Central Drugs Standard Control Organisation

(Medical Devices Division)

Guidance Document

Title : Requirements for Conducting Clinical Trial(s) of Medical Devices in India

Date : 04.08.2010

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A. Preface:

In India import, manufacturing, sale and distribution Medical devices is regulated under Drugs and Cosmetics Act and Rules. At present, Medical Devices notified by Central Government are regulated under the said Act. List of notified medical devices is available on CDSCO website i.e. www.cdsco.nic.in.

The proposed "Requirements for Conducting Clinical Trial (s) of Medical Devices in India" are being uploaded for the information of all stakeholders likely to be affected thereby for comments, if any.

Any person interested making any suggestions on the proposed draft guidance documents may do so in writing for consideration of the CDSCO with in a period of 20 days from the date of its uploading through post to the Drugs Control General (India), CDSCO, FDA Bhavan, Kotla Road, New Delhi – 110002 and through email at cdamdi@gmail.com

The document is intended to provide non-binding guidance for conducting clinical trial (s) of medical devices in India.

B. Requirements for Conducting Clinical Trials of Medical Devices in India

Note: All information/reports/data should be in English only. It is expected that the information submitted in the form of hard copy shall a be submitted in the form of soft copy.

The application for conducting clinical trials for Medi in India should include following documents/information but not limited to:

1. **Covering Letter**: Indicating the precise intent of the application (e.g. whether the application is for Feasibility study or Safety and Efficacy study/Post Market study and purpose for conducting the study), name and address of the manufacturer as well as applicant, name of the device ich clinical trial is to be carried out along with a list of documents attached (Index) along with any other relevant information regarding the subject application. It should be signed by Authorized Signatory, clearly reflecting the name and designation of the Authorized Signatory.

2. **Duly filled Application** in **Form 44** as prescribed in Drugs & Cosmetics Act and Rules there under, signed and stamped by the authorized signatory, clearly indicating the name and designation of the Authorized Signatory. Performa for Form 44 is enclosed at **Annexure – I**. T*echnical* data pertaining to the subject Medical Device should be submitted as per **Annexure II**.

3. **Requisite Fee** as per the provisions of Drugs & Cosmetics Act and Rules there under in the Form of TR6 Challan issued by Bank Baroda. Fee can be submitted at notified branches of Bank of Baroda under the Head of Account "0210 - Medical and Public Health, 04 - Public Health, 104 - Fees and Fines" adjustable to Pay and Account Officer, DGHS, New Delhi in the form of a Treasury Challan. Performa for Treasury Challan (TR 6) is annexed at **Annexure - III**. TR6 Challan receipt (in original) needs to be submitted clearly specifying the fee deposited. The fee to be paid is as follows:

    I. For Feasibility Study (i.e. Safety and efficacy study); which is equivalent to Phase I trials in case of drugs: Rs 50, 000/-

    II. For Pivotal Study (i.e. Confirmatory trials); which is equivalent to Phase II/III trials in case of drugs: Rs 25, 000/-

4. **Delegation of Responsibility:** Declaration from the sponsor required to be submitted in original on Sponsor's letterhead stating the extent of delegation of responsibilities to the Principle Investigator.

5. **Protocol:** Information to be submitted in Protocol is enclosed at **Annexure IV**.

6. **Global Regulatory status of the device: (particularly in 5 GHTF countries i.e. USA, Australia, Japan, Canada and European Union)**

   I. **Clinical trial in each participating country:** Copies of regulatory approval letters, IRB/EC approvals, number of study centres per country, number of subjects recruited (Protocol specific) from participating countries (if available)

   - **Regulatory status of device in other countries (if applicable)**
     1. Approved
     2. Marketed (if marketed a copy of package insert)
     3. Withdrawn, if any, with reasons
     4. Free sale certificate or certificate of analysis, as appropriate
     5. ISO Certificates and/or CE certificate (if available)

7. **Investigator's Undertakings:** as enclosed at Annexure VII

8. **Ethics committee approval letters (if available):** Information for constitution of Ethics Committee and Format for approval of Ethics Committee is enclosed at Annexure VIII

9. **Informed consent form:** Checklist for study Subject's informed consent documents and Format of informed consent form for Subjects participating in a clinical trial are enclosed at Annexure IX

10. **Case Record Form:** Format for Case Record Form should be submitted.

11. **Patient Record Form:** Format for Patient Record Form should be submitted.

