

Draft Guidance for Registration of Clinical Research Organisation (CRO)

TABLE OF CONTENTS

SECTIONS	CONTENTS	PAGE NO.
Section A	Introduction	3
Section B	Rules And Regulations Related to Registration of Clinical Research Organisations	5
Section C	Requirement For the Submission of Documents For Registration	8
Section D	Responsibilities of CRO	10
Section E	SOP For Registration Of CRO	11
Section F	Record Keeping And Data Handling	12
Section G	References	16
Section H	Abbreviations	17
Section I	Letter of Undertaking	18
Section J	Template for authorisation letter	19

SECTION A

INTRODUCTION:

This Guidance has been developed in conformity with New Drugs and Clinical Trials Rules, 2019 under Drugs and Cosmetics Act 1940 and GCP Guidelines of India for the purpose of submission of registration of Clinical Research Organisation application.

The Central Government, after consultation with the Drugs Technical Advisory Board, amend the New Drugs and Clinical Trial Rules 2019, vide GSR 581(E) dated 19 Sept 2024. They shall come into force on and from the 1st day of April, 2025. In the New Drugs and Clinical Trials Rules, 2019 (hereinafter referred to as the principal rules), in rule 2, in sub-rule (1), after clause (i), the following clause shall be inserted, namely:- '(ia) "Clinical Research Organisation" means the sponsor or a body, commercial or academic or of other category, owned by an individual or an organisation having status of legal entity by whatsoever name called, to which the sponsor may, delegate or transfer in writing, some or all of the tasks, duties or obligations regarding clinical trial or bioavailability or bioequivalence study.

DEFINITIONS:

Clinical Trial: - A systematic study of pharmaceutical products on human subjects – (whether patients or non-patient volunteers) – in order to discover or verify the clinical, pharmacological (including pharmacodynamics / pharmacokinetics), and / or adverse effects, with the object of determining their safety and / or efficacy.

Clinical Research Organisation :- means the sponsor or a body, commercial or academic or of other category, owned by an individual or an organisation having status of legal entity by whatsoever name called, to which the sponsor may, delegate or transfer in writing, some or all of the tasks, duties or obligations regarding clinical trial or bioavailability or bioequivalence study.

Central Licensing Authority: means the authority appointed by the Central Government to perform the duties of the licensing authority under these rules and includes any person to whom the powers of a licensing authority may be delegated under Rule 22 of Drugs and cosmetics Act 1940

Bioavailability and Bioequivalence studies: bioavailability as the rate and extent of drug absorption into systemic circulation from its dosage form. Bioequivalence is established when two similar dosage forms reach systemic circulation at the same relative rate and extent.

New Drug: A drug, including bulk drug substances which has not been used in the country and has not been recognised as effective and safe by the Licensing Authority for the proposed claims

Investigational New Drug: A drug or biological drug that has not been approved for general use by the FDA. It is used in a clinical trial to investigate its safety and efficacy.

OBJECTIVE

The CRO is also responsible for implementing and maintaining Quality Assurance system to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol and Good Clinical Practice Guidelines issued by CDSCO, Directorate General of Health Services, Govt. of India as well as all applicable statutory provisions of New Drugs and Clinical Trials Rules, 2019 under Drugs and Cosmetics Act, 1940. Standard operating procedures should be documented to ensure compliance with GCP and applicable regulations.

SECTION B

RULES AND REGULATIONS RELATED TO REGISTRTION OF CLINICAL RESEARCH ORGANISATIONS

38A. Registration of Clinical Research Organisation.- Without prejudice to anything contained in any other provisions of these rules, no Clinical Research Organisation shall conduct any clinical trial or bioavailability or bioequivalence study of new drug or investigational new drug in human subjects without registration granted by the Central Licencing Authority under these rules.

38B. Application for Registration of Clinical Research Organisation.- (1) The Clinical Research Organisation shall make an application in Form CT-07B (**Annexure I**) to the Central Licencing Authority for the purpose of registration for conducting clinical trial or bioavailability or bioequivalence study. Provided that any bioavailability or bioequivalence study centre already registered under rule 44, shall be deemed to be registered under this Chapter for the purposes of bioavailability or bioequivalence study. (2) The application for registration shall be accompanied by a fee as specified in the Sixth Schedule along with such documents and other information as specified in the Ninth Schedule.

