treatment."

[116] Yogini Oke and Shreya Shrivastava, How India's regulatory pitfalls helped Covishield and Covaxin get rapid approval, THE PRINT (Jan. 08, 2021, 12.54 PM IST), https://theprint.in/opinion/how-indias-regulatory-pitfalls-helped-covishield-and-covaxin-get-rapid-approval/581676/ (Last visited May 18, 2022).

According to this mechanism, "if remarkable efficacy is observed with a defined dose in a Phase II CT of an investigational new drug for the unmet medical needs of serious and life-threatening diseases in the country, it may be considered for grant of marketing approval by the CLA based on Phase II CT data," "it may be considered for grant of marketing approval by the CLA."

However, "additional post-licensure studies may be required to be conducted after approval to generate data on a larger population to further verify and describe the clinical benefits, as per the protocol approved by CLA.

Even though the provision clarifies the expedited approval procedure, it does not address the nature of the permission issued or which will rule for such a drug which is the outcome of such an expediated CT process.

This creates a vacuum and ambiguity on the discretion of DCGI. This particular issue is exacerbated in the current scenario by the fact that the DCGI's conditions are not yet available in the public domain.

The CTs law in US provides that the public has to be notified or alerted on the approval of a product for 'Emergency use' and the notify the fact that the product is yet to complete the whole procedure of approval from the authorities.

That is, while administering the COVID-19 vaccination in large groups, they should be aware of the vaccine's possible benefits and hazards, as well as the extent to which such benefits and risks are unclear.

Despite the fact that no country has made vaccination mandatory, the government's rules for dealing with the COVID-19 pandemic include mandatory vaccination for numerous purposes, such as travelling, attending restaurants, malls, and so on; otherwise, they will not be allowed to do so. This is subject to limitations and conditions, but the ability to refuse a vaccine or drug is restricted in some way.

It took almost a year for bringing of Covid drug and licensing it for the use of the general public, this is due to lack of proper regulatory clarity regarding the expediated process of drug approval. This ambiguity and lack of clarity puts a question as to the

safety of these vaccines on the humans. There is no transparency on the process of approval of the same and puts a question as to the efficacy.

The regulatory framework in countries like USA, provides for a clear process in case of rapid approval or emergencies approval of medications with the FDA approved control under the Federal FDC Act and the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 to support the provision of an un - authorized drug during an announced state of emergency.

That is how the system differs with that of India, where the post-approved conditions under the discretion of the DCGI/CLA, the law explicitly addresses both before and post components of such emergency approval. The D & C Act and other guidelines are found insufficient in terms of keeping up with current disease and medication development.

Even though the NDCTR came into being in 2019, there are no evidences of the competency to deal with the current pandemic.

## 5.8 Conclusion

Various health issues have emerged as a result of changes in lifestyle and the environment**,** which may be adversarial to health of people. Due to these circumstances, there is very much need for developing new efficient drugs for the protection of the human population. Before a new molecule can be commercialised, it must go through a series of rigorous preclinical and clinical trials.

The CT industry in India has experienced remarkable expansion in recent years, owing to economic globalisation, and is consequently one of the country's most promising economic sectors. The outsourcing of CTs to India by numerous international pharmaceutical companies may be to blame for the rapid growth of CTs. Furthermore, the country's infrastructure, which includes comprehensive treatment, a wide range of common ailments, ethnic diversity, English-speaking health care specialists, and medical and information technologies, makes it ideal for conducting CTs.

CTs are thus methods to check the effectiveness and safety of new drugs on humans. Before a group of people (participants) is subjected to clinical investigations, their

consent must be obtained. However, because the participants' safety is a top priority, the sponsors and investigators must adhere to ethical guidelines and use GCP. And launching new drugs should not adversely affect the trial participants and compromise with their safety.

The growth of India's medicinal research sector has been clouded by reports of anomalies in CT administration. These ethical infractions in the sector have highlighted regulatory gaps, causing the regulatory system to struggle to adequately oversee CTs.

As a result, Indian authorities modified the regulatory system's flaws in 2016 to improve the regulatory systems for reviewing clinical studies. These revisions were made after a lot of examination, a lot of media attention, a lot of input from non-governmental organisations, Supreme Court hearings, and expert committee recommendations.