12. **Relevant published literature** for the subject device/predicate device (s) should be submitted.

13. **Investigator's Brochure:** Investigators brochure should be submitted.

14. **Suspected Unexpected Serious Adverse Reaction (SUSAR)** from other participating countries if any reported and summary of any reported problems should be submitted.

15. **Affidavit** from the sponsor that the study has not been discontinued in any country and in case of discontinuation the reasons for such a discontinuation and that the applicant would further communicate to DCG (I) about the future discontinuation and Investigator's Brochure containing the summarized information is based on the facts.

16. Any other specific relevant information w.r.t. Subject device.

17. Clinical Study Report: Structure, contents and format for Clinical Study Report is enclosed at Annexure X**.**

C. Annexures

Annexure I	Format for Form 44
Annexure II	Technical Data To Be Submitted Along With The Application For The Subject Medical Device
Annexure III	Format for TR6 Challan
Annexure IV	Contents of The Proposed Protocol For Conducting Clinical Trials
Annexure V	Phase study assessment
Annexure VI	Data elements for reporting serious adverse events occurring in a clinical trial
Annexure VII	Undertaking by the investigator
Annexure VIII	Ethics Committee and Format For Approval Of Ethics Committee
Annexure IX	Checklist for study subject's informed consent documents and format of Informed Consent Form
Annexure X	Structure, contents and format for clinical study report

Annexure I

Form 44

(See rules 122A, 122B, 122D and 122 DA)

Application for grant of permission to import or manufacture a New Drug or to undertake clinical trial.

I/We*…… (Name of the Authorised Person) of M/s..... (Full address, Telephone no, x No and e-mail) hereby apply for grant of permission for import of and/or clinical trial or for approval to manufacture a new drug or fixed dose combination or subsequent permission for already approved new drug. The necessary information / data is given below :

I. Particulars of Subject device

i. Generic name

ii. Brand name

iii. Composition of device

iv. Specifications/standards of device

v. Qualitative and quantitative particulars of the constituents

vi. Information on sterility and stability of the product

vii. Labeling details

viii. Variations in shape, style or size of the device, if applicable

ix. Physician manual and promotional literature (Literature insert) in English. (If any)

x. Packaging description including pack sizes

xi. Risk classification (in country of origin as well as in 5 GHTF countries i.e. EU, USA, Japan, Canada, Australia)

xii. List of accessories or device to be used in conjunction with subject medical device

xiii. Indication w.r.t. Which clinical study is to be carried out

xiv. Name and address of the manufacturer/contract manufacturer(s)

xv. Regulatory status of the subject device (particularly 5 GHTF countries i.e. EU, USA, Japan, Canada, Australia)

II. Technical data submitted along with the application as per Annex II. All the information provided with the application should be indexed properly with page no's.

A total fee of rupees ..... (in words)..... has been credited to the Government under the Head of Account ..... (Photocopy of receipt is enclosed).

Place.....
Dated :.....

Signature of the Applicant
(Name & Designation)
Seal / Stamp

Note: **Delete whichever is not applicable.*

Annexure II

TECHNICAL DATA TO BE SUBMITTED ALONG WITH THE APPLICATION FOR THE SUBJECT MEDICAL DEVICE

A. For All Medical Devices

a. Design Analysis Data: The Design Analysis for a medical device means, its Physical and Metrological Standardization and its comparison to the previously approved device of the si ilar type. Design control or Design analysis is a predefined procedure of the medical device at the time of manufacturing. The Design Analysis should be carried out in accordance with the established International standards for the device (e.g. ISO standards) and a comprehensive report including the basic design features of the device, drawings, and tests adapted for design analysis (with specifications) and rationale for selecting those tests and design control procedures. If available international standards are not followed for a device, then an explanation must be included for justifying deviation m those standards.

b. Biocompatibility Data: Attributes to the biocompatibility Analysis include-

a. Body Contact
   i. Surface: Skin, Mucosal, Breached
   ii. External Communicating: Indirect blood,
   iii. Tissue/Bone, Blood
   iv. Implant: Tissue/Bone, Blood
b. Contact Duration
   i. Limited (<24h)
   ii. Prolonged (24h-30 days)
   iii. Permanent (>30 days)
c. Protocol for carrying out biocompatibility study
d. Tests conducted for establishing biocompatibility (along with test reports) and rationale for selecting those tests
e. Summary report of the biocompatibility study including the conclusion of the study