38C. Grant of registration to Clinical Research Organisation.- (1) The Central Licencing Authority may, after scrutiny of the information and requirements furnished with the application under rule 38B and such further enquiry, if any, as may be considered necessary, – (i) if satisfied, that the requirements of these rules have been complied with, grant registration to the applicant in Form CT-07C (**Annexure II**) within a period of forty-five working days from the date of receipt of the application; or (ii) if not satisfied, reject the application, for reasons to be recorded in writing, within a period of forty-five working days reckoned from the date of the receipt of the application ; or (iii) If satisfied, that any deficiency in the application is required to be rectified, it shall inform the applicant of the deficiency not later than forty-five working days from the date of receipt of the application, to rectify the deficiencies within such period as may be specified by it: Provided that where the applicant rectifies the deficiency within the period so specified, the Central Licencing Authority, shall if satisfied, grant registration to the applicant or if not satisfied, reject the application within a period of ninety days reckoned from date of the receipt of the rectification. (2) In case of rejection of application under sub-rule (1), the applicant may request the Central Licencing Authority to reconsider the application within a period of sixty days from the date of rejection of the application on payment of fee as specified in the Sixth Schedule and submission of required information and documents. (3) Any applicant aggrieved by the decision of the Central Licencing Authority under sub-rule (1) or sub-rule (2), may file an appeal within forty-five days from the date of such decision, before the Central Government and Government may, after such enquiry and after giving an opportunity of being heard to the appellant, dispose of the appeal within a period of sixty days from the date of receipt of the appeal.

38D. Validity period and renewal of registration of Clinical Research Organisation. - (1) The registration granted under rule 38C shall remain valid for a period of five years from the date of its grant, unless suspended or cancelled by the Central Licencing Authority. (2) An application for renewal of registration shall be made in Form CT-07B to the Central Licencing Authority along with documents as specified in the Ninth Schedule prior to date of expiry of its registration: Provided that if the application for renewal of registration is received by the Central Licencing Authority prior to the date of expiry, the registration shall continue to be in force until the orders are passed by the Central Licencing Authority on the application. (3) The Central Licencing Authority shall, after scrutiny of information enclosed with the application and such further enquiry, if any, as may be considered necessary, if satisfied, shall renew the registration in Form CT-07C and in case of rejection or rectification of deficiency, if any, the procedure as specified in rule 38C shall apply.

38E. Inspection of Clinical Research Organisation registered with Central Licencing Authority.- The Clinical Research Organisation registered by the Central Licencing Authority under rule 38C, shall allow any officer authorised by the Central Licencing Authority, who may be accompanied by an officer authorised by the State Licencing Authority, to enter the premises of the Clinical Research Organisation with or without prior consent, to inspect, search or seize, any record, document, investigational product and other related material and reply to queries raised by the inspecting authority in relation to functioning of the Organisation.

38F. Suspension or cancellation of registration of Clinical Research Organisation- (1) Where any Clinical Research Organisation fails to comply with any provision of the Act and these rules, the Central Licencing Authority may, after giving an opportunity to show cause and after affording an opportunity of being heard, by an order in writing, take one or more of the following actions, namely:- (a) withdraw show cause notice issued under sub-rule (1); (b) issue warning in writing to the Clinical Research Organisation describing the deficiency or defect observed during inspection or otherwise, which may affect adversely the right or well-being of trial subject or the validity of any study conducted; (c) reject the results of the clinical trial or the bioavailability or bioequivalence study; (d) suspend for such period as considered appropriate or cancel the registration granted under rule 38C; (e) debar the organisation to conduct any clinical trial study or bioavailability or bioequivalence study in future for such period as considered appropriate by the Central Licencing Authority.

