Available online on 15 Mar, 2026 at https://ijdra.com/index.php/journal

International Journal of Drug Regulatory Affairs

Published by Diva Enterprises Pvt. Ltd., New Delhi
Associated with Delhi Pharmaceutical Sciences & Research University
Copyright© 2013-26 IJDRA

Review Article **Open Access**

Comprehensive Comparison of Clinical Trial Protocol & Clinical Investigation Plan in Different Countries

Sedamaki Chaitanya, Dhulipudi Hara Naga Ganesh, Rudra Vaishno, Prasanthi D.*

Department of regulatory affairs, G. Pulla Reddy College of Pharmacy, Osmania University, Hyderabad, Telangana, India 500028.

Abstract

Clinical research involving investigational medicinal products and medical devices is governed by region-specific regulatory frameworks that define the planning, review, and conduct of studies. The clinical trial protocol (CTP) and clinical investigation plan (CIP) serve as core regulatory documents required for approval and oversight. This review compares regulatory requirements for CTPs and CIPs in India, the United States, and the European Union, with a focus on definitions, structure, submission pathways, ethical considerations, and regulatory oversight. Across all regions, strong emphasis is placed on participant safety, scientific rationale, and compliance with good clinical practice. Common elements include study background, objectives, methodology, risk assessment, and data management. However, differences exist in terminology, approval processes, and region-specific expectations, particularly for medical device investigations and risk classification. Understanding both harmonised principles and jurisdiction-specific requirements can support regulatory compliance and facilitate efficient planning of multinational clinical research studies.

Conclusion: Despite differences in terminology, approval pathways, and regulatory authorities, a clear understanding of both global standards and region-specific requirements is essential for ensuring regulatory compliance and enabling efficient multinational clinical research.

Keywords: Clinical trial protocol; Clinical investigation plan; Regulatory requirements; medical device regulation; CDSCO; FDA; European Union

Article Info: Received 19 Jan 2026; Review Completed 25 Feb 2026; Accepted 05 Mar 2026

Cite this article as:
Sedamaki C, Dhulipudi Hara NG, Rudra V, Prasanthi D. Comprehensive Comparison of Clinical Trial Protocol & Clinical Investigation Plan in Different Countries. Int. J. Drug Reg. Affairs [Internet]. 2026 Mar 15 [cited 2026 Mar 15]; 14(1):12-20. Available from:
https://ijdra.com/index.php/journal/article/view/844

DOI: 10.22270/ijdra.v14i1.844
*Corresponding author. E-mail address: prasanthidhanu@gmail.com (D. Prasanthi)

1. Introduction

Clinical research for drugs and medical devices is governed by internationally recognised standards to ensure participant safety, data integrity, and ethical conduct. For medicinal products, the cornerstone guideline is ICH E6 – Good Clinical Practice (GCP), (1) while for medical devices, the corresponding global standard is ISO 14155 – Clinical Investigation of Medical Devices for Human Subjects. (2)

Under ICH E6, drug trials are conducted according to a well-defined Clinical Trial Protocol (CTP), which describes the study objectives, design, methodology, statistical considerations, and safety monitoring. ISO 14155 provides the ethical and scientific framework for device investigations through the Clinical Investigation Plan (CIP). The CIP outlines the rationale, design, conduct, and analysis of a medical device study, with a strong focus on risk management, device performance, and subject protection. (2)

The adoption of ICH E6 for drug trials and ISO 14155 for medical device investigations has had a significant global impact on clinical research. These standards have harmonised how Clinical Trial Protocols (CTPs) and Clinical Investigation Plans (CIPs) are designed and conducted across regions, reducing variability in study quality and ethical oversight. Regulatory authorities worldwide—including the CDSCO, FDA and EU.

1.1 Core Definitions

a) Clinical Trial Protocol (CTP)

As per ICH E6 Good Clinical Practice, a Clinical Trial Protocol is: A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a clinical trial. It provides the basis for conducting, monitoring, auditing, and reporting a clinical trial involving medicinal products in compliance with GCP.

The guideline draws from current good clinical practices in places like the World Health Organization (WHO),

Australia, Canada, the Nordic countries, Japan, the United States, and the European Union. (1)

b) ISO 14155:2020 – Clinical Investigation Plan (CIP)

A Clinical Investigation Plan, as outlined in ISO 14155:2020, is essentially a detailed roadmap for running a clinical study on a medical device with human participants. It lays out the reasoning behind the study, its goals, how it's designed, the step-by-step methods, how it'll be monitored, the stats involved, and who's organizing it all. This document serves as the go-to guide to keep everything ethical, scientific, and on track. (2)

Table 1. Comparison Between Clinical Trial Protocol (CTP) And Clinical Investigation Plan (CIP). (1,2)

