ICMR Bioethics Unit

ETHICAL GUIDANCE FOR

NON-REGULATORY CLINICAL TRIALS

WHO Collaborating Centre for Strengthening Ethics in Biomedical and Health Research

Contents

Abbreviations

AE	Adverse Event
CDSCO	The Central Drugs Standard Control Organization
CLA	Central Licensing Authority
CSR	Corporate Social Responsibility
CTRI	Clinical Trials Registry – India
DSMB	Data Safety and Monitoring Board
DHR	Department of Health Research
GCP	Good Clinical Practice
ICD	Informed Consent Document
ICMR	Indian Council for Medical Research
IND	Investigational New Drug
NRCT	Non-Regulatory Clinical Trial
NDCT	New Drugs and Clinical Trial
SAE	Serious Adverse Event
SME	Subject Matter Expert
SOP	Standard Operating Procedures
TMF	Trial Master File

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1.Background

A clinical trial is a type of research/study that prospectively assigns human participants or groups of participants to one or more health-related intervention(s) to evaluate their effects on health outcomes. Health-related intervention(s) may be pharmacological or non-pharmacological including- drugs, medical devices, vaccines, biosimilars, biologics, phytopharmaceuticals, radiopharmaceuticals, diagnostic tools, public health interventions, psychosocial/neurobehavioral/socio-behavioral interventions pertaining to health, technologies, surgical techniques, procedures and other therapies. [1] In the context of a clinical trial, an intervention refers to any deliberate departure from the existing standard of care, where such a standard exists.

Clinical trials in India may be broadly categorized into Regulatory clinical trials and Non-regulatory clinical trials, based on their intent and regulatory pathway. Regulatory clinical trials are undertaken to generate evidence on the safety, efficacy, or tolerability of a new drug or investigational new drug, and are conducted with the objective of obtaining marketing authorization. Such trials require approval from the Central Drugs Standard Control Organization (CDSCO). In contrast, Non-Regulatory Clinical Trials (NRCTs) are interventional studies involving human participants that evaluates health-related interventions for academic, scientific or public health purposes without the intent of seeking marketing approval.

NRCTs may involve pharmacological health interventions that have already been approved by CDSCO for marketing or non-pharmacological health interventions which are not under the purview of CDSCO. As specified under the New Drugs and Clinical Trials (NDCT) Rules 2019 , academic or non-regulatory clinical trial on a pharmacological intervention may be conducted using a 'drug already approved for a certain claim and initiated by any investigator, academic or research institution for a new indication or new route of administration or new

[1] Specific categories within the definition may require additional considerations. For further guidance, refer to Section 7, Clinical Trials of Drugs and Other Interventions, in the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants 2017 and other relevant guidelines pertaining to the specific category.

dose or new dosage form, where the results of such a trial are intended to be used only for academic or research purposes and not for seeking approval of the Central Licensing Authority or regulatory authority of any country for marketing or commercial purpose.'

Additionally, NRCTs include but are not limited to comparator or comparative effectiveness trials using approved and marketed products to generate further evidence on efficacy, effectiveness, or real-world performance, trials providing data on the off-label use of approved drugs, as well as assessing the effectiveness of interventions in new populations or in public health and social science contexts. Methodologically, NRCTs employ interventional (experimental) designs and often compare an approved intervention with the standard of care. Exceptionally, when the research question requires and when there is a clear scientific and ethical justification, an NRCT may be conducted as a single arm study without a comparator.

NRCTs are predominantly investigator-initiated, often conducted within academic or research settings. These studies are driven by scientific, clinical or public health objectives, including the advancement of medical knowledge, improving existing health interventions, and generation of evidence to inform future research, policy and clinical practice. In these trials, the responsibility for the design, conduct, oversight, and reporting rests with the investigator(s) with support from the institution, fulfilling a role analogous to that of a sponsor in regulatory clinical trials. Some of the examples of NRCTs are given below in Box 1.

