

## INDEX

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## 1. APPLICATIONS FOR INVESTIGATIONAL NEW DRUGS (INDs)

#	Documents required to be submitted	Status	
		Yes	No
1	Application for (permission for manufacture /import/clinical trial – purpose should be clearly mentioned)		
2	Name of the applicant		
3	Name of the New Drug		
	a. Composition of the New Drug		
	b. Dosage Form		
	c. Proposed indication for the New Drug		
4	Application in Form 44 complete in all respect duly signed and stamped by authorized person of the firm		
5	Treasury Challan of INR 50,000 (for Phase I) or INR 25,000 (for Phase II / III)		
8	Copy of valid manufacturing license in Form 25/28 along with copy of form 29		
9	Source of bulk drugs.		
10.	Information on active ingredients		
	a) Physiochemical data (Chemical name and Structure, Physical properties etc.)		
	b) Analytical data (elemental analysis, NMR spectrum, IR Spectrum, UV spectrum etc.)		
	c) Complete monograph specification including identification, identity/quantification of impurities, enantiomeric purity, assay etc.)		
	d) Certificate of analysis		
	e) Validation [assay method, impurity estimation method, residual solvent/other volatile impurities(OVI) estimation method]		
	f) Reference standard characterization,		
	g) Material safety data sheet.		
11	Data on Formulation:		
	a) Details on Dosage Form		
	b) Master manufacturing formula		
	c) Details of the formulation (including inactive ingredients)		
	d) Finished product specification		
	e) In process quality control check		
	f) Excipient compatibility study		
	g) Validation of analytical method		

	h) Certificate of analysis including identification, pH, content uniformity, impurities, assay etc.		
	i) Dissolution data in case of oral dosage forms as appropriate		
	j) Stability study evaluation as per requirements of schedule Y		
<b>12</b>	<b>Animal Pharmacology including summary of the study, general pharmacological actions, specific pharmacological actions, follow-up and supplemental safety Pharmacology Studies, Pharmacokinetics including absorption, distribution; metabolism; excretion</b>		
<b>13</b>	<b>Animal toxicology data as per Schedule Y.</b>		
	<b>a. systemic toxicity studies,</b>		
	<b>i. single dose toxicity</b>		
	<b>ii. repeated dose toxicity</b>		
	<b>b. Male Fertility Study</b>		
	<b>c. Female Reproduction and Developmental Toxicity Studies (for all drugs proposed to be studied or used in women of child bearing age)</b>		
	<b>d. Local toxicity</b>		
	<b>i. Dermal toxicity (for products meant for topical (dermal) application)</b>		
	<b>ii. Ocular toxicity (for products meant for ocular instillation)</b>		
	<b>iii. Inhalation toxicity (conducted with the formulation proposed to be used via inhalation route)</b>		
	<b>iv. Vaginal toxicity (for products meant for topical application to vaginal mucosa)</b>		
	<b>v. Photoallergy or dermal phototoxicity (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential)</b>		
	<b>vi. Rectal tolerance test (For all preparations meant for rectal administration)</b>		
	<b>e. Genotoxicity</b>		
	<b>f. Allergenicity/Hypersensitivity</b>		
	<b>g. Carcinogenicity (Carcinogenicity studies should be performed for all drugs that are expected to be clinically used for more than 6 months as well as for drugs used frequently in an intermittent manner in the treatment of chronic or recurrent conditions. However, completed rodent carcinogenicity studies are not needed in advance of the conduct of large scale clinical trials, unless there is a special concern for the patient population)</b>		
	<b>Reports of following toxicity studies should be submitted alongwith clinical trial applications of different Phases for INDs:</b>		

**For Phase I Clinical Trials**

- Systemic Toxicity studies
  - (i) Single dose toxicity studies
  - (ii) Dose Ranging Studies
  - (iii) Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure.
- Male fertility study
- In-vitro genotoxicity tests
- Relevant local toxicity studies with proposed route of clinical application (duration depending on proposed length of clinical exposure)
- Allergenicity/Hypersensitivity tests (when there is a cause for concern or for parenteral drugs, including dermal application)
- Photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent 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 submitted while 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 the non-clinical safety data needed for obtaining the permission for Phase I trial, as per the list provided above must be submitted.
- Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure
- In-vitro and In-vivo genotoxicity tests.
- Segment II reproductive/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 submitted while obtaining the permissions for Phase I and II trials, with appropriate references.
- In case of an application for directly initiating a Phase III trial - complete details of the non-clinical safety data needed for obtaining the permissions for Phase I and II trials, as per the list provided above must be provided.
- Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure
- Reproductive/developmental toxicity studies
- In-vitro and In-vivo genotoxicity tests.
- 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

	<p>where there are indications of possible adverse effects on foetal development).</p> <ul style="list-style-type: none"> <li>• Carcinogenicity studies (when there is a cause for concern or when the drug is to be used for more than 6 months).</li> </ul>		
<b>14</b>	<b>Human / Clinical pharmacology (Phase I) including summary of the study and reports</b>		
	<b>i. Summary</b>		
	<b>ii. Specific Pharmacological effects</b>		
	<b>iii. General Pharmacological effects</b>		
	<b>iv. Pharmacokinetics, absorption, distribution, metabolism, v. excretion</b>		
	<b>vi. Pharmacodynamics / early measurement of drug activity</b>		
<b>15</b>	<b>Therapeutic exploratory trials (Phase II) including summary of the study and reports</b>		
<b>16</b>	<b>Therapeutic confirmatory trials (Phase III) including summary of the study and individual study reports with listing of sites and Investigators.</b>		

## **17. STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL TRIAL PROTOCOL**

#	Documents required to be submitted	Status	
		Yes	No
1.	Title Page		
2.	Table of Contents		
3.	Study Objective(s) (primary as well as secondary) and their logical relation to the study design.		
4.	Study Design		
5.	Study Population		
6.	Subject Eligibility - Inclusion Criteria and Exclusion Criteria		
7.	Study Assessments		
8.	Study Treatment		
9.	Adverse Events		
10.	Ethical Considerations		
11.	Study Monitoring and Supervision		
12.	Study Monitoring and Supervision		
13.	Investigational Product Management		
14.	Data Analysis		
15.	Undertaking by the Investigator: This shall include all the details / elements as mentioned in the Appendix VII of Schedule-Y.		
16.	Informed consent documents (patient information sheet, informed consent form etc.) as per Appendix V of Schedule-Y should mention the following: "In case of study related injury or death M/s. «NAME OF THE COMPANY» will provide complete medical care along with compensation for the injury or death".		