Aspect	Clinical Trial Protocol (CTP)	Clinical Investigation Plan (CIP)
Regulatory Submission	Submitted to ethics committees and regulatory agencies for approval	Submitted to ethics committees and authorities; basis for approvals in medical device trials
Focus on Safety and Performance	Emphasizes drug safety, efficacy, and compliance with clinical research principles	Emphasizes device safety, performance, clinical benefit, and compliance with device-specific standards
Format	Detailed and prescriptive; often lengthy	Structured per ISO 14155; detailed and includes justification based on prior data and clinical evaluation

2. Clinical Trial Protocol (CTP) in India

Section 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), along with DTAB guidance, establishes the New Drugs and Clinical Trials Rules (NDCT) 2019 as India's regulatory framework for clinical trial protocols. Clinical trials on new drugs can only be initiated after obtaining permission from the Central Licensing Authority and approval from the respective Ethics Committee. Moreover, any administrative, logistic changes or minor amendments in the approved protocol must be notified to the Central Licensing Authority within thirty days. This system is designed to guarantee ethical, open, and standards-compliant clinical trials at national and global levels. (3)

2.1 Contents of Clinical Trial Protocol:

Contents of CTP are broadly divided into two main sections: the Title Page and the Table of Contents.

The Title Page includes the full clinical study title, protocol and study numbers, protocol version with dates, name and IND number of the investigational drug, sponsor and contract research organisation details, investigator qualifications with their institutional affiliations, clinical trial site locations, and participating clinical laboratories or facilities. (3)

The Table of Contents outlines key sections of the protocol such as background and introduction summarizing preclinical and clinical experience; study rationale including design and methodology overview; defined primary and secondary objectives linked to the study design; a detailed study design explaining trial type, treatment arms, randomization, and blinding; study population and eligibility criteria; plans for study assessments and procedures; study conduct activities including medical history, exams, and lab tests; treatment details describing dosing, administration, and adjustments; adverse event monitoring and reporting; ethical considerations covering risk-benefit, Ethics Committee oversight, informed consent (see Figure 1), and confidentiality; procedures for monitoring data collection and Case Report Form completion; investigational product management; statistical data analysis methods; investigator undertakings; and appendices containing supportive documents like consent forms and study manuals. (3)

2.2 Approval Process and Timelines:

The NDCT Rules specify clear timelines for the regulatory review process. For investigational new drugs developed within India, the Central Licensing Authority must complete their review within 30 working days of submission. For global clinical trials or drugs already approved in certain regulated countries, this review period extends to 90 working days. Importantly, the rules provide an "automatic approval" feature: if no response is received from the Central Licensing Authority within these timelines and all Ethics Committee approvals are in place, the sponsor may proceed after notifying the authority via Form CT-4A. Ethics Committee approval is mandatory, and the trial can only commence after both the Central Licensing Authority and Ethics Committee have granted permission. (4)

3. Clinical Trial Protocol in the United States of America:

3.1 FDA Clinical Trial Protocol

Every planned clinical study or trial requires a submitted clinical protocol. An original IND application without one count as incomplete. Protocols for follow-up studies not included in the initial IND application may be submitted later as Protocol Amendments. (5)

3.2 Required protocol elements

All clinical trial protocols, regardless of phase, must include study's objectives and purpose, along with complete investigator information, including names, addresses, qualifications, study sites, sub investigators, and IRB details.

They must clearly define participant inclusion and exclusion criteria and provide an estimated sample size. The study design should describe any control groups and outline methods to minimize bias. Detailed information on dose selection, maximum dose, and exposure duration must be provided. The protocol should also specify all

planned assessments needed to meet study objectives and include comprehensive safety monitoring procedures, such as clinical evaluations, laboratory tests, and other measures to track drug effects and ensure participant safety. (5)

Format of Informed Consent Form according to NDCT 2019:

2. Format of informed consent form for Subjects participating in a clinical trial—

Informed Consent form to participate in a clinical trial

Study Title:

Study Number:

Subject's Initials:..... Subject's Name:.....

Date of Birth/ Age:.....

Address of the Subject.....

Qualification.....

Occupation: Student or Self-Employed or Service or Housewife or Others (Please click as appropriate).

Annual Income of the subject:

Name and address of the nominees and his relation to the subject (for the purpose of compensation in case of trial related death).

Place Initial box (Subject)

(i) I confirm that I have read and understood the information [ ]

Sheet dated.....for the above

study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and [ ]

that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purposes. [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression)
of the Subject/Legally Acceptable Representative:

Date:...../...../

Signatory'sName:.....

Signature of the Investigator:.....Date:...../...../

Study Investigator's Name:.....

Signature of the Witness.....e:...../...../

Name of the Witness:.....