B. For Moderate/ High Risk Medical Devices:

a. For Phase I study [Feasibility / First in Man Trials]:

i. Animal Study data as prescribed below:

Device performance for its actions (Including mechanical, electrical, thermal, radiation and any other of this type) and Safety data in Healthy and with pathology Animal Model (intended to be treated by such medical device) demonstrating absolute tissue reaction to active and basic parts of the devices, on Local tissue and on whole organism, Clearly recording Local, general and systemic adverse events/ Risks/ Potential sks and Performance of device in line with intended use, and conclusion whether safe / unsafe for human use. Wherever possible, Histopathology, pathophysiology and pathoanatomy should be carried out.

ii. If the active component of device is defined as drug, data for its animal studies as per schedule Y should be submitted

iii. Characteristics of good animal study

1. Powered high
2. Staged randomization
3. Defined Methodology for induction / selection
4. Live and killed studies
5. Defined measurement

b. For Phase II/III Study [Pivotal Trials]:

i. Animal study data as prescribed above

ii. Human Clinical Research data for the previous phase

Annexure III

TR6 CHALLAN

T.R. - 6.
(See Rule 92)
Challan No.

Please indicate whether	Civil
	Defence
	Railways
	Posts & Telegraphs

Challan of cash paid into Treasury/Sub-Treasury .....
Bank of Baroda, K.G. Marg, New Delhi

To be filled by the remitter				To be filled by the Department Officer or the Treasury		
By whom Tendered	Name (designation) and address of the person on whose behalf money is paid	Full particular of the remittance and/of authority (If any)	Amount	Head of Account	Accounts Officer by whom adjustable	Order to the Bank
Name			Rs. P.			
				0210-Medical + Public Health, 04-Public Health, 104-Fee and Fines	Pay and Accounts Offices, DGHS, New Delhi	Date Correct, Receive and grant receipt (Signature and full Designation of the Officer ordering the money to be paid in).
Signature		Total				
(in words) Rupees_____				To be used only in the case of remittance to the Bank through Departmental officer or the Treasury Officer.		
Received payment (in words) Rupees						
Treasurer	Accountant	Date		Treasury Officer Agent or Manager		

P.T.O.

Note:

1. In the case of payment at the Treasury, receipts for sums less than Rs. 50,000.00 do not require the Signature of the Treasure Officer but only of the Accountant and the Treasurer. Receipts for cash and cheques paid for service postage stamps should be given in form T.R. 5.

2. Particulars of money tendered should be given below.

3. In case where direct credit at the Bank are permissible the column, “Head of Account” will be filled in by the Treasury Officer or Accountant General as the case may be on receipt of the Bank's Daily Sheet.

Particulars	Amount	
	Rs.	P.
Coins		
Notes (with details)		
Cheque (with details)		
Total Rs.		

Annexure IV

CONTENTS OF THE PROPOSED PROTOCOL FOR CONDUCTING CLINICAL TRIALS

Protocol: Should include following points:

I. **Title page:**

a. Full title of Clinical study

b. Protocol/Study No. and Protocol Version No. with Date

c. The Investigational Device Name

d. Complete name and address of the sponsor and contract organization.

e. list of investigators who are conducting the study, their respective institution and affiliations and site locations

f. Name(s) of clinical laboratories and other department / or facilities participating in the study.

II. **Table of Contents:** A table of contents including a list of all appendices**.**

a. Background and Introduction

1. Preclinical Experiences
2. Clinical Experiences

Previous clinical work with the new Medical devices should be reviewed here and description of how the current protocol extends existing data should be provided. Relevant information regarding Design analysis data, Biocompatibility data for all medical devices as well pharmacological, toxicological and other biological properties of medical devices containing any medicinal substance and previous efficacy and safety e should be described.

b. Study rationale: this section should describe a brief summary of background information relevant to the study design and protocol methodology. The reason for performing this study in particular population included by the protocol should be provided**.**

c. Study Objective

i. Primary

ii. Secondary (if any)

d. Study Design

i. Overview of study design: **including description of the type of study (i.e. double blind, multicentre, placebo controlled etc.)**

ii. Flow Chart of the study

iii. A brief description of the methods and procedures to be used during the study

iv. Discussion of Study design; discussion details, rationale for the design chosen for this study

v. Planned overall duration,

vi. Definition of study population,

vii. Follow up,

viii. Statistical analysis plan

e. Study Population: the number of subjects required to be enrolled in the study at the investigative site and by all sites along with a brief description of the nature of the subject population required is also mentioned.

f. Subject Eligibility:

i. Inclusion Criteria

ii. Exclusion Criteria

g. Study Assessment: Plan, procedure and method to be described in detail **(Phase study assessment for medical devices is described in Annexure V)**

h. **Study Conduct stating the types of study activities and follow up that would be included in this section would be:** medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG), diagnostic tests, symptom measurement, adverse event review, etc.

