Global Clinical Trial

1. Application For Global Clinical trial

Sr. No.	Contents	YES, Indicate Annexure No.	No
1.	Name & Address of the Applicant:-		
2.	Name & Address of the Sponsor:-		
3.	Authorization Letter from Sponsor in favour of Applicant:-		
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 & Strength:-		
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. (a)	Patient Information Sheet (PIS)/ Informed consent form (ICF) as per revised Appendix V of Schedule "Y" including the following clauses. (A) Statement describing the financial compensation and medical management as under:- (a) In the event of an injury occurring to the clinical trial subjects, such subjects shall be provided free medical management as long as required. (b) In the event of a trial related injury or death, the sponsor or his representative, whosoever has obtained permission from licensing authority for conduct of clinical study shall provide financial compensation for the injury or death. (B) In serial no. 02 of an Appendix V, the following shall be included : Address of the subject: Qualification: Occupation: Student/Self-employed /service/ Housewife / Other(Please tick as appropriate) Annual income of subject: Name and address of the nominee and his/her relation to the subject (for the purpose of compensation in case of trial related death. (C) After the name of witness occurring at the end, the following shall be inserted: "Copy of the patient information sheet and duly filled ICF shall be handed over to the subject or his/her attendant"		
11.(b)	Undertaking by the Sponsor/Sponsors representative/applicant to the licensing authority to		

	provide medical management and compensation in case of clinical trial related injury or death for which subjects are entitled to compensation as required under rule 122DAB (6).		
11.(c)	Declaration regarding financial status of the applicant vis-à-vis medical management and compensation to be paid to the trial participants (in case of injury or death in clinical trial).		
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(es)		
	(a) Trial sites detail (whether it is equipped with super specialty or multi-specialty facilities and emergency facilities with Institutional ethics committee)		
	(b) Furnish details on the total number of trials being undertaken currently by the proposed Investigator.		
16.	Name(s) 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:- (Whether new drug in India or an already approved molecule)		
20.	a. Present status of proposed study in other participating countries. b. In case of premature termination/closeout of the study in other participating countries submit reasons thereof.		
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 in same area where the site is located)		
24.	Investigators Brochure:-		
25.	Investigational Medicinal Products Dossier (IMPD):		
25 (a)	Information on active Ingredients: Drug information (Generic Name, Chemical Name or INN) Physicochemical Data including:		
	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):-		
	v. Name and address of manufacturing sites for the experimental drug.		
	vi. GMP status of the manufacturing site(s) and for the Investigational products (enclose copy of relevant regulatory approvals).		
	vii. Package insert (If the drug is marketed in any Country)		
	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 • For biological drugs relevant characterization information shall be submitted.		
25 (b)	Data on Formulation:		
	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		
26.	Affidavit declaring that the information about study drug as mentioned in Investigators Brochure is correct and based on available facts:-		
27.	As per the protocol, whether the subjects will receive the Standard Care. (Give declaration)		
28.	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:-		
29.	Details of the contract entered by the sponsor with the investigator/institutions with regard to financial support, amount of fees, honorarium, payments in kind etc. to be paid to the investigator. In case no contract has yet been entered with any Investigator / Institution, plan for financial support, fees, honorarium, and payments in kind etc. to be paid to the investigator.		
30.	Undertaking by the sponsor for application of marketing authorization in India after successful completion of clinical trial.		

31.	**Pre-Clinical and Clinical data**		
31.(A)	**Pre-Clinical data**		
(a)	**Animal Pharmacological Data**:-		
	Summary		
	Specific pharmacological actions		
	General pharmacological actions		
	Follow-up and Supplemental Safety Pharmacology Studies		
	Pharmacokinetics: absorption, distribution; metabolism; Excretion		
(b)	**Animal Toxicological Data As Per Schedule Y:**		
	a) systemic toxicity studies, i. single dose toxicity ii. repeated dose toxicity b) Male Fertility Study c) Female Reproduction and Developmental Toxicity studies for all drugs proposed to be studied or used in women of child bearing age) d) Local toxicity i. Dermal toxicity (for products meant for topical (dermal) application) ii. Ocular toxicity (for products meant for ocular instillation) iii. Inhalation toxicity (conducted with the formulation proposed to be used via inhalation route) iv. Vaginal toxicity (for products meant for topical application to vaginal mucosa) v. Photo allergy or dermal photo toxicity (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) vi. Rectal tolerance test (For all preparations meant for rectal administration) e) Genotoxicity f) Allergenicity/Hypersensitivity 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)		
(c)	Name, address of the laboratory / laboratories with accreditation certificate /Authorization certificates for all animal toxicological reports		

