Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health and Family Welfare
Government of India

New Drugs Division

Frequently Asked Questions (FAQs) on New Drugs and Clinical Trials

Feedback/Suggestions, if any, in this regard, may be submitted to:

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Notice:

The replies to the FAQs are aimed only for creating public awareness about regulation of New Drugs and Clinical Trials and are not meant to be used for legal or professional purposes. The readers are advised to refer to the statutory provisions of Drugs and Cosmetics Act & Rules and respective Guidelines / Clarifications issued by CDSCO from time to time for all their professional needs.

FAQs on New Drugs and Clinical Trials

1. Whether the New Drugs and Clinical Trial Rules, 2019 (NDs & CTs Rules, 2019) is applicable only for New Drugs and Investigational New drugs for human use?

Yes. Regulation for New drugs for veterinary use will continue to be as per Part XA of the Drugs and Cosmetics Rules, 1945.

2. What is a "new drug"?

A new drug means;

i. a drug, including active pharmaceutical ingredient or phytopharmaceutical drug, which has not been used in the country to any significant extent has not been approved as safe and efficacious by Central Licencing Authority (CLA) i.e. DCG(I) with respect to its claims; or

ii. a drug approved by the CLA for certain claims and proposed to be marketed with modified or new claims including indication, route of administration, dosage and dosage form; or

iii. a fixed dose combination of two or more drugs, approved by CLA separately for certain claims and proposed to be combined for the first time in a fixed ratio, or where the ratio of ingredients in an approved combination is proposed to be changed with certain claims including indication, route of administration, dosage and dosage form; or

iv. a modified or sustained release form of a drug or novel drug delivery system of any drug approved by the Central Licencing Authority; or

v. a vaccine, r-DNA derived product, living modified organism, monoclonal anti-body, stem cell derived product, gene therapeutic product or xenografts, intended to be used as drug;

3. What is an "investigational new drug (IND)"

An "investigational new drug (IND)" means a new chemical or biological entity or substance that has not been approved for marketing as a drug in any country.

4. What is a "subsequent new drug"?

A subsequent new drug means a drug approved by the Central Licencing Authority for certain claims and proposed to be marketed with modified or new claims including indication, route of administration, dosage and dosage form. A subsequent new drug also includes a new drug already approved in the country.

5. Whether modified/sustained/prolonged/controlled release, etc and NDDS of an approved drug are considered as new drug forever and it requires permission from the CLA prior to obtaining manufacturing license from the State Licencing Authority (SLA)?

Yes. As per clause (w) of rule 2 of the New Drugs and Clinical Trials Rules, 2019 modified/sustained/prolonged/controlled release, etc and NDDS of an approved drug are always considered as new drug and hence, require prior permission from CLA before obtaining the manufacturing license from the SLA for such products.

6. What is a "similar biologic"?

A "similar biologic" means a biological product which is similar in terms of quality, safety and efficacy to reference biological product licensed or approved in India, or any innovator product approved in International Council of Harmonization (ICH) member countries.

7. How long a new drug is considered to be a new drug?

A new drug which is a modified or sustained release form of a drug or Novel Drug Delivery System (NDDS) of any drug approved by the Central Licencing Authority; or a vaccine, recombinant Deoxyribonucleic Acid (r-DNA) derived product, living modified organism, monoclonal anti-body, stem cell derived product, gene therapeutic product or xenografts, intended to be used as drug shall continue to be a new drug forever. However, new drugs covered other than above categories shall be considered as a new drug for a period of 4 years of their approval by the CLA.

8. What is an "orphan drugs"?

An "orphan drug" means a drug intended to treat a condition which affects not more than 5 lakh persons in India.

9. What is "clinical trial"?

A "clinical trial" in relation to a new drug or investigational new drug means any systematic study of such new drug or investigational new drug in human subjects to generate data for discovering or verifying its,

(i) clinical or;
(ii) pharmacological including pharmacodynamics, pharmacokineticsor;
(iii) adverse effects,

with the objective of determining the safety, efficacy or tolerance of such new drug or investigational new drug

10. What is an "academic clinical trial"?

An "academic clinical trial" means a clinical trial of 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 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 Licencing Authority or regulatory authority of any country for marketing or commercial purpose.

11. Whether permission is required from the DCG (I) for conduct of an academic clinical trial?

No permission for conducting an academic clinical trial shall be required for any drug from the CLA where, —

(i) the clinical trial in respect of the permitted drug formulation is intended solely for academic research purposes for a new indication or new route of administration or new dose or new dosage form; and

(ii) the clinical trial referred to in clause (i) has been initiated after prior approval by the Ethics Committee for clinical trial; and

(iii) the observations generated from such clinical trial are not required to be submitted to the Central Licencing Authority; and

(iv) the observations of such clinical trial are not used for promotional purposes.

However, in the event of a possible overlap between the academic clinical trial and clinical trial or a doubt on the nature of study, the Ethics Committee concerned shall inform the DCG (I) in writing indicating its views within thirty working days from the receipt of application to that effect.

12. Whether compensation, medical management in case of injury or death of trial subjects is applicable in case of academic clinical trial?

The academic clinical trial shall be required to be conducted in accordance with the approved clinical trial protocol, ethical principles specified in National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, notified by the ICMR with a view to ensuring protection of rights, safety and wellbeing of trial subject during conduct of such clinical trial. Therefore, ethical principles including compensation, medical management in case of injury or death etc. as prescribed in National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, notified by the ICMR are applicable for academic clinical trials.

13. Who can apply for grant of permission to conduct clinical trial or BA/BE study of new drugs in human subjects?

Any person or institution or organisation having permanent establishment in India who intends to conduct clinical trial or BA/BE study of a new drug or an investigational new drug can submit application for clinical trial or BA/BE study.

14. How can an application for grant of permission to conduct clinical trial of new drug or investigational new drug be made?

An application for grant of permission to conduct clinical trial of new drug or investigational new drug shall be made in Form CT-04.
The application should be accompanied by the necessary documents as specified under Second Schedule along with the fees as specified under Sixth Schedule of the NDs & CTs Rules, 2019.

15. Whether permission is required from the CLA for conduct of clinical trial in India?

Yes. Any sponsor or investigator intended to initiate a clinical trial for new drug or investigational new drug shall obtain permission from CLA in Form CT-06. The applicant shall submit application in Form CT-04 along with all other necessary documents specified under Second Schedule and fees as specified under Sixth Schedule of CT Rules 2019. However, no fee is required for such application from a person from an institution or organization funded or owned, wholly or partially by the Central Government or by a State Government.

16. Whether Phase-I (first-in-human) study of a new drug discovered or developed outside India can be permitted to be conducted in India?

No. For new drug substances discovered or developed in countries other than India, Phase I data should be submitted along with the application. After submission of Phase I data generated outside India to the Central Licensing Authority, permission may be granted to repeat Phase I trials or to conduct Phase II trials and subsequently Phase III trial concurrently with other global trials for that drug.

17. Under what circumstances relaxation, abbreviations, omission or deferment of non- clinical and clinical data may be considered for approval of Clinical Trial and New Drug?