New regulations were recently announced in 2019, revising the 2016 regulations to bring additional modifications to the clinical research sector. These guidelines aimed to define the parameters of new drug CT and phase IV studies, as well as post-trial access to new pharmaceuticals, clinical trial approval validity, equality, remuneration, and monitoring, all of which have been discussed elsewhere.

While the NDCTR has made important reforms to medical trial and drug development supervision, this research suggests that more room in the existing structure is necessary for volunteer welfare and protection. As alleged, the trial rules assist the funders by allowing for chosen appeal proceedings.

As a result, providing the respondents with the right to challenge and be addressed in choices affecting their health and safety is the first step toward strengthening them. Furthermore, as shown, the clinical trial system lacks not only participant rights but also openness. There is a need of methods for achieving transparency by making primary and secondary trial data public and incorporating participants in the decision-making process.

Instead of just listing the stage of a study when the medicine can be given a green light, the fast approval procedure has to be revamped to prioritise safety and provide better clarity about the bar for "remarkable efficacy." In the absence of these, the regulator is free to skirt the regulations and give in to external pressure by authorising the drug despite the lack of adequate efficacy data. In the present, it is expected that new knowledge and breakthroughs in the area will pave the path for improved legislation that benefits both patients and sponsors.

# CHAPTER 6

# Conclusion & Suggestions

## 6.1 Introduction

The current aspects of Law Relating to Clinical Trials in India analysed in this thesis is observed as an evolving area. The subject certainly needs better attention, scrutiny and further improvement. Such initiative is important in order to build up a stable legal system in India. This system should be sufficiently flexible for clinical testing activities of international drug development procedures. It should be well-developed to ensure the safety and advantage of India's medical drug testing framework and the human participants who are integral part of the clinical trial procedure.

This final chapter of this paper provides the thesis summary and author's suggestions on the narrated subject to motivate future upgrade in the clinical trial legal system.

## 6.2 Thesis Summary

CTs are described as an organised experimental and thorough study executed on humans with the intent of assessing the effectiveness and safety of novel pharmaceuticals by detecting or establishing therapeutic, pharmacological (comprised with pharmacokinetic and pharmacodynamic) or detrimental impact.

CTs is a prominent topic in research around the world because it is vital for the future of innovative drug processing, drug delivery mechanisms, dosage regimens, surgical and examination procedures, instruments, and cures, among other areas.

Clinical research evidence is required for the launch of any new medicine. Whether it's a specific chemical composition or an established pharmaceutical being sold for a new indication, clinical studies are required. Clinical evidence is also expected before a new preparation, drug delivery system, or even a new fixed dose mix can be launched.

As a result, it should come as no surprise that clinical research has a lot of potential, because drug releases are impossible without supporting data. Clinical research should not be considered an afterthought to preclinical research.

It has immense scope and benefits not just for trained healthcare, drug companies, and med tech specialists, but also for monitoring agencies, the government, and society at large.

The pharmaceutical industry in India is one of the speedy-growing in the country, with tremendous advances gained over the past. From being an included this economy in the 1950s toward being identity and widely acclaimed as a supplier of high-quality, low-cost, bulk mixtures and pharmaceuticals, the company has grown to become self-sufficient and globally recognized.

A number of factors have contributed to India's prominence as a clinical testing hub, and global corporations have chosen it as their preferred location. For starters, there are a slew of government-funded medical and pharmaceutical institutions with cutting-edge facilities that might serve as perfect sites for multi-centre clinical studies.

Secondly, the population of India is huge, the folks are well aware, talented and trained also, capable when comes to English language ability. Most importantly, there is an abundance of clinical statistics provided. India is a superior alternative in terms of cost savings since this cost of conducting a clinical study here is 50 to 75 percent cheaper than in the United States or the countries of European Union.

Another advantageous factor is that R&D costs in India are far below, when compared to various other Industrialised economies, which is helpful in NDDR along with NDDS projects at a reasonable cost. In addition, clinical trial expenditures in India are around one-third of what they are in major drug-producing countries like Europe and the United States.