(d)	Reports of following toxicity studies should be submitted along with clinical trial applications of different Phases for INDs: **For Phase 1 Clinical Trial** • 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 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).		
31.(B)	**Clinical Data**		
	I. Human / Clinical pharmacology (Phase I):- • Summary • Specific Pharmacological effects • General Pharmacological effects • Pharmacokinetics, absorption, distribution, metabolism, excretion • Pharmacodynamics / early measurement of drug activity		
	II. Therapeutic exploratory trials (Phase II):- • Summary • Study reports		
	III. Therapeutic confirmatory trials (Phase III):- • Summary • Individual study reports with listing of sites and Investigators.		
	Special studies:- • Summary • Bio-availability / Bio-equivalence. • Other studies e.g. geriatrics, paediatrics, pregnant or nursing women.		
	iv. PMS/ PSUR data (Phase IV):-		

Note: Details of Animal Pharmacology & Animal Toxicology studies required to be carried out will be as per Appendix IV & 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.

- **Submit the Executive summary (as per the attached format) in hard as well as soft copy.**

2. 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	Annex. 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(Tabular Form) 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.	Copies of approval for the proposed amendment from the Ethics Committees involved in all trial sites.			
8.	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	Annex. 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 (Tabular Form) with earlier protocol to be presented with rationale.			

3. Checklist for Import License (GCT)

1. In case of fresh Test License

S.No.	CONTENTS	YES	NO	Annex. No.
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 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			
6.	GMP Status of the manufacturing site where the investigational product is manufactured.			

NOTE: Separate application under Form 12 and fees are required for import from different countries.

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

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

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4. Checklist for Site Addition/ Deletion/ Closure/ Change in PI

A. Site Addition

S. No.	CONTENTS	YES	NO	Annex 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.	(a) CV/ Statement of Qualification			
	(b) Furnish details on the total number of trials being undertaken currently by the proposed Investigator.			
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.	Details of the medical facility /Hospitals: Number of beds, Whether it is equipped with super specialty or multi-specialty facilities and emergency facilities.			
9.	Whether the study site has institutional Ethics Committee or Independent Ethics Committee			
10.	Name, address and registration number of Institutional Ethics Committee			

B. Site Closure/Deletion

S. No.	CONTENTS	YES	NO	Annex 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			
10.	Safety measures after discontinuation &/or premature closure/termination of the study/study site.			
11.	Ethic committee opinion for premature close-out of the study site vis-à-vis & rights of the subjects enrolled & exposed to the study drug.			

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C. Change in Site Address

S. No.	CONTENTS	YES	NO	Annex No.
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 on Original letter lead of new site. (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/old site and the proposed/new site)			
8.	Whether the clinical study site is a Private Clinic/Private hospital/Nursing home/ Govt. Hospital.			
9.	Details of the medical facility /Hospitals: Number of beds, Whether it is equipped with super specialty or multi-specialty facilities and emergency facilities.			
10.	Name, address and registration number of Institutional Ethics Committee			
11.	Subject enrolment status at the earlier/old site			

D. Change in Investigator

S. No.	CONTENTS	YES	NO	Annex No.
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 and MCI registration certificate copies.			
7.	Copy of Ethics committee approval letter, if available			

E	Revised ICD in the view of compensation clause as per G.S.R. 53(E) dated 30th Jan 2013
F	Undertaking by the applicant to the licensing authority as required under G.S.R. 53(E) dated 30th Jan 2013

Note: E and F are to be submitted for all on going trials also.

