ANNEXURE: 07 **AF/IEC/07/06/V-8.3**

Contents of the proposed protocol for the conducting clinical trial

a. Full title of the clinical study,

b. Protocol, Study number, and protocol version number with date.

c. The Investigational New Drug (IND) name/number of the investigational drug.

d. Complete name and address of the Sponsor and contract research organization if any.

e. List of the investigators who are conducting the study, their respective institutional affiliations and site locations

f. Name of clinical laboratories and other departments and/or facilities participating in the study.

Table of Contents

1. Background and introduction
    a. Preclinical experience
    b. Clinical experience:

        Previous clinical work with the new drug should be reviewed here and a description of how the current protocol extends existing data should be provided. If this is an entirely new indication, how this drug was considered for this should be discussed. Relevant information regarding pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should be described.
2. Study rationale: This section should describe a brief summary of the background information relevant to the study design and protocol methodology. The reasons for performing this study in the particular population included by the protocol should be provided.
3. Study objective (primary as well as secondary) and their logical relation to the study design.
4. Study design
    a. **Overview of the study design:** Including a description of the type of study (i.e., double-blind, multicentre, placebo controlled, etc.), a detail of the specific treatment groups and number of study Subjects in each group and investigative site, Subject number assignment, and the type, sequence and duration of study periods.
    b. Flow chart of the study
    c. A brief description of the methods and procedures to be used during the study.

d. Discussion of study design: This discussion details the rationale for the design chosen for this study.

5. Study population: the number of subjects required to be enrolled in the study at the investigative site and by all sites along with a brief description of the nature of the subject population required is also mentioned.
6. Subject eligibility

a. Inclusion criteria

b. Exclusion criteria

7. Study assessments-plan, procedures and methods to be described in detail.
8. Study conduct stating the types of study activities that would be included in this section would be: medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG), diagnostic testing such as pulmonary function tests, symptom measurement, dispensation and retrieval of medication, Subject cohort assignment, adverse event review, etc.

   Each visit should be described separately as Visit 1, Visit 2, etc.

   Discontinued subjects: Describes the circumstances for Subject withdrawal, dropouts, or other reasons for discontinuation of Subjects. State how dropouts would be managed and if they would be replaced describe the method of handling of protocol waivers if any. The person who approves all such waivers should be identified and the criteria used for specific waivers should be provided.

   Describes how protocol violations will be treated, including conditions where the study will be terminated for noncompliance with the protocol.
9. Study treatment-
   a. Dosing schedule (dose, frequency, and duration of the experimental treatment) Describe the administration of
   b. Placebos and/or dummy medications if they are part of the treatment plan. If applicable, concomitant drug(s),
   c. Their doses, frequency, and duration of concomitant treatment should be stated.
   d. Study drug supplies and administration: A statement about who is going to provide the study medication and that the investigational drug formulation has been manufactured following all regulations Details of the product stability, storage requirements and dispensing requirements should be provided. Dose modification for study drug toxicity:

Rules for changing the dose or stopping the study drug should be provided Possible drug interactions

e. Concomitant therapy: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a Subject is not allowed to use during parts of or the entire study. If any washout periods for prohibited medications are needed prior to enrolment, these should be described here.
f. Blinding procedures: A detailed description of the blinding procedure if the study employs a blind on the Investigator and/or the Subject
g. Un-blinding procedures: If the study is blinded, the circumstances in which un-blinding may be done and the mechanism to be used for un-blinding should be given

10. Adverse Events:

Description of expected adverse events should be given.

Procedures used to evaluate an adverse event should be described.

11. Ethical considerations: Give the summary of:
    a. Risk/benefit assessment:
    b. Ethics committee review and communications
    c. Informed consent process
    d. Statement of subject confidentiality including ownership of data and coding procedures.
    e. Vulnerability
    f. Privacy and Confidentiality
12. Study monitoring and supervision
13. Investigational Product Management:
    a. Give investigational product description and packaging (stating all ingredients and the formulation of the investigational drug and any placebos used in the study)
    b. The precise dosing required during the study
    c. Method of packaging, labelling and blinding of study substances
    d. Method of assigning treatments to subjects and the subject identification code numbering system
    e. Storage conditions for study substances

f. Investigational product accountability: Describe instructions for the receipt, storage, dispensation, and return of the investigational products to ensure a complete accounting of all investigational products received, dispensed, and returned or destroyed.

g. Describe policy and procedure for handling unused investigational products.