The requirement of non-clinical and clinical data may be relaxed, abbreviated, omitted or deferred under life threatening or serious disease conditions or rare diseases and for drugs intended to be used in the diseases of special relevance to Indian scenario or

unmet medical need in India, disaster or special defence use e.g. haemostatic and quick wound healing, enhancing oxygen carrying capacity, radiation safety, drugs for combating chemical, nuclear, biological infliction etc. However, such relaxation, abbreviations, omission or deferment of data will be evaluated on case-by-case basis depending on the nature of the new drugs, proposed indication, etc.

18. **What are the timelines for disposal of application for conduct of clinical trial and BA/BE study of new drugs?**

In general, the timeline for disposal of an application for conduct of clinical trial and BA / BE study is 90 working days from the date of receipt of application. However, if the drug is discovered in India or research and development of the drug are being done in India and also the drug is proposed to be manufactured and marketed in India then the timeline for disposal of an application for conduct of such clinical study is 30 working days from the date of receipt of application. In such case, if no response is issued by the CDSCO within 30 working days, the clinical trial will be considered to be deemed approved.

19. What is the timeline for disposal of an application for clinical trial which is a part of discovery, research and manufacture of a new drug in India?

The application submitted to CLA for grant of permission to conduct clinical trial of a new drug discovered in India or research and development of the drug are being done in India and also the drug is proposed to be manufactured and marketed in India, such application shall be disposed by way of grant of permission or rejection or processed by way of communication to rectify any deficiency of the application, as the case may be, as specified in rule 22, by the CLA within a period of 30 working days from the date of the receipt of the application. If no communication has been received from the CLA to the applicant within the said period, the permission to conduct clinical trial shall be deemed to have been granted.

20. When an application for clinical trial can be considered as a part of discovery, research and manufacture of new drug in India for applicability of 30 working days timeline for disposal of the application?

In this regard, it may be considered that discovery and research and development of the drug mentioned under this provision primarily mean discovery/innovation, research and development of new biological or chemical entity. However, it may also include discovery/innovation, research and development of novel drug delivery system of new drugs with significant improvement in terms of safety, efficacy of the delivery system over the conventional form.

21. Whether CDSCO can review clinical trial which has been considered deemed approved under the Form CT-4A and take legal action if found non-compliant to regulatory provisions?

Yes. CDSCO can review such clinical trial any time even after the timeline of 30 working days and in case of non compliance with any provision of the Act and the Rules, the CDSCO, 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:—

(i) issue warning in writing describing the deficiency or defect observed , which may affect adversely the right, or well- being of a trial subject or the validity of clinical trial conducted;

(ii) reject the results of clinical trial;

(iii) suspend for such period as considered appropriate or cancel the permission granted.

(iv) debar the investigator or the sponsor including his representatives to conduct any clinical trial in future for such period as considered appropriate by the Central Licencing Authority.

22. **Can I initiate a clinical trial straightway after deemed approval?**

No. The information to initiate clinical trial of new drug or investigational new drug shall be made required to be submitted to CDSCO in Form CT-04A duly filled and signed before initiation of the clinical trial. As per the requirement, any sponsor or investigator shall before initiating the clinical trial is required to inform the CDSCO in Form CT-4A. On the basis of the said information the CDSCO shall take on record the Form CT-4A which shall become part of the official record and shall be called automatic approval of the CLA.

23. Whether registration of clinical trial in ICMR-CTRI is mandatory?

Yes. Before enrollment of first participant in any clinical trial, registration in CTRI is mandatory.

24. Whether global clinical trial (GCT) is also required to be registered in ICMR-CTRI?

Yes, in case of multi-country trial or GCT, where India is a participating country, which have already been registered in an international registry, are also required to be registered in the CTRI. In the CTRI, details of Indian investigators, trial sites, Indian target sample size and date of enrollment are captured. After a trial is registered, applicants are expected to regularly update the trial status or other aspects in this regard.

25. What is the validity of clinical trial permission to initiate a clinical trial?

The permission to initiate clinical trial granted in Form CT-06 or automatic approval in Form CT 4A shall remain valid for a period of 2 years from the date of its issue, unless extended by the CLA.

26. What is an Interventional study?

A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.

27. What is a non-interventional / observational study?

A non-interventional / observational study means a study in which the investigator does not assign the participants to any specific interventions/treatment.

28. Whether systematic clinical study of a drug (not covered under the definition of new drug) in human beings requires permission from the CLA?

No clinical trial of new drugs shall be conducted without prior approval of CLA and new drug is defined under clause (w) of rule 2 of New Drugs and Clinical Trials Rules, 2019. A new drug is approved in respect of its composition, dosage form, indication, use, patient population etc. A new drug is approved for marketing to be used for treatment of disease in patients or in certain cases in healthy persons for prophylactic use such as vaccine. Therefore, in case the drug is truly not a new drug, in respect of composition, dosage form, indication, use, patient population etc. no permission from CLA may be required for conduct of such study of such drug in human beings. However, if such study is covered under category of observational study or non-interventional study, the same will be regulated as per the Fifth Schedule of the New Drugs and Clinical Trials Rules, 2019. Study of such drug in human beings if covered under the definition of Biomedical and Health Research, the same will be regulated as per the regulatory provisions prescribed under Chapter IV of the New Drugs and Clinical Trials Rules 2019 (to be effective after 180 days from 19-03-2019) shall be applicable.

29. What is regulatory control on observational/non-interventional study/clinical study of a drug which is not a new drug?

In case of observational/non-interventional study/clinical study of a drug which is not a new drug, no approval from the CLA is required. However, for confirmation that the study protocol is truly a protocol for an observational/non-interventional study, it is advised that the applicant should submit the protocol to the CLA and wait for its response. Otherwise, after initiation of such study without prior approval of CLA, if it is considered by CLA not to be truly an observational/non-interventional study/clinical study of a drug which is not a new drug, regulatory action as per the provisions of the New Drugs and Clinical Trials Rules, 2019 will be enforced.

30. Is any permission required from the CLA to conduct observational and non-interventional study of a new drug?

Yes. Such studies are conducted with a new drug under approved conditions of its use under a protocol approved by Central Licencing Authority with scientific objective. Inclusion or exclusion of subject are decided as per the recommended use as per prescribing information or approved package insert. In such studies the study drugs are the part of treatment of patient in the wisdom of the prescriber included in the protocol. However, the regulatory provisions and guidelines applicable for clinical trial of a new drug are not applicable in such cases as the drugs are already approved for marketing.

31. Whether prior approval of ethics committee is mandatory for submission of application and obtaining permission from CDSCO to conduct a clinical trial?

No. Submission and approval of clinical trial by Ethics Committee (EC) and CDSCO may go in parallel. However, if EC approval is available, the same should be submitted alongwith the application to CDSCO.

32. Whether ethics committee approval is mandatory to initiate a clinical trial?

Yes. Clinical trial at each site shall be initiated after the approval of the clinical trial protocol and other related documents by the Ethics Committee for that site, registered with the CLA.