Box 1: Some of the examples of NRCTs

- Comparator/ comparative effectiveness trials using approved and marketed products to generate additional evidence on efficacy or effectiveness, or real-world performance.
- Research evaluating the use of the same approved medicine at a lower dose to reduce side effects while maintaining clinical effectiveness.
- Research on the application of approved medical devices in different patient populations to assess their safety and effectiveness in new contexts.
- Non-pharmacological interventions, such as the use of Kangaroo Mother Care (KMC) in low birth weight neonates, behavioral intervention studies aimed at improving public health outcomes, such as lifestyle modification, mental health support, or adherence to treatment.

2.Scope

This guidance aims to support the ethical design, conduct, review, and oversight of NRCTs. It is applicable to all interest-holders involved in Non-Regulatory Clinical Trials, including investigators, collaborative research groups, institutions, ethics committees, postgraduate students, funding bodies and industry partners.

3. Scientific Review

A thorough scientific review is required for all NRCT proposals before seeking Ethics Committee approval, to ensure meaningful and robust research outcomes.

3.1 The Scientific review helps to assess the scientific validity, methodological rigor, feasibility, and relevance, ensuring that the proposed research can generate reliable evidence.

3.2 Scientific review may be conducted through an institutional Scientific Review Committee or by engaging external peer reviewers, subject matter experts, or independent consultants with appropriate expertise.

3.3 This Scientific Review Committee should be multidisciplinary and should have clinical experts, laboratory experts, research methodology experts, and at least one biostatistician.

3.4 The recommendations of the Scientific Review Committee shall be shared with the investigator, who shall make necessary revisions (if any), and seek final Scientific Review Committee approval. This approval document including its recommendations must be submitted to the Ethics Committee when their approval is sought.

4.Ethics Review

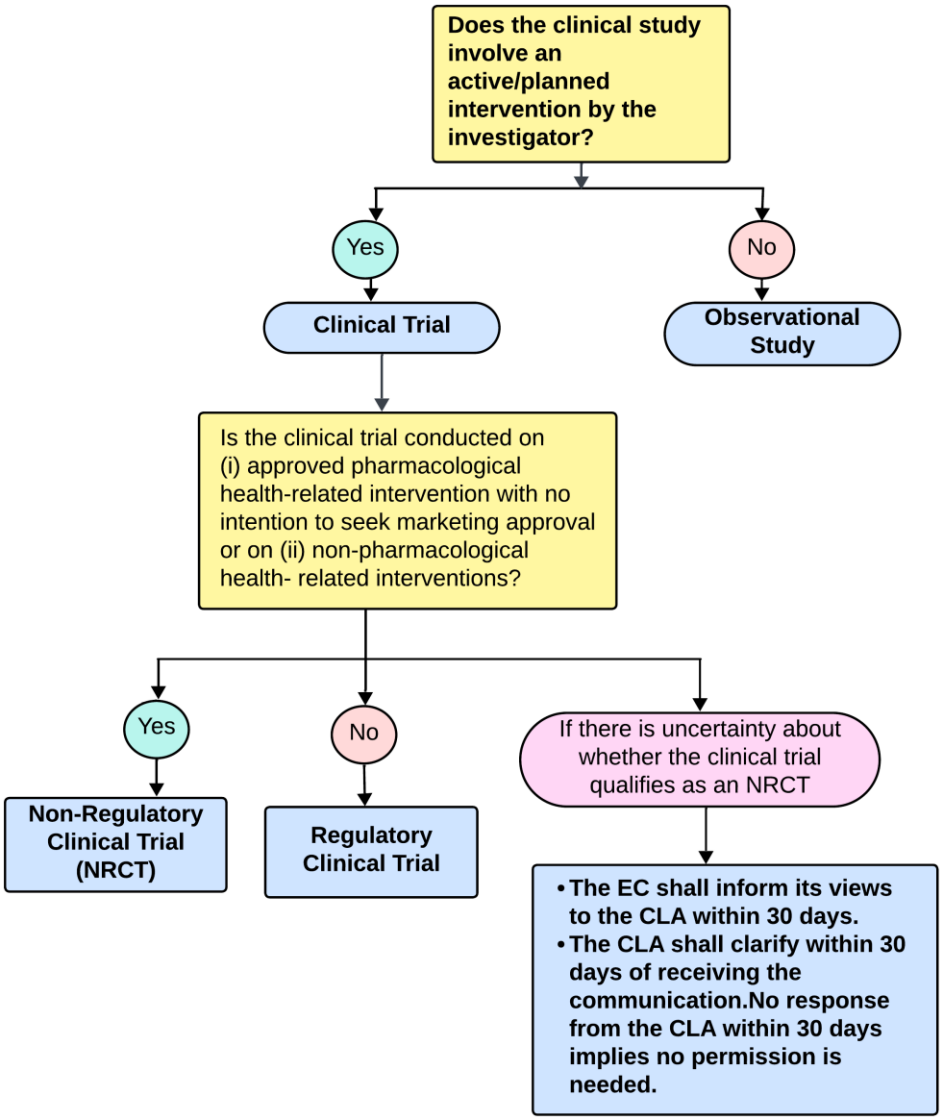
The Ethics Committee is responsible for ethics review, approval and oversight and monitoring to ensure that the rights, safety, dignity and well-being of participants are protected throughout the conduct of the trial. Non-Regulatory Clinical Trials (NRCTs) shall be initiated only after approval by the Ethics Committee.

