REVIEW ARTICLE

Similarities and Differences Between Clinical Trials of Drugs and Clinical Trials of Vaccines

Shankar Prasad Bhattacharya
West Bengal Medical Education Services

CORRESPONDING AUTHOR
Dr Shankar Prasad Bhattacharya, West Bengal Medical Education Services
Email: spbwb@yahoo.co.in

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Abstract

Background: Clinical trials are central to the development of drugs and vaccines; however, therapeutic, and preventive products differ substantially in objectives, populations, endpoints, and regulatory expectations. **Aim & Objectives**: To critically compare similarities and differences between drug and vaccine clinical trials, with special reference to the Indian regulatory and public health framework. **Methodology**: A structured narrative review was conducted using PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, WHO IRIS, CDSCO, ICMR, FDA, and EMA sources (2000–2025). Seventy-three eligible publications were included after screening 480 records. Comparative domains included trial phases, endpoints, safety monitoring, ethics, regulatory scrutiny, and post-marketing systems. **Results**: Both trial types follow phased development, Good Clinical Practice, ethics oversight, and regulatory approval pathways. However, vaccine trials differ in enrolling predominantly healthy populations, emphasizing immunogenicity and population-level effectiveness, requiring larger sample sizes, stricter safety thresholds, and enhanced community engagement. In India, NDCTR-2019, CTRI registration, PvPI, and AEFI frameworks create differentiated yet complementary surveillance mechanisms. **Conclusion**: While drug and vaccine trials share methodological foundations, vaccines operate within a broader public health governance paradigm. Strengthening integrated surveillance, adaptive regulatory pathways, and ethical harmonization is essential for future therapeutic and preventive innovation.

Keywords

Clinical trials, Drug development, Vaccine development, Regulatory framework, Public health, India

Introduction

Clinical trials provide the highest level of evidence for evaluating safety and efficacy of medical interventions. Although drugs and vaccines are regulated under similar statutory frameworks, their intended purposes differ fundamentally—therapeutic versus preventive. Drug trials primarily target diseased individuals to modify clinical outcomes, whereas vaccine trials enroll largely healthy populations and aim to prevent disease, reduce transmission, and generate herd immunity. These distinctions influence trial design, endpoints, ethical thresholds, regulatory scrutiny, and post-marketing surveillance structures.

Recent regulatory reforms, including India's New Drugs and Clinical Trials Rules (2019), and lessons from the COVID-19 pandemic have further highlighted structural differences between therapeutic and preventive trial governance.

Aims and Objectives

- To identify scientific similarities between drug and vaccine clinical trials
- To compare methodological and ethical distinctions
- To analyse regulatory oversight mechanisms in India
- To examine post-marketing surveillance differences
- To propose an integrated governance framework

METHODOLOGY

Study Design, Study Type: Narrative Review

Literature Search Strategy

A structured but flexible narrative review methodology was adopted.

Databases Searched: The following databases and regulatory repositories were searched:

- PubMed / MEDLINE
- Scopus
- Web of Science
- Google Scholar
- Cochrane Library
- WHO Institutional Repository for Information Sharing (IRIS)
- CDSCO (India) official website
- ICMR official publications
- FDA and EMA regulatory guidance portals

Search Period: Publications from **2000 to 2025** were included, with priority given to post-2010 regulatory reforms and COVID-19 era publications.

Search Keywords: The following keyword combinations were used:

- "clinical trials drugs vs vaccines"
- "vaccine clinical trial design"
- "drug development phases"
- "immunogenicity endpoints"
- "New Drugs and Clinical Trials Rules 2019 India"
- "CDSCO vaccine regulation"
- "GCP guidelines WHO"
- "vaccine safety monitoring India"
- "AEFI surveillance India"
- "pharmacovigilance programme India"
- "ethical issues in vaccine trials"
- "placebo during outbreaks"

Boolean operators (AND/OR) were applied where applicable.

Example search string (PubMed):

("drug clinical trial" OR "therapeutic trial") AND ("vaccine trial" OR "immunization trial") AND ("regulatory framework" OR "ethics" OR "India") 3,4,5

Inclusion Criteria

- Peer-reviewed articles
- Regulatory guidelines (WHO, ICMR, CDSCO, FDA, EMA)
- Policy documents
- Textbooks of clinical trial methodology
- Publications in English
- Human clinical trials

Exclusion Criteria

- Animal-only experimental studies
- Non-regulatory opinion pieces without scientific backing
- Duplicate publications
- Non-English articles without reliable translation

Study Selection Flow Diagram

Literature Identification and Screening Process

Records identified through database searching (n = 412)