Each visit/follow up should be recorded separately as Visit 1, Visit 2, etc.

Discontinued Subjects: Describes the circumstances for Subject withdrawal, dropouts, or other reasons for discontinuation of Subjects . State how dropouts would be managed and if they would be replaced

Describe the method of handling of protocol waivers and violations, if any.

i. Study Endpoints

i. Primary

ii. Major Secondary Endpoints

iii. Other secondary Endpoints

j. Risk Analysis

i. General Definition

ii. Device Component related risks.

iii. Potential Benefit

k. Adverse Event Management (As per Annexure VI)

i. Definition

ii. Notification of Serious adverse event and Serious adverse device effect

iii. Device Failure and Malfunctioning

iv. Clinical Event Committee (CEC)

l. **Ethical Considerations:** Give the summary of:

- Risk/benefit Assessment
- Ethics Committee review and communications
- Informed consent process
- Statement of subject confidentiality including ownership of data and coding procedures (if any)

m. Study monitoring and supervision: A description of study monitoring policies and procedures should be provided along with proposed frequency of site monitoring visits, and who is expected to perform monitoring.

Case Record Form (CRF) completion requirements, including who gets which copies of the forms and any specifics required in filling out the forms

CRF correction requirements, including who is authorized to make corrections on the CRF and how queries about study data are handled and how errors, if any, are to be corrected should be stated.

n. Investigational Product Management:

(1) Give Investigational product description and packaging (stating all components of the investigational devices)
(2) All other accessories required along with the device during the study.
(3) Method of packaging, labelling, of study substances.
(4) Method of assigning treatments to Subjects and the Sub identification code numbering system.
(5) Describe policy and procedures for handling unused investigat devices

o. Data Analysis:

Provide details of the statistical approach to be followed including sample size, how the sample size was determined, including as mptions made in making this determination, efficacy endpoints (primary as well as secondary) and safety endpoints.

p. Statistical considerations

i. The reason for choice of sample size shall be stated, cluding the level of significance to be used, the power of the trial, possible differences in the incidences of investigation variables in the study population and expected drop-out rates together with justification for these aspects;

ii. Provision for interim analysis, where applicable, and criteria for termination of the investigation on the statistical grounds.

iii. Procedure for reporting any deviation from the original statistical plan and it must be described with justification.

iv. The criteria for selection of subjects to be included the analysis with justification

v. The procedure for accounting all the data, together with treatment of missing, unused or spurious data, together with justif ation for excluding particular information from testing of the hypothesis.

Annexure V

PHASE STUDY ASSESSMENT

Clinical Trial Phases in case of medical devices are identified as follows:-

1. Phase I study: [Feasibility / First in Man Trials]: demonstrating Feasibility of the device for human use depending upon safety and performance. (Randomization control or historical control)

A. Characteristics of Good Phase I study

i. Equal or at least 1:2 Randomizations

ii. Following Standards of international device safety regulation

iii. Blinded (least possible)

iv. Powered high

v. Primary study hypothesis is performance (Efficacy in Pivotal studies)

vi. "Closest control"

vii. Multicentre

viii. Dual evaluation

- Clinical follow up
- Follow up by qualitative and quantitative invasive methods

ix. Defined concomitant medication

x. Natures / definitions of Endpoints defined by standard institutions / texts/ bodies

2. Phase II/ III study [Pivotal Trials]: For High Risk Medical Devices the **Pivotal Trials** and/or Wider population, real world trials, well randomized and statistically qualified should be submitted for further study permission.

A. If Phase II / III data reveals safety and adequate performance,

i. Marketing approvals could be given to the devices with moderate to high risk

ii. Conditional marketing approvals can be given to medical devices with Very high risk – with submission of post marketing surveillance study data of 10 - 25% of total sales for 2 years

B. If Phase II / III Study data is inadequate with good Feasibility data

i. Premarketing surveillance can be called IDE (Investigational device Exemption)

C. If Feasibility data and Phase II / Phase III data is not adequate –

i. Further randomized data will be called

Note: If the data of any study is not significant enou the approval may be barred / restricted.