4.1 As in all clinical research involving human participants, Ethics Committees reviewing NRCTs must be duly registered at DHR through NAITIK portal.

4.2 If, during ethics review, there is uncertainty on whether a proposed study qualifies as an NRCT, the Ethics Committee must notify the Central Licensing authority (CLA)[2] within 30 working days (see figure 1).

[2] The Central Licensing Authority (CLA) refers to the CDSCO (Central Drugs Standard Control Organization), which is responsible for granting licenses and approvals for new drugs, medical devices and clinical trials.

Figure 1: Decision Tree for Determining if a study qualifies as Non-Regulatory Clinical Trial



4.3 The Ethics Committee shall evaluate the social value, anticipated benefits and risks, payment for participation, privacy and confidentiality, community considerations, qualifications of investigators, adequacy of study sites, potential conflicts of interests, adequacy of plans for medical management and compensation for study related injuries, informed consent process and all other relevant ethical aspects of the proposed NRCT before granting approval.

4.4 Any Payments made for participation must be reasonable and subject to approval by the Ethics Committee (EC) to prevent any undue inducement or coercion.

4.5 The NRCTs comparing approved and marketed interventions may have very low or minimal risks to participants, since the product is already determined to be safe and has been approved and marketed. Accordingly, the principal investigator must categorise each NRCT as either “Minimal risk” or “More than minimal risk” based on the foreseeable risk and inherent risk factors associated with the intervention.

4.6 The Ethics Committee must review, validate and formally endorse this risk classification when it conducts the detailed protocol review.

4.7 When an EC decides that a study has more than minimal risk, it shall provide a note on the specific reasons and on additional safeguards required.

4.8 To facilitate this, a reference risk categorization is proposed to assist interest-holders in assessing the level of risk (see Table 1) and some examples of NRCTs with suggested risk categorisation is given in Annexure.

Table 1: Framework for risk categories in Non-Regulatory Clinical Trial (NRCTs)

Risk level	Description[3]	Notes for Ethics Committee
Minimal Risk	Probability and/or severity of anticipated adverse events or discomfort from NRCT intervention-related foreseeable risk(s) is low or not greater than what is expected from activities of daily life or routine examination. (Most NRCTs are expected to be in minimal risk category, since only regulator approved and marketed interventions are to be used in NRCT)	Since the study involves minimal risk, no additional safeguards would be required. Routine monitoring by the Ethics Committee is sufficient; and insurance coverage is not necessary.
More than minimal Risk	Probability and/or severity of anticipated adverse events or discomfort from NRCT-intervention-related foreseeable risk(s) is greater than what is encountered in daily life or routine examination.	In cases where the EC decides that the risk is higher to participants due to participation in NRCT, one or more of the following safeguards may be recommended by the EC, as appropriate: • Inbuilt mechanisms (such as research corpus and/or insurance) to cover for medical management of adverse events and compensation for SAEs related to trials • Intensive periodic monitoring • Constitution of a Data Safety and Monitoring Board

4.9 Certain studies may inherently have some risk involved. More than minimal risk studies include a spectrum of risk profiles as any risk beyond that encountered in daily life or routine examination comes under this category. The classification under the "More than Minimal Risk" category does not automatically imply high or unacceptable risk, but includes a range of risk categories.