33. Is ethics committee approval required for conducting clinical trial at a site?

Yes. Clinical trial shall be initiated only after approval of the trial protocol and other related documents by the ethics committee for that site, registered under rule 8.In case an Ethics Committee of a trial site rejects the approval of the protocol, the details

of the same should be submitted to the CLA prior to seeking approval of another Ethics Committee for conduct of the trial at the same site.

34. In absence of local ethics committee which Ethics committee can approve a clinical trial?

If a clinical trial site does not have its own ethics committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the ethics committee of another trial site. Provided that the approving ethics committee for clinical trial shall be responsible for the study at the trial site and the same shall be located within the same city or within a radius of 50 kms of the actual clinical trial site.

35. Whether the approval of ethics committee should be intimated to CLA?

Yes. The approval granted by the ethics committee of each site shall be intimated along with copy of such approval to the CLA within a period of 15 working days of such approval.

36. Whether the enrollment status of trial subject should be informed to CLA?

Yes. The status of enrolment of the trial subjects shall be intimated to the CLA on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier.
Further, six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted in SUGAM portal.
In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to CLA.

37. When a laboratory under clinical trial shall be deemed to be registered with CLA?

The laboratory owned by any person or a company or any other legal entity and utilized by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the CLA and may be used for test or analysis of any drug for and on behalf of CLA.

38. Can a clinical trial be initiated after two years of its approval by CLA?

No. A CLA approved clinical trials shall be initiated by enrolling the first subject within a period of 2 year from the date of grant of permission, failing which the sponsor or investigator should get prior permission from CLA before initiating the trial. **T**he permission to initiate clinical trial granted in Form CT-06 or automatic

approval in Form CT 4A shall remain valid for a period of 2 years from the date of its issue, unless extended by the CLA.

39. What is a post-trial access?

A "post-trial access" means making a new drug or investigational new drug available to a trial subject after completion of clinical trial through which the said drug has been found beneficial to the trial subject during clinical trial, for such period as considered necessary by the investigator and the ethics committee.

40. What is the procedure for providing post trial access to a clinical trial subject?

Where any investigator of a clinical trial of investigational new drug or new drug has recommended post-trial access of the said drug after completion of clinical trial to any trial subject and the same has been approved by the Ethics Committee for clinical trial, the post-trial access shall be provided by the sponsor of such clinical trial to the trial subject free of cost, —

(i) if the clinical trial is being conducted for an indication for which no alternative therapy is available and the investigational new drug or new drug has been found to be beneficial to the trial subject by the investigator; and

(ii) the trial subject or legal heir of such subject, as the case may be, has consented in writing to use post-trial investigational new drug or new drug; and the investigator has certified and the trial subject or his legal heir, as the case may be, has declared in writing that the sponsor shall have no liability for post-trial use of investigational new drug or new drug.

41. How long post trial access of a new drug can be provided to a trial patient?

This will depend on the recommendation of the Investigator and Ethics Committee, consent from the patient/legal heir and approval from CDSCO.

42. What are the regulatory actions that could be taken in case of non-compliance to the regulatory provisions for clinical trial?

If any person or institution or organization to whom permission has been granted under rule 22 in Form CT-06 or rule 23 in Form CT-4A fails to comply with any provision of the Act and these rules, the CLA 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:

(i) issue warning in writing describing the deficiency or defect observed during inspection or otherwise, which may affect adversely the right, or well- being of a trial subject or the validity of clinical trial conducted;

(ii) reject the results of clinical trial;

(iii)suspend for such period as considered appropriate or cancel the permission

granted.

(iv) debar the investigator or the sponsor including his representatives to conduct any clinical trial in future for such period as considered appropriate by the CLA.

43. Where should I make my appeal to revoke suspension of my clinical trial?

If any person or an institution or an organization to whom permission has been granted under rule 22 in Form CT-06 or rule 23 in Form CT-4A or the sponsor is aggrieved by the order of suspension of clinical trial by the CLA, the person or the institution or the organization may, within a period of 60 working days of the receipt of the order, make an appeal to the Government of India in the Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi.

44. What is a bioavailability and bioequivalence (BA/BE) study?

(i) "bioavailability study" means a study to assess the rate and extent to which the drug is absorbed from a pharmaceutical formulation and becomes available in the systemic circulation or availability of the drug at the site of action;

(ii) "bioequivalence study" means a study to establish the absence of a statistically significant difference in the rate and extent of absorption of an active ingredient from a pharmaceutical formulation in comparison to the reference formulation having the same active ingredient when administered in the same molar dose under similar conditions;

45. Whether permission from CLA is required to conduct BA/BE study of new drug and investigational new drug in human subjects?

Yes. Any person or institution or organization who intends to conduct BA/BE study of a new drug or an investigational new drug in human subjects shall obtain permission for conducting the BA/BE study from the CLA by making an application in Form CT-05. However, no permission from CLA is required for conduct of any BA/BE study in animals.

46. What are the necessary documents to be submitted for grant of permission to conduct BA/BE study in human subjects?

For grant of permission to conduct BA/BE study of any new drug or investigational new drug the application shall be accompanied by a fee as specified in Sixth Schedule and such other information and documents as specified in the Table 2 of the Fourth Schedule of the rules.

47. Is permission required to conduct a BA/BE study of a drug (not covered under the definition of new drug) in human subjects?

A new drug is approved in respect of its composition, dosage form, indication, use, patient population etc. A new drug is approved for marketing to be used for treatment of disease in patients or in certain cases in healthy persons for prophylactic use such as vaccine. Therefore, in case the drug is truly not a new drug, in respect of composition, dosage form, indication, use, patient population etc. no permission from CLA may be required for conduct of BA/BE study of such drug. However, such study will be covered under the definition of Biomedical and Health Research on Human Participants and the regulatory provisions prescribed under Chapter IV of the New Drugs and Clinical Trials Rules 2019 (to be effective after 180 days from 19-03-2019) shall be applicable.

48. Is ethics committee approval required for conducting BA/BE study in human subjects?

Yes. Such BA/BE study shall be initiated only after approval of the BA/BE study protocol and other related documents by the ethics committee for that site, registered under rule 8.

(i) in case an Ethics Committee of a BA/BE study centre rejects the approval of the protocol, the details of the same should be submitted to the CLA prior to seeking approval of another Ethics Committee for conduct of the BA/BE study at the same centre.

(ii) the approval granted by the registered Ethics Committee shall be intimated to CLA within a period of 15 working days of the grant of such approval.

49. If a BA/BE center is not having its own ethics committee, how can a BA/ BE study be initiated at that centre?

If a BA/BE study center does not have its own ethics committee at that site, it may initiate the study after obtaining approval of the protocol from the institutional ethics committee of another institution, or an independent ethics committee constituted as per rule 11. Such ethics committee shall accept the responsibility for the study at the center and shall be located within the same city or within a radius of 50 km of the study center.

50. Whether ICMR-CTRI registration is mandatory to initiate a bioavailability and bioequivalence study in human beings?

At present registration of BA/BE study of investigational new drugs in human beings with the Clinical Trial Registry of India (CTRI) is mandatory before enrolling the first subject for the study.