Clinical trial outsourcing to India is a particularly appealing choice for US corporations since it alleviates their logistical and budgetary concerns. Because the opportunity to enrol in an exploratory drug study is a healthcare jackpot for many in India, recruitment is faster and easier logistically.

India provides ease in expenses to pharmaceutical companies in US and Western Europe. This advantage is offered as a result of low-cost expenditure in conducting trials in India and India is abundant with health facilities, large patient traffic needed

for the trials, research organisations, staffs with fluency in English language etc. Diverting trials to India has also helped the pharmaceutical companies to cut down their trial expenditures up to 60 % as per the data given by New Zealand Journal of Medicine.

The Clinical Research industry, on the other hand, has been caught in a bind due to India's shifting regulatory landscape. Between 2005 and 2010, there was a rise of projects, followed by a steady reduction in the past five years. As a result of this paradigm shift, the government has enacted new rules that include more strict procedures to ensure compliance and the proper conduct of clinical research.

The downward trend may be linked back to a series of events that began with national and international complaints of unethical techniques, such as failing to get informed consent from subjects for trial participation. India's Supreme Court intervened in the legal proceedings and postponed permissions for new clinical trials in the case of Swasthya Adhikar Manch, Indore v. Union of India, in response to concerns about participating member individuality and safeness, as well as public benefit litigation from non-governmental groups.

New policies were implemented in 2013 as amendments to Schedule Y of the D & C Rules, enabling ethics committee certification and AV footage of informed consent sessions, which really is a requirement, distinct to India.

Clinical trials are exclusively used in India to explore "new medications," with BMHR pertaining to all other elementary, technical, functional, and clinical research.

The NDCT Rules of 2019 are the stepping point in India to incorporate non-drug-related research (i.e., BMHR) within the legislative coverage (before, regulatory processes in India were primarily focused on "new drug" research).

The primary operational objective of the new regulation has been to improve regulatory monitoring over the investigators, sponsors, ethical committees, and institutions, ensuring rights of the trial subjects, safety, and their well-being protected.

Despite this, there are still some areas of worry. The executive's attempt to establish a method for rewarding study participant in the accidental death or harm, for example,

could be seen as an endeavour by the executive to move beyond its authority and into the sphere of the courts.

Section 12 and 33 of the D & C Act, over which the NDCT Rules was constructed did not by itself give any standards for providing remuneration for the participants.

Monopolistic trends in the CRO sector have gone unnoticed. The necessity for bridging trials for ethnically varied groups to verify medication appropriateness is not addressed because India has such a large ethnic variety. The cost-cutting waiver programme of easy CTs approval for faster access to new pharmaceuticals can put people's health at risk and result in a poor/incomplete CTs procedure.

### 6.4 Significant Changes done in 2019 NDCTR

Under the New Rules, DCGI is the CLA. Anyone planning to perform a clinical trial, bioavailability research, or bioequivalence studies must form and register an EC. Only once the EC has approved the experiment or study, it may be carried out. The application for conducting a clinical study must be submitted to the CLA using SUGAM, the CDSCO's online platform[117].

The New Drugs and Clinical Trials Rules, 2019, supersede Part X-A of the Drugs and Cosmetics Rules, 1945, and Schedule Y of the rules. The new law has given scientists and ethical researchers greater alternatives for promoting scientific and ethical study. The new rule expands the scope of drug development and approval.

The disposal of a new drug application must be completed within 90 days. It also gives the option of accelerated approval on the condition of completing a post- marketing trial. Expedited Review can be requested by sponsors. Pre-submission and post-submission meetings are mentioned in the rule.

The current law covers prescription treatments, innovative treatment products for human use, clinical trials, bio comparable studies, bio availability investigations, and ECs.

[117] Essenese Obhan ,et al., India: Changes To The Regulatory Framework For Clinical Trials In India, OBHAN A.(2019).

For innovative pharmaceuticals that have been authorized and marketed in other countries for more than two years, perinatal studies, animal toxicity studies, teratogenic studies, reproductive studies, mutagenicity and carcinogenicity studies are not necessary.

In the event of revised or new claims and NDDS, the law has reduced the need for non-clinical and clinical evidence. The law gives us the option of exclusion in certain cases.