Figure 1. Informed Consent Form

Protocol submission: A separate protocol must be provided for each planned study; later-added studies follow §312.30(a). (6)

- Phase 1 protocols: Less detailed; provide an investigation outline, estimated patient numbers, safety exclusions, and dosing plans. Only safety-critical elements (vital signs, labs, toxicity

monitoring) require detailed description. Non-critical design changes are reported annually. (6)

- Phase 2–3 protocols: Must be fully detailed. Should include built-in alternatives or contingencies for anticipated design deviations (e.g., early crossover for non-responders). (6)

3.3 Approval Process

Upon IND submission, the FDA has a 30-day period to review the protocol and may place a clinical hold if safety concerns arise. If no hold is issued, the sponsor can start the trial after receiving IRB approval. Protocol amendments generally require prior FDA and IRB approval unless addressing immediate safety issues. After clinical trials, sponsors file a New Drug Application (NDA) or Biologics License Application (BLA) for marketing approval, with FDA targeting 10 months for standard reviews or 6 months for priority ones. This step-by-step approach precisely assesses research while protecting participants. (7)

Next Page Reset Form

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0014
Expiration Date: September 30, 2026
See PRA Statement on page 3.

NOTE: No drug/biologic may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40)

1. Center *(select one)* ☐ CDER ☐ CBER
2. Name of Sponsor
3. Date of Submission *(mm/dd/yyyy)*
4. Sponsor Address
   - Address 1 *(Street address, P.O. box, company name c/o)*
   - Address 2 *(Apartment, suite, unit, building, floor, etc.)*
   - City
   - State/Province/Region
   - Country
   - ZIP or Postal Code
5. Telephone Number *(Include country code if applicable and area code)*
7A. IND Number *(If previously assigned)*
7B. IND Type *(select one)* ☐ Commercial ☐ Research
6. Name of Drug *(Include all available names: Trade, Generic, Chemical, or Code)* Continuation Page for #6
8A. (Proposed) Indication for Use
Is this indication for a rare disease (prevalence <200,000 in U.S.)? ☐ Yes ☐ No
Does this product have an FDA Orphan Designation for this indication? ☐ Yes ☐ No
If yes, provide the Orphan Designation number for this indication:
Continuation Page for #8
8B. SNOMED CT Indication Disease Term *(Use continuation page for each additional indication and respective coded disease term)*
9. Phase of Clinical Investigation to be conducted ☐ Phase 1 ☐ Phase 2 ☐ Phase 3 ☐ Other *(Specify)*:
10. List numbers of all Investigational New Drug Applications (21 CFR Part 312), New Drug Applications (21 CFR Part 314), Drug Master Files (21 CFR Part 314.420), and Biologics License Applications (21 CFR Part 601) referred to in this application.
11. IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.. Serial Number
12A. This submission contains the following *(Select all that apply)*
☐ Initial Investigational New Drug Application (IND) ☐ Response to Clinical Hold ☐ Response To FDA Request For Information
☐ Request For Reactivation Or Reinstatement ☐ Annual Report ☐ General Correspondence
☐ Development Safety Update Report (DSUR) ☐ Other *(Specify)*:

Protocol Amendment	Information Amendment	Request for	IND Safety Report
☐ New Protocol	☐ Chemistry/Microbiology	☐ Meeting	☐ Initial Written Report
☐ Change in Protocol	☐ Pharmacology/Toxicology	☐ Proprietary Name Review	☐ Follow-up to a Written Report
☐ New Investigator	☐ Clinical/Safety	☐ Special Protocol Assessment	
☐ PMR/PMC Protocol	☐ Statistics	☐ Formal Dispute Resolution	
☐ HF Validation Protocol	☐ Clinical Pharmacology		
☐ Use-Related Risk Analysis			