**18. STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL STUDY REPORTS**

#	Documents required to be submitted	Status	
		Yes	No
1.	Title Page		
2.	Study Synopsis		
3.	Statement of compliance with the 'Guidelines for Clinical Trials on Pharmaceutical Products in India		
4.	List of Abbreviations and Definitions		
5.	Table of contents		
6.	Copy of Ethics Committee approval		
7.	Study Team		
8.	Introduction		
9.	Study Objective		
10.	Investigational Plan		
11.	Trial Subjects		
12.	Efficacy evaluation		
13.	Safety Evaluation		
14.	Discussion and overall Conclusion		
15.	List of References		

**Note:**

1. All items mentioned above may not be applicable to all drugs. The items not relevant to a particular new drug should be marked with "Not Applicable (NA)".

2. In case the application is for clinical trial permission :-

- (a) adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available
  
- (b) In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated alongwith justification / reasons for the change.
  
- (c) **Ethics Committee Approval:** Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
  
- (d) The proposed clinical trial study centers should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

**2. CHECKLIST FOR ACCEPTABILITY OF APPLICATION PERTAINING TO GRANT OF PERMISSION TO IMPORT OR MANUFACTURE NEW DRUGS GOING TO BE INTRODUCED FOR THE FIRST TIME IN THE COUNTRY FOR SALE OR TO UNDERTAKE CLINICAL TRIALS**

#	Documents required to be submitted	Status	
		Yes	No
1	<b>Application for permission to import or manufacture new drugs for sale or to undertake clinical trials</b> - Purpose should be clearly mentioned.		
	a. Name of the applicant		
	b. Name of the New Drug		
	c. Composition of the New Drug		
	d. Proposed indication		
2	<b>Application in Form 44</b> should be complete in all respect and signed by the authorized person of the firm with name and designation		
3	<b>Treasury Challan of Rs.50,000</b> and should mention the name of the New Drug including correct head of the account, payable at, bank clearance, etc.		
4	<b>Copy of valid manufacturing license in Form 25/28 along with copy of Form 29</b>		
5	<b>Source of bulk drugs</b> a) In-house b) Other than in-house. If source is other than in-house, a copy of consent letter from manufacturer of the bulk drug should be submitted and the manufacture of the bulk drug should also file application for the bulk drug.		
6	<b>Information on active ingredients</b>		
	a) Physiochemical data (Chemical name and Structure, Physical properties etc.)		
	b) Analytical data (elemental analysis, NMR spectrum, IR Spectrum, UV spectrum etc.)		
	c) Complete monograph specification including identification, identity / quantification of impurities, enantiomeric purity, assay etc.)		
	d) Certificate of analysis		
	e) Validation [assay method, impurity estimation method, residual solvent/other volatile impurities(OVI) estimation method]		
	f) Reference standard characterization,		
	g) Material safety data sheet.		
7	<b>Data on Formulation:</b>		
	a) Master manufacturing formula		
	b) Details of the formulation (including inactive ingredients)		
	c) Finished product specification		
	d) In process quality control check		

	e) Excipient compatibility study		
	f) Process validation		
	g) Validation of analytical method		
	h) Certificate of analysis including identification, pH, content uniformity, impurities, assay etc.		
	i) Dissolution data in case of oral dosage forms as appropriate		
	j) Stability study evaluation as per requirements of schedule Y		
<b>8</b>	<b>Animal Pharmacology</b> including summary of the study, general pharmacological actions, specific pharmacological actions, follow-up and supplemental safety Pharmacology Studies, Pharmacokinetics including absorption, distribution; metabolism; excretion		
<b>9</b>	<b>Animal toxicology data as per Schedule Y.</b>		
	<b>h. Systemic toxicity studies,</b>		
	i. single dose toxicity		
	ii. repeated dose toxicity		
	<b>i. Male Fertility Study</b>		
	<b>j. Female Reproduction and Developmental Toxicity Studies</b> (for all drugs proposed to be studied or used in women of child bearing age)		
	<b>k. Local toxicity</b>		
	<b>vii. Dermal toxicity</b> (for products meant for topical (dermal) application)		
	<b>viii. Ocular toxicity</b> (for products meant for ocular instillation)		
	<b>ix. Inhalation toxicity</b> (conducted with the formulation proposed to be used via inhalation route)		
	<b>x. Vaginal toxicity</b> (for products meant for topical application to vaginal mucosa)		
	<b>xi. Photoallergy or dermal phototoxicity</b> (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential)		
	<b>xii. Rectal tolerance test</b> (For all preparations meant for rectal administration)		
	<b>l. Genotoxicity</b>		
	<b>m. Allergenicity/Hypersensitivity</b>		
	<b>n. Carcinogenicity</b> (Carcinogenicity studies should be performed for all drugs that are expected to be clinically used for more than 6 months as well as for drugs used frequently in an intermittent manner in the treatment of chronic or recurrent conditions. However, completed rodent carcinogenicity studies are not needed in advance of the conduct of large scale clinical trials, unless there is a special concern for the		

	patient population)		
<b>10</b>	<b>Human / Clinical pharmacology (Phase I) including summary of the study and reports</b>		
<b>11</b>	<b>Therapeutic exploratory trials (Phase II)</b>		
<b>12</b>	<b>Therapeutic confirmatory trials (Phase III).</b>		
<b>13</b>	<b>Regulatory status in other countries, as appropriate.</b>		
	a) Names of the countries where the drug is marketed / approved along with package insert circulated in those countries and since when it is marketed in those countries. <i>Specific names of countries where the drug is marketed should also be mentioned in the covering letter.</i>		
	b) Names of the countries where the drug is withdrawn, if any, with reasons ( Information in respect of restrictions imposed, if any, on the use of the drug in other countries, e.g. dosage limits, exclusion of certain age groups, warning about adverse drug reactions etc.)		
	c) In case import of drug, Free sale certificate (FSC) or Certificate of Pharmaceutical Product (COPP), as appropriate.		
<b>14</b>	<b>Copy of proposed prescribing information.</b> The prescribing information (package insert) shall comprise the following sections: generic name; composition; dosage form/s, indications; dose and method of administration; use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.); contra-indications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.		
<b>15</b>	<b>Proposed Draft specimen of the label and carton.</b> The drafts of label and carton texts should comply with provisions of Rules 96 and 97.		
<b>16</b>	If the study drug is intended to be imported for the purposes of examination, test or analysis, the application for import of small quantities of drugs for such purpose should also be made in Form 12.		

**17. STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL TRIAL PROTOCOL:**

#	Documents required to be submitted	Status	
		Yes	No
1.	Title Page		
2.	Table of Contents		
3.	Study Objective(s) (primary as well as secondary) and their logical relation to the study design.		
4.	Study Design		
5.	Study Population		
6.	Subject Eligibility - Inclusion Criteria and Exclusion Criteria		
7.	Study Assessments		
8.	Study Treatment		
9.	Adverse Events		
10.	Ethical Considerations		
11.	Study Monitoring and Supervision		
12.	Study Monitoring and Supervision		
13.	Investigational Product Management		
14.	Data Analysis		
15.	Undertaking by the Investigator: This shall include all the details / elements as mentioned in the Appendix VII of Schedule-Y.		
16.	Informed consent documents (patient information sheet, informed consent form etc.) as per Appendix V of Schedule-Y should mention the following: "In case of study related injury or death M/s. (NAME OF THE COMPANY) will provide complete medical care along with compensation for the injury or death".		

