CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
DIRECTORATE GENERAL OF HEALTH SERVICES
MINISTRY OF HEALTH AND FAMILY WELFARE
GOVERMENT OF INDIA

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A. INTRODUCTION

The office of Drugs Controller General (India) at CDSCO (HQ) FDA Bhawan, New Delhi receives applications from applicants requesting for the approval to carry out BA/BE studies for export purpose with various pharmaceutical dosage formulations on Indian subjects to ensure the demonstration of the safety and tolerability of generics against corresponding innovator drugs to ensure they are comparable as per requirement of concerned regulatory agencies. The assessment of 'interchangeability' between the investigational product and the innovator product is carried out by a study of "in vivo equivalence" or "bioequivalence" (BE) study.

Accordingly, the office of DCGI review the application as per New Drugs and Clinical Trial Rules, 2019 of Drugs and Cosmetics Act 1940 & Rules 1945 & Indian Good Clinical Practices (GCP) Guidelines and issue Permission in Form CT-07 and Import Licence in Form CT-17 for import of investigational product to conduct BA/BE studies to generate data for overseas registration.

Purpose: To have harmonization in the documents submitted by applicant for their applications seeking permission to conduct bioavailability/ bioequivalence study for export purpose only and for grant of license for importing the test and/or reference products to be utilized in the proposed study. This will also facilitate the reviewers to take uniform decisions and thereby shorten the application processing time.

Scope: Bioavailability and Bioequivalence studies are required by regulations to ensure therapeutic equivalence between a pharmaceutical equivalent test product and a reference product. The focus of this guidance document is for the submission of documents for getting approval to conduct bioequivalence study in human subjects for Export purpose and to import drug products (test and/or reference), if required.

Bioavailability study: 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.

Bioequivalence study: 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.

Good Clinical Practice Guidelines: Good Clinical Practice Guideline for conduct of Clinical studies in India formulated by Central Drugs Standard Control Organization (CDSCO) and adopted by Drugs Technical Advisory Board (DTAB).

New Drugs: As per New Drugs & Clinical Trial Rules, 2019,

(i) a drug, including active pharmaceutical ingredient or phytopharmaceutical drug, which has not been used in the country to any significant extent, except in accordance with the provisions of the Act and the rules made thereunder, as per conditions specified in the labelling thereof and has not been approved as safe and efficacious by the Central Licensing Authority with respect to its claims; or

(ii) a drug approved by the Central Licensing Authority 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 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 Licensing Authority; or

(v) 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;

Explanation- The drugs, other than drugs referred to in sub-clauses (iv) and (v), shall continue to be new drugs for a period of four years from the date of their permission granted by the Central Licensing Authority and the drugs referred to in sub-clauses (iv) and (v) shall always be deemed to be new drugs.

Note:- It is informed that BA/BE Division for Export deals with applications related to Drugs except Biological products.

B. APPLICATION CHECKLIST FOR FILING THE APPLICATION

All applications for BA/BE permission or acknowledgement to prior intimation for Export purpose will fall under either one of the following categories in SUGAM portal:-

1. Application acknowledgement to prior intimation for Export purpose as per the Rule 31 (2) of the New Drugs and Clinical Trial Rules, 2019 (*in case of single-dose, two-period, two-sequence, two-treatment, bioavailability or bioequivalence studies in normal healthy adult human volunteers (for export purpose only), of oral dosage form of a drug (other than drugs of Cytotoxic, Hormone, Narcotic and Psychotropic substances categories and not a drug of Narrow Therapeutic Index or a drug having highly variable pharmacokinetics) already approved in India or any one of the countries namely, United State of America, European Union, Japan, Australia, Canada and United Kingdom*).
2. Application for BA/BE Permission for Export purpose [A Drug not approved in India].
3. Application for BA/BE Permission for Export purpose [New Drugs already approved in the country]
4. Application for Import license (CT-16) for BA/BE study for Export purpose of Drugs [which are not covered under the definition of New Drug]

Firm needs to submit documents for various categories of applications (as defined above) as per the checklist below:

B.1. Application acknowledgement to prior intimation for Export purpose as per the Rule 31 (2) of the New Drugs and Clinical Trial Rules, 2019

1. Application in Form CT-05 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details.
2. Bharatkosh receipt of Rs. 2,00,000/- (Medical and Public Health Account: 0210).
3. Application in Form CT-16 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details and its detailed utilization and justification.