4.10 Further the risk related to the study participation must be seen and considered by the EC rather than risks that are unrelated or may be due to existing illness or disease conditions or other such reasons.

4.11 The Ethics Committee shall apply a proportionate, case-by-case approach and require enhanced safeguards only when justified by the NRCT's nature and level of risk.

4.12 Although NRCTs typically involve approved pharmacological or non-pharmacological interventions and are therefore not intended to be high risk, the actual level of risk depends on factors such as how the intervention is used, in what setting, participant population and what additional procedures are required, etc.

[3] However, the actual occurrence of adverse events may vary depending on individual characteristics and study-specific factors.

4.13 For More than Minimal Risk NRCTs with a foreseeably high likelihood of AEs or SAEs, the Ethics Committee shall, at the time of protocol review, ascertain the adequacy of additional safeguards, including intensive monitoring and compensation mechanisms.

5.Informed consent process

Informed consent is a fundamental ethical requirement in NRCTs. Informed consent process must clearly distinguish between research and routine medical care. It is intended to protect the autonomy, rights, and welfare of participants by ensuring that their participation is voluntary and based on adequate information and understanding.

5.1 Informed consent process should be simplified to ensure participants understand the exploratory nature and purpose of the NRCT. It must clearly explain the methodology proposed, potential benefits, risks, alternative treatments and the right to voluntarily participate or withdraw at any time.

5.2 In cases where the investigators is also the treating physician, the informed consent must clearly disclose this and clarify that participation decisions will not affect standard clinical care.

5.3 Participants should be informed if the NRCT involves an approved health-related intervention including any specific modification being tested, such as a change in the formulation, route of administration (e.g., oral to dermal, oral to intravenous), dose adjustment or comparative evaluations, and their potential implications.

5.4 The informed consent process must detail payment or reimbursement, medical management and compensation for research-related injury, funding sources, insurance coverage, and confidentiality measures including data storage and handling.

5.5 Informed consent process should include contact information of the research team, and outline the plans for benefit sharing and publication.

5.6 In NRCTs involving industry collaborators, the informed consent document (ICD) must clearly disclose the industry's contributions, including drug supplies and any other support received.

6. Adverse Events (AEs) and Serious Adverse Events (SAEs)

6.1 Reporting of AEs and SAEs

Since approved health-related interventions are used in NRCTs, the occurrence of adverse events is less likely. Nevertheless, timely identification, documentation, reporting of adverse Events (AEs) and Serious Adverse Events (SAEs) is essential to protect participant safety and maintain public trust in research. In the unfortunate event of adverse events occurring in NRCTs, the following steps must be undertaken.

6.1.1 All Serious Adverse Events (SAEs) must be reported by investigators to the Ethics Committee and the head of the institution within 24 hours of knowledge of the event. Reporting of SAE may be done through email or other agreed digital methods. (including on non-working days).

6.1.2 Further, the investigator must submit a report on how the SAE was related to the research within 14 days to the Ethics Committee.

6.1.3 Ethics committee is responsible for reviewing the relatedness of the SAE to the research (causality assessment), as reported by the investigator. Ethics Committee adjudicates whether any harm or injury is attributable to participation in the NRCT, and such determinations are binding for medical care and compensation.

6.1.4 In view of the volume of work for Ethics Committees, additional subcommittees can be constituted, and independent consultants/subject matter experts may be invited for the causality assessment in case of SAEs.

6.1.5 The Ethics Committee must review all SAE reports to identify trends or emerging risks that may warrant protocol modifications and make necessary recommendations.

6.1.6 All Adverse events must be logged and listed in the continuing reports as suggested by the Ethics Committee on a case-to-case basis.