**18. Protocol of Bioequivalence study along with Informed Consent document and undertaking by Investigator in case of Oral Dosage Forms having systematic absorption. In case of biowaiver, justification should be submitted.**

**19. STRUCTURE, CONTENTS AND FORMAT FOR CLINICAL STUDY REPORTS:**

#	Documents required to be submitted	Status	
		Yes	No
1.	Title Page		
2.	Study Synopsis		
3.	Statement of compliance with the 'Guidelines for Clinical Trials on Pharmaceutical Products in India		
4.	List of Abbreviations and Definitions		
5.	Table of contents		
6.	Copy of Ethics Committee approval		
7.	Study Team		
8.	Introduction		
9.	Study Objective		
10.	Investigational Plan		
11.	Trial Subjects		
12.	Efficacy evaluation		
13.	Safety Evaluation		
14.	Discussion and overall Conclusion		
15.	List of References		

**Note:**

1. All items mentioned above may not be applicable to all drugs. The items not relevant to a particular new drug should be marked with “Not Applicable (NA)”.
2. Application for both bulk as well as formulation is required to be submitted. Proposal for grant of permission to manufacture only bulk drug will be considered after approval of it's formulation.
3. In case the application is for clinical trial permission:
  - a. Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.
  - b. In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated along with justification / reasons for the change.
  - c. Ethics Committee Approval: Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
  - d. The proposed clinical trial study centres should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

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### 3. Application for Global Clinical Trial

<u>CONTENT</u>	<u>YES</u>	<u>NO</u>
1. Name of the Applicant:-		
2. Name of the Sponsor:-		
3. Authorisation Letter from Sponsor:-		
4. Treasury Challan along with Form 44 (amount):-		
5. Treasury Challan along with Form 12 (amount):-		
6. Name of the Study Drug:-		
7. Dosage form:-		
8. Therapeutic class:-		
9. Study Protocol:- Phase of Study:-		
10. Undertaking by the Investigators as per Appendix VII of Schedule 'y' :- (Ethics Committee should be of same area where the site is located and details of the committee should be mentioned)		
11. Patient Information Sheet (PIS)/ Informed consent form (ICF) as per Appendix V of Schedule 'y' :- The following clause should be added "In case of study related injury or death, M/s (applicant) will provide complete medical care along with compensation for the injury or death".		
12. Justification for conducting the study in India:-		
13. Details of Export of Biological Samples:-		
14. Application for Export NOC for biological samples:-		
15. List of Investigators in India including site Address:-		
16. Name of the Participating Countries:-		
17. Total Number of patients to be enrolled globally:-		
18. Total Number of patients to be enrolled in India:-		
19. Status of Drug in India & other countries:-		
20. Status of the proposed study in other participating countries:-		
21. If any Clinical trial of the Investigational Product has been Withdrawn/discontinued in any country or rejected/refused by any Regulatory Agency if so details of the same.		
22. Approvals of the proposed protocol from other participating countries (Notification to USFDA and IRB Approvals in case USA is a participating country).		
23. Ethics Committee approvals if available:- (Ethics Committee should be of same area where the site is located.)		
24. Investigators Brochure:-		
25. Investigational Medicinal Products Dossier (IMPD):-		
<u>25 (a) Information on active ingredients:</u> <u>Drug information (Generic Name, Chemical Name or INN) &amp; Physicochemical</u> <u>Data including:</u> i. Chemical name and Structure - Empirical formula, Molecular weight		

ii. Analytical Data: Elemental analysis, Mass spectrum, NMR spectra, IR spectra, UV spectra, Polymorphic identification		
iii. Stability Studies: Data supporting stability in the intended container closure system for the duration of the clinical trial.		
iv. Certificate of Analysis (COA):- Note: While adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.		
<u>25 (b) Data on Formulation:</u>		
i. Dosage form		
ii. Composition		
iii. Master manufacturing formula		
iv. Details of the formulation (including inactive ingredients)		
v. In process quality control check		
vi. Finished product specification & Method of Analysis		
vii. Certificate of analysis		
viii. Excipient compatibility study		
ix. Validation of the analytical method.		
x. Stability Studies: Data supporting stability in the intended container closure system for the duration of the clinical trial. Note: While adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.		
26 Affidavit declaring that the information about study drug as mentioned in Investigators Brochure is correct and based on available facts:-		
27 Affidavit declaring that the study has not been discontinued in any country. In case of discontinuation the reasons for such a discontinuation would be communicated:-		
Technical Documents:- 1) Package Insert:- (if the drug is marketed in any country		

<p>2) Pre-clinical Data:-</p> <p>I. Animal Pharmacological Data:-</p> <ul style="list-style-type: none"> <li>▪ Summary</li> <li>▪ Specific pharmacological actions</li> <li>▪ General pharmacological actions</li> <li>▪ Follow-up and Supplemental Safety Pharmacology Studies</li> <li>▪ Pharmacokinetics: absorption, distribution; metabolism; Excretion</li> </ul>		
<p><b>II. Animal toxicology data as per Schedule Y.</b></p> <ol style="list-style-type: none"> <li>a. systemic toxicity studies,       <ol style="list-style-type: none"> <li>i. single dose toxicity</li> <li>ii. repeated dose toxicity</li> </ol> </li> <li>b. Male Fertility Study</li> <li>c. Female Reproduction and Developmental Toxicity Studies</li> <li>d. (for all drugs proposed to be studied or used in women of child bearing age)</li> <li>e. Local toxicity       <ol style="list-style-type: none"> <li>i. Dermal toxicity (for products meant for topical (dermal) application)</li> <li>ii. Ocular toxicity (for products meant for ocular instillation)</li> <li>iii. Inhalation toxicity (conducted with the formulation proposed to be used via inhalation route)</li> <li>iv. Vaginal toxicity (for products meant for topical application to vaginal mucosa)</li> <li>v. Photoallergy or dermal phototoxicity (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential)</li> <li>vi. Rectal tolerance test (For all preparations meant for rectal administration)</li> </ol> </li> <li>f. Genotoxicity</li> <li>g. Allergenicity/Hypersensitivity</li> <li>h. Carcinogenicity (Carcinogenicity studies should be performed for all drugs that are expected to be clinically used for more than 6 months as well as for drugs used frequently in an intermittent manner in the treatment of chronic or recurrent conditions. However, completed rodent carcinogenicity studies are not needed in advance of the conduct of large scale clinical trials, unless there is a special concern for the patient population)</li> </ol> <p>Reports of following toxicity studies should be submitted alongwith clinical trial applications of different Phases for INDs:</p> <p>For Phase I Clinical Trials</p> <ul style="list-style-type: none"> <li>• Systemic Toxicity studies       <ol style="list-style-type: none"> <li>(i) Single dose toxicity studies</li> <li>(ii) Dose Ranging Studies</li> </ol> </li> </ul>		

(iii) Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure.