4. Bharatkosh receipt of Rs. 5000/- (Medical and Public Health Account: 0210) for each study drug.
5. Valid Copy of Form CT-14, issued by Central Licensing Authority and Licence in Form-29 issued by State Licencing Authority.
6. BA/BE Centre approval copy in CT-09 issued by Central Licensing Authority, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.
7. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per Table 4 of the Third Schedule along with CV & MCI Registration number.
8. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
9. Report of any study related deaths during last 3 years at BA/BE centre. If yes, the copy of intimation should be submitted.
10. Address details of the IEC location and study site location.
11. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio visual recording system as per requirements of Second Schedule.
12. Copy of approval of protocol from the Ethics Committee.
13. Copy of registration of Ethics Committee under Rule – 8 from the Central Licensing Authority.
14. The study synopsis.
15. Undertaking letter from the sponsor or applicant (if the Sponsor is a foreign entity) stating that complete medical management in accordance with Rule 40 and an undertaking letter from the sponsor stating that compensation in case of study related injury or death shall be provided in accordance with Rule 39.
16. Published reports of Pharmacokinetic and Pharmacodynamics studies carried out in healthy subjects/patients demonstrating safety and tolerability of the drug formulation / molecule.

17. Regulatory approval status of the drug indicating the strength, dosage form and countries where the drug is marketed, approved, approved as Investigational New Drug or withdrawn, if any, with reasons.
18. Copy of approval status of the Drug in India or any one of the countries namely, INDIA, USA, EU, Japan, Australia, Canada and UK.
19. Package insert/ prescribing information of the product in case the drug is approved for marketing in the country or other country.
20. Chemical and Pharmaceutical information (including stability data (minimum three months accelerated & real time).
21. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case of Oral Solid dosage forms.

B.2. Application for BA/BE Permission for Export purpose [A Drug not approved in India].

1. Application in Form CT-05 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details.
2. Bharatkosh receipt of Rs. 2,00,000/- (Medical and Public Health Account: 0210).
3. Application in Form CT-16 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details and its detailed utilization and justification.
4. Bharatkosh receipt of Rs. 5000/- (Medical and Public Health Account: 0210) for each study drug.
5. Valid Copy of Form CT-14, issued by Central Licensing Authority and Licence in Form-29 issued by State Licencing Authority.
6. BA/BE Centre approval copy in CT-09 issued by Central Licensing Authority, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations.

7. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per Table 4 of the Third Schedule along with CV & MCI Registration number.
8. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
9. Report of any study related deaths during last 3 years at BA/BE centre. If yes, the copy of intimation should be submitted.
10. Address details of the IEC location and study site location.
11. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio visual recording system as per requirements of Second Schedule.
12. Copy of approval of protocol from the Ethics Committee, if available.
13. Copy of registration of Ethics Committee under Rule – 8 from the Central Licensing Authority.
14. The study synopsis.
15. Undertaking letter from the sponsor or applicant (if the Sponsor is a foreign entity) stating that complete medical management in accordance with Rule 40 and an undertaking letter from the sponsor stating that compensation in case of study related injury or death shall be provided in accordance with Rule 39.
16. Animal pharmacological and toxicological data, Clinical Trial Data – as per Second Schedule.
17. Published reports of Pharmacokinetic and Pharmacodynamics studies carried out in healthy subjects/patients demonstrating safety and tolerability of the drug formulation / molecule.
18. Regulatory approval status of the drug indicating the strength, dosage form and countries where the drug is marketed, approved, approved as Investigational New Drug or withdrawn, if any, with reasons.
19. Restrictions on use, if any, in countries where marketed or approved.
20. Free sale certificate or Certificate of Analysis, as appropriate.