51. Is registration of BA/BE study centre with the CLA mandatory?

Yes. Registration of BA/BE study centers with CLA, that are involved in conduct of BA/BE study of new drugs or investigational drugs in human subjects is mandatory. Such study center shall not conduct any BA/BE study of new drugs or investigational drugs without being registered with CLA.

52. How to make an application for registration of a BA/BE study center?

Any person/sponsor or investigator who intends to conduct BA/BE study in a center should obtain registration from the CLA before initiating any such study. For the purpose of registration, an applicant shall make an application to CLA in Form CT-08 along with the informations and documents as specified in fourth schedule and fees as specified in the sixth schedule.

53. What is the timeline for processing of registration for a BA/BE study center with the CLA?

After evaluating the application in Form CT-08, the CLA may grant registration to the applicant in Form CT-09 within the period of 90 working days from the date of receipt of application. If the registration is denied for some reasons, the applicant may file an appeal within 45 days on receipt of such rejection before the Government in the Ministry of Health and Family Welfare, Nirman Bhavan, New Delhi-110011.

54. What is the validity period of registration of BA/BE study centre?

The registration granted under rule 47 in Form CT-09 shall remain valid for a period of 5 years from the date of its issue, unless suspended or cancelled by the CLA.

55. What is the procedure to renew registration of BA/BE study center?

The BA/BE center shall make an application for renewal of registration in Form CT-08 along with documents as specified in the Fourth Schedule at least 90 days prior to date of expiry of its registration.

56. Is change in ownership of BA/BE study center required to be informed to CLA?

Yes. If there is any change in constitution or ownership of the bioavailability and bioequivalence study center, the center shall intimate about the change in writing to the CLA within 30 days of such change.

57. For how long the BA/BE study data of new drug or investigational new drug is required to be maintained in BA/BE study center?

The study center shall maintain data, records, and other documents related to the conduct of the BA/BE study in human beings for a period of 5 years after completion of such study or for at least 2 years after the expiration date of the batch of the new drug or investigational new drug studied.

58. How to submit application for permission to conduct BA/BE study in human subjects from CLA?

Any person/sponsor or investigator who intend to conduct BA/BE study of new drug or investigational new drug in human subjects should application in Form CT-05 to CLA along with necessary documents specified under Table 2 of forth schedule and fees as specified under sixth schedule.

Note: No fee shall be payable for conducting a bioavailability or bioequivalence study in human subjects by an institution or organization owned or funded wholly and partially by the Central Government or a State Government.

59. What is the time line for processing of application for grant of permission to conduct BA/BE study in human subjects?

After evaluating application in Form CT-05 and submitted documents, if satisfied, that the requirements of these rules have been complied with, CLA is required to grant permission to conduct BA/BE study for a new drug or investigational new drug in Form CT-07 within 90 working days from the date of receipt of the application.

60. In case of termination of BA/BE study, should I inform CLA about the same?

Yes. In case of termination of any BA/BE study, the detailed reasons for such termination shall be communicated to the CLA within 30 working days of such termination.

61. In case of SAE or study related death, should I have to inform CLA?

(i) in case of an injury during BA/BE study of new drug or Investigational New Drug (IND) to the subject of such study, complete medical management and compensation shall be required to be provided in accordance with the Chapter VI of the Rules and details of compensation provided in such cases shall be intimated to the CLA within 30 days of the receipt of order the CLA.

(ii) In case of study related death or permanent disability of any subject, compensation shall be required to be provided in accordance with Chapter VI and

the same shall be intimated to CLA within thirty days of receipt of the order of the CLA.

62. Can I initiate study in human beings at any time after the approval of the CLA?

The BA/BE study shall be initiated by enrolling the first subject within a period of 1 year from the date of grant of permission, failing which prior permission from the CLA shall be required.

63. What action can be taken for non-compliance to the rules in conduct of BA/BE study?

Any sponsor or investigator to whom permission has been granted fails to comply with any provision of the Act and the rules, the CLA may take one or more of the following actions:

(i) issue warning in writing describing the deficiency or defect observed during inspection or otherwise, which may affect adversely the rights, or well- being of a subject enrolledin the study or the validity of bioavailability or bioequivalence study conducted;

(ii) reject the results of BA/BE study, as the case may be;

(iii) suspend for such period as considered appropriate or cancel the permission

(iv) debar the investigator or the sponsor including his representatives, to conduct any BA/BE study in future for such period as considered appropriate by the CLA.

64. How to apply for permission to manufacture new drug or investigational new drug for CT or BA/BE or for examination, test and analysis?

(i) Any person who intends to manufacture a formulation as well as API of a new drug or investigation new drug for CT or BA/BE study or for examination, test and analysis shall submit application in CT-10 for obtaining permission from the CLA to manufacture such new drug.

(ii) Any person who intends to manufacture a formulation of a new drug after obtaining API from an approved source for CT or BA/BE study or for examination, test and analysis shall submit application in CT-10 for obtaining permission from the CLA in Form CT-11to manufacture such new drug.

(iii) Any person who intends to manufacture a formulation of a new drug after obtaining API from an unapproved source for CT or BA/BE study or for examination, test and analysis shall submit application in CT-12 for obtaining permission from the CLA in Form CT-14 to manufacture such new drug. In such case, the API manufacturer is also required to submit application to CLA in

Form-CT 13 for obtaining permission in Form CT-15 to manufacture and supply the unapproved API to the formulator for development of the formulation.

(iv) Any person who intends to manufacture a formulation of an investigational new drug after obtaining the unapproved API from another manufacturer for CT or BA/BE study or for examination, test and analysis shall submit application in CT-12 for obtaining permission from the CLA in Form CT-14 to manufacture such investigational new drug. In such case the API manufacturer is also required to submit application to CLA in Form CT-13 for obtaining permission in Form-CT-15 to manufacture and supply the unapproved API to the formulator for development of the formulation.

65. Where should I submit my application for obtaining permission to manufacture new drug or investigational new drug for CT or BA/BE study?

Such application is required to be submitted to the CDSCO, HQ at FDA Bhavan, New Delhi alongwith the application for grant of permission to conduct the CT or BA/BE study, as the case may be.

66. Where should I submit my application for obtaining permission to manufacture new drug or investigational new drug only for examination, test and analysis and not for CT or BA/BE study (in human subjects)

Such application is required to be submitted to the respective Zonal/ Sub-zonal offices of CDSCO.

67. What is the validity period of permission granted in Form CT-11 /CT-14/CT-15 to manufacture a formulation or API of a new drug or an investigational new drug to conduct CT or BA/BE study or for examination, test and analysis?

The permission granted in Form CT-11/CT-14/CT-15 to manufacture a formulation or API of a new drug or an investigational new drug to conduct CT or BA/BE study or for examination, test and analysis shall remain valid for a period of 3 years from the date of its issue, unless suspended or cancelled by CLA. In exceptional circumstances the CLA may extend the period of the permission granted for a further period of 1year.