3. For Active Medical Devices: The data for its active component independently should be submitted as per schedule Y

A. If the active component is biochemical in action, its Pharmacological data as per schedule Y

B. or Radiation, thermodynamic, Magnetic and sound- based active component human safety ranges and design control stating that the device has these uses these components within safety limits.

Annexure VI

DATA ELEMENTS FOR REPORTING SERIOUS ADVERSE EVENTS OCCURRING IN A CLINICAL TRIAL

1. Patient Details

- Initials & other relevant identifier (hospital/OPD record number etc.)*
- Gender
- Age and/or date of birth
- Weight
- Height

2. Suspected Device(s)

- Generic name of the Device*.
- Indication(s) for which suspect device was prescribed or tested.
- Starting date and time of day.
- Stopping date and time, or duration of treatment

3. Other Treatment(s)

- Provide the same information for concomitant devices a for the suspected Devices(s).

4. Details of Suspected Adverse Drug Reaction(s)

- Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.*
- Start date (and time) of onset of reaction.
- Stop date (and time) or duration of reaction.
- Setting (e.g., hospital, out-patient clinic, home, nursing home).

5. Outcome

- Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.
- For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.
- Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

6. Details about the Investigator*

- Name
- Address
- Telephone number
- Profession (speciality)
- Date of reporting the event to Licensing Authority:
- Date of reporting the event to Ethics Committee overseeing the site:
- Signature of the Investigator

Note: Information marked * must be provided."

Annexure VII

UNDERTAKING BY THE INVESTIGATOR

1. Full name, address and title of the Principal Investigator (or Investigator(s) when there is no Principal Investigator)
2. Name and address of the medical college, hospital or other facility the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, and / or any other statement(s) of qualification(s))
3. Name and address of all clinical laboratory facilities to be used in the study.
4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.
5. Names of the other members of the research team (Co- or sub-Investigators) who will be assisting the Investigator the conduct of the investigation (s).
6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.
7. Commitments:

   (i) I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary Ethics Committee and regulatory approvals have been obtained.

   (ii) I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval / favorable opinion from the Ethics Committee of the amendment, except where necessary to eliminate an immediate hazard(s) to the trial Subjects or when the change(s) involved are only logistical or administrative in nature.

   (iii) I agree to personally conduct and/or supervise the clinical trial at my site.

   (iv) I agree to inform all Subjects, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics comm e review and approval specified in the GCP guidelines are met.

   (v) I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory and GCP guidelines.

   (vi) I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug.

(vii) I agree to ensure that all associates, colleague loyees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their ob ions in meeting their commitments in the trial.

(viii) I agree to maintain adequate and accurate records and to make those records available for audit / inspection by the Sponsor, Ethics Committee, Licensing Authority or their authorized representatives, in accordance with regulatory and GCP provisions. I will fully cooperate with any study related audit conducted by regulatory officials or authorized representatives of the Sponsor.

(ix) I agree to promptly report to the Ethics Committee all changes in the clinical trial activities and all unanticipated problems involving risks to human Subjects or others.

(x) I agree to inform all unexpected serious adverse e to the Sponsor as well as the Ethics Committee within seven days of their occurence.

(xi) I will maintain confidentiality of the identification of all participating study patients and assure security and confidentiality of study data.

(xii) I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in clinical trials

8. Signature of Investigator with Date

Annexure VIII

ETHICS COMMITTEE

The number of persons in an Ethics Committee should have atleast seven members. Ethics Committee should appoint, from among its members, a Chairperson (who is from outside the institution) and a Member Secretary. Other members should be a mix of medical/non-medical, scientific and non-scientific persons, including lay public, to reflect the different viewpoints.

For review of each protocol the quorum of Ethics Committee should be atleast 5 members with the following representations:

- basic medical scientists.
- clinicians
- legal expert
- social scientist / representative of non-governmental voluntary agency / philosopher / ethicist / theologian or a similar person
- lay person from the community.

In any case, the ethics committee must include at least one member whose primary area of interest / specialization is nonscient c and at least one member who is independent of the institution / trial site. Besides, there should be appropriate gender representation on the Ethics Committee. If required, Subject experts may be invited to offer their views. Further, on the requirement of research area, e.g. Orthopedics, cardiovascular etc. specific patient groups may also be represented in the Ethics Committee as far as possible.