21. Package insert/ prescribing information of the product in case the drug is approved for marketing in the country or other country.
22. Chemical and Pharmaceutical information (including stability data (minimum three months accelerated & real time).
23. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case of Oral Solid dosage forms.
24. For multiple dose BE study adequate supporting safety data and PK/PD should be submitted covering the duration of period for which the study has to be conducted. For all Injectables, the sub-acute toxicity should be submitted on the Test product, studied in at least two species for minimum 14 days. If Regulatory Guidance is available, provide a copy of the same.
25. For conducting Bio-equivalence studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances and radioactive substances in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted. If regulatory guidance is available, provide a copy of the same.
26. For conducting Bio-equivalence studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances and radioactive substances in Patients a Scientific justification with special emphasis on Safety with a proper Risk Evaluation and Mitigation Strategy should be submitted.

B.3. Application for BA/BE Permission for Export purpose [New Drugs already approved in the country].

1. Application in Form CT-05 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details.
2. Bharatkosh receipt of Rs. 200000/- (Medical and Public Health Account: 0210).

3. Application in Form CT-16 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details and its detailed utilization and justification.
4. Bharatkosh receipt of Rs. 5000/- (Medical and Public Health Account: 0210) for each study drug.
5. Valid Copy of Form CT-11 issued by Central Licensing Authority and Licence in Form-29 issued by State Licencing Authority.
6. BA/BE Centre approval copy in CT-09 issued by Central Licensing Authority, along with details of number of beds provided at the centre (CRO) including ICU beds for effective handling of SAEs in emergency situations
7. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per Table 4 of the Third Schedule along with CV & MCI Registration number.
8. Sponsor's Authorization letter duly signed by the Authorized Signatory on company letterhead.
9. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio visual recording system as per requirements of Second Schedule.
10. Copy of approval of protocol from the Ethics Committee, if available.
11. Copy of registration of Ethics Committee under Rule – 8 from the Central Licensing Authority.
12. The study synopsis.
13. Undertaking letter from the sponsor or applicant (if the Sponsor is a foreign entity) stating that complete medical management in accordance with Rule 40 and an undertaking letter from the sponsor stating that compensation in case of study related injury or death shall be provided in accordance with Rule 39.
14. Report of any study related deaths during last 3 years at BA/BE centre. If yes, the copy of intimation should be submitted.
15. Address details of the IEC Location and study site location.

16. Published reports of Pharmacokinetic and Pharmacodynamics studies carried out in healthy subjects/ patients demonstrating safety and tolerability of the drug formulation.
17. Package insert/ prescribing information of the product.
18. Chemical and Pharmaceutical data including stability data (minimum three months accelerated & real time) as per Table 2 of Second Schedule.
19. Certificate of Analysis (COA) of representative batches (both Test & Reference formulations) to be used in the BE study along with dissolution profile in case of Oral Solid dosage forms.
20. For multiple dose BE study adequate supporting safety data and PK/PD should be submitted covering the duration of period for which the study has to be conducted.
21. For all injectables, the sub-acute toxicity should be submitted on the Test product, studied in at least two species for minimum 14 days. If Regulatory Guidance is available, provide a copy of the same.
22. For conducting Bio-equivalence studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances and radioactive substances in Healthy Human subjects a Scientific justification with special emphasis on Safety of subjects with a proper Risk Mitigation Strategy should be submitted. If regulatory guidance is available, provide a copy of the same.
23. For conducting Bio-equivalence studies with reference to Cytotoxic drugs, Hormonal preparations, Narcotic and Psychotropic substances and radioactive substances in Patients a Scientific justification with special emphasis on Safety with a proper Risk Evaluation and Mitigation Strategy should be submitted.

B.4. Application for Import license (Form 11) for BA/BE study for Export purpose of Drugs [which are not covered under the definition of New Drug].