68. What I should do if a new drug manufactured under Form CT-11 /CT-14/CT-15 expires?

If the new drug manufactured for purposes of CT or BA/BE study or for examination, test and analysis is left over or remains unused or gets damaged or its specified shelf life has expired or has been found to be of sub- standard quality, the same shall be destroyed and action taken in respect thereof shall be recorded.

69. How to apply for grant of license to manufacture new drugs or investigational new drugs for CT or BA/BE study or for examination, test and analysis by SLA?

After obtaining permission in CT-11 or CT-14 or CT-15 as the case may be, the person, who intends to manufacture the new drug or investigational new drugs for CT or BA/BE study or for examination, test and analysis of new drugs or investigational new drugs, shall make an application for grant of license to manufacture the new drug or investigational new drugs by the respective State Licensing Authority (SLA) in accordance with the provisions of the Act and the Drugs and Cosmetics Rules, 1945.

70. What is the labeling a new drug or investigational new drug manufactured under Form CT-11,CT-14 & CT-15?

Any new drug or investigational new drug manufactured under Form CT-14 & Form CT-15 shall be kept in containers bearing labels, indicating the name of the drug or code number, batch or lot number, wherever applicable, date of manufacture, use before date, storage conditions, name of the institution or organization or the center where the CT or BA/BE study is proposed to be conducted, name and address of the manufacturer, and the purpose for which it has been manufactured.

71. How to import a new drug for conducting clinical trial or BA/BE study or for examination, test and analysis?

Any person or institution or organization who intends to import a new drug or any such substance for clinical trial or BA/BE study or for examination, test and analysis shall make an application in Form CT-16 to the CLA. The application shall be accompanied by a fees specified in the Sixth Schedule and such other information and documents as specified in Form CT-16.

72. Where an application for import of new drugs for CT, BA/BE study or for examination, test and analysis should be submitted?

In case of import of such drugs for CT or BA/BE study, the application in Form-CT-16 should be submitted to the CDSCO, HQ. However, in case of import of such drugs only for examination, test and analysis and not for any CT, BA/BE study, the application in CT-16 should be submitted to the respective Zonal/Sub-zonal offices of CDSCO.

73. Whether application in Form 12 under Drugs and Cosmetics Rules, 1945 can be submitted for import of new drugs for CT, BA / BE study or for examination, test and analysis?

No. For import of new drugs for CT, BA / BE study or for examination, test and analysis. The application should be submitted in Form CT 16. However, for import of a drug (not a new drug) for such purpose, the application should be submitted in Form 12 as prescribed under Drugs and Cosmetics Rules, 1945. Such applications for the purpose of examination, test and analysis are required to be submitted to the respective zonal / sub –zonal offices of CDSCO.

74. What is the timeline for disposal of application under Form CT-16?

After evaluating the Form CT-16 and documents if satisfied, that the requirements of these rules have been complied with, grant the licence to import the new drug or investigational new drug for CT or BA/BE study or for examination, test and analysis in Form CT-17 within a period of 90 working days from the date of receipt of the application.

75. What is the validity period of license granted in Form CT-17?

The license granted under rule 68 in Form CT-17 shall remain valid for a period of 3 years from the date of its issue, unless suspended or cancelled by CLA. In exceptional circumstances the CLA may extend the period of the license granted under rule 68 for a further period of 1 year.

76. Who can apply for grant of permission to import and market a new drug?

Any person/ organization having a valid wholesale license for sale and distribution of drugs under the Drugs and Cosmetics Rules, 1945 can make application to CLA for grant of permission to import the new drug.

77. How can an application for grant of permission to import a new drug be made?

Any person who intends to import a new drug in the form of API or formulation shall make application in Form CT-18 to CDSCO, FDA Bhawan, Kotla Road, New Delhi-110002 as per the relevant checklist to obtain permission in Form CT-19.
The details of the information/data required to be submitted along with the application in Form CT-18 are as under;

Sl No	Purpose	As per Schedule	Documents as per Table	Fees
1	For grant of permission to import a new drug, in the form of active pharmaceutical ingredient which is a new drug not approved earlier	Second	Table 1/4 as applicable	**as per Sixth Schedule**
2	A new drug proposed to be marketed by any person is a new drug having unapproved new molecule	Second	Table 1	**As per Sixth Schedule**
3	A new drug is proposed to be marketed which has been approved as a new drug in the country	Second	Table 2	**As per Sixth Schedule**
4	A new drug which is already permitted for certain claims, is now proposed to be marketed by any person for new claims, new indication or new dosage form or new route of administration or new strength	Second	Table 3	**As per Sixth Schedule**
5	A new drug which is a fixed dose combination	Second	Table 1 or 2 or 3, as the case may be	**As per Sixth Schedule**
6	A new phyto-pharmaceutical drugs is proposed to be manufactured/ imported	Second	Table 4	**As per Sixth Schedule**

Note:- For biological product, 'Guidance for Industry for Biotechnological / Biological Product' document should also be referred. For similar biologics, 'Guidance on Similar Biologics' document should also be referred. Both the documents are available on CDSCO website.

78. What are the provisions under which animal toxicology data requirement may be relaxed for consideration of proposal of new drug approval?

Submission of animal toxicology, reproduction studies, teratogenic studies, perinatal studies, mutagencity and carcinogenicity alongwith the application for import or manufacture of new drug, may be modified or relaxed in case of new drugs approved and marketed for more than two years in other countries, if the CLA is satisfied that there is adequate published evidence regarding the safety of the drug.

79. Under what conditions the requirement of local clinical trial for approval of a new drug already approved in other countries can be waived?

Local clinical trial waiver for approval of a new drug already approved in other countries can be considered under following conditions:

A. The new drug is approved and marketed in countries specified by the CLA under rule 101 and if no major unexpected serious adverse events have been reported, and there is no probability or evidence, on the basis of existing knowledge, of difference in Indian population of the enzymes or gene involved in the metabolism of the new drug or any factor affecting pharmacokinetics and pharmacodynamics, safety and efficacy of the new drug, and the applicant has given an undertaking in writing to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug as per design approved by the CLA

B. For import of a new drug for which the CLA had already granted permission to conduct a global clinical trial which is ongoing in India and in the meantime such new drug has been approved for marketing in a country specified under rule 101, and there is no probability or evidence, on the basis of existing knowledge, of difference in Indian population of the enzymes or gene involved in the metabolism of the new drug or any factor affecting pharmacokinetics and pharmacodynamics, safety and efficacy of the new drug, and the applicant has given an undertaking in writing to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug as per design approved by the CLA.

C. Further, in general, the requirements of non-clinical and clinical data may be relaxed, abbreviated, omitted or deferred under life threatening or serious disease conditions or rare diseases and for drugs intended to be used in the diseases of special relevance to Indian scenario or unmet medical need in India, disaster or special defense use e.g. haemostatic and quick wound healing, enhancing oxygen carrying capacity, radiation safety, drugs for combating chemical, nuclear, biological infliction etc. However, such relaxation, abbreviations, omission or deferment of data will be evaluated on case-by-case basis depending on the nature of the new drugs, proposed indication, etc.