### 6.4 Prospects of 2019 NDCTR for India's Pharmaceutical Businesses

The new laws are expected to encourage clinical research in the country by establishing a more open approach that results in speedier approvals than previous restrictions.

If the restrictions implemented in 2019 yield results in 2019-20 and save time & expense for global enterprises, the market might expand to 8.5-9 per cent from 2019-2021 and then speed up quicker (2022-2026 to roughly >12 percentage) terms of number of clinical trials filed in India.

Drug companies choosing India as a market for performing local clinical research earn added features if their drugs are licensed and commercialised in the European Union, Canada, the United Kingdom, the United States, Australia, and Japan.

As per the new legislation, any drug developed in India or developed in India that is intended to be made and supplied in India must be licensed for clinical trials by the CLA within 30 working days.

The licence to undertake a clinical trial is deemed to have been authorized if the CLA does not interact with the request within the time range stipulated.

The DCGI will now consider data acquired anywhere outside the nation, simplifying and speeding up the application processing.

Foreign companies located in the United States and Europe who have been eyeing China as a testing ground have yet to build trust in the country, and are checking up on the environment following the new rule's introduction in 2019.

Except from it, the proposed laws will eliminate pointless investigations, accelerate the availability of new drugs in the country, reduce drug costs, and make life simpler for drug businesses to operate.

## 6.5 Scope of Improvements of India's 2019 New Clinical Trial Rules

To reap the benefits of clinical trials, the country's goal should be to increase clinical research while maintaining high standards for patient safety and data accuracy. A clinical trial should be prepared and carried out by a skilled investigator who adheres to the most up-to-date norms and regulations while keeping thorough records and reporting[118].

Maintaining the highest standards is critical, since any lapse could undermine public trust and participation of the subjects in clinical trials, ultimately affecting the supply of safe and effective treatments.

To create healthy competition and break down the monopoly, more mid and smaller businesses in the CRO area should be rewarded. The expense of conducting trials in India will be reduced as a result of this. This sector can lose its path and become entangled in the complexities of trials if it is not carefully fostered.

In contrast to market segments like African countries, where interaction is a big problem, or Western Europe, where the cost of testing is high and people with the disease have few medical problems, but vocabulary is a huge impediment, Indonesia, where transit is a difficulty, India provides facility, simple and systematic policies (as of 2019 rules), and the government has a natural propensity to support more companies keeping in view the Indian market as a site for clinical trials.

## 6.6 Suggestions and Future Possibility of India's Clinical Trial Legal System

To develop a better legal framework well-suited for conducting international clinical trials India's clinical trial legal model needs to particularly emphasize on:

[118] Social Justice Article, Drugs and Clinical Trials Rules, 2019, 2019, https://www.drishtiias.com/to-the-points/Paper2/drugs-and-clinical-trials-rules-2019.

1. Adequate awareness skill building provisions for investigators and proper assessment to ensure their eligibility in clinical trial procedure. This will help in better participant selection, assistance for their well-being of the participants of the trial and management of human subject care.

2. Clinical Trial System should be made more legally valid and convincing among general public to gather their trust and support for the betterment of the procedure. This will be helpful to increase the participation of the population in the trials.

3. Adequate encouragement and sufficient employment options should be incorporated to recruit capable staff for clinical trial processes in India. The recruitments be made open conveniently based on regions. Recruitment policy should regularly evaluate demand, regional availability of suitable candidates, pattern of clinical trials and future scope of the procedure. Recruiting staffs for the process based on region or with the hold of local language, will help in counselling of the trial participants throughout the trial process and also eliminate any kind of discrepancies, which will lead to the stoppage of the trial process.

4. Both medical and non-medical candidates should be made aware of the prospects of Clinical Trial market prospects to motivate them to become a clinical trial staff. Awareness and skill building units should be built in every region, particularly emphasizing the disease prone area.

5. EC plays a major role in a clinical trial so it's important that systematic Ethical Committee infrastructure that should be uniformly established and maintained to assure a transparent clinical trial set up. The contrary provisions in the Rule 25 of NDCTR, which infers differently on the requirement of EC, should be amended to bring in clarity in the roles of ECs. EC role and structure should be properly aligned to avail their timely and prompt support and coordination during clinical trial process.