6.2. Medical Management

Medical management refers to the provision of free, timely, and appropriate treatment to any participant who experiences harm—whether an Adverse Event (AE) or Serious Adverse Event (SAE) —during their participation in an NRCT.

6.2.1 Medical management includes clinical care in accordance with the standard of care, psycho-social support, referrals and access to required healthcare facilities

6.2.2 The investigator, with support from the institution, should arrange for free, and appropriate medical care to participants for adverse events, at least until it is proved to be unrelated to the NRCT intervention.

6.3 Payment of Compensation

Compensation refers to the financial support provided, in addition to medical management, to participants or their legal heirs in cases where temporary or permanent injury, disability, or death occurs and is determined to be causally related to participation in the NRCT.

6.3.1 Compensation applies only to AEs or SAEs that are determined to be causally related to the NRCT intervention and is relevant only in cases of more than minimal risk NRCTs.

6.3.2 Institutions are encouraged to arrange for insurance coverage or a research corpus to cover for such eventualities. In case of funded projects, the same can be inbuilt in the budget submitted to funding agencies.

6.3.3 The Ethics Committee must determine the quantum of compensation to be provided to the participant.

6.3.4 The maximum compensation in NRCTs per eligible event should follow the formulae provided under the seventh schedule of New Drugs and Clinical Trials Rules, 2019 for clinical trial related injury or death. When determining the quantum of compensation, the Ethics Committee should consider the extent of injury (temporary/permanent, short/long term), loss of wages, and all other relevant ethical considerations.

7. Monitoring

Monitoring in NRCTs refers to the process of overseeing the progress of the research, to ensure that it is conducted, documented, and reported in compliance with the approved protocol, institutional policies, Standard Operating Procedures (SOPs), and applicable ethical guidelines.

7.1 Monitoring systems may be set up at various levels such as institutional, departmental or investigator level, through different mechanisms to ensure compliance to trial procedures, data quality and adequate safety measures for research participants.

7.2 Ethics Committees shall ascertain the appropriate method and frequency for monitoring of NRCTs based on the trial's risk level, the experience of the investigators, involvement of vulnerable population and the complexity of the study design. More intensive monitoring may be required for more than minimal risk trials.

7.3 Due to the inherent nature of the trial or other reasons, if the NRCT is determined to have more than minimal risk and requiring intensive monitoring, a Data Safety Monitoring Board (DSMB) may be recommended.

7.4 After reviewing the study data, blinded or unblinded, as required, DSMB will provide a report to the investigator who in turn submits the same to Ethics Committee.

7.5 Ethics Committee shall have mechanisms to monitor the conduct of the approved research at appropriate intervals, through continuing review reports or site visits (if needed) to ensure ongoing ethical compliance throughout the study.

7.6 Ongoing research must be reviewed at least once a year. Studies involving more than minimal risk may require more frequent review (quarterly or half-yearly).

8.Post Graduate Student Thesis/ Doctoral Research

Many students from medical and other health science disciplines undertake Non-Regulatory Clinical Trials as part of their postgraduate thesis. This involvement provides valuable hands-on research experience and helps nurture their development as physician-scientists and future researchers.

8.1 Post graduate students, as trainees, can engage in NRCTs as a part of their academic thesis work under the supervision of experienced investigator(s) who serve as their guide(s) for the study.

8.2 The guide(s) and/or host institution retain full responsibility and accountability for all aspects of the trial including safeguarding participants, maintaining data integrity, and ensuring compliance with ethical requirements.

8.3 Institutions, Scientific Review Committees, Ethics Committees, funding agencies and the broader scientific community should strive to create a facilitatory environment for

students conducting NRCTs by providing necessary financial or administrative support to prevent impediments in academic progress.

8.4 Ethics Committees should generally allow only minimal risk NRCTs for postgraduate student thesis/doctoral research.

8.5 Ethics Committees should assess funding support as well as continuity plans for NRCTs to address scenarios where students exit the program before completing the trial or fulfilling post-trial responsibilities. Institutions must establish clear guidelines to document and transfer such responsibilities to qualified faculty to ensure the trial's completion and continued care of participants.