80. Is BA / BE study required in case of manufacture of a new drug already approved and marketed in other country, where local clinical trial is waived off?

In case of an application of a new drug already approved and marketed in other countries, where local clinical trial in India which waived off or not found

scientifically justified for its approval for manufacturing first time in the country, bioequivalence studies of such drugs, as appropriate, is required to be carried out and the test batches manufactured for the purpose shall be inspected before its approval.

81. What are the conditions under which requirement of local Phase IV clinical trial, in case of approval of a new drug with local clinical trial waiver, can be relaxed?

CDSCO may relax such requirement of local Phase IV clinical trial, where the new drug is indicated in life threatening or serious diseases or diseases of special relevance to Indian health scenario or for a condition which is unmet need in India such as XDR tuberculosis, hepatitis C, H1N1, dengue, malaria, HIV, or for the rare diseases for which drugs are not available or available at a high cost or if it is an orphan drug.

82. How to apply for License to import a new drug for sale or for distribution?

After obtaining permission from CLA to import new drug for sale or for distribution the applicant shall make an application as per provisions of the Drugs and Cosmetics Rules, 1945 for grant of import license to import and market the new drug. The application shall be accompanied by the permission in Form CT-19 or Form CT-20.

83. Who can file application to CLA for grant of permission to manufacture new drugs for sale or distribution?

A person/organization having a valid drug manufacturing license for any drug issued under the Drugs and Cosmetics Act, 1940 and Rules, 1945 can file an application for grant of permission to manufacture new drugs for sale or distribution.

84. Presently, I am not a manufacturer of any drug. I want to manufacture new drug for the first time in my facility. How can I proceed?

In such case the person/organization having established a manufacturing facility can submit application to CDSCO for grant of permission to manufacture new drug for sale and distribution. However, simultaneously, he has to approach the concerned SLA and file application for grant of manufacturing license under the Drugs and Cosmetics Rules, 1945.

85. How can I submit application for grant of permission to manufacture a new drug for sale and distribution?

A person/organization who intends to manufacture new drug in the form of active pharmaceutical ingredient or pharmaceutical formulation, as the case may be, for sale or distribution, shall make an application for grant of permission to the Central

Licencing Authority in Form CT-21 along with information as specified in the Second Schedule and fee as specified in the Sixth Schedule:

Provided that no fee shall be required to be paid along with the application for manufacture of a new drug based on successful completion of clinical trials from Phase I to Phase III under these Rules in India, where fee has already been paid by the same applicant for conduct of such clinical trials.

86. Can I file application for approval of only API (bulk drug) of a new drug molecule not approved in the country?

No. An application for grant of permission to manufacture a new drug for sale or distribution in the form of active pharmaceutical ingredient having a new drug molecule not approved earlier in the country shall be required to be accompanied by an application for grant of permission to manufacture for sale or distribution of pharmaceutical formulation of the said new drug which is required for evaluation of safety and efficacy of the new drug.

87. What are the information required to be submitted along with an application in Form CT -21 for grant of permission to manufacture a new drug?

The details of the information/data required to be submitted along with the application in Form CT-21 are as under as per the laid down checklists.

Sl No	Purpose	As per Schedule	Documents required as per	Fees
1	a new drug, proposed to be manufactured, having unapproved new molecule.	Second	Table 1	**As per Sixth Schedule**
2	a new drug, proposed to be manufactured which has been approved as a new drug.	Second	Table 2	**As per Sixth Schedule**
3	a new drug which is already permitted for certain claims, is now proposed to be manufactured for new claims, namely new indication or new dosage form or new route of administration or new strength	Second	Table 3	**As per Sixth Schedule**
4	new drug which is a fixed dose combination	Second	Table 1 or 2 or 3	**As per Sixth Schedule**
5	a person who intends to market phyto - pharmaceutical drugs	Second	Table 4	**As per Sixth Schedule**

Note:- For biological product, 'Guidance for Industry for Biotechnological / Biological Product' document should also be referred. For similar biologics, 'Guidance on Similar Biologics' document should also be referred. Both the documents are available on CDSCO website.

88. What is the timeline for disposal of application in Form CT-21 for grant of permission to manufacture new drugs?

After evaluating application in Form CT-21 and documents, if satisfied, that the requirements of these rules have been complied with, the CLA grant permission to manufacture new drug, in the form of active pharmaceutical ingredient for sale or for distribution in Form CT-22 or pharmaceuticalformulation for sale or for distribution in Form CT-23, as the case may be, within a period of 90 working days from the date of receipt of its application in Form CT-21.

89. How to apply for Licence to manufacture a new drug for sale or for distribution?

After obtaining permission from CLA to import new drug for sale or for distribution the applicant shall make an application as per provisions of the Drugs and Cosmetics Rules, 1945 to the concerned SLA for grant of manufacturing license for the new drug. The application shall be accompanied by the permission in Form CT-22 or Form CT-23, as the case may be obtained in favor of the applicant.

90. Is an importer or manufacturer allowed to market a new drug for unapproved indication?

No. Under any circumstances, the manufacturer or importer of new drug cannot market a new drug for an indication not approved by CLA. No such indication should be mentioned in the package insert/ promotional literature of the new drug.

91. What is accelerated approval process for new drugs?

Accelerated approval process may be allowed to a new drug for a disease or condition, taking into account its severity, rarity, or prevalence and the availability or lack of alternative treatments, provided that there is a prima facie case of the product being of meaningful therapeutic benefit over the existing treatment.

(a) In such case, the approval of the new drug may be based on data generated in clinical trial where surrogate endpoint shall be considered rather than using standard outcome measures such as survival or disease progression, which are reasonably likely to predict clinical benefit, or a clinical endpoint. These should be measurable earlier than irreversible morbidity or mortality (IMM) and reasonably likely to predict clinical benefit.

(b) After granting accelerated approval for such drug, the post marketing trials shall be required to validate the anticipated clinical benefit.

(c) Accelerated approval may also be granted to a new drug if it is intended for the treatment of a serious or life-threatening condition or disease of special relevance to the country, and addresses unmet medical needs. This provision is intended to facilitate and expedite review of drugs so that an approved product can reach the therapeutic armamentarium expeditiously.

(d) If the remarkable efficacy is observed with a defined dose in the Phase II clinical trial of investigational new drug for the unmet medical needs of serious and life threatening diseases in the country, it may be considered for grant of marketing approval by the Central Licencing Authority based on Phase II clinical trial data. In such cases, additional post licensure studies may be required to be conducted after approval to generate the data on larger population to further verify and describe the clinical benefits, as per the protocol approved by the Central Licencing Authority.

(e) The type of information needed to demonstrate the potential of a drug to address an unmet medical need will depend on the stage of drug development. Early in development, such potential should be sufficiently demonstrated based on nonclinical models, a mechanistic rationale and pharmacologic data. Later in development, prior to new drug approval such potential should be demonstrated through clinical data to address an unmet medical need.