6. Better Capacity Building of EC to enhance their eligibility and expertise. To boost convenient, timely and updated knowledge transfer, India is adopting wide use

of ICT based tools to serve for information distribution. Accordingly, support, funding and infrastructural policies should be enforced.

Note[119]: The COHRED developed the RHInnO, an online platform that gives researchers access to an easy-to-use automated system that allows them to track the research process throughout its entire life cycle. This is helpful for research institutions and researchers to publish their data, findings, make calls for proposals of research etc. Its 'ethical' is helpful to review the process, track the progress etc.

7. Legal policies should be more integrated and collaborative in terms of information transfer and communication processes. Each and every segment involved in the procedure should be permitted to access necessary information and establish communication without any bias or suppression.
8. Strict reporting and record keeping of SAEs occurrence on human subjects should be made mandatory in the Clinical trials in India, just like in USA etc. So that not only the people related to the trial, but also the general public can have information about SAEs. The monitoring and evaluation should be honest, on-time and accurate to minimize or properly evaluate such occurrence.
9. Balanced provisions and priority for the sponsors, investigators and human participants to seek legal protection, raise issues and claim compensation in terms of clinical trial anomalies. That serves for an unbiased and neutral process eliminating the chances of ethical mistreatment.
10. Fair compensation procedure to ensure benefits to the human subjects on happening of any SAEs should be properly drafted. Proper procedure for determining compensation has to be laid down taking into all factors necessary. Bringing in No fault compensation, which was in the draft rules of NDCT, in the actual rules would alleviate the problems related to erroneous compensation etc.
11. Systematic, organized and well monitored informed consent procedure should be compulsorily done in each clinical trial process, with proper proof and evidence, so that subjects are not kept in dark.

[119] Subramani Poongothai et al., supra note 3.

12. Legal transparency for feasible innovation and drug development applications as per global standard should be evolved and updated as per the advancement of clinical trial system. More transparency in the system of clinical trials would improve the number of trials in the country and will ensure safety and efficacy.
13. The duplication of rules as a result of numbering the rules of D&C Rules and NDCT Rules could be avoided by differently numbering them, to avoid confusion as to which rules.
14. The CTRI website should made properly functional and should be mandated to updated the results of each trials & the current progress in between specified intervals.
15. India's Clinical Trial Legal Policies should possess its own uniqueness and give scope to the international laws as applicable under specific conditions ensuring control as well as smoothness of functionality guaranteeing the legitimacy and security of the procedure.

## 6.7 Conclusion

The Clinical trial system in India can be improved in the years ahead and the time of it reaching in par with the Clinical trial system like of USA or any other country is not far, if the authorities and the rules related to Clinical trial system is made stricter, with clarity and unambiguous. Hence the hypothesis of the research that' The NDCTR are not comprehensive' stands proven, as there are still deficiencies in the rules relating to CTs. At present the Clinical trial rules, though have come to a better position than that before some years, still the rules are not comprehensive and have deficiencies and challenges faced in many aspects, related to EC, compensation, safety etc. Some of the suggestions, mentioned in these chapters, if brought into the NDCTR rules and the system of CTs, would definitely help to improvise the system by filling the deficiencies and making India, the most suitable, feasible & preferred option to conduct Clinical trials.

# BIBLIOGRAPHY

**Books**

1. LILY SRIVASTAVA, LAW AND MEDICINE 163-194 (2013 ed., Universal Law Publishing house) (2013).
2. NANDITA ADHIKANI, LAW AND MEDICINE 356-384 (4th ed., Central Law Publications) (2015).
3. SHAUN D PATTISON, MEDICAL LAW AND ETHICS (South Asian ed., Sweet & Maxwell) (2017).
4. VIJAY MALIK, LAW RELATING TO DRUGS AND COSMETICS 1559-1600 (EBC Books) (2016).