(2) Any Clinical Research Organisation aggrieved by the order of the Central Licencing Authority under sub-rule (1), may within a period of sixty days from the date of the receipt of the order, make an appeal to the Central Government and the Central Government may, after such enquiry, as deemed necessary and after affording an opportunity of being heard, pass such orders in relation thereto as may be considered appropriate in the facts and circumstances of the case.”

Fees for Registration of CRO:

Requisite amount should be paid through Bharath Khosh receipt along with the application.

The fee as per sixth schedule of NDCT Rules, 2019 for registration of recommendation of application is as follows:

4A	38B	Application for Grant/Renewal of Clinical Research Organisation Registration	5,00,000
4B	38C	Reconsideration of application for registration of Clinical Research Organisation	1,00,000

NOTES:

- The CRO shall submit the application in Form CT-07B (online) through SUGAM portal.
- Whenever new rules are published, the new Rules will prevail over this guidance.

SECTION C

REQUIREMENT FOR THE SUBMISSION OF DOCUMENTS FOR REGISTRATION:

1. Authority under which the CRO has been constituted (upload authority letter from authorised person of CRO)
2. Details of the constitution of the CRO and registration of the legal entity by local authority (Name & Address of the Director) to be provided.
3. Application in the form CT-07B duly signed by the competent person as per Ninth Schedule for the grant of registration of Clinical Research organisation constituted under Rule 38B of New Drugs and Clinical Trials Rules, 2019
4. Bharat Khosh receipt for the fees as per Sixth Schedule of New Drugs and Clinical Trials Rules, 2019
5. Details of in-charge person responsible for overall activities of the organisation as per clause 1(i) of Ninth Schedule of NDCT Rules, 2019.
6. Details of facilities, resources, personnel, training etc.
 - 4.1. Details of CRO facilities, resources and staff for handling any oversight of clinical trials and bioavailability or bioequivalence studies
 - 4.2. Educational qualification, training records of CRO staff
7. Organogram of the organisation including brief Curriculum Vitae of key personnel
8. SOP for ensuring that the trials and bioavailability or bioequivalence studies are adequately monitored and the trial or study related responsibilities transferred to it, partially or fully, by the sponsor are discharged effectively and efficiently
9. SOP for implementing of quality assurance and quality control as per standard operating procedures designed for the purpose and such standard operating procedures shall be well documented
10. SOP for maintaining complete data, documentations and other related records accurately including checking and ensuring that the essential documents required for the conduct of the trial are maintained properly by the investigators
11. SOP for ensuring the investigators receive all documents and trial or study related supplies needed to conduct the clinical trial or bioavailability or bioequivalence study properly
12. SOP for transferring and assuming study related duties by CRO
13. List of Standard Operating Procedures with salient highlights about specific areas to be scrutinised
14. Details of education programmes to help its investigators carry out the research studies as per the guidelines and regulations applicable to such trials and studies including imparting trainings as to protocol adherence, good clinical practices guidelines, informed consent process, and investigators responsibilities for good clinical practices compliance

15. SOP for maintenance of records (written documents, electronic, magnetic or optical records, scans, etc.), such as protocols, approvals from the Central Licencing Authority and Ethics committee, investigators particulars, blank consent forms, monitor reports, audit certificates, relevant correspondence, reference pages, completed and the final reports.
16. A brief profile of the specific activities or services undertaken by the organisation including facilities, resources and infrastructure
17. Undertaking for all documentation and communication shall be dated, filed and preserved safely for a period of five years after completion of such study or for at least two years after the expiration date of the batch of the new drug or investigational new drug studied, whichever is later.
18. Undertaking for strict confidentiality shall be maintained during access and retrieval procedures
19. Undertaking for constitution or ownership of the Clinical Research Organisation, the organisation shall intimate about the change in writing to the Central Licencing Authority within thirty days of such change.
20. Details of accreditation or approval of other regulatory agencies, if any, (self-attested copy of certificate)
21. Copy of agreement with third party service providers for site management, translation, biostatistics, data management, and laboratory services etc;
22. An undertaking to declare that-
 - a. we shall comply with the conditions imposed on the registration certificate along with the adherence to other guidelines like Good Clinical Practices guidelines and provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940), and the New Drugs and Clinical Trials Rules, 2019;
 - b. We shall comply with such further requirements, if any, as may be specified by the Government of India, under the Act and the rules made thereunder;
 - c. We shall allow the Central Licencing Authority or any person authorised by him in that behalf to enter and inspect the premises and to examine the process or procedure and documents in respect of any clinical trial conducted by us.