8.6 Ethics Committee must plan to hold special or unscheduled meetings to meet the deadlines related to student thesis submission, as per requirement.

8.7 For risk stratification of the studies undertaken by PG/ PhD etc. should be as stated in the general section, but the responsibility of the implementation should be on the guide. This will help in improve the quality of such research.

9. Data Management and Documentation

In NRCTs, data management and documentation are especially important as these studies are conducted outside formal regulatory frameworks and involve human participants. Robust data practices ensure ethical accountability, scientific validity, and responsible data sharing, while safeguarding participant rights and confidentiality at all stages of the research.

9.1 A data management plan must be included in the research protocol, clearly defining procedures for data collection, storage, and timelines (including responsible personnel, location, methods). This must outline measures to ensure data integrity.

9.2 NRCTs may be conducted with essential documentation as detailed in table 2. Additional documentation may be included as required on a case-to-case basis.

Box 2: Essential Documentation for Trial Master File

❖ The following documents should be invariably filed in the trial master file

- CVs and GCP training certificates.
- Final trial protocol and amendments
- EC approval letters and correspondence
- CTRI Registration
- Informed Consent Documents (ICDs)
- SAE and AE logs and reports
- Participant logs (screening, enrolment, withdrawal)
- Monitoring reports (if applicable)
- Training logs of study team
- Budget and funding details
- COI declarations
- Other relevant approvals/ documents

9.3 All trial-related documents should be archived in safe and secure condition by the host institution for at least 3 years after study completion.

9.4 Anonymized NRCT data may be made available in centralized data repositories, databases and platforms in India, for long term periods to enable transparent and meaningful knowledge exchange, while avoiding research waste, particularly for studies with significant social value and public health implications.

9.5 Investigators are encouraged to publish results regardless of the outcome (positive or negative) in accordance with the ICMJE criteria, to contribute to good research practices and avoid research waste.

10.Responsible Conduct of Research

Understanding and adherence to the respective roles and responsibilities of investigators and institutions are essential to ensure ethical conduct, regulatory compliance, scientific integrity and effective coordination in the conduct of Non-Regulatory Clinical Trials (NRCTs). The key responsibilities are outlined below:

10.1 Role of investigators

10.1.1 Investigator must obtain approval from the Scientific Review Committee (SRC) and Ethics Committee (EC), prior to the initiation of the NRCT.

10.1.2 Investigators must register NRCTs prospectively with ICMR's Clinical Trials Registry – India (CTRI) website before initiating the study, promoting public access to trial information and outcomes. Subsequent modifications in the trial protocol if any, and final study reports should be reflected in the CTRI.

10.1.3 Investigator must ensure that adequate infrastructure, trained manpower, and operational capacity are available for the conduct of the NRCT.

10.1.4 Investigators must ensure comprehensive budgeting for all NRCT costs covering personnel, supplies, and research-specific clinical procedures to ensure participants incur no additional expenses due to participation in research and are fairly reimbursed; institutions and funders should have a provision for budget to cover unforeseen expenses and prevent costs falling on participants or the PI's personal resources.

10.1.5 Investigators must ensure compliance with applicable guidelines and Good Clinical Practice (GCP) and institutional policies, and must maintain a Trial Master File (TMF).

10.1.6 Investigators must disclose all forms of industry involvement, including financial support, resource provision, advisory roles, and potential conflicts of interest, in the protocol, Ethics Committee submissions, study related documents, and the informed consent document.

10.2 Role of institutions

10.2.1 Institutions must establish mechanisms and policies for research governance including mechanisms for data management, monitoring of ongoing research, management of conflict of interest, reporting and inquiry into scientific misconduct, and initial and continuing training of researchers and Ethics Committee members.

10.2.2 Institutions may establish a dedicated research office to facilitate research, manage grants and oversee compliance with ethical and scientific standards.

10.2.3 Institutions should have their Ethics Committees registered with DHR through the NAITIK Portal and is supported with appropriate infrastructure, Ethics Committee secretariat, and "protected time" for the Member Secretary.