1. Covering letter of the firm.
2. Regulatory status of the Drug in India indicating strength & dosage form.

3. Application in Form 12 duly signed, by the Authorized signatory with details of name and designation along with relevant drugs details and its detailed utilization and justification.
4. Bharatkosh receipt of Rs. 5000/- (Medical and Public Health Account: 0210) for each study drug.
5. The study protocols, Informed Consent Form (ICF) or Patient Information Sheet (PIS) along with audio visual recording system.
6. Copy of approval of protocol from the Ethics Committee.
7. Copy of registration of Ethics Committee under Rule – 8 from the Central Licensing Authority.
8. Undertaking by the Principal Investigator (PI) in original duly signed on a company letterhead as per Table 4 of the Third Schedule along with CV & MCI Registration number.
9. The study synopsis along with published literature for the study design.

If the study to be conducted with old drugs in healthy subject, then application shall be submitted to respective Zonal Office of CDSCO.

If the study to be conducted with old drugs in patients, then application shall be submitted to CDSCO (HQ).

Note: All above requirements are general in nature, however depending on the nature of the drug, disease and studies, further specific information may also be required to be furnished by the firm.

C. FORM CT-05 (refer rule 33):-

Application for grant of permission to conduct Bioavailability or Bioequivalence studies shall be made in Form CT-05 along with applicable fees and digitally signed by the applicant (authorized signatory) who will sponsor the study or where the study will be conducted. Refer New Drugs and Clinical Trial Rules 2019 for the format of Form CT-05 along with tooltips.

FORM CT-05

(See rule 33)

APPLICATION FOR GRANT OF PERMISSION TO CONDUCT BIOAVAILABILITY OR BIOEQUIVALENCE STUDY

I/We, ...

(name and full postal address of the applicant) of .....

..... *(**name of the authorized person, company name and full postal address along with postal code**)* hereby apply for grant of permission to conduct bioavailability or bioequivalence study (*strike off whichever is not applicable*) of new drug or investigational new drug, the details of which are as under :

1.Name of applicant:	***The name of the Firm/ Company/ Organization as per the records of MOA/ AOA/ Registrar of Companies (ROC) shall be mentioned.***
2. Nature and constitution: (proprietorship, partnership including limited liability partnership, company, society, trust, other to be specified)	***The constitution nature of the Firm/ Company/ Organization i.e. proprietorship, partnership including Limited Liability Partnership, private or public company, society, trust, other to be specified***
3. (i) Sponsor address, telephone number, mobile number, fax number and e-mail id:	***1. In case the applicant and sponsor are same for the applied product, then name and address, telephone number, mobile number, fax number and e-mail id.*** ***2. The name and address of the applicant authorised by the sponsor, in case of CRO with its address, telephone number, mobile number, fax number and e-mail id.***
(ii) Study address, telephone number, mobile number, fax number and e-mail id:	***The name and address of the BA/BE study site proposed by the applicant shall be mentioned including telephone number, mobile number, fax number and e-mail id***
(iii) Address for correspondence: [corporate or registered office or bioavailability or bioequivalence study centre]	***The Corporate or Registered office address of Organization responsible for managing BA/BE study including telephone number, mobile number, fax number and e-mail address of the firm shall be specified for correspondence.***

4. Details of new drug or investigational new drug and study centre [As per Annexure].
5. Study protocol number with date: ***The details of Protocol no., Version no. and date shall be mentioned.*** ***If the protocol is revised, then firm shall submit the revise CT 05 mentioning the final version of the protocol.***
6. Fee paid on _____Rs._____ Receipt or challan or transaction ID ._____. ***Bharat Kosh Payment receipt/challan/transaction id details. The firm shall capture the details of the challan fee idin the legal Form CT 05same as the Bharat Kosh Payment receipt/challan/transaction id enclosed.***
7. I have enclosed the documents as specified in the Fourth Schedule of the New Drugs and Clinical Trials Rules,2019. ***Firm should ensure that the documents enclosed are complete in all aspects as per the checklist refereeing Fourth Schedule of the New Drugs and Clinical Trials Rules,2019.***
8. I hereby state and undertake that: (i) I shall comply with all the provisions of the Drugs and Cosmetics Act, 1940, and the New Drugs and Clinical Trials Rules, 2019.

Place: …….
Date: …….....