SECTION D

RESPONSIBILITIES OF CRO:

1. **Protocol design and development:** CROs assist sponsors in creating robust and scientifically sound study protocols that define the scope, objectives, and methodologies of the clinical trial.
2. **Patient recruitment and retention:** CROs employ various strategies to identify and enroll eligible patients for clinical trials, ensuring that participant targets are met. They also focus on patient retention through engagement and support.
3. **Regulatory and ethics compliance:** CROs navigate complex regulatory requirements and ensure adherence to ethical considerations, protecting the rights and well-being of study participants.
4. **Clinical trial operation:** CROs manage the day-to-day operations of clinical trials, including site selection, monitoring, data collection, and adverse event reporting, among other activities.
5. **Data management and biostatistics:** CROs employ advanced technologies and robust data management systems to collect, scrutinize, and analyze trial data, generating high-quality evidence to support regulatory submissions.
6. **Quality assurance and control:** CROs implement comprehensive quality assurance measures to ensure that clinical trials are conducted in accordance with Good Clinical Practice (GCP) guidelines, industry standards, and regulatory requirements.
7. The Sponsor/CRO shall have formal and legal agreement / contract with the Investigator(s) / Institution(s) on the following terms:
 - a. To conduct the Study in compliance with New Drugs and Clinical Trial Rules 2019, GCP, other applicable regulatory requirements and the Protocol agreed to by the Sponsor and given approval / favourable opinion by the Ethics Committee
 - b. To comply with the procedures for data recording, and reporting
 - c. To permit monitoring, auditing and inspection
 - d. To retain the study related essential documents until the Sponsor informs the Investigator(s) / Institution(s) in writing that these documents are no longer needed

SECTION E

SOP FOR REGISTRATION OF CRO:

1. SOP for transferring and assuring study related duties by CRO, List of Standard Operating Procedures with salient highlights about specific areas to be scrutinised
2. SOP to ensure that the trials and bioavailability or bioequivalence studies are adequately monitored and the trial or study related responsibilities transferred to it, partially or fully, by the sponsor are discharged effectively and efficiently
3. SOP for ensuring implementing of quality assurance and quality control as per standard operating procedures designed for the purpose and such standard operating procedures shall be well documented
4. SOP for maintaining complete data, documentations and other related records accurately including checking and ensuring that the essential documents required for the conduct of the trial are maintained properly by the investigators
5. SOP for ensuring the investigators receive all documents and trial or study related supplies needed to conduct the clinical trial or bioavailability or bioequivalence study properly
6. SOP for maintenance of records (written documents, electronic, magnetic or optical records, scans, etc.), such as protocols, approvals from the Central Licencing Authority and Ethics committee, investigators particulars, blank consent forms, monitor reports, audit certificates, relevant correspondence, reference pages, completed and the final reports.

SECTION F

RECORD KEEPING AND DATA HANDLING

The CRO shall maintain

1. Data, record, registers and other documents related to the functioning and review of clinical trial or bioavailability study or bioequivalence study, as the case may be, for a period of five years after completion of such clinical trial.
2. the curriculum vitae of all staff of CRO
3. standard operating procedures followed by CRO
4. National and international guidelines followed by the CRO
5. copies of the protocol, data collection formats, case report forms, investigators brochures, etc., submitted for review
6. all correspondence with committee members and investigators regarding application, decision and follow up
7. agenda of all Ethics Committee meetings and minutes of all Ethics Committee meetings with signature of the Chairperson
8. copies of decisions communicated to applicants
9. records relating to any order issued for premature termination of study with a summary of the reasons
10. final report of the study including microfilms, compact disks or video recordings; recommendation given by Ethics Committee for determination of compensation
11. records relating to the serious adverse event, medical management of trial subjects and compensation paid.