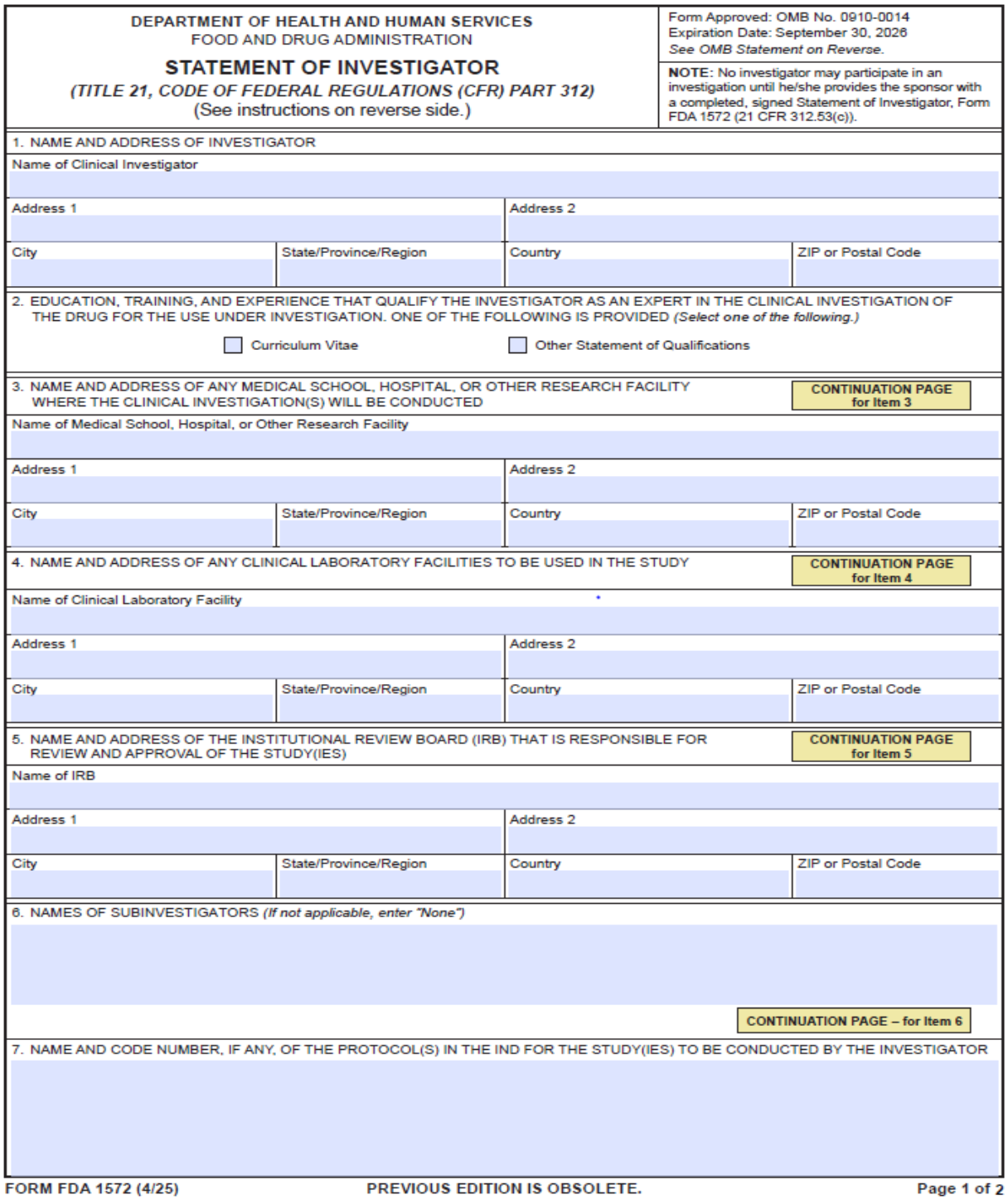
12B. Does the submission contain: Digital Health Technology (DHT) data or a proposal to collect DHT data? ☐ Yes ☐ No
13. For Originals, is the product a combination product (21 CFR 3.2(e))? ☐ Yes ☐ No
Combination Product Type *(See instructions)*
Request for Designation (RFD) Number

For FDA Use Only

CBER/DCC Receipt Stamp	DDR Receipt Stamp	Division Assignment
		IND Number Assigned

FORM FDA 1571 (3/25) - PREVIOUS EDITION OBSOLETE Page 1 of 3 PSC Publishing Services (301) 443-6740 EF

Figure 2. FDA Form 1571



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014
Expiration Date: September 30, 2026
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

Name of Clinical Investigator

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED *(Select one of the following.)*

☐ Curriculum Vitae ☐ Other Statement of Qualifications

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED — CONTINUATION PAGE for Item 3

Name of Medical School, Hospital, or Other Research Facility

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY — CONTINUATION PAGE for Item 4

Name of Clinical Laboratory Facility

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES) — CONTINUATION PAGE for Item 5

Name of IRB

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

6. NAMES OF SUBINVESTIGATORS *(If not applicable, enter "None")*

CONTINUATION PAGE – for Item 6

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

FORM FDA 1572 (4/25) PREVIOUS EDITION IS OBSOLETE. Page 1 of 2

Figure 3. Form 1572

4. Clinical Trial Protocol (CTP) In the European Union

4.1 Regulatory Framework

The European Union Clinical Trials Regulation (EU CTR) No 536/2014 uniquely harmonizes EU-member states in clinical trial submissions and oversight through CTIS since Jan 31, 2022. Managed by the European Medicines Agency (EMA) through the Clinical Trials Information System (CTIS), the regulation facilitates a centralized single-entry portal for multinational trial applications. (8) It emphasises transparency, requiring public availability of trial data while protecting commercially confidential information and personal data. The EU CTR replaces the earlier Clinical Trials Directive to foster innovation, improve safety standards, and increase efficiency by allowing joint assessment by national competent authorities and ethics committees. (9,10)

4.2 Contents of Clinical Trial Protocol

The clinical Trial Protocol under EU CTR must comprehensively outline objectives, design, methodology, statistical plans, and organization. Identification details such as the full title, EU trial number, protocol code, version, date, and sponsor information should be clear and accessible. Protocol content includes detailed descriptions of the

investigational medicinal product (IMP), dosage, and justification; study population criteria, including inclusion/exclusion; study design specifics such as endpoints, control measures, and blinding to minimise bias; and data and sample management processes. Statistical plans must justify sample sizes and define analysis methods. The protocol outlines subject management, including recruitment and follow-up, IMP accountability, monitoring, mechanisms to maintain blinding, and plans for post-trial care. It should also address publication policies, clinical data confidentiality, data breach management, and compliance with data protection legislation. (9)