Digital Signature
(Name and designation)

(Digital signature of the authorsied person stated above should sign herein with his name, designation and company name)

Annexure:

Details of new drug or investigational new drugs:

Names of the new drug or investigational new drug:	***Names of the new drug shall be mentioned as generic name*** ***OR*** ***investigational new drug with INN code/ chemical name/ product codeof the product shall be mentioned and not a trademark or product brand name.***
Therapeutic class:	***Therapeutic class for the proposed drug***
Dosage form:	***Details of Dosage form shall be mentioned for*** ***eg. Oral Tablets-*** *IR, Modified release/ PR/ER/SR tablets, bilayered tablets)****,*** ***Capsules-*** *Hard/ Soft gelatin* ***Topical use-*** *gel/ lotion, transdermal patches****,*** ***Injection-****Lyophillized powder for injection, Liquid*

	injection, liposomal drug delivery systems, Nanosomal drug delivery systems, Suspension for injection ***Metered dose Inhalers, Dry powder inhalation, ORAL-*** *Syrup, suspension, granules for oral suspension, modified release/ nanosomal suspension etc.*
Composition:	***Composition of the formulation including details of excipients & its quantity as per proposed label. It should specify the content of drug per unit dosage form, each 5ml, each ml etc.***
Indications:	***Detail of Indications for which CT is proposed shall be mentioned.***

Details of study centre:

Names and address of study centre	***Name and address of the BABE Study centre for Clinical facility and bio-analytical facility. ****
Ethics committee details:	***Name and address of the Ethics Committee with details of Ethics Committee Registration number. ****

**** Further, in case of Multi-centric studies, details of the Study Center / Site along with Ethics Committee details should be listed.***

D. FORM CT-16 (refer rule 67):

An application for grant of licence to import New Drug for Clinical Trial or Bioavailability or Bioequivalence study or for examination, test and analysis, shall be made in Form CT-16 and digitally signed by the applicant (authorized signatory) who will sponsor the study or where the study will be conducted. Refer New Drugs and Clinical Trial Rules 2019 for the format of Form CT-16.

FORM CT-16

(See rule 67)

APPLICATION FOR GRANT OF LICENCE TO IMPORT NEW DRUG OR INVESTIGATIONAL NEW DRUG FOR CLINICAL TRIAL OR BIOAVAILABILITY OR BIOEQUIVALENCE STUDY OR FOR EXAMINATION, TEST AND ANALYSIS

I/We, ...*(name and address of the applicant)* of M/s .... *(**name of the authorized person, company name and full postal address along with postal code**)* hereby apply for grant of licence to import new drug or investigational new drug for clinical trial bioavailability or bioequivalence study or for examination, test and analysis.

The details of the application are as under:

1. Name of applicant:	***The name of the Firm/ Company/ Organization as per the records of MOA/ AOA/ Registrar of Companies (ROC) and registered with IT cell CDSCO shall be mentioned.***
2. Nature and constitution of applicant: (proprietorship, partnership including limited liability partnership, company, society, trust, other to be specified)	***The constitution nature of the Firm/ Company/ Organization i.e. proprietorship, partnership including Limited Liability Partnership, private or public company, society, trust, other to be specified***
3.(i) Corporate or registered office address including telephone number, mobile number, fax number and e-mail id:	***3. In case the applicant and sponsor are same for the applied product, then name and address, telephone number, mobile number, fax number and e-mail id.*** ***4. The name and address of the applicant authorised by the sponsor, in case of registered CRO with its address, telephone number, mobile number, fax number and e-mail id.*** ***The address shall be same as registered with IT cell of CDSCO.***
(ii) Applicant's address including telephone number, mobile number, fax number and e- mail id:	***The name and address of the BA/BE study site proposed by the applicant shall be mentioned including telephone number, mobile number, fax number and e-mail id and the address shall be same as registered with IT cell of CDSCO.***
(iii) Address for correspondence:	***The Corporate or Registered office address of Organization responsible for managing BA/BE study including telephone number, mobile number, fax number and e-mail address of the firm shall be specified for correspondence.***
4. Details of new drugs to be imported [As per Annexure]. ***The firm needs to submit details of the drug with dosage form and dose.***	
5. Particulars of overseas Manufacturer, Manufacturing sites [As per Annexure]. ***The details of Protocol no., Version no. and date shall be mentioned.*** ***If the protocol is revised, then firm shall submit the revise CT 05 mentioning the final version of the protocol.***	
6. Fee paid on _____Rs_____ receipt or challan or transaction ID _____. ***Bharat Kosh Payment receipt/challan/transaction id details. The firm shall capture the details of the challan fee idin the legal Form CT 05same as the Bharat Kosh Payment receipt/challan/transaction id enclosed.***	