10.2.4 Institutions without an Ethics Committee may engage a Host EC via a Memorandum of Understanding (MoU), provided the Host Ethics Committee has access to all study records and is able to perform site monitoring.

10.2.5 For trials involving more than minimal risk to the participants, the institute must ensure provision for free management of trial related adverse events and mechanisms for compensation, including insurance coverage where applicable, as per Ethics Committee recommendations.

10.2.6 A Data Safety and Monitoring Board (DSMB) may be constituted, as recommended by the Ethics Committee. Institutions may also consider establishing a common DSMB for multiple studies, provided there is no conflict of interest.

10.2.7 Industry may conduct NRCTs independently or in collaboration with academic or public institutions. When conducted in partnership, the industry may provide support in the form of drugs, materials, funding, infrastructure, or technical expertise. Regardless of the nature or extent of industry involvement, the overall responsibility for the ethical and scientific conduct of the NRCT lies with the host institution and the Principal Investigator, unless specific responsibilities have been formally delegated through written agreements.

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Annexure

Table: Some Examples of non-regulatory clinical trials with suggested risk categorisation

S.No	Study Title	Brief Description of Study Methods	Risk Category
1.	A study conducted in a clinical setting to compare 60000 IU Cholecalciferol (Vitamin D3) oral solution versus 60000 IU capsules for the treatment of Vitamin D3 deficiency	Investigators will randomly assign participants with documented Vitamin D3 deficiency to receive either Vitamin D3 oral solution or Vitamin D3 capsules (both approved) and assess effectiveness and adherence.	Minimal Risk
2.	A study conducted in a tertiary health care setting to evaluate educational support for Kangaroo Mother Care (KMC) adherence	A randomized study comparing standard verbal instructions vs. illustrated flip-charts to teach mothers the correct KMC positioning and duration for stable low-birth-weight infants.	Minimal Risk
3.	Study conducted in an academic setting to evaluate the effectiveness of two video-based ECG teaching modules among medical interns	Investigators will assign medical interns to one of two standardized video-based ECG teaching modules and assess their ECG interpretation performance as part of the study.	Minimal Risk
4.	A study conducted in a clinical setting to compare digital versus manual reminders for medication adherence	Investigators will randomly assign patients with chronic hypertension to receive either automated SMS reminders (digital group) or standard verbal counselling (manual group) and assess medication adherence over a defined period.	Minimal Risk
5.	Study conducted in an academic setting to evaluate the effective antimicrobial therapy and Mortality-Related risk factors for infections caused by carbapenem-Resistant Acinetobacter baumann (CRAB)	Investigators will assign CRAB patients to one or more approved antimicrobial therapy regimens and assess response to therapy as part of the study	More than minimal Risk
6.	A comparative evaluation study conducted in a tertiary care teaching hospital setting to evaluate the efficacy of Triamcinolone versus platelet-rich plasma in lateral Epicondylitis.	Investigators will randomly assign patients with lateral epicondylitis to receive either Triamcinolone or platelet-rich plasma (both approved) therapy and assess their effect on resolution of epicondylitis	More than minimal Risk

7.	A hospital based comparative study between Bipolar versus Monopolar Transurethral Resection of prostate in patients with Benign Prostatic Hyperplasia	Investigators will randomly assign patients with Benign Prostatic Hyperplasia to receive either Bipolar or monopolar Transurethral Resection (surgical techniques) and assess their effect on resection time	More than minimal Risk
8.	A hospital-based study to evaluate the efficacy of two therapeutic regimens for pain reduction in patients with Stage IV Pancreatic cancer	Investigators will randomly assign patients with Stage IV Pancreatic cancer to receive an approved and marketed therapy either via self-determined dosing or physician-determined dosage, to assess effects on pain reduction	More than minimal Risk
9.	A study conducted in a clinical setting to evaluate Naproxen Sodium for the treatment of Rheumatoid Arthritis	Investigators will administer Naproxen Sodium to participants with Rheumatoid Arthritis to evaluate its effectiveness, representing a new indication for a previously approved drug.	More than minimal Risk
10.	A study conducted in a clinical setting to evaluate the effect of Atorvastatin on insulin resistance in patients with Type 2 Diabetes	Investigators will administer Atorvastatin to participants with Type 2 Diabetes to study its effects on pancreatic function and insulin resistance, beyond its approved use for hyperlipidaemia.	More than minimal Risk
11.	A study conducted in a clinical setting to evaluate Sacubitril/Valsartan for right ventricular dysfunction	Investigators will administer Sacubitril/Valsartan to participants with right ventricular dysfunction to assess its effectiveness in a new cardiac indication beyond its approved use for left ventricular heart failure.	More than minimal Risk
12.	A study conducted in a clinical setting to compare Metoprolol versus Clonidine for blood pressure management in acute stroke	Investigators will randomly assign patients with acute stroke to receive either Metoprolol or Clonidine (both approved) and assess blood pressure control, and short-term clinical outcomes.	More than minimal Risk