(Annexure 1)

“FORM CT-07B

[See rules 38B (1) and 38D (2)]

APPLICATION FOR REGISTRATION / RENEWAL OF CLINICAL RESEARCH ORGANISATION

I/We, ... (name, designation and full postal address of the applicant) of hereby apply for grant of registration of my/Our Clinical Research Organisation. The details of the application are as under:

1. Name of the Applicant:	
2. Nature and constitution of applicant: (proprietorship, partnership including limited liability partnership, company, society, trust, other to be specified)	
3.(i) Applicant's address including telephone number, mobile number, fax number and e- mail id: (ii) Address for correspondence: [corporate or registered office of the Clinical Research Organization]	
4. Details of accreditation, if any, (self-attested copy of certificate to be attached):	
5. Fee paid on Rs. Receipt or challan or transaction ID	
6. I have enclosed the documents as specified in the Table 1 of Ninth Schedule of the New Drugs and Clinical Trials Rules, 2019.	
7. I hereby state and undertake that: (i) I shall comply with the conditions imposed on the registration certificate along with the adherence to other guidelines like Good Clinical Practices guidelines and provisions of the Drugs and Cosmetics Act, 1940, and the New Drugs and Clinical Trials Rules, 2019. (ii) I shall comply with such further requirements, if any, as may be specified by the Government of India, under the Act and the Rules made thereunder. (iii) I shall allow the Central Licencing Authority and/or any person authorised by him in that behalf to enter and inspect the premises and to examine the process/procedure and documents in respect of any clinical trial conducted by us.	

Place:

Date

Digital Signature

(Name and designation)

Annexure II

FORM CT- 07C
[See rules 38C and 38D (3)]

GRANT OR RENEWAL OF REGISTRATION OF CLINICAL RESEARCH ORGANISATION

Registration No. -----

The Central Licencing Authority hereby registers (Name and full address with contact details of the applicant) for conduct of clinical trial or bioavailability or bioequivalence study of new drugs and investigational new drugs under the New Drugs and Clinical Trials Rules, 2019.

Place:
Date:

Central Licencing Authority
Stamp"

Conditions of registration :

The registration granted under rule 38C or renewal granted under rule 38D shall be subject to the conditions specified in rule 25, rule 35 and the requirements specified in the Ninth Schedule including the following conditions:-

- (i) the organisation shall maintain the facilities and adequately qualified and trained personnel as specified in the Ninth Schedule for performing its functions;
- (ii) the organisation shall initiate conduct of any clinical trial or bioavailability or bioequivalence study of any new drug or investigational new drug in human subjects after approval of the protocol and other

related documents by the Ethics Committee for clinical trial or bioavailability or bioequivalence study, as the case may be, and permission of such study granted by the Central Licencing Authority;

- (iii) where a clinical trial site or bioavailability or bioequivalence centre does not have its own Ethics Committee, the study at that site or centre may be initiated after obtaining approval of the protocol from another Ethics Committee of another trial site or an independent Ethics Committee for clinical trial or bioavailability or bioequivalence study registered under rule 8:

Provided that the approving Ethics Committee shall be responsible for the study at the trial site or centre, as the case may be, and both the approving Ethics Committee and the trial site or the centre are located within the same city or within a radius of fifty kilometer of the trial site or the centre.

- (iv) the Central Licencing Authority shall be informed about the approval of the Ethics Committee for clinical trial or bioavailability or bioequivalence study;
 - (v) clinical trial of new drug or investigational new drug shall be registered with the Clinical Trial Registry of India before enrolling the first subject for the study;
 - (vi) bioavailability or bioequivalence study of investigational new drug shall be registered with the Clinical Trial Registry of India before enrolling the first subject for the study
 - (vii) study shall be conducted in accordance with the approved protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and provisions of the Act and these rules;
 - (viii) in case of termination of any such study prematurely, the detailed reasons for such termination shall be communicated to the Central Licencing Authority immediately;
 - (ix) any report of serious adverse event occurring during study to the subject of such study shall, after due analysis, be forwarded to Central Licencing Authority within fourteen days of its occurrence in the format as specified in Table 5 of the Third Schedule and in compliance with the procedures as specified in rule 42;
 - (x) in case of an injury to the study subject during study, the complete medical management and compensation in the case of study related injury shall be provided in accordance with the provisions of Chapter VI and details of compensation paid to the trial subject in such cases shall be intimated to the Central Licencing Authority within thirty days of receipt of the order;
-