7. I hereby state and undertake that: (i) I shall comply with all the provisions of the Drugs and Cosmetics Act, 1940 and Chapter IX of the New Drugs and Clinical Trials Rules, 2019. (ii) The new drug to be imported from M/s..... shall be used exclusively for the purpose of clinical trial and no part of it shall be diverted to the domestic market.

Place: …….
Date: …….....

Digital Signature
(Name and designation)

(Sugam generated and Digitally signed by the authorsied person stated above with his name, designation and company name)

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug:	***Names of the new drug shall be mentioned as generic name OR investigational new drug with INN code/ chemical name/ product codeof the product shall be mentioned and not a trademark or product brand name.***
Therapeutic class:	***Therapeutic class for the proposed drug***
Dosage form:	***Details of Dosage form shall be mentioned for eg. Oral Tablets- IR, Modified release/ PR/ER/SR tablets, bilayered tablets), Capsules- Hard/ Soft gelatin Topical use- gel/ lotion, transdermal patches, Injection-Lyophillized powder for injection, Liquid injection, liposomal drug delivery systems, Nanosomal drug delivery systems, Suspension for injection Metered dose Inhalers, Dry powder inhalation, ORAL- Syrup, suspension, granules for oral suspension, modified release/ nanosomal suspension etc.***
Composition:	***Composition of the formulation including details of excipients & its quantity as per proposed label. It should specify the content of drug per unit dosage form, each 5ml, each ml etc.***
Indications:	***Detail of Indications for which CT is proposed shall be mentioned.***

Details of manufacturer and manufacturing site:

Name and address of manufacturer (full address with telephone, fax and e-mail address of the manufacturer)	***The firm needs to submit Name and address of manufacturer (full address with telephone, fax and e-mail address of the manufacturer)***
Name and address of manufacturing site (full address with telephone, fax and e-mail address of the manufacturing site)	***The firm needs to submit Name and address of manufacturing site (full address with telephone, fax and e-mail address of the manufacturing site)***

**** Further, in case of Multi-centric studies, details of the Study Center / Site along with Ethics Committee details should be listed.***

FORM 12
(See rule 34 of Schedule Y)

Application for licence to import drugs for purpose of examination, test or analysis I,… ……***(name and address of the applicant)*** ……resident of ……***(name of the authorized person, company name and full postal address along with postal code)*** ……. by occupation……(***occupation of the applicant)*** ……. hereby apply for a licence to import the drugs specified below for the purposes of examination, test or analysis at ***…….(name of the proposed site)***.....from.....(***name of the importer country)……***and I undertake to comply with the conditions applicable to the licence.

1 [A fee of rupees..... has been credited to Government under the head of Account —0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines‖ under the Drugs and Cosmetics Rules, 1945—Central vide Challan No…….dated……(attached in original).]

Name of drugs	Quantities which may be imported
Names of the new drug shall be mentioned as generic name OR investigational new drug with INN code/ chemical name/ product code of the product shall be mentioned and not a trademark or product brand name.	***Proposed quantity***

Place……..
Date……

Signature
signed by the authorsied person stated above with his name, designation and company name)

- **Payment of application Fee:-**The fees prescribed under these rules, in case of application made in Form CT-05, Form CT-16 & Form 12 to the Central Licensing Authority, shall be paid through online Bharatkosh only.

E. UTILIZATION/JUSTIFICATION OF THE QUANTITY REQUIRED TO BE IMPORTED FOR BA/BE STUDY

Quantities of drugs required to be imported under Form CT-17 licence should be justified. Utilization/justification should be duly signed by the Authorized Signatory. The detailed utilization break up for quantity of drug product mentioned in Form CT-16/Form 12 shall be submitted.