- Male fertility study
- In-vitro genotoxicity tests
- Relevant local toxicity studies with proposed route of clinical application (duration depending on proposed length of clinical exposure)
- Allergenicity/Hypersensitivity tests (when there is a cause for concern or for parenteral drugs, including dermal application)
- Photo-allergy or dermal photo-toxicity test (if the drug or a metabolite is related to an agent 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 submitted while 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 the non-clinical safety data needed for obtaining the permission for Phase I trial, as per the list provided above must be submitted.
- Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure
- In-vitro and In-vivo genotoxicity tests.
- Segment II reproductive/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 submitted while obtaining the permissions for Phase I and II trials, with appropriate references.
- In case of an application for directly initiating a Phase III trial - complete details of the non-clinical safety data needed for obtaining the permissions for Phase I and II trials, as per the list provided above must be provided.
- Repeat-dose systemic toxicity studies of appropriate duration to support the duration of proposed human exposure
- Reproductive/developmental toxicity studies
- In-vitro and In-vivo genotoxicity tests.
- 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 of possible adverse effects on foetal development).  
Carcinogenicity studies (when there is a cause for concern or when the drug is to be used for more than 6 months).

<p>3) Clinical Data:</p> <p>I. Human / Clinical pharmacology (Phase I):-</p> <ul style="list-style-type: none"> <li>▪ Summary</li> <li>▪ Specific Pharmacological effects</li> <li>▪ General Pharmacological effects</li> <li>▪ Pharmacokinetics, absorption, distribution, metabolism, excretion</li> <li>▪ Pharmacodynamics / early measurement of drug activity</li> </ul> <p>II. Therapeutic exploratory trials (Phase II):-</p> <ul style="list-style-type: none"> <li>▪ Summary</li> <li>▪ Study reports</li> </ul>		
<p>III. Therapeutic confirmatory trials (Phase III):-</p> <ul style="list-style-type: none"> <li>▪ Summary</li> <li>▪ Individual study reports with listing of sites and Investigators.</li> </ul>		
<p>Special studies:-</p> <ul style="list-style-type: none"> <li>▪ Summary</li> <li>▪ Bio-availability / Bio-equivalence.</li> <li>▪ Other studies e.g. geriatrics, paediatrics, pregnant or nursing women.</li> </ul>		
<p>4) PMS/ PSUR data (Phase IV):-</p> <p>Note: Details of Animal Pharmacology &amp; Animal Toxicology studies required to be carried out will be as per Appendix IV &amp; Appendix III of Schedule Y of Drugs and Cosmetics Rules respectively. Depending upon the nature of new drugs and disease(s) specific additions/deletions may be made to the above requirement.</p>		

#### 4. Checklist for Protocol Amendment (GCT )

##### Classification for major protocol amendment:

1. Amendment with respect to age limit of subject, dose, and treatment duration.
2. Increase in number of subjects
3. Amendment in study design
4. Amendment in inclusion or exclusion criteria
5. Amendment in safety or efficacy parameters
6. Any other changes which has impact on safety of the subject

##### Checklist for Major Protocol Amendment:

S.No.	CONTENTS	YES	NO
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Copy of the amended protocol		
5.	Changes made in comparison with earlier protocol to be presented with rationale and major changes should be highlighted		
6.	Safety and efficacy data in support of proposed amendment		
7.	Regulatory approval from participating key country/countries (in case of language other than English, English Translated version along with Translation Certificate)		

##### Checklist for Minor Protocol Amendment:

S.No.	CONTENTS	YES	NO
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Copy of the amended protocol		
5.	Changes made in comparison with earlier protocol to be presented with rationale.		

## **5. Checklist for Import License (GCT)**

### **1. In case of fresh Test License**

<b>S.No.</b>	<b>CONTENTS</b>	<b>YES</b>	<b>NO</b>
1.	Covering letter		
2.	TR-6 challan of required amount; bank's stamp for cheque realization(a fee of one hundred rupees for a single drug and an additional fee of fifty rupees or each additional drug).		
3.	Application in Form-12, sign, date, stamp, country from which the drugs to be imported		
4.	Justification for quantity to be imported		
5.	Copy of CT permission letter		

The following additional documents need to be submitted in case of Test License of balance quantity/ additional quantity / expiry of validity of test licence

1. Debit sheet
2. Justification for the additional quantity to be imported

## 6. Amended Checklist for Site Addition/ Deletion/ Closure/ Change in PI

### a. Site addition

S.No.	CONTENTS	YES	NO
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Undertaking by the Investigators as per Appendix VII of Schedule "Y":- (Ethics Committee should be of same area where the site is located.)		
5.	CV/ Statement of Qualification		
6.	Copy of Ethics committee approval letter, if available		
7.	Whether the clinical study site is a Private Clinic/Private Hospital/Nursing Home/Govt Hospital.		
8.	In case of nursing home/hospital, details of the number of beds available.		
9.	In case of hospital, details of: whether it is equipped with super specialty or multispecialty facilities.		
10.	Whether the study site has Institutional Ethics Committee or Independent Ethics Committee.		
11.	In case of Independent Ethics Committee, SOPs should be submitted along with details of composition of the committee.		

### b. Site Closure / Deletion

S.No.	CONTENTS	YES	NO
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Reason for closure		
5.	Subject enrolment status		
6.	Procedure for subject follow up at the given site		
7.	Copy of Ethics committee notification		
8.	Copy of Ethics committee approval letter, if available		
9.	Copy of summary report		

**c. Change in Site Address**

<b>S.No.</b>	<b>CONTENTS</b>	<b>YES</b>	<b>NO</b>
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Reason for site address change		
5.	Undertaking by the Investigators as per Appendix VII of Schedule" Y":- (Ethics Committee should be of same area where the site is located.)		
6.	CV/ Statement of Qualification		
7.	Copy of Ethics committee approval letter(earlier site and the proposed site), if available		
8.	Whether the clinical study site is a Private Clinic/Private Hospital/Nursing Home/Govt Hospital.		
9.	In case of nursing home/hospital, details of the number of beds available.		
10.	In case of hospital, details of: whether it is equipped with super specialty or multispecialty facilities.		
11.	Whether the study site has Institutional Ethics Committee or Independent Ethics Committee.		
12.	In case of Independent Ethics Committee, SOPs should be submitted along with details of composition of the committee.		