**Articles**

1. Akanksha Rani and Vikesh Kumar Shukla, *Impact of rules for New Drug and Clinical Trial in India*, 8 INT. J. D. R. A. 25-30 (2020).
2. Akhilesh Dubey et al., *New Drugs and Clinical Trials Rules, 2019: Towards Fast-track Accessibility of New Drugs to the Indian Population*, 53 INT. J. P. E. R. S451 (2019).
3. Amar Jesani and Sandhya Srnivasan, *New Drugs and Clinical Trials Rules, 2019: The market trumps ethics and participant rights*, 4 IND. J. M. E. 89-91(2019).
4. Ankita Chakravarty and Ambedkar Bhavan, *Unethical Clinical Trials in India: A Selective Preliminary Overview*, 27 EUBIOS J. A. I. B. (2017).
5. Ashna Ashesh and Zubin Dash, *Inadequacies Of Clinical Trial Regulations In India*, 5 NUJS L. R. 379 (2012).
6. Bushra Shamim, *Good Clinical Practice (GCP): A Review*, 2 PHARMATUTOR 20-29 (2014).
7. David B. Fogel, *Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review*, 11 CONTEMPORARY C. T. C. 156-164 (2018).
8. Essenese Obhan , et al., *India: Changes To The Regulatory Framework For Clinical Trials In India*, OBHAN A. (2019).
9. Himani Bhakuni, *Informed consent to clinical research in India: A private law remedy*, 20 SAGE P. J. 256 (2020).

10. Hitt Sharma and Sameer Parekh, *Clinical Trials Regulations in India*, 1 PHARM. R. A., 1-e118 (2012).
11. Jan Borysowski et al., *Legal Regulations, Ethical Guidelines and Recent Policies to Increase Transparency of Clinical Trials*, 86 BRITISH J. C. P. 679–686 (2020).
12. Josmar K. Alas et al., *Regulatory Framework for Conducting Clinical Research in Canada*, 44 THE C. J. N. S. 2 (2017).
13. Kalindi Naik, *Clinical Trials in India: History, Current Regulations, and Future Considerations*, THE SCHOOL OF HEALTH SCIENCES EASTERN MICHIGAN UNIVERSITY, Michigan, 2-3 (2017).
14. Khalid Mahmood, *Forewarned is Forearmed! Unethical Drug Trials in the Developing Countries*, 6 JOURNAL D. U. H. S. K. 79 (2012).
15. Madhuri Jadhav and Arun Bhatt, *Ethics in clinical research in India: A survey of clinical research professionals' perceptions*, 4 PERSPECT. C. R. (2013).
16. Mark Yarborough, *Do we really know how many clinical trials are conducted ethically? Why research ethics committee review practices need to be strengthened and initial steps we could take to strengthen them*, 47 J. M. E. 572-579 (2021).
17. Mohammed Imran et al., *Clinical Research Regulation in India- History, Development, initiatives, Challenges and Controversies: Still Long Way to Go*, 5 JOURNAL P. B. S. 2–9 (2013).
18. Mohit Hans, Suresh Kumar Gupta, *Comparative evaluation of pharmacovigilance regulation of the United States, United Kingdom, Canada, India and the need for global harmonized practices*, 9(4), PERSPECT. C. R. 170-174 (2018).
19. Mukesh Yadav et al., *Compensation Issue in Clinical Trials Recent Indian Scenario*, 36, JOURNAL I. A. F. M. (2014).
20. A Nair, *Clinical research: Regulatory uncertainty hits drug trials in India*, THE P. J. (2015).
21. Neelu Singh et al., *New drugs and clinical trials rules 2019: Changes in responsibilities of the ethics committee*, 11 PERSPECT. C. R. 37 (2020).
22. Nisha Venugopal and Gayatri Saberwal, *A Comparative AnalysisOf Important Public Clinical Trial Registries, And A Proposal For An Interim Ideal One*, 16 PLoS O. (2021).