***Note:** Some examples of non-regulatory clinical trials are presented in the table above. These examples may be hypothetical and are presented here only for learning purpose. "Approved" here means health related interventions approved by CDSCO for marketing purpose.*

Glossary

Biomedical and Health Research: Research including studies on basic, applied and operational research designed primarily to increase scientific knowledge about diseases and conditions (physical or socio-behavioral), their detection, cause and evolving strategies for health promotion, prevention, or amelioration of disease and rehabilitation including clinical research.

Clinical trial registry: An official platform for registering a clinical trial, such as Clinical Trial Registry-India.

Clinical Trial: A clinical trial is any research/study that prospectively assigns human participants or groups of humans to one or more health-related intervention(s) to evaluate the effects on health outcomes. The intervention could be drugs, vaccines, biosimilars, biologics, phytopharmaceuticals, radiopharmaceuticals, diagnostic agents, public health interventions, socio-behavioural interventions, technologies, devices, surgical techniques or interventions involving traditional systems of medicine, etc.

Compensation: Provision of financial payment to the research participants or their legal heirs when temporary or permanent injury or death occurs due to research participation.

Confidentiality: Keeping information confidential which an individual has disclosed in a relationship of trust and with the expectation that it shall not be divulged to others without permission.

Independent consultant: An expert who gives advice, comments and suggestions to the Ethics Committees and has no affiliation to the involved institute or industry or researchers proposing the research protocols. This individual has no voting power for decision making.

Informed Consent Process: It is the process by which a patient learns about and understands all aspects of the NRCT including the purpose, benefits, and potential risks of a health intervention, and agrees to participate in the trial.

Informed consent document (ICD): Written signed and dated document confirming a participant's willingness to voluntarily participate in a particular research, after having been

informed of all aspects of the research that are relevant for the participant's decision to participate. It includes Participant Information Sheet and Informed Consent Form.

Placebo: Placebo means an inactive substance visually identical in appearance to a drug being tested in a clinical trial.

Principal investigator: An individual who initiates and takes full responsibility for the conduct of NRCTs; if there is more than one such individual, they may be called co-principal investigators/ co-investigators.

Research related injury: Harm or loss that occurs to an individual as a result of participation in research, irrespective of the manner in which it has occurred, and includes both expected and unexpected adverse events and serious adverse events related to the intervention, whenever they occur.

Risk: Probability and severity of harm or discomfort to research participants.

Scientific Review Committee: A group of experts who assess the scientific validity and methodological rigor of a clinical trial proposal before it undergoes ethical review.

Serious Adverse Event: An event when participant suffers from life-threatening injury requiring hospitalization, prolongation of hospitalization, requirement of intervention to prevent permanent impairment or damage or significant disability/incapacity, congenital anomaly, or death.

Social scientist: A person who is an expert on societal and social behavior with specialization/experience in the area.

SOP (standard operating procedure): Detailed written instructions in a certain format describing all activities and actions to be undertaken by an organization to achieve uniformity in performance of a specific function.

Funder: An individual, institution, private company, government or non-governmental organization from within or outside the country who supports the research and is responsible for its funding.

Standard of care: Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by health care professionals. Also, standard medical care, or standard therapy.