**d. Change in Investigator**

<b>S.No.</b>	<b>CONTENTS</b>	<b>YES</b>	<b>NO</b>
1.	Covering letter		
2.	Copy of CT permission letter		
3.	Copy of previous protocol amendment approval letter, if any		
4.	Reason for change of Investigator in same site		
5.	Undertaking from new Investigators as per Appendix VII of Schedule" Y":- (Ethics Committee should be of same area where the site is located.)		
6.	CV/ Statement of Qualification		
7.	Copy of Ethics committee approval letter, if available		

**7. Checklist for Grant of permission to manufacture/import of Bulk Drug already approved in the country**

#	Documents required to be submitted	Status	
		Yes	No
1.	Name of Applicant		
2.	Name of Drug		
3.	Therapeutic Class		
4.	Date of Approval		
5.	Application in Form-44 duly filled and signed by the competent authority		
6.	Treasury Challan of Rs. 50,000/- upto 1 year from initial approval and Rs. 15,000/- for other drugs upto 4 years		
7A.	For manufacturing:-  Copy of manufacturing license in Form-25/ Form-26 for any bulk drug to manufacturer and Form-29		
7B.	For import:-  Copy of drug sale license in Form 20B and 21B		
8.	Pharmaceutical & Chemical Information		
8A.	Manufacturing Process including in process control		
8B.	Specifications and methods of analysis		
8C.	Structural elucidation data		
9.	Sub-acute toxicity data generated with the applicant 's bulk drug in two species		
10.	Stability data of three different lots as per Schedule –Y of Drugs and Cosmetics Rules		
11.	CDTL Test report		

\* In case the application is for grant of NOC for lab testing the documents at serial no 9 & 10 may be submitted at the time of approval of bulk drug.

## 8. Approvals of a New drug (Formulation) already approved in the country

#	Documents required to be submitted	Enclosed	
		Yes	No
1.	<b>Application for permission to Manufacture /Import: (Purpose should be mentioned clearly)</b>		
2.	<b>Name of the applicant</b>		
3.	<b>Name of the New Drug</b>		
	<b>a. Composition of the New Drug</b>		
	<b>b. Dosage Form</b>		
	<b>c. Proposed indication for the New Drug</b>		
4.	<b>Details of the approval of the New Drug in the country</b>		
	<b>a. Approved Dosage Form</b>		
	<b>b. Approved composition</b>		
	<b>c. Approved indication</b>		
5.	<b>Application in Form 44 duly signed and stamped by authorized personal</b>		
6.	<b>Treasury Challan of INR 15,000 New Drug approved in India for more than one year, or INR 50,000 of New Drug is approved for less than one year duly signed and stamped by Bank of Baroda</b>		
7.	<b>Copy of valid manufacturing license in Form 25/28/26</b>		
8.	<b>Copy of Test license in form 29</b>		
9.	<b>Source of bulk drugs along with current regulatory status of the source with copy of Form 46A/45A. (if obtained)</b>		
10.	<b>Information on active ingredients:</b>		
	a) Brief Chemical & pharmaceutical data		
	b) Specification		
	c) Method of Analysis		
	d) Certificate of Analysis		
11.	<b>Data on Formulation</b>		
	a) Master manufacturing formula		
	b) Manufacturing Procedure		
	c) Finished product specification		
	d) Finished product Method of Analysis		
	e) Finished product Certificate of Analysis		
	f) In process quality control check		
	g) Stability study data evaluation as per requirements of schedule Y		
	h) Dissolution Release Profile (in case of oral dosage form)		
	i) Copy of proposed Package Insert which should include generic name of all active ingredients; composition; dosage form/s, indications; dose and method of administration; use in special populations; contraindications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.		

	j) Draft specimen of Label and Carton		
12.	Bio Equivalence study Protocol in case BE Permission / BE report in case of Final approval. ( for oral dosage form.)		
12.1.	Justification on Bio equivalence study waiver, if requested		
13.	In case of injectable formulation, sub-acute toxicity data conducted with the applicant drug formulation.		

**Note :**

In case the application is for clinical trial / Bio equivalence permission:

- a. Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.
- b. In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated along with justification / reasons for the change.
- c. Ethics Committee Approval: Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
- d. The proposed clinical trial study centres should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

**9. A drug already approved by the Licensing Authority mentioned in Rule 21 proposed to be marketed with new indication**

#	Documents required to be submitted	Enclosed	
		Yes	No
1.	<b>Application for permission to Manufacture /Import/Clinical trial: (Purpose should be mentioned clearly)</b>		
2.	<b>Name of the applicant</b>		
3.	<b>Name of the New Drug</b>		
	<b>a. Composition of the New Drug</b>		
	<b>b. Dosage Form</b>		
	<b>c. Proposed indication for the New Drug</b>		
4.	<b>Details of the approval of the New Drug in the country</b>		
	<b>a. Approved Dosage Form</b>		
	<b>b. Approved composition</b>		
	<b>c. Approved indication</b>		
5.	<b>Application in Form 44 duly signed and stamped by authorized personal</b>		
6.	<b>Treasury Challan of INR 15,000 New Drug approved in India for more than one year, or INR 50,000 of New Drug is approved for less than one year and not submitted challan earlier for the same drug.</b>		
7.	<b>Copy of valid manufacturing license in Form 25/28/26</b>		
8.	<b>Copy of Test license in form 29</b>		
9.	<b>In case of new drug, Source of bulk drugs along with current regulatory status of the source with copy of Form 46A/45A. (if obtained)</b>		
10.	<b>Information on active ingredients:</b>		
	a) Brief Chemical & pharmaceutical data		
	b) Specification		
	c) Method of Analysis		
	d) Certificate of Analysis		
11.	<b>Data on Formulation</b>		
	a) Master manufacturing formula		
	b) Manufacturing Procedure		
	c) Finished product specification		
	d) Finished product Method of Analysis		
	e) Finished product Certificate of Analysis		
	f) In process quality control check		
	g) Stability study evaluation as per requirements of schedule Y		
	h) Dissolution Release Profile (in case of oral dosage form)		
	i) Copy of proposed Package Insert which should include generic name of all active ingredients; composition; dosage form/s, indications; dose and method of administration; use in special populations; contraindications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.		
j) Draft specimen of Label and Carton			
<i>Sr No 9 to 11 is not applicable, if applicant holds manufacturing or Import and marketing permission for the proposed drug product [ Except 11(i) and 11(j)]</i>			
12.	<b>Therapeutic Rationale and justification for the proposed Additional Indication</b>		

13.	<b>Regulatory status in other countries, as appropriate.</b>		
	a) Names of the countries where the the drug is marketed/approved for proposed indication alongwith package insert and/or copies of approval in key countries.		
	b) Names of the countries where the drug is withdrawn, if any, with reasons		
	c) Free sale certificate (FSC) or Certificate of Pharmaceutical Product (COPP), in case of import.		
14	<b>Clinical trial protocol in case of proposed Additional dosage form is not approved in key countries. (Ckecklist already given in New Drug application)</b>		
15	<b>Justification on Clinical trial waiver, if requested.</b>		
16	Published report of Clinical trial/Journal/literature with respect to proposed Additional Indication.		