23. Nusrat Shafiq et al., *On-Site Monitoring of Clinical Trials by an Ethics Committee in India: A Road Less Travelled*, 17 RES. E. 45- 54 (2020).
24. Parveen Jain and Rahul Chauhan, *India's New Drugs and Clinical Trials Rules: An Industry Perspective*, 7 REGULATORY F. (2019).
25. Pikee Saxena and Rohit Saxena, *Clinical Trials: ChangingRegulations in India*, 39 INDIAN J. C. M. 197–202 (2014).
26. Pooja Agarwal and Priyanka B, *Regulations Governing Clinical Trials In India, Europe And USA- A Comparative Study*, 5 INT. J.D. R. A, 30-39 (2017).
27. Prajapati Vishal et al., *A Review On Drug Approval Process For Us, Europe And India*, 2 INT. J. D. R. A. 1- 11 (2014).
28. Roli Mathur, *Handbook On National Ethical Guidelines For Biomedical And Health Research Involving Human Participants*, I.C. M. R (2018).
29. Royal Patel et al., *Present era of drug safety in India: An overview*,2 JOURNAL P. D. R. 3-4 (2021).
30. S. B. Thorat et al., *Clinical Trial: A Review*, 1 ARTICLE 019, 101- 102 (2010).
31. Sandhiya Selvarajan, et al., *Clinical trials in India: Where do we stand globally?*, 4 INT. S. C. R. 160-164 (2013).
32. Sangeeta Kumari, et al., *Hidden duplicates: 10s or 100s of Indian trials, registered with ClinicalTrials.gov, have not been registered in India, as required by law*, 15 PLOS O. e0234925 (2020).
33. Shivaprakash G and Pallavi LC, *New Drugs and Clinical Trial Rules 2019, What is New? Our Views from Ethical Perspective*, 67 JOURNAL A. P. I. 75-76 (2019).
34. Subramani Poongothai et al., *Why are Clinical Trials Necessary in India?*, 5 PERSPECT. C. R. 55-56 (2014).
35. Suneha Kasal and Swini Khara, *Reviewing the New Drugs andClinical Trials Rules, 2019: Lessons from the COVID-19Pandemic*, NAT. L. S. I. R. (2021), https://nlsir.com/reviewing-the-new-drugs-and-clinical-trials-rules-2019-lessons-from-the-covid- 19-pandemic/ (Last visited May 05, 2022).

**Reports**

1. K. Bangarurajan, Regulations and Guidelines Specific to Ethics Schedule Y and CDSCO-GCP,CDSA,https://www.kem.edu/wp content/uploads/2019/12/Regulations_Dr.Bangaruranjan-Well-drfine-Drug-ministry.pdf(Last visited Mar.18,2022).
2. ECCHR Case Summary, Human Rights Violations in Clinical Trials in India, The case of The HPV Vaccination Project, ECCHR (Feb.11,2014,https://www.ecchr.eu/fileadmin/Fallbeschreibungen/Case_Summary Clinical_Trials 2014-02-11.pdf(Last visited April 15, 2022).
3. India Correspondent BMJ, India: Doctors Call For Investigation Into Allegations Of Ethical Abuse In Covid-19 Vaccine Trial, BMJ 372 (2021).
4. ISCR Report, New Drugs and Clinical Trial Rules, 2019, ISCR (2019), https://www.rgcb.res.in/documents/New%20drugs%20and%20clin ical%20trial%20rules%202019.pdf (Last visited Mar. 22, 2022).
5. Social Justice Article, Drugs and Clinical Trials Rules, 2019, 2019, https://www.drishtiias.com/to-the-points/Paper2/drugs-and-clinical-trials-rules-2019.
6. Suzanne White Junod, FDA and Clinical Drug Trials: A Short History, U.S. FOOD AND DRUG ADMINISTRATION, Available Online at https://www.fda.gov/media/110437/download(Last visited Feb.05, 2022).
7. Therapeutic Product Directorate Report, Overview of Regulation of Clinical Trials in Canada, Vol-2(1),Health Canada,https://admin.ich.org/sites/default/files/inline-files/Overview_of_Regulation_of_Clinical_Trials_in_Canadapdf.pdf.

**Internet Sources**

1. Abanti Bose, Law regarding emergency use authorization of vaccines in India, iPLEADERS (Dec. 06,2021), https://blog.ipleaders.in/law-regarding-emergency-use- authorization-of-vaccines-in-india/ (Last visited May 17, 2022).
2. Divya Rajagopal ET Bureau, PIL Filed Against Illegal Drug Trials, THE ECONOMICS TIMES| INDUSTRY (Feb. 06, 2012, 07:54 PM IST), https://economictimes.indiatimes.com/industry/healthcare/biotech/

pharmaceuticals/pil-filed-against-illegal-drug trials/articleshow/11780731.cms?from=mdr (Last visited April 21, 2022).