4.3 Approval Process

Sponsors submit clinical trial applications through CTIS, triggering a coordinated evaluation by all concerned EU member states within roughly 45 days. A consolidated assessment report is issued, followed by a single national decision authorizing or rejecting the trial. Trials may proceed only after all approvals are granted. The system also manages amendments, safety updates, and annual safety reports, ensuring continuous oversight. The EU CTR's unified approach reduces duplicative submissions and supports efficient multinational trial operations, enhancing patient safety and data transparency across the region. (10)

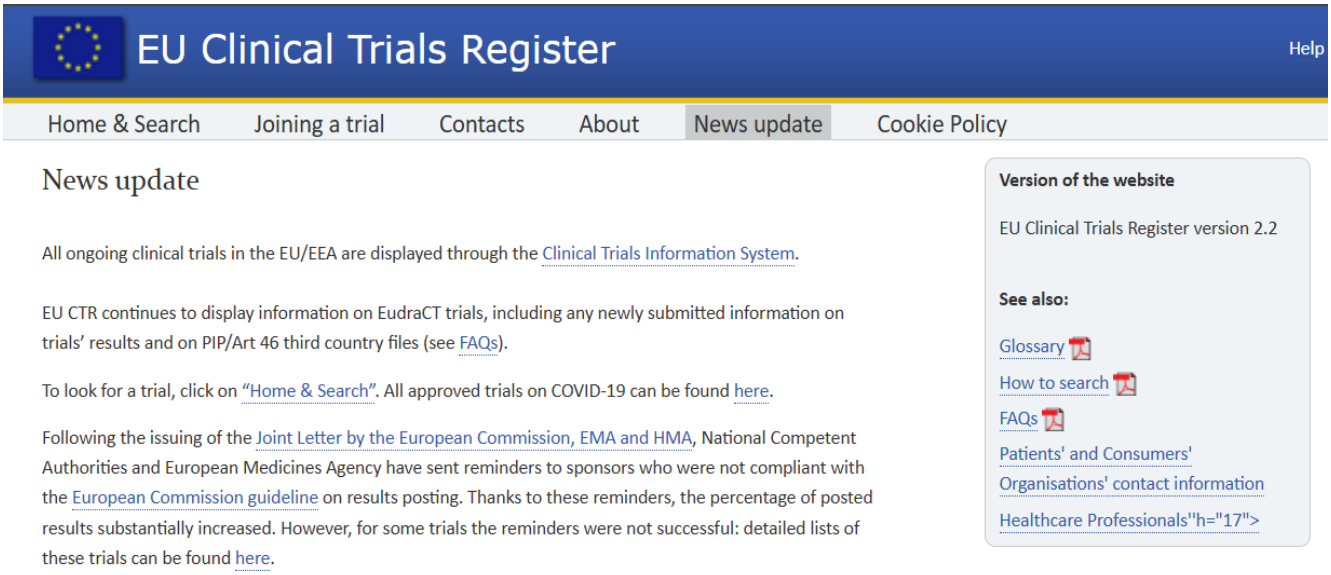


Figure 4. Describing the EU Clinical Trials Register (EU CTR)

5. Clinical Investigation Plan (CIP) In India

5.1 Medical Devices Regulatory Framework

India regulates medical devices under the Medical Devices Rules, 2017, which classify devices into four risk-based categories (Class A, B, C, and D). (11) Clinical investigations for medical devices follow principles aligned with ISO 14155:2020 while incorporating India-specific requirements. (12)

5.2 CIP Requirements and Contents

The Clinical Investigation Plan for medical devices in India must address the study rationale, objectives, and scientific justification, detailed study design and methodology aligned with ISO 14155, risk management integration per ISO 14971, subject eligibility criteria with demographic and clinical parameters, safety monitoring and adverse event management, device-specific procedures including device accountability and training, informed consent processes with language and cultural considerations, and data collection, monitoring, and quality control measures. (12)

For higher-risk devices (Class C and D), clinical investigations are generally mandatory unless adequate clinical evidence exists from similar devices. The CIP must demonstrate a comprehensive risk-benefit analysis and include specific monitoring plans. (12)

5.3 Approval and Ethics Requirements

Medical device clinical investigations require approval from registered Ethics Committees. The submission may be made through the MedDev Portal or SUGAM portal depending on device classification and study scope. Sponsors must ensure compliance with Indian GCP guidelines and maintain device accountability throughout the investigation. (12)

6. Clinical Investigation Plan in the United States

6.1 FDA Device Regulation

The FDA supervises medical device clinical investigations governed by 21 CFR Part 812 through the Investigational Device Exemption (IDE) pathway. Devices are divided as either Significant Risk (SR) or Non-Significant Risk (NSR), which influences the regulatory requirements (21 CFR 812.2, 812.3, 812.20). (13,14)