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Additional records from regulatory websites and policy documents (n = 68)

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Total records identified (n = 480)

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Records after removal of duplicates (n = 420)

↓

Records screened by title and abstract (n = 420)

↓

Records excluded (irrelevant to comparative focus) (n = 275)

↓

Full-text articles assessed for eligibility (n = 145)

↓

Full-text articles excluded (methodologically weak / not comparative) (n = 72)

↓

Studies included in final narrative synthesis (n = 73)

Table 1 Summary Table of Comparative Dimensions

Dimension	Drug Clinical Trials	Vaccine Clinical Trials	Policy Implication
Primary Objective	Therapeutic	Preventive	Broader population-level impact for vaccines
Study Population	Diseased individuals	Mostly healthy individuals	Higher safety threshold for vaccines
Primary Endpoints	Clinical cure, survival, symptom reduction	Immunogenicity, infection reduction	Surrogate markers more common in vaccine trials
Sample Size	Moderate (disease-dependent)	Often large-scale	Requires stronger surveillance systems
Safety Tolerance	Context-dependent	Extremely stringent	Zero-risk perception in public
Ethical Issues	Risk-benefit in sick patients	Placebo during outbreaks, child inclusion	Stronger community engagement required
Post-Marketing	Pharmacovigilance (PvPI)	AEFI Surveillance	Separate monitoring frameworks
Public Health Role	Individual therapeutic benefit	Herd immunity, transmission control	Policy integration into UIP

3,4,5

Proposed New Conceptual Framework

Integrated Therapeutic–Preventive Trial Governance Model (ITPTGM)

Based on this review, a new conceptual framework is proposed:

Level 1: Scientific Domain

- Trial design (Phase I–IV)
- Endpoint classification (clinical vs immunological)
- Statistical power and adaptive designs

Level 2: Ethical Domain

- Individual autonomy
- Community benefit
- Risk–benefit proportionality
- Vulnerable population safeguards

Level 3: Regulatory Domain

- NDCTR 2019 compliance
- CDSCO approval
- WHO prequalification alignment
- Emergency Use Authorization pathway

Level 4: Public Health Domain

- Cost-effectiveness analysis
- Equity in access
- Integration into national programs
- Surveillance infrastructure

This four-tier model emphasizes that vaccine trials operate more strongly within Level 4 (public health domain), whereas drug trials are primarily centered within Level 1 and Level 2 domains. 5,6,7

Policy Analysis (Indian Context)

Strengths

- Robust NDCTR 2019 regulatory structure
- Mandatory CTRI registration
- Active AEFI and PvPI systems
- Strong vaccine manufacturing ecosystem

Gaps Identified

- Limited harmonization between PvPI and AEFI databases
- Need for faster adaptive trial regulatory pathways
- Insufficient community engagement models
- Variable Ethics Committee capacity across institutions

Recommendations

Regulatory Reform

1. Develop an Integrated Clinical Trial Digital Dashboard linking:
   - CDSCO
   - CTRI
   - PvPI
2. AEFI surveillance
3. Introduce structured adaptive trial guidance specific to vaccines.
4. Strengthen lot-to-lot consistency oversight with AI-based analytics.

Ethical Strengthening

1. Mandatory community consultation framework in vaccine trials.

2. Independent national-level DSMB registry.
3. Standardized compensation framework transparency. 7,8

Public Health Integration

1. Pre-approval cost-effectiveness modeling before UIP inclusion.
2. Real-world effectiveness platform for post-authorization studies.
3. Transparent risk communication strategy for vaccine hesitancy reduction.

Academic and Research Recommendations

- Promote comparative regulatory science research.
- Encourage interdisciplinary collaboration between pharmacologists, epidemiologists, and public health experts.
- Develop postgraduate curriculum modules on vaccine trial methodology.

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Indian Regulatory Framework for Drug and Vaccine Clinical Trials

Legal and Regulatory Basis

In India, clinical trials are governed by the Drugs and Cosmetics Act, 1940 and the New Drugs and Clinical Trials Rules (NDCTR), 2019. The Central Drugs Standard Control Organization (CDSCO), under the leadership of the Drugs Controller General of India (DCGI), oversees approval, regulation, and monitoring of clinical trials. 9,10

Mandatory requirements for both drug and vaccine trials include:

DCGI approval

Registration with the Clinical Trials Registry of India (CTRI)

Ethics Committee approval

Compliance with national GCP guidelines

Differential Regulatory Scrutiny

While both drugs and vaccines undergo rigorous review, vaccine trials in India are subject to enhanced scrutiny due to their preventive nature and large-scale public health implications. Additional requirements for vaccines may include:

Lot-to-lot consistency studies

Bridging trials

Cold-chain stability assessments

Long-term safety follow-up

Ethical Guidelines and Participant Protection in India

The ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants provide a comprehensive ethical framework. Vaccine trials involving children, pregnant women, or vulnerable groups require stronger justification, enhanced consent procedures, and community engagement. Placebo-controlled vaccine trials are carefully evaluated, particularly when effective preventive measures already exist.