92. What is an unmet medical need?

An unmet medical need is a situation where treatment or diagnosis of disease or condition is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs).

93. What are the conditions under which quick or expeditious process can be sought for approval of new drugs?

i) In situation where the evidence for clinical safety and efficacy have been established even if the drug has not completed the all or normal clinical trial phases, the sponsor or applicant may apply to the Licensing authority for expedited review process wherein the Licensing authority will examine and satisfy the following conditions. -

(a) it is for a drug that is intended to treat a serious or life threatening or rare disease or condition;

(b) if approved, the drug would provide a significant advantage in terms of safety or efficacy;

(c) there is substantial reduction of a treatment-limiting adverse reaction and enhancement of patient compliance that is expected to lead to an improvement in serious outcomes;

(ii) the sponsor or applicant may also apply to the Licensing authority for expedited review process for new drugs developed for disaster or defence use in extraordinary situation, such as war time, the radiation exposure by accident or intention, sudden deployment of forces at areas with higher health risk, where specific preventive and treatment strategy is required, where new intervention in the form of new drug, route of delivery or formulation has been developed and where real life clinical trial may not be possible. The permission for manufacture of such new drug may be granted if following conditions are satisfied: -

(a) The preclinical data makes a case for claimed efficacy;

(b) there is no possibility of obtaining informed consent from the patient or his legally acceptable representative, as the case may be, adopting inclusion and exclusion criteria and strict protocol adherence by each subject;

(c) there is no established management or therapeutic strategy available as on date and proposed intervention has clear possible advantage;

(d) such approval can be used only for one time. The subsequent approval shall only be granted once detailed efficacy report of such intervention is generated.

(iii) the new drug is an orphan drug as defined in clause (x) of rule 2 of these Rules.

94. What are the requirements of data and information required for approval of new claims namely indication, dosage, dosage from, route of administration, NDDS, etc of a drug already approved by CLA? Is it same as for any unapproved new drug?

i) In case a drug already approved by the Central Licencing Authority for certain claims, which is now proposed to be clinically tried or marketed with modified or new claims, namely, indications, dosage, dosage form (including sustained release dosage form) and route of administration or novel drug delivery system (NDDS), the requirements of data and information for permission to import or manufacture of such new drug for sale or to undertake clinical trial shall depend on nature and regulatory status of the drug for the new claim in other country. Application for approval of manufacture or import of such new drug or to undertake Clinical trial may differ from application for a new drug molecule in that they allow the applicant and regulatory authority to rely at least in part, on the safety or efficacy data of drug formulation already approved. However, additional non-clinical or clinical data may be necessary to substantiate the new claims considering the following:-

(A) Chemical and pharmaceutical information will be same as prescribed in this Schedule. However, the data requirements may be omitted depending on whether the drug formulation is already approved and marketed in the country by

the applicant in the same dosage form for certain indication. If it is approved and marketed, no further chemical and pharmaceutical data is required to be submitted.

(B) The animal pharmacological and toxicological data and clinical data needed in such cases will usually be determined on case-by-case basis depending on the type of new claims being made by the applicant as well as the mechanism of action, patho-physiology of the disease or condition, safety and efficacy profile in the respective conditions or population and clinical data already generated with the drug in the approved claim. The requirements may be abbreviated or relaxed or omitted as considered appropriate by the Central Licencing Authority under following conditions:

(a) the drug is already approved and marketed in other country for the proposed new claim;

(b) clinical data supporting the benefit-risk ratio in favour of the drug in the proposed new claim is available;

(c) the clinical trial doesn't involve a route of administration, dose, patient population that significantly increases the risk associated with the use of the drug.

(ii) In case of an application for permission to undertake clinical trial of a new drug formulation, which is already approved in the country, no chemical and pharmaceutical data and non-clinical and clinical data is required to be submitted provided the clinical trial is proposed to be conducted with a new drug manufactured or imported by a firm under necessary new drug permission or import registration and license, as the case may be granted by the Central Licencing Authority.

95. How can a new drug not approved in the country be imported by Government hospital and government Medical institutions for treatment of their patients?

A medical officer of a Government hospital or a Government medical institution, may import new drug, which has not been permitted in the country under Chapter X of these rules, but approved for marketing in the country of origin for treatment of a patient suffering from life threatening disease or disease causing serious permanent disability or disease requiring therapies for unmet medical needs, by making an application duly certified by the Medical Superintendent of the Government hospital or Head of the Government medical institution, as the case may be, to the Central Licencing Authority in Form CT-24.

The application shall be accompanied by such other particulars and documents as are specified in Form CT-24 along with fee as specified in the Sixth Schedule.

96. Is there any provision for import of a new drug not approved in the country of export, even for treatment of patients by Govt. autonomous hospitals?

No. The new drug must be approved for marketing in the country of origin for import by Govt/autonomous hospitals treatment of a patient suffering from life threatening disease or disease causing serious permanent disability or disease requiring therapies for unmet medical needs, by making an application duly certified by the Medical Superintendent of the Government Hospital or Head of the Government medical institution, as the case may be, to the Central Licencing Authority in Form CT-24 and the license in this regard will be issued by CLA in Form CT 25.

97. Is there any provision for manufacture of a new drug not approved in the country even for treatment of patients by Govt./ autonomous hospitals?

There are provisions (Rules 91 -96 of the New Drugs and Clinical Trials Rules, 2019) for manufacture of a new drug not approved in the country but under clinical trial for treatment of patients by Govt. / autonomous hospitals/Govt. medical institutions.

98. How much quantity of unapproved new drug can be imported in Form CT-25 by the Govt./ Autonomous Hospitals/institutions?

The quantity of any single drug imported on the basis of license shall not exceed one hundred average dosages per patient but in exceptional circumstances the CLA may allow to import of unapproved new drugs in larger quantities depending on the condition and requirement of such patient.

99. What is the validity period of Form CT-25?

The license shall remain valid for a period of 3 years from the date of its issue.

100. Who will maintain the stock & record of the drug obtained in Form CT-25?

The registered pharmacist of the hospital/institution shall maintain a record with due countersigned by the Medical Superintendent. The Government Hospital shall submit half yearly report about the status and stock of unapproved new drugs imported, utilized and destroyed.

101. What should I do, if the shelf life of the drug obtained in Form CT-25 expires?

If the drug is left over or remains unused or gets damaged or its specified shelf life has expired or has been found to be of sub-standard quality, the same shall be destroyed and action taken shall be recorded by registered pharmacist.

102. What is the procedure to apply in Form CT-26 for permission to manufacture an unapproved new drug?

If any manufacturer intends to manufacture an unapproved new drug, he shall obtain the consent in writing from the patient to whom the drug has been prescribed or his legal heirs and make an application to the ethics committee of the Government hospital for recommendation to manufacture the drug. After obtaining the recommendation the manufacturer shall make an application in Form CT-26. The application should be accompanied by consent in writing from the patient or his legal heirs along with the fee as specified in the Sixth Schedule.