6.2 IDE Application Requirements

For Significant Risk devices, sponsors must submit an IDE application to the FDA, including device description with engineering specifications, preclinical testing results, clinical protocol with objectives, patient selection, study design, and risk analysis, investigator qualifications and institutional commitments, informed consent documents and IRB approval, and device labelling and instructions for use (21 CFR 812.20–

812.35). (15,16) Non-Significant Risk device investigations require IRB approval but abbreviated IDE procedures without FDA submission. The IRB makes the determination of risk category based on FDA guidance (21 CFR 812.2(b)). (13)

6.3 Study Design Considerations

Medical device investigations in the US often Seek to establish safety and effectiveness for the intended use, device performance endpoints, procedural success rates, and comparative effectiveness against the standard of care or predicate devices. Studies may employ early feasibility studies, pivotal trials, or post-market surveillance designs depending on device risk and regulatory pathway (FDA Guidance documents complementing 21 CFR Part 812). (14)

6.4 Monitoring and Compliance

FDA device investigations require adherence to Good Clinical Practice, protocol compliance monitoring, adverse event and device deficiency reporting, and documentation of device accountability. IRB oversight continues throughout the investigation with annual reviews and reporting of modifications (21 CFR 812.150–812.160; 21 CFR Part 56). (13,14)

7. Clinical Investigation Plan in the European Union

7.1 EU Medical Device Regulation Framework

The European Union Medical Device Regulation (EU) 2017/745 (MDR) establishes comprehensive requirements for clinical investigations of medical devices. Annex XV of the MDR specifically addresses clinical investigations, with Chapter II, Section 3 detailing CIP content requirements. (15)

7.2 CIP Content Requirements Under MDR Annex XV

The MDR requires the CIP to contain specific elements as outlined in Annex XV, including identification of sponsor, investigators, and investigation sites with a synopsis of the clinical investigation covering objectives, design, ethical aspects, monitoring, quality measures, selection criteria, target populations, sample size, treatment schedules, follow-up duration, and statistical plan. The rationale and justification section must provide an evaluation of preclinical testing results and prior clinical investigations, an evaluation of relevant clinical data, a description of clinical development stage, and a justification for the study design based on clinical evaluation. Additional requirements include risk analysis and management strategies, comprehensive benefit-risk assessment, device description with intended purpose and claimed performance, study objectives and hypotheses with primary and secondary endpoints, detailed statistical considerations with sample size justification and power calculation, monitoring plan with risk-based approach, data management and quality assurance procedures, and subject selection criteria with clear inclusion and exclusion parameters. (15)

7.3 ISO 14155:2020 Integration

The EU framework explicitly references ISO 14155:2020 as the international standard for Good Clinical Practice in device investigations. The standard's Annex A provides a comprehensive template for CIP content that aligns with MDR requirements while offering additional implementation guidance. (16, 17)

7.4 Approval Process

Manufacturers must submit the CIP and supporting documentation to National Competent Authorities (NCAs) and Ethics Committees in each participating member state. The assessment considers scientific validity, ethical acceptability, risk-benefit balance, subject protection measures, and compliance with MDR requirements. (18) For Class III and implantable devices, you usually need clinical trials unless there's already enough proof they work or special rules let you skip them. Post-Market Clinical Follow-up (PMCF) is required for all device classes, with enhanced requirements for higher-risk devices. (19)

7.5 MDCG Guidance 2024-3

The Medical Device Coordination Group published MDCG 2024-3 guidance providing a detailed interpretation of CIP content requirements under MDR Annex XV. (20) This guidance clarifies expectations for each CIP section, integrates ISO 14155:2020 requirements with EU-specific elements, emphasises risk-based approaches throughout planning and conduct, and provides practical recommendations without introducing new legal requirements. (17)

8. Different Comparisons of CTP and CIP

This section includes a comparative analysis of regulatory requirements for clinical documentation across major regions. Table 2 outlines the differences and similarities in the Clinical Trial Protocol (CTP) among India, the US, and the EU, whereas Table. 3 compares the Clinical Investigation Plan (CIP) requirements across India, the US, and the EU.

Table 2. Comparison Table 2. Clinical Trial protocol (CTP) - India, US, and EU

Aspect	India	US	EU
Regulatory Authority	CDSCO (Central Drugs Standard Control Organisation)	FDA (Food and Drug Administration)	EMA + National Competent Authorities (NCAs)
Protocol Basis	NDCTR 2019 + ICH-GCP	FDA 21 CFR 312 + ICH-GCP	EU CTR 536/2014 + ICH-GCP
Submission Type	CTA (Form CT-04) includes protocol	IND Application includes protocol	Clinical Trial Application via EU-CTIS includes protocol
Language	English; ICF must be in local	English	Country-specific languages