**Note :**

In case the application is for clinical trial / Bio equivalence permission:

- a.** Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.
- b.** In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated along with justification / reasons for the change.
- c.** Ethics Committee Approval: Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
- d.** The proposed clinical trial study centres should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

**10. A drug already approved by the Licensing Authority mentioned in Rule 21 and proposed to be marketed as a 'New Dosage Form / New Route of Administration'.**

#	Documents required to be submitted	Enclosed	
		Yes	No
1.	<b>Application for permission to Manufacture /Import/Clinical trial: (Purpose should be mentioned clearly)</b>		
2.	<b>Name of the applicant</b>		
3.	<b>Name of the New Drug</b>		
	a. <b>Composition of the New Drug</b>		
	b. <b>Proposed Dosage Form</b>		
	c. <b>Proposed indication for the New Drug</b>		
4.	<b>Details of the approval of the New Drug in the country</b>		
	a. <b>Approved Dosage Form and route of administration</b>		
	b. <b>Approved composition</b>		
	c. <b>Approved indication</b>		
5.	<b>Application in Form 44 duly signed and stamped by authorized personal</b>		
6.	<b>Treasury Challan of INR 15,000 New Drug approved in India for more than one year, or INR 50,000 of New Drug is approved for less than one year and not submitted challan earlier for the same drug.</b>		
7.	<b>Copy of valid manufacturing license in Form 25/28/26</b>		
8.	<b>Copy of Test license in form 29</b>		
9.	<b>In case of new drug, Source of bulk drugs along with current regulatory status of the source with copy of Form 46A/45A. (if obtained)</b>		
10.	<b>Information on active ingredients:</b>		
	a) <b>Brief Chemical &amp; pharmaceutical data</b>		
	b) <b>Specification</b>		
	c) <b>Method of Analysis</b>		
	d) <b>Certificate of Analysis</b>		
11.	<b>Data on Formulation</b>		
	a) <b>Master manufacturing formula</b>		
	b) <b>Manufacturing Procedure</b>		
	c) <b>Finished product specification</b>		
	d) <b>Finished product Method of Analysis</b>		
	e) <b>Finished product Certificate of Analysis</b>		
	f) <b>In process quality control check</b>		
	g) <b>Stability study evaluation as per requirements of schedule Y</b>		
	h) <b>Dissolution Release Profile (in case of oral dosage form)</b>		
	i) <b>Copy of proposed Package Insert which should include generic name of all active ingredients; composition; dosage form/s, indications; dose and method of administration; use in special populations; contraindications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.</b>		
	j) <b>Draft specimen of Label and Carton</b>		
12	<b>Therapeutic Rationale and justification for the proposed new dosage form / new route of administration</b>		

13.	<b>Regulatory status in other countries, as appropriate.</b>		
	a) Names of the countries where the the drug is marketed/approved for proposed Dosage Form / New Route of Administration alongwith package insert and/or copies of approval in key countries.		
	b) Names of the countries where the drug is withdrawn, if any, with reasons		
	c) Free sale certificate (FSC) or Certificate of Pharmaceutical Product (COPP), in case of import.		
14	<b>Clinical trial protocol in case of proposed Additional dosage form is not approved in key countries. (Ckecklist already given in New Drug application)</b>		
15	<b>Bio Equivalence study requirement (in case of oral dosage form as appropriate as per Appendix X of Schedule Y)</b>		
16	Justification on Clinical trial and Bio equivalence study waiver, if requested.		
17	<b>Animal toxicology data as per Schedule Y.</b>		
	<b>o. Systemic toxicity studies,</b>		
	i. single dose toxicity		
	ii. repeated dose toxicity		
	<b>p. Local toxicity</b>		
	<b>a. Dermal toxicity</b> (for products meant for topical (dermal) application)		
	<b>b. Ocular toxicity</b> (for products meant for ocular instillation)		
	<b>c. Inhalation toxicity</b> (conducted with the formulation proposed to be used via inhalation route)		
	<b>d. Vaginal toxicity</b> (for products meant for topical application to vaginal mucosa)		
	<b>e. Photoallergy or dermal phototoxicity</b> (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential)		
	<b>f. Rectal tolerance test</b> (For all preparations meant for rectal administration)		
18	Published report of Clinical trial/Journal/literature with respect to proposed Dosage Form / New Route of Administration.		

**11. A drug already approved by the Licensing Authority mentioned in Rule 21 now proposed to be marketed as a 'Modified release dosage form'.**

#	Documents required to be submitted	Enclosed	
		Yes	No
1.	<b>Application for permission to Manufacture /Import/Clinical trial: (Purpose should be mentioned clearly)</b>		
2.	<b>Name of the applicant</b>		
3.	<b>Name of the New Drug</b>		
	a. <b>Composition of the New Drug</b>		
	b. <b>Dosage Form</b>		
	c. <b>Proposed indication for the New Drug</b>		
4.	<b>Details of the approval of the New Drug in the country</b>		
	a. <b>Approved Dosage Form</b>		
	b. <b>Approved composition</b>		
	c. <b>Approved indication</b>		
5.	<b>Application in Form 44 duly signed and stamped by authorized personal</b>		
6.	<b>Treasury Challan of INR 15,000 New Drug approved in India for more than one year, or INR 50,000 of New Drug is approved for less than one year and not submitted challan earlier for the same drug.</b>		
7.	<b>Copy of valid manufacturing license in Form 25/28/26</b>		
8.	<b>Copy of Test license in form 29</b>		
9.	<b>In case of new drug, Source of bulk drugs along with current regulatory status of the source with copy of Form 46A/45A. (if obtained)</b>		
10.	<b>Information on active ingredients:</b>		
	a) Brief Chemical & pharmaceutical data		
	b) Specification		
	c) Method of Analysis		
	d) Certificate of Analysis		
11.	<b>Data on Formulation</b>		
	a) Master manufacturing formula		
	b) Manufacturing Procedure		
	c) Finished product specification		
	d) Finished product Method of Analysis		
	e) Finished product Certificate of Analysis		
	f) In process quality control check		
	g) Stability study evaluation as per requirements of schedule Y		
	h) Dissolution Release Profile (in case of oral dosage form)		
	i) Copy of proposed Package Insert which should include generic name of all active ingredients; composition; dosage form/s, indications; dose and method of administration; use in special populations; contraindications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.		
	j) Draft specimen of Label and Carton		
12	<b>Therapeutic Rationale and justification for the proposed new dosage form / new route of administration</b>		