103. What is the timeline for disposal of application in Form CT-26?

After evaluating the application in Form CT-26 and other documents, if satisfied, that the requirements of these rules have been complied with, the CLA may grant permission to manufacture unapproved new drug but under clinical trial for the treatment of patient of serious or life threatening disease in Form CT-27and the permission may be granted within a period of 90 working days from the date of application.

104. How much quantity of a new drug can be imported in Form CT-27?

The quantity of any single drug imported on the basis of permission shall not exceed one hundred average dosages per patient but in exceptional circumstances the CLA may allow tomanufacture unapproved new drugs in larger on the basis of prescription and recommendation of ethics committee.

105. What is the validity period of Form CT-27?

The permission shall remain valid for a period of 1 year from the date it has been issue.

106. Who will maintain the stock & record of the drug obtained in Form CT-27?

The registered pharmacist shall maintain a record with due countersigned by the Medical Superintendent.

107. What to do, if the new drug obtained/manufactured in Form CT-27 expires?

If the drug is left over or remain unused or get damaged or its specified shelf life has expired or has been found to be of sub-standard quality, the same shall be destroyed and action taken shall be recorded by manufacturer.

108. How to obtain license for manufacture of a new the drug under Form CT-27?

After obtaining permission the person intending to manufacture an unapproved new drug shall make an application for grant of license to manufacture the new drug under the provisions of the Act and the Drugs and Cosmetics Rules, 1945, and the application shall be accompanied by Form CT-27.

109. Whether the provision of pre-submission meeting is available with CDSCO?

Yes.

110. **Who should request for pre-submission meeting with CDSCO?**

Any person who intends to make an application for grant of license or permission for import or manufacture of new drugs or to conduct clinical trial may request by making an application in writing.

111. What are the particulars to be submitted for pre-submission meeting?

This will depend on the kind of guidance required by the applicant. The applicant should submit the relevant particulars and documents referred in the Second Schedule, as available with the applicant, to support his proposal along with fee as specified in the Sixth Schedule.

112. Whether the provision of post-submission meeting is available with CDSCO?

Yes.

113. **Who should request post-submission meeting with CDSCO?**

The applicant desires to seek clarification in person in respect of pending applicationmay make an application for a post-submission meeting with the officer designated by CLA within a period of 15 days from the date the query was received for seeking guidance with regards to the queries concerning pending application.

114. How to schedule a post-submission meeting with CDSCO?

The applicant should clearly state the points on which clarification is required and the designated officer shall inform the time and date scheduled for post submission meeting. The application for post-submission meeting shall be accompanied with the fee as specified in the Sixth Schedule.

115. Whether all rules regulations applicable for clinical trial are applicable for Phase IV clinical trial?

Yes

116. **What is a post marketing surveillance study or observational or non-interventional study for active surveillance?**

Such studies are conducted with a new drug under approved conditions of its use under a protocol approved by Central Licencing Authority with scientific objective. Inclusion or exclusion of subject are decided as per the recommended use as per prescribing information or approved package insert.
In such studies the study drugs are the part of treatment of patient in the wisdom of the prescriber included in the protocol. The regulatory provisions and guidelines applicable for clinical trial of a new drug are not applicable in such cases as drugs are already approved for marketing.

117. What are the toxicity study data required to be submitted for conduct of CT of new drug or investigational new drug?

For Phase I Clinical Trials:
Systemic Toxicity studies:-

(I) Single dose toxicitystudies
(II) Dose Ranging Studies
(III) Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed humanexposure.

Male fertility study:

In-vitro genotoxicity tests, -

Relevant local toxicity studies with proposed route of clinical application (durationdepending on proposed length of clinical exposure).

Allergenicity or Hypersensitivity tests (when there is a cause for concern or forparenteral drugs, including dermal application).

Photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to anagent causing photosensitivity or the nature of action suggests such a potential).

For Phase II Clinical Trials:
Provide a summary of all the non-clinical safety data (listed above) already submittedwhile obtaining the permissions for Phase I trial, with appropriate references.

In case of an application for directly starting a Phase II trial - complete details of thenonclinical safety data needed for obtaining the permission for Phase I trial, as per the listprovided above must be submitted.
Repeat-dose systemic toxicity studies of appropriate duration to support the duration ofproposed human exposure.

In-vivo genotoxicity tests.
Segment II reproductive or developmental toxicity study (if female patients of child bearing age are going to be involved).

For Phase III Clinical Trials:
Provide a summary of all the non-clinical safety data (listed above) already submittedwhile obtaining the permissions for Phase I and II trials, with appropriate references. In caseofan application for directly initiating a Phase III trial - complete details of the non-clinical safetydata needed for obtaining the permissions for Phase I and II trials, as per the list provided abovemust be provided.
Repeat-dose systemic toxicity studies of appropriate duration to support the duration ofproposed human exposure.

Reproductive or developmental toxicity studies

Segment I (if female patients of child bearing age are going to be involved), and Segment III (for drugs to be given to pregnant or nursing mothers or where there are indications ofpossible adverse effects on foetal development).

Carcinogenicity studies (when there is a cause for concern or when the drug is to be usedfor more than 6 months).

For Phase IV Clinical Trials:
Provide a summary of all the non-clinical safety data (listed above) already submitted while obtaining the permissions for Phase I, II and III trials, with appropriate references.
In case an application is made for initiating the Phase IV trial, complete details of the non-clinical safety data needed for obtaining the permissions for Phase I, II and III trials, as per the list provided above must be submitted.
Application of Good Laboratory Practices (GLP) –
The animal studies be conducted in an accredited laboratory. Where the safety pharmacology studies are part of toxicology studies, these studies should also be conducted in an accredited laboratory

118. Whether animal toxicology study data generated as per ICH guidelines is acceptable?

Yes. While, the animal toxicology requirements as referred in clause 2 of Second Schedule should be viewed as general guidance for drug developments, animal toxicology studies may be planned, designed and conducted as per the International Council of Harmonization (ICH) guidelines to promote safe, ethical development and availability of new drugs with reduced use of animals in accordance with the 3R (reduce/refine/replace) principles.

119. What are the data required to be submitted along with the application to conduct clinical trial or import or manufacture of a new phytopharmaceutical drug?

Application for permission to conduct clinical trial or import or manufacture of a new phytopharmaceutical drug shall be accompanied with the data/information as per the Table 4 of the Second Schedule and fees as per Sixth Schedule of New Drugs & Clinical Trials Rules, 2019. For further clarification, please refer the Checklist and FAQs already available in the CDSCO website.

120. For how many days the samples of test and reference drug product of BA/BE shall be retained?

All samples of test and reference drug products used in bioavailability or bioequivalence study should be retained by the organisation carrying out the bioavailability or bioequivalence study for a period of 5 years after the conduct of the study or one year after the expiry of the drug, whichever is later.

121. What are the data required to be submitted along with the application to conduct BA/BE study of new drug or investigational new drug?

Data requirement will be as per the Table 2 of the Fourth Schedule.

122. What are the data required to be submitted along with the application to conduct BA/BE study of new drug already approved?

Data requirement will be as per the Table 3 of the Fourth Schedule.

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