14. Data Analysis: Provide details of the statistical approach to be followed including sample size, how the sample size was determined, including assumptions made in making this determination, efficacy endpoints (primary as well as secondary) and safety endpoints.

    Statistical analysis: Give complete details of how the results will be analyzed and reported along with the description of statistical tests to be used to analyze the primary and secondary endpoints defined above. Describe the level of significance, statistical tests to be used, and the methods used for missing data; method of evaluation of the data for treatment failures, non-compliance, and Subject withdrawals; rationale and conditions for any interim analysis if planned.

    Describe statistical considerations for Pharmacokinetic (PK) analysis, if applicable.

15. Undertaking by the Investigator

16. Appendices: Provide a study synopsis, copies of the informed consent documents (patient information sheet, Informed consent form etc.); Case Record Form (CRF) and other data collection forms; a summary of relevant preclinical safety information and any other documents referenced in the clinical protocol.

    1. Protocol- if any amendments- Summary of changes
    2. Investigator brochure
    3. CRF
    4. Patient materials Diaries if applicable
    5. Final/Draft Clinical Trial Agreement
    6. CV, MRC and GCP of PI
    7. CTRI
    8. DCGI Approval Letter/Submission letter
    9. Sponsoring agent Details
    10. Study or site-specific insurance
    11. ICDs –all vernacular languages – Translation and back translation certificates

ANNEXURE: 02 **AF/IEC/02/08/V-8.3**

Format for Summary and Detailed Protocol

Protocol Title: PI/CoI-Name:

Sponsor/CRO Name:

Sl. No.	Enclosures:	Page Nos.
1.	Face sheet	
2.	Undertaking of Principal, Co-investigator and Collaborators	
3.	Brief Bio-data of investigators	
4.	conflict of interest, if applicable	
5.	Summary of study protocol, if the protocol amended Summary of Changes version and date	
6.	Detailed protocol version and date	
7.	Participant Information sheet version and date	
8.	Informed Consent Document version and date	
9.	Translation and Back translation certificates	
10.	Funding Agency / sponsor's letter	
11.	Investigator Brochure version and date	
12.	Final CTA/Draft	
13.	GCP Training Certificate of Principal Investigator/ Co-Investigators/Collaborators	
14.	CTRI	
15.	DCGI submission/Approval letter	
16.	Investigator Undertaking	
17.	Study/site Specific Insurance [Who it covers and validity]	
18.	Any other relevant documents	

ANNEXURE: 03 **AF/IEC/03/08/V-8.3**

UNDERTAKING BY THE INVESTIGATOR

1. Full name, address and title of the Principal Investigator (or Investigators when there is no Principal Investigator).
2. Name and address of the medical college, hospital or another facility where the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, or any other statements of qualifications)
3. Name and address of all clinical laboratory facilities to be used in the study.
4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.
5. Names of the other members of the research team (Co-or sub-Investigators) who will be assisting the Investigator in the conduct of the investigations.
6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.
7. Commitments:

i. I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary ethics committee and regulatory approvals have been obtained.

ii. I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval or favorable opinion from the ethics committee of the amendment, except where necessary to eliminate an immediate hazard to the trial subject or when the changes involved are only logistical or administrative in nature.

iii. I agree to personally conduct or supervise the clinical trial at my site.

iv. I agree to inform all trial subject, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the New Drugs and Clinical Trials Rules, 2019 and Good Clinical Practices guidelines are met.

v. I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory requirements and Good Clinical Practices guidelines.

vi. I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug.

vii. I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the trial.

viii. I agree to maintain adequate and accurate records and to make those records available for audit or inspection by the Sponsor, ethics committee, Central Licencing Authority or their authorized representatives, in accordance with regulatory provisions and the Good Clinical Practices guidelines. I will fully cooperate with any study-related audit conducted by regulatory officials or authorized representatives of the Sponsor.

ix. I agree to promptly report to the ethics committee all changes in the clinical trial activities and all unanticipated problems involving risks to human subjects or others.

x. I agree to inform all serious adverse events to the Central Licencing Authority, sponsor as well as the ethics committee within twenty-four hours of their occurrence. In case, of failure to do so, I shall furnish the reason for the delay to the satisfaction of the Central Licencing Authority along with the report of the serious adverse event.

xi. I will maintain the confidentiality of the identification of all participating subjects and assure security and confidentiality of study data.

xii. I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in clinical trials.

xiii. Declaration of Conflict of Interest

8. Signature of Investigator with date