13.	<b>Regulatory status in other countries, as appropriate.</b>		
	a) Names of the countries where the the drug is marketed/approved for proposed Modified Dosage Form alongwith package insert and/or copies of approval in key countries.		
	b) Names of the countries where the drug is withdrawn, if any, with reasons		
	c) Free sale certificate (FSC) or Certificate of Pharmaceutical Product (COPP), in case of import.		
14.	<b>Clinical trial protocol in case of proposed Additional dosage form is not approved in key countries. (Ckecklist alreedy given in New Drug application)</b>		
15	<b>Bio Equivalence study requirement (in case of oral dosage form as appropriate as per Appendix X of Schedule Y)</b>		
16	Justification on Clinical trial and Bio equivalence study waiver, if requested.		
17.	Published report of Clinical trial/Journal/literature with respect to proposed Modified Dosage Form.		

**Note :**

In case the application is for clinical trial / Bio equivalence permission:

- a. Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.
- b. In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated along with justification / reasons for the change.
- c. Ethics Committee Approval: Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
- d. The proposed clinical trial study centres should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

**12. A drug already approved by the Licensing Authority mentioned in Rule 21 proposed to be marketed with Additional Strength**

#	Documents required to be submitted	Enclosed	
		Yes	No
1.	<b>Application for permission to Manufacture /Import/Clinical trial: (Purpose should be mentioned clearly)</b>		
2.	<b>Name of the applicant</b>		
3.	<b>Name of the New Drug</b>		
	a. <b>Composition of the New Drug</b>		
	b. <b>Dosage Form</b>		
	c. <b>Proposed indication for the New Drug</b>		
4.	<b>Details of the approval of the New Drug in the country</b>		
	a. <b>Approved Dosage Form</b>		
	b. <b>Approved composition</b>		
	c. <b>Approved Strength along with Indication</b>		
5.	<b>Application in Form 44 duly signed and stamped by authorized personal</b>		
6.	<b>Treasury Challan of INR 15,000 New Drug approved in India for more than one year, or INR 50,000 of New Drug is approved for less than one year and not submitted challan earlier for the same drug.</b>		
7.	<b>Copy of valid manufacturing license in Form 25/28/26</b>		
8.	<b>Copy of Test license in form 29</b>		
9.	<b>in case of new drug, Source of bulk drugs along with current regulatory status of the source with copy of Form 46A/45A. (If obtained)</b>		
10.	<b>Information on active ingredients:</b>		
	a) Brief Chemical & pharmaceutical data		
	b) Specification		
	c) Method of Analysis		
	d) Certificate of Analysis		
11.	<b>Data on Formulation</b>		
	a) Master manufacturing formula		
	b) Manufacturing Procedure		
	c) Finished product specification		
	d) Finished product Method of Analysis		
	e) Finished product Certificate of Analysis		
	f) In process quality control check		
	g) Stability study evaluation as per requirements of schedule Y		
	h) Dissolution Release Profile (in case of oral dosage form)		
	i) Copy of proposed Package Insert which should include generic name of all active ingredients; composition; dosage form/s, indications; dose and method of administration; use in special populations; contraindications; warnings; precautions; drug interactions; undesirable effects; overdose; pharmacodynamic and pharmacokinetic properties; incompatibilities; shelf-life; packaging information; storage and handling instructions.		
	j) Draft specimen of Label and Carton		
12.	<b>Therapeutic Rationale and justification for the proposed Additional Strength</b>		

13	<b>Regulatory status in other countries, as appropriate.</b>		
	a) Names of the countries where the the drug is marketed/approved for proposed additional strength alongwith package insert and/or copies of approval in key countries.		
	b) Names of the countries where the drug is withdrawn, if any, with reasons		
	c) Free sale certificate (FSC) or Certificate of Pharmaceutical Product (COPP), in case of import.		
14	<b>Clinical trial protocol in case of proposed Additional dosage form is not approved in key countries. (Ckecklist alreedy given in New Drug application)</b>		
15	<b>Bio Equivalence study requirement (in case of oral dosage form as appropriate as per Appendix X of Schedule Y)</b>		
16	Justification on Clinical trial and Bio equivalence study waiver, if requested.		
17	Published report of Clinical trial/Journal/literature with respect to proposed Additional Strength.		

**Note :**

In case the application is for clinical trial / Bio equivalence permission:

- a. Adequate chemical and pharmaceutical information should be provided to ensure the proper identity, purity, quality & strength of the investigational product, the amount of information needed may vary with the Phase of clinical trials, proposed duration of trials, dosage forms and the amount of information otherwise available.
- b. In case of applications for protocol amendments of already approved studies, applicants should submit copy of approval of protocol, amended new protocol, summarized list of all the new changes incorporated along with justification / reasons for the change.
- c. Ethics Committee Approval: Ethical approval should be obtained from Ethics Committee located in the same area where the clinical trial site is located.
- d. The proposed clinical trial study centres should be geographically distributed in the country and should also include clinical sites which have their own Institutional Ethics Committee.

**13. Application for BE NOC for Export, of a new molecule not approved in India but approved in the other countries.**

S. No	Documents	Yes	No
1	Application in Form-44 duly signed, stamped & dated by the competent authority with name and designation.		
2	Treasury Challan: Rs 25000/- BE NOC & T/L (Brand Name & Generic Name of the drug in form 12)		
3	A copy of the approval granted to the BE study centre by CDSCO		
4	Regulatory status of the drug in other country		
5	Names of the countries where the drug is currently being marketed (to be mentioned in the covering letter also)		
6	Prescribing information/Package literature on the international product		
7	Chemical & Pharmaceutical data including stability data		
8	Non-clinical & clinical data as per Appendix- I of schedule Y along with Published data BA/BE study carried out in healthy volunteers		
9	In the case of multiple dose BE study adequate supporting safety data including published report of BA/BE carried out in the subjects.		
10	Sponsor's Authorization letter duly signed by the competent authority on their letterhead.		
11	Undertaking by the Principal Investigator (PI) as per appendix VII of schedule "Y" of Drugs and Cosmetic Rules.		
12	The study synopsis		
13	The study protocols		
14	Complete Informed consent form/Patient Information Sheet Informed consent Documents should include "in case of study related injury the ( <i>name of the applicant</i> ) will provide complete medical care along with compensation for injury". Further compensation for participation in the study should be paid to the volunteers proportionately at the end of each period of the study.		
	IEC Location : /study site location : The Location of Ethics committee vis-a-vis location of the study site		
	<ul style="list-style-type: none"> <li>Authority under which ethics committee has been</li> </ul>		

	<p>constituted.</p> <ul style="list-style-type: none"> <li>• Composition of Ethics committee</li> <li>• Review and decision making process of the Ethics committee.</li> <li>• Source and methods of recruitment for volunteers</li> <li>• ICF process followed for the study</li> </ul> <p>*The above information is not required if the information already submitted earlier with application, However the firm should mention the reference of the submission.</p>		
15	Complete Certificate of Analysis of same batches (both test & reference formulations) to be used in the BE study along with dissolution profile.		
16	In the case of Injectable preparation the sub-acute toxicity should be submitted on the product of the sponsor, generated in two species for adequate duration.		
17	Depending on the nature of the drug like cytotoxic agent, hormonal preparations etc. Proper justification for conducting studies on healthy volunteers/patients or male/ female should be submitted, published report of BA/BE carried out in the subjects.		