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Executive Summary

Protocol Title and No. :

Section I : Investigational Medicinal Product

1	Investigational Product Name	
1.1	Therapeutic class / Indication	

2.	**Summary of Chemical and Pharmaceutical Information**	
2.1	Chemical Name	
2.2	Dosage Form / composition	
2.3	Details of manufacturing site of IMP and its GMP status.	
2.4	Summary of stability data	

Product	Primary Package	Storage Condition	Shelf-life

3	**Brief Summary of non-clinical studies**	
3.1	**Animal Pharmacology**	Summary: Specific pharmacological actions: General pharmacological actions: Follow-up and Supplemental Safety Pharmacology Studies: Pharmacokinetics: absorption, distribution; metabolism; excretion

Classifications		Study No.	Species	Dosing route	Duration	Test articles	Dose (mg/kg)	GLP Compliance	Result
Assay									
In Vitro Studies									
In Vivo Studies									

3.2	**Animal Toxicology**	a) Systemic toxicity studies, i. Single dose toxicity ii. Repeated dose toxicity b) Male Fertility Study c) Female Reproduction and Developmental Toxicity Studies (For all drugs proposed to be studied or used in women of child bearing age) d) Local toxicity ii. Dermal toxicity (for products meant for topical/dermal application) iii. Ocular toxicity (for products meant for ocular instillation) iv. Inhalation toxicity (conducted with the formulation proposed to be used via inhalation route) v. Vaginal toxicity (for products meant for topical application to vaginal mucosa)

		vi. Photo allergy or dermal photo toxicity (required if the drug or a metabolite is related to an agent causing photosensitivity or the nature of action suggests such a potential) vii. Rectal tolerance test (For all preparations meant for rectal administration) e) Genotoxicity f) Allergenicity/Hypersensitivity g) Carcinogenicity
3.3	Whether toxicity study data submitted is as per requirement of Schedule Y. If not specify and same along with Justification.	

4.	**Summary of clinical studies**	
4.1	Phase I	
4.2	Phase II	
4.3	Phase III	
4.4	Summary of Phase I/II/III	Human / Clinical pharmacology (Phase I) • Summary • Specific Pharmacological effects • General Pharmacological effects • Pharmacokinetics, absorption, distribution, metabolism, excretion • Pharmacodynamics Therapeutic exploratory trials (Phase II) • Summary • Study reports as given in Appendix II of Schedule Y Therapeutic confirmatory trials (Phase III) • Summary • Individual study reports with listing of sites and Investigators. Special studies • Summary • Bio-availability / Bio-equivalence. • Other studies e.g. geriatrics, paediatrics, pregnant or nursing women
4.5	Proof of concept studies, if any	
5.	**Justifications for the proposed studies:**	

Phases	Description	No. of Subjects	Primary Endpoint	Secondary Endpoint

5.1	Scientific rationale for the study and justification of dose level and treatment duration (Provide reference to specific studies which have been used to arrive at close / treatment duration)	
5.2	Justification for inclusion of special populations e.g. pediatrics, geriatrics, pregnant women etc, if any.	
5.3	Comparator (if placebo is used a comparator, provide justification in light of requirement of therapy for trial subjects	

Section II: Summary of Protocol

Sr. No.	Item	Details
1.	Protocol Title	
2.	Patient Population	
3.	Study design including flow chart of the study	
4.	Subject eligibility criteria	
5.	Assessment of efficacy	
6.	Assessment of safety	
7.	Clinical laboratories participating in the study	
8.	Summary of data analysis plan	
9.	Names of the participating countries in the proposed study.	
10.	Regulatory status of the protocol under consideration. If approved, Whether copy of approval / copy of notification (in case of USFDA) should be submitted.	
11.	Details of Investigational sites in India along with investigators and details of respective ethics committees (EC).	
12.	Names of EC who have already approved or rejected the study proposal.	
13.	Whether undertaking of all the investigators as per appendix VII of Schedule Y has been submitted.	
14.	Total number of subject proposed to be enrolled globally.	
15.	Total number of subject proposed to be enrolled in India.	
16.	Whether patient information sheet and informed consent form, as per appendix V of schedule Y submitted. Please annex. Copy.(It should include compensation clause as per GSR 53(E) dated 30 Jan 2013	
17.	Brief summary on Standard of care proposed to be provided to the subject	

Section III: Regulatory Status of Drug

Sr. No.	Subject	
1.	Regulatory status of Investigational Product (IP) including comparator, if any, globally, if approved and marketed copy of package insert circulated in those countries.	
2.	Regulatory status of IP including comparator, if any, in India	

Section IV: Description of PI & Sites

Sr. No	Name of PI	Site Name & Address	Institutional Ethics Committees Name & Address	Private Clinic/ Private Hospital / Nursing Home/ Govt. Hospital	Super specialty/ Multispecialty Facilities	EC Registration Number