3. Khaitan & Co, Delhi High Court permits in-house expert of a contesting party to be a part of Confidentiality Club, LEXOLOGY (June 17, 2020), https://www.lexology.com/library/detail.aspx?g=68bfa72e-f5db- 4f0a-8634-da7cd448cfc3 (Last visited April 11, 2022).
4. Malia Politzer and Vidya Krishnan, The Dark Underbelly of India's Clinical Trials Business, MINT (Oct 11, 2012, 12:20 AM IST), https://www.livemint.com/Politics/D0gBgwCn3huK72S06p8K5H/ The-dark-underbelly-of-Indias-clinical-trials-business.html (Last accessed April 25, 2022).
5. Maureen Bennett and Jan Murray, Conducting Clinical Trials in the US and Abroad: Navigating the Rising Tide of Regulation and Risk, Squire, Sanders & DempseyL.L.P., https://www.squirepattonboggs.com/~/media/files/insights/publications/2009/10/conducting-clinical-trials-in-the-us-and-abroad-/files/ssdcentral68696v2draftwhitepaperconductingclinic/fileattachment/ssdcentral68696v2draftwhitepaperconductingclinic. pd f.
6. Mritryunjay Seal, Clinical Trials in India and Role of a Legal Expert in the Ethics Committee, 2018, https://www.latestlaws.com/articles/clinical-trials-in-india-and-role-of-a-legal-expert-in-the-ethics-committee-by-mrityunjoy-seal(last accessed April 05, 2022).
7. National Institute of Infectious Diseases Review: USA vs India Clinical Trials, CLINGREGS SURVEY (2021) (Last visited Apr. 03, 2022).
8. Neha Dixit, Churu Drug Trials: Four Months On, Dalit Victims Report Severe Damage To Health And Caste-Based Harassment, THE CARAVAN (Sep. 11, 2018), https://caravanmagazine.in/health- and-education/churu-drug-trials-four-months-on-dalit-victims- report-severe-damage-to-health-and-caste-based-harassment (April 15, 2022).
9. Pharm-Olam Report, Reconsidering India as a Clinical Trial Location Revised Regulations Warrant a Fresh Look, PHARM- OLAM, https://cdn2.hubspot.net/hubfs/4238150/PharmOlam_March2018/P DF/pharm-

olam_india_clinical_trials_white_paper_1.pdf?t=1524594556831 (Last visited Mar. 12, 2022).

10. S Srinivasan, India's new clinical trial rules weaken safety nets for participants, SCROLL.IN - LAX STANDARDS (Apr. 04, 2019, 02.30 P.M.), https://scroll.in/pulse/918874/new-clinical-trial-rules- weaken-safety-nets-for-trial-participants-to-promote-research (Last visited May 21, 2022).
11. Sanil Manavalan and Catherine Sinfield, Conducting Clinical Trials In India: Opportunities And Challenges, Clinical Leader, CLINICAL LEADER - GUEST COLUMN (Aug. 8, 2017),https://www.clinicalleader.com/doc/conducting-clinical-trials-in- india-opportunities-and-challenges-0001 (Last visited May 11, 2022).
12. Soibam Rocky Singh, PIL Against Covaxin Trial On 2-18 Age Group: Hc Seeks Centre's Stand, THE HINDU (May 19, 2021, 12:18 IST), https://www.thehindu.com/news/national/pil-against- covaxin-trial-on-2-18-age-group-hc-seeks-centres- stand/article34593271.ece (Last visited April 19, 2022).
13. Subhash C. Mandal and Moitreyee Mandal, Evolution of clinical trial regulation in India, CONFERENCE: 2ND INTERNATIONAL & 4TH NATIONAL CONFERENCE OF INDIAN SOCIETY FOR RATIONAL PHARMACOTHERAPEUTICS at: Kolkata (2012) (Last visited Mar. 19, 2022).
14. Yogini Oke and Shreya Shrivastava, How India's regulatory pitfalls helped Covishield and Covaxin get rapid approval, THE PRINT (Jan. 08, 2021, 12.54 PM IST), https://theprint.in/opinion/how-indias-regulatory-pitfalls-helped-covishield-and-covaxin-get-rapid-approval/581676/ (Last visited May 18, 2022).