F. REPLIES IN RESPONSE TO QUERIES

Upon review of submitted online application, the query will be issued with respect to deficiency. **In response to the query, firm shall submit reply in proper manner within 30 days from the date of receipt of query issued by this Directorate. If no reply is received within the stipulated time, the necessary action as per the provision of New Drugs & Clinical Trial Rules, 2019 will be initiated.**

G. APPLICATION FOR POST APPROVAL CHANGES (AMENDMENT / NOTIFICATION) IN ALREADY ISSUED BA/BE PERMISSION FOR EXPORT PURPOSE

Applicant shall apply for amendment if there is any change in proposed study, for which permission to conduct BA/BE Study in Form CT-07 & Licence to import New Drugs in Form CT-17 *and licence to import old drug for patient studies in* Form 11 has already been issued by this Directorate. The criteria for post approval changes are as follows:-

Major Changes:

1. Change of study site.
2. Transfer of BA/BE Permission from one CRO to another CRO.
3. Transfer of BA/BE Permission from CRO to Sponsor.
4. Change of Principal Investigator.

5. Site addition/ deletion with respect to patient studies.
6. Change in study protocol with respect to change in study design, study treatment, Dosage Form, composition, study periods, change in laboratory parameters (safety) and other changes viz. increase in number of study subjects, increase in volume of blood sample collection, increase in total blood loss, increase in sampling time points for PK parameters etc.
7. Change in Bio analytical site.
8. Change in reference product/ brand name/ manufacturer details etc.
9. Change in Import License in Form CT-17/Form 11 e.g. quantity to be imported, change in details of manufacturer & manufacturing site, country from where drug would be imported, change in pack size etc.
10. Change in Ethics Committee.
11. Any other changes that may affect subject/ patient safety.

Minor Changes:

1. If there is reduction in number of subjects, total blood loss & sampling frequency.
2. Correction of minor typographical error in study related documents-Protocol, ICF.
3. Any other changes that may not affect the subject/ patient safety.

Note: The application for transfer of BE Permission from one CRO to another CRO and from CRO to Sponsor, shall be accompanied by adequate fee as per New Drugs & Clinical Trial Rules, 2019.

Documents required for submission of amendments:

(i) Copy of earlier issued BE Permission / Form CT-07.
(ii) List of changes in tabular form along with detailed rationale / justification for the changes made.
(iii) Copy of Revised protocol/ ICF, if applicable,
(iv) Other relevant document on case to case basis along with justification etc.

Note: Firm shall obtain amendment approval from this Directorate for Major Changes and submit notification for the Minor Changes and obtain acknowledgement letter, before initiation of the study.

Documents to be submitted before initiation of study:

- Conditions which are mentioned in the issued BE Permission, to be submitted before initiation of the study.
- Accelerated and Real time stability data sufficient to cover storage, shipment and uses of Investigational product.
- COA of test product for the batch on which, proposed study is to be conducted.
- Any other document, as committed by the firm at the time of submission of the application, based on which BE Permission had been issued.

Note to Applicant:

Firm need to submit annual status of the permission issued, study conducted and final outcome of the study to this Office.

H. NOTE TO APPLICANT:

Application for grant of BE-Permission for export purpose may not be considered in following cases:

(i) Inadequate safety data in healthy subjects/ patients, as applicable.

(ii) Drug (molecule) falling under Narcotic Drugs and Psychotropic Substances (NDPS) not approved in India.

(iii) Study Protocols with different study design in single application.

(iv) Inadequate documents with respect to applicable checklist.

I. ABBREVIATIONS:

BA: Bioavailability
BE: Bioequivalence
CLA: Central Licensing Authority
COA: Certificate of Analysis
CRO: Contract Research Organization
CV: Curriculum Vitae
DCG (I): Drugs Controller General (India)

IEC: Independent/Institutional Ethics Committee
ICF: Informed Consent Form
ICU: Intensive Care Unit
GCP: Good Clinical Practices
MCI: Medical Council of India
PI: Principal Investigator
PIS: Patient Information Sheet
PK/PD: Pharmacokinetics/Pharmacodynamics