	languages		+ English
Key Focus	Ethics, safety, compensation, local population	Scientific robustness, safety reporting, pharmacology	Harmonization across EU, transparency, safety
Compensation Requirements	Mandatory for injury; strict rules	No mandatory compensation rules	Compensation rules vary by member state
SAE Reporting Timeline	24 hrs (to sponsor), 14 days to CDSCO/EC	7 days (fatal/life-threatening), 15 days (others)	7 days (fatal/life-threatening), 15 days (others)
Ethics Committee	EC registered with CDSCO	IRB approval required	Ethics Committee + national approvals
Protocol Content Standard	ICH-GCP E6 + NDCTR-specific requirements	FDA IND content + ICH-GCP	EU CTR + ICH-GCP
Informed Consent	Strict, multi-language, compensation details required	Must meet 21 CFR 50; English acceptable	Must comply with GDPR + local languages
Monitoring Requirements	GCP-compliant monitoring; can be sponsor or CRO	FDA requires monitoring adequate to ensure quality	Risk-based monitoring encouraged; EMA guidance
Investigational Product (IP) Labelling	Must follow NDCTR labelling	Must follow FDA labelling requirements	EU Annex VI labelling rules
Data Protection	Indian GCP + new DPDP Act (where applicable)	HIPAA compliance	GDPR-compliant data protection
Protocol Deviations	Serious deviations must be reported to EC/CDSCO	Must be documented; significant ones to FDA	Must be reported through CTIS when affecting safety
Role of DSMB	Required for high-risk trials	Required for many Phases 3 trials	Recommended for pivotal/long-term studies
Archival Period	Minimum 5 years after study completion	At least 2 years after marketing application approval or discontinuation	Usually 25 years (varies by country)

Table 3. Comparison of Clinical Investigation Plan (CIP) - India, US, And EU

Aspect	India (CDSCO)	United States (FDA)	European Union (MDR/IVDR)
Regulatory Framework	Medical Devices Rules, 2017 & NDCT Rules, 2019	FDA 21 CFR 812 (IDE)	EU MDR 2017/745 & IVDR 2017/746
Applicable Products	Medical devices (Class A-D)	Medical devices ((IDE)	Medical devices & IVDs
Primary Standard	ISO 14155:2020 + Indian requirements	ISO 14155:2020 (voluntary); FDA regulations mandatory	ISO 14155:2020 & MDR Annex XV
Document Name	Clinical Investigation Plan (CIP)	Investigational Device Exemption (IDE) Application	Clinical Investigation Plan (CIP)
Governing Annex/Section	Rule 13-16, Medical Devices Rules, 2017	21 CFR 812	Annex XV, Chapter II, Section 3
Submission Portal	MedDev Portal / SUGAM	FDA Electronic Submissions Gateway	National Competent Authority portals / EUDAMED
Risk-Benefit Analysis	Mandatory for Class C & D	Required - risk assessment under 21 CFR 812	Mandatory - comprehensive risk-benefit per Annex XV
Statistical Justification	Required with sample size calculation	Required with endpoint justification	Mandatory with power calculation
Ethics Approval	Ethics Committee approval mandatory	IRB approval required	Ethics Committee in each member state
Monitoring Requirements	Risk-based monitoring per ISO 14155	Per FDA regulations & study protocol	Detailed monitoring plan per ISO 14155

9. Conclusion

In conclusion, each regulatory system India's reformative NDCT Rules, 2019, the U.S. FDA's structured IND and IDE pathways and the EU's harmonised CTR and MDR, demonstrates distinct strengths shaped by regional priorities yet united by common principles of Good Clinical Practice and alignment with ICH and ISO 14155 guidelines.

Beyond regulatory alignment, these frameworks symbolise humanity's collective pursuit of progress where scientific innovation harmonises with moral responsibility. As cross-border collaboration intensifies, the emphasis on data integrity, subject safety, and

equitable access will define the next era of clinical development.

Acknowledgements

We would like to express our sincere gratitude to IJDRA Journal for publishing our work.

Conflict of Interest

he author declares that there is no conflict of interest regarding the publication of this article.

Financial Disclosure statement:

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reference

1. ICH E6 – Good Clinical Practice (GCP) ICH Harmonised Guideline: Guideline for Good Clinical Practice E6(R2). Step 4 final version [Internet]. Geneva: ICH; 2016 Nov 09 [cited 2025 Oct 29]. Available from: https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf
2. Frestedt JL. Comparing ICH E6 and ISO 14155 for drug and device clinical trials. PowerPoint presentation presented at: 26th Annual SOCRA Conference; 2017 Oct 6; Lake Buena Vista (FL) [Internet]. US: Frestedt; 2017 Oct 06 [cited 2025 Oct 31]. Available from: https://frestedt.com/wp-content/uploads/2022/07/14155-ICH-E6-R2-9-5-17-2246.pdf
3. Indian Society for Clinical Research. Ministry of Health and Family Welfare, Government of India. New Drugs and Clinical Trials Rules, 2019 [Internet]. India: ISCR; 2019 Mar 19 [cited 2025 Oct 31]. Available from: https://www.rgcb.res.in/documents/New%20drugs%20and%20clinical%20trial%20rules%202019.pdf.
4. National Institute of Allergy and Infectious Diseases. Clinical research regulation timelines: India [Internet]. India: NIH;2015 Sep 23 [cited 2026 Jan 9].Available from: https://clinregs.niaid.nih.gov/country/india#timeline_of_review
5. Intuition Labs. What is a clinical trial protocol? A guide to its design [Internet]. intuitionlabs [cited 2026 Jan 9]. Available from: https://intuitionlabs.ai/articles/clinical-trial-protocol-guide
6. Food and Drug Administration, Department of Health and Human Services. 21 Code of Federal Regulations (CFR) Part 312.30 – Protocol amendments [Internet]. e-CFR; 2026 Jan 16 [cited 2025 Mar 12]. Available from: https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-B/section-312.30
7. Frederick National Laboratory for Cancer Research. Content of an investigational new drug (IND) application [Internet]. Frederick; 2019 Nov 26 [cited 2026 Jan 9]. Available from: https://frederick.cancer.gov/sites/default/files/2022-04/Content_of_an_Investigational_New_Drug_Application_(IND).pdf
8. European Commission. Clinical Trials Regulation (EU) No 536/2014: guidance document [Internet]. EU:EC; 2024 Mar 01[cited 2025 Oct 10]. Available from: https://health.ec.europa.eu/document/download/f5ad2a13-4a41-4ada-81a1-2854783c75c0_en
9. Sermes CRO. Assessment and approval of clinical trials in CTIS: theoretical versus actual timelines [Internet]. Sermescro; 2023 Nov 10 [cited 2026 Jan 9]. Available from: https://www.sermescro.com/language/en/assessment-and-approval-of-clinical-trials-in-ctis-theoretical-versus-actual-timelines/
10. Central Drugs Standard Control Organisation. Medical Devices Rules, 2017 [Internet]. India: CDSCO;2017 Jan 31 [cited 2025 Sept 9]. Available from: https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2022/m_device/Medical%20Devices%20Rules,%202017.pdf
11. Biotech Consortium India Ltd. Medical Devices Rules, 2017 and ISO standards [Internet]. India:CDSCO; 2020 Feb 29 [cited 2026 Jan 9]. Available from: https://www.biotech.co.in/sites/default/files/2020-01/MDR17-%20Regulations.pdf
12. United States Food and Drug Administration. Investigational Device Exemptions; 21 CFR Part 812 [Internet]. US: ecfr.gov; 2026 [cited 2026 Jan 9].Available from:https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-812
13. United States Food and Drug Administration. Investigational Device Exemption (IDE) application [Internet]. US: USFDA; 2025 Nov 18 [cited 2026 Jan 9]. Available from: https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-application
14. European Union. Regulation (EU) 2017/745 on medical devices: Annex XV [Internet]. UK:legislation.gov.uk; 2026 [cited 2025 Oct 10] Available from: https://www.legislation.gov.uk/eur/2017/745/annex/XV/adopted
15. Clinical Leader. Clinical investigation plans: the role of MDCG in the context of EU MDR Annex XV and ISO standards [Internet]. Clinical Leader; 2024 May 22 [cited 2026 Jan 9]. Available from: https://www.clinicalleader.com/doc/clinical-investigation-plans-the-role-of-mdcg-in-the-context-of-eu-mdr-annex-xv-iso-0001
16. Medical Device Coordination Group. MDCG 2024-3: guidance on clinical investigation plans under EU MDR [Internet]. EU:EC; 2024 Mar [cited 2026 Jan 9].Available from: https://health.ec.europa.eu/document/download/690de85a-ac17-45ea-bb32-7839540c25c4_en
17. Bitrai C, & Prasanthi D. EU MDR Regulatory Update and Compliance Strategies. Asian Journal of Pharmaceutical Research and Development. 2025; 13(6):54–60. DOI: https://doi.org/10.22270/ajprd.v13i6.1652
18. Wagner H. From Reviewer to Consultant: Transforming Regulatory Affairs in the MDR Transition. Int. J. Drug Reg. Affairs [Internet]. 2025 Dec15 [cited 2025 Dec 15]; 13(4):48-51. Available from: https://ijdra.com/index.php/journal/article/view/819
19. Anjuman Z, Srichakritha T, Prasanthi D. Coordinating Research and evidence for Medical Devices (CORE MD) and beyond. Int. J. Drug Reg. Affairs [Internet]. 2024 Dec15 [cited 2024 Dec 15]; 12(4):69-81. Available from: http://ijdra.com/index.php/journal/article/view/723
20. Wadge JV, Patil SB. Comparative Study of Medical Device Regulation in US, EU and Canada. Int J Drug Reg Affairs [Internet]. 2025Mar.15 [cited 2026Jan.28];13(1):6-11. Available from: https://www.ijdra.com/index.php/journal/article/view/735