- (xi) in case of death, permanent disability, injury other than death and permanent disability, as the case may be, of a study subject, compensation shall be provided in accordance with the provisions of Chapter VI and details of compensation paid to the trial subject or his legal heir, as the case may be, in such cases shall be intimated to the Central Licencing Authority within thirty days of receipt of the order;
 - (xii) if there is any change in constitution or ownership of the Clinical Research Organisation, the organisation shall intimate about the change in writing to the Central Licencing Authority within thirty days of such change;
 - (xiii) the clinical research organisation shall maintain data, records, and other documents related to the conduct of the clinical trials for a period of five years after completion of such study or for at least two years after the expiration date of the batch of the new drug or investigational new drug studied, whichever is later;
 - (xiv) the Clinical Research Organisation shall allow any officer authorised by the Central Licencing Authority who may be accompanied by an officer authorised by State Licencing Authority to enter the premises with or without prior notice, to inspect any record, statistical observation or results or any documents related to clinical trials and furnish information to the queries raised by such authorised person, in relation to the conduct of the said study;
 - (xv) the Central Licencing Authority may, if considered necessary, impose additional condition, in writing with justification, in respect of specific clinical trials regarding the objective, design, subject population, subject eligibility, assessments, conduct and treatment of such specific study".
-

SECTION G

REFERENCES:

1. New Drugs and Clinical Trial Rules, 2019
2. Indian GCP Guidelines
3. GSR 581(E) dated 19.09.2024

SECTION H

ABBREVIATIONS:

BA: Bioavailability

BE: Bioequivalence

NOC: No Objection Certificate

TL: Test Licence

PI: Principal Investigator

IEC: Independent/Institutional Ethics committee

ICF: Informed Consent Form

PIS: Patient Information Sheet

GCP: Good Clinical Practices

CoA: Certificate of Analysis

CRO: Clinical Research Organization

PK/PD: Pharmacokinetics/Pharmacodynamics

SECTION I

<On Company Letterhead>

LETTER OF UNDERTAKING

I, (Mr/Ms/Dr).....S/o or D/o.....is authorized person of
M/s..... (name of CRO) hereby
undertake that:

1. All documentation and communication shall be dated, filed and preserved safely for a period of five years after completion of such study or for at least two years after the expiration date of the batch of the new drug or investigational new drug studied, whichever is later.
2. Strict confidentiality shall be maintained during access and retrieval procedures
3. Constitution or ownership of the Clinical Research Organisation, the organisation shall intimate about the change in writing to the Central Licencing Authority within thirty days of such change.
4. Comply with the conditions imposed on the registration certificate along with the adherence to other guidelines like Good Clinical Practices guidelines and provisions of the Drugs and Cosmetics Act, 1940 (23 of 1940), and the New Drugs and Clinical Trials Rules, 2019;
5. Comply with such further requirements, if any, as may be specified by the Government of India, under the Act and the rules made thereunder;
6. Allow the Central Licencing Authority or any person authorised by him in that behalf to enter and inspect the premises and to examine the process or procedure and documents in respect of any clinical trial conducted by us.

Signature of Authorised Signatory:

Name:

Designation:

Seal of the Company / Firm / Organisation:

SECTION J

<On Company Letterhead>

TEMPLATE FOR AUTHORISATION LETTER

You are requested to submit authority letter as per the format. TO WHOM IT
MAY CONCERN This is to declare that I/we.....(Head of
Institute/Director) hereby authorize the formation
of(Name of Clinical Research Organisation)
under.....(Name & address of the organization under which the
Clinical Research Organisation). The Clinical Research Organisation will
function under our authority as per Rules & Regulations notified by MoH&FW.

Name & Signature

HOD/Director