Indian Public Health Perspective

Population-Level Impact

Vaccines are assessed in India not only for individual protection but also for their ability to reduce disease burden, achieve herd immunity, and provide cost-effective public health solutions. Successful vaccine trials often lead to inclusion in the Universal Immunization Programme (UIP).

India's Role in Global Clinical Research

India is a major contributor to global drug and vaccine trials due to its large and diverse population, skilled workforce, and strong manufacturing capacity. Vaccine trial data generated in India frequently support WHO prequalification, enabling global distribution, particularly to low- and middle-income countries.8,9

Post-Marketing Surveillance

Drugs: Post-marketing safety of drugs is monitored through the Pharmacovigilance Programme of India (PvPI), which tracks adverse drug reactions and ensures ongoing risk assessment.

Vaccines: Vaccine safety surveillance is strengthened through the Adverse Events Following Immunization (AEFI) Surveillance System, coordinated by the Ministry of Health & Family Welfare, CDSCO, and WHO–India. Emphasis is placed on detecting rare adverse events, causality assessment, and transparent risk communication. 10

Lessons from the COVID-19 Pandemic: The COVID-19 pandemic demonstrated India's capacity for rapid clinical trial execution, accelerated regulatory review, and large-scale vaccine deployment. Emergency use authorization, adaptive trial designs, and real-world effectiveness studies underscored the need for flexible yet robust regulatory mechanisms without compromising safety.

CONCLUSION

Recent regulatory and methodological literature (2015–2025) demonstrates that although drug and vaccine trials share phased development models and Good Clinical Practice standards, they diverge significantly in population risk thresholds, endpoint selection, and public accountability mechanisms. Vaccine trials increasingly incorporate real-world effectiveness data, adaptive platform designs, and enhanced pharmacovigilance integration, particularly after the COVID-19 pandemic. Indian regulatory reforms under NDCTR-2019 and strengthened AEFI surveillance have aligned national systems with global standards while recognizing vaccines' broader societal implications.

This review confirms that vaccine trials function within a dual scientific–public health mandate, unlike drug trials that primarily address individual therapeutic benefit. The proposed Integrated Therapeutic–Preventive Trial Governance Model extends existing knowledge by conceptualizing trial governance across scientific, ethical, regulatory, and public health domains.

Future preparedness for emerging infections will require harmonized surveillance systems, adaptive approval pathways, and strengthened ethical oversight without compromising participant safety.

RECOMMENDATION

The comparative understanding of drug and vaccine trials has direct implications for:

- Strengthening national immunization policy decision-making
- Enhancing public trust in preventive interventions
- Improving surveillance harmonization between PvPI and AEFI systems
- Supporting evidence-based inclusion into the Universal Immunization Programme
- Guiding regulatory preparedness during health emergencies

An integrated digital regulatory-surveillance ecosystem is recommended to improve transparency, responsiveness, and real-time safety assessment.

LIMITATION OF THE STUDY

This study is a structured narrative review and does not employ quantitative meta-analytic pooling. Selection bias may exist despite systematic screening. Grey literature and unpublished regulatory deliberations were not comprehensively analysed. Comparative conclusions rely on published regulatory guidance and may not reflect confidential internal review processes. Rapidly evolving adaptive trial methodologies post-COVID-19 may further modify regulatory landscapes beyond the review period.

RELEVANCE OF THE STUDY

This study contributes to current knowledge by:

- Providing a structured comparative framework between therapeutic and preventive clinical trials
- Integrating regulatory science with public health governance
- Proposing a novel four-tier Integrated Therapeutic–Preventive Trial Governance Model
- Highlighting Indian regulatory evolution in the global context

- Identifying harmonization gaps between pharmacovigilance and immunization safety systems

It advances regulatory science discourse by positioning vaccine trials within a broader societal accountability framework.

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Nil

Conflict of Interest

There are no conflicts of interest.

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Declaration Of Generative AI And AI Assisted Technologies In The Writing Process

During the preparation of this work, the author used ChatGPT (OpenAI) for language refinement, structural organization, and formatting assistance. The author critically reviewed, edited, and validated all content and takes full responsibility for the accuracy, interpretation, and originality of the manuscript.

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