**14. Application for BE NOC for Export, of a New Drugs approved in India within period of 1 year:-**

S. No	Documents	Yes	No
1	Application in Form-44 duly signed, stamped & dated by the competent authority with name and designation.		
2	Treasury Challan: Rs 25000/- BE Noc & T/L (Brand Name & Generic Name of the drug in form 12)		
3	A copy of the approval granted to the BE study centre by CDSCO		
4	Regulatory status of the drug in India		
6	Published data BA/BE study carried out in healthy volunteers		
7	Sponsor's Authorization letter duly signed by the competent authority on their letterhead.		
8	Undertaking by the Principal Investigator (PI) as per appendix VII of schedule "Y" of Drugs and Cosmetic Rules.		
9	The study synopsis		
10	The study protocols		
11	Complete Informed consent form/Patient Information Sheet Informed consent Documents should include "in case of study related injury the ( <i>name of the applicant</i> ) will provide complete medical care along with compensation for injury". Further compensation for participation in the study should be paid to the volunteers proportionately at the end of each period of the study.		
	IEC Location : /study site location : The Location of Ethics committee vis-a-vis location of the study site		
	<ul style="list-style-type: none"> <li>• Authority under which ethics committee has been constituted.</li> <li>• Composition of Ethics committee</li> <li>• Review and decision making process of the Ethics committee.</li> <li>• Source and methods of recruitment for volunteers</li> <li>• ICF process followed for the study</li> </ul> <p>*The above information is not required if the information already submitted earlier with application, However the firm should mention the reference of the submission.</p>		
12	Chemical & Pharmaceutical data including stability data, Complete Certificate of Analysis of same batches (both test & reference formulations) to be used in the BE study along with dissolution profile.		
13	In the case of multiple dose BE study adequate supporting safety		

	data including published report of BA/BE carried out in the subjects.		
14	In the case of Injectable preparation the sub-acute toxicity should be submitted on the product of the sponsor, generated in two species for adequate duration.		
15	Depending on the nature of the drug like cytotoxic agent, hormonal preparations etc. Proper justification for conducting studies on healthy volunteers/patients or male/ female should be submitted.		
16	If the study is proposed with new dosage form, new route of administration, higher strength of the drug, supporting safety data including published report of BA/BE carried out in the subjects.		

**15. Application for BE NOC for Export, of a New Drugs approved within period of more than 1 year & less than 4 years:**

S. No	Documents	Yes	No
1	Application in Form-44 duly signed, stamped & dated by the competent authority with name and designation.		
2	Treasury Challan: Rs15000/- BE Noc & T/L (Brand Name & Generic Name of the drug in form 12)		
3	A copy of the approval granted to the BE study centre by CDSCO		
4	Regulatory status of the drug in India		
5	Sponsor's Authorization letter duly signed by the competent authority on their letterhead.		
6	Undertaking by the Principal Investigator (PI) as per appendix VII of schedule "Y" of Drugs and Cosmetic Rules.		
7	The study synopsis		
8	The study protocols		
9	Complete Informed consent form/Patient Information Sheet Informed consent Documents should include "in case of study related injury the ( <i>name of the applicant</i> ) will provide complete medical care along with compensation for injury". Further compensation for participation in the study should be paid to the volunteers proportionately at the end of each period of the study.		
	IEC Location : /study site location : The Location of Ethics committee vis-a-vis location of the study site		
	<ul style="list-style-type: none"> <li>• Authority under which ethics committee has been constituted.</li> <li>• Composition of Ethics committee</li> <li>• Review and decision making process of the Ethics committee.</li> <li>• Source and methods of recruitment for volunteers</li> <li>• ICF process followed for the study</li> </ul> <p>*The above information is not required if the information already submitted earlier with application, However the firm should mention the reference of the submission.</p>		
10	Chemical & Pharmaceutical data including stability data, Complete Certificate of Analysis of same batches (both test & reference formulations) to be used in the BE study along with dissolution profile.		
11	In the case of multiple dose BE study adequate supporting safety data including published report of BA/BE carried out in the		

	subjects.		
12	In the case of Injectable preparation the sub-acute toxicity should be submitted on the product of the sponsor, generated in two species for adequate duration.		
13	Depending on the nature of the drug like cytotoxic agent, hormonal preparations etc. Proper justification for conducting studies on healthy volunteers/patients or male/ female should be submitted.		
14	If the study is proposed with new dosage form, new route of administration, higher strength of the drug, supporting safety data including published report of BA/BE carried out in the subjects.		

**16. Application for BE NOC for Export, of a drug product in modified release form irrespective of their approval status:-**

S. No	Documents	Yes	No
1	Application in Form-44 duly signed, stamped & dated by the competent authority with name and designation.		
2	Treasury Challan: Rs 15000/- BE NOC & T/L (Brand Name & Generic Name of the drug in form 12)		
3	A copy of the approval granted to the BE study centre by CDSCO		
4	Regulatory status of the drug in India		
5	Sponsor's Authorization letter duly signed by the competent authority on their letterhead.		
6	Undertaking by the Principal Investigator (PI) as per appendix VII of schedule "Y" of Drugs and Cosmetic Rules.		
7	The study synopsis		
8	The study protocols		
9	Complete Informed consent form/Patient Information Sheet Informed consent Documents should include "in case of study related injury the ( <i>name of the applicant</i> ) will provide complete medical care along with compensation for injury". Further compensation for participation in the study should be paid to the volunteers proportionately at the end of each period of the study.		
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12	In the case of Injectable preparation the sub-acute toxicity should be submitted on the product of the sponsor, generated in two species for adequate duration.		
13	Depending on the nature of the drug like cytotoxic agent, hormonal preparations etc. Proper justification for conducting studies on healthy volunteers/patients or male/ female should be submitted.		
14	If the study is proposed with new dosage form, new route of administration, higher strength of the drug, supporting safety data including published report of BA/BE carried out in the subjects.		

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