Only those Ethics Committee members who are independent of the clinical trial and the Sponsor of the trial should vote / provide opinion in matters related to the study.

FORMAT FOR APPROVAL OF ETHICS COMMITTEE

To

Dr.

Dear Dr. _____

The Institutional Ethics Committee / Independent Ethics Committee (state name of the committee, as appropriate) reviewed and di ssed your application to conduct the clinical trial entitled "……" on …….(date).

The following documents were reviewed:

a) Trial Protocol (including protocol amendments), dated_____ Version no (s)._____

b) Patient Information Sheet and Informed Consent Form (including updates if any) in English and/or vernacular language.

c) Investigator's Brochure, dated_____, Version no._____

d) Proposed methods for patient accrual including advertisement (s) etc. proposed to be used for the purpose.

e) Principal Investigator's current CV.

f) Insurance Policy / Compensation for participation and for serious adverse events occurring during the study participation.

g) Investigator's Agreement with the Sponsor.

h) Investigator's Undertaking (Annexure VII).

The following members of the ethics committee were present at the meeting held on (date, time, place).

_____ Chairman of the Ethics Committee

_____ Member secretary of the Ethics Committee

_____ Name of each member with designation

We approve the trial to be conducted in its presented form.

The Institutional Ethics Committee / Independent Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

Yours sincerely,

Member Secretary, Ethics Committee.

Annexure IX

INFORMED CONSENT

CHECKLIST FOR STUDY SUBJECT'S INFORMED CONSENT DOCUMENTS

1.1 *Essential Elements:*

a. Statement that the study involves research and explanation of the purpose of the research
b. Expected duration of the Subject's participation
c. Description of the procedures to be followed, including all invasive procedures and
d. Description of any reasonably foreseeable risks or discomforts to the Subject
e. Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.
f. Disclosure of specific appropriate alternative procedures or therapies available to the Subject.
g. Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records
h. Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)
i. Compensation and/or treatment(s) available to the Subject in the event of a trial-related injury
j. An explanation about whom to contact for trial related queries, rights of Subjects and in the event of any injury
k. The anticipated prorated payment, if any, to the Subject for participating in the trial
l. Subject's responsibilities on participation in the trial
m. Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Subject is otherwise entitled
n. Any other pertinent information

1.2 *Additional elements, which may be required*

a. Statement of foreseeable circumstances under which the Subject's participation may be terminated by the Investigator without the Subject's consent.

b. Additional costs to the Subject that may result from p ipation in the study.

c. The consequences of a Subject's decision to withdraw from the research and procedures for orderly termination of participation by Subject.

d. Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.

e. A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or foetus, if the Subject is or may become pregnant), which are currently unforeseeable

f. Approximate number of Subjects enrolled in the study

FORMAT OF INFORMED CONSENT FORM FOR SUBJECTS PARTICIPATING IN A CLINICAL TRIAL

Informed Consent form to participate in a clinical trial

Study Title:

Study Number:

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

Please initial box (Subject)

(i)	I confirm that I have read and understood the information sheet dated ___ for the above study and have had the opportunity to ask questions.	[ ]
(ii)	I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	[ ]
(iii)	I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.	[ ]
(iv)	I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)	[ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____ Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness _____ Date:_____/_____/_____

Name of the Witness: _____

Annexure X

Structure, contents and format for Clinical Study Report

1. Title Page: This page should contain information about:

- the title of the study,
- the protocol code,
- name of the investigational device tested,
- development Phase,
- indication studied,
- a brief description of the trial design,
- the start and end date of patient accrual and
- the names of the Sponsor and the participating Institutes (Investigators).

2. Study Synopsis (1 to 2 pages): A brief overview of the study from the protocol development to the trial closure should be given here. This section will only summarize the important conclusions derived from the study.

3. Statement of compliance with the 'Guidelines for Clinical Trials on Pharmaceutical Products in India : GCP Guidelines' issued by the Central Drugs Standard Control Organization, Ministry of Health, Government of India.

4. List of Abbreviations and Definitions

5. Table of contents

6. Ethics Committee:

This section should document that the study was conducted in accordance with the ethical principles of Declaration of Helsinki. A detailed description of the Ethics Committee constitution and date(s) of approvals of trial documents for each of the participating sites should be provided. A declaration should state that EC notifications as per Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organization and Ethical Guidelines for Biomedical Research on Human Subjects, issued by Indian Council of Medical Research have been followed.

7. Study Team: Briefly describe the administrative structure of the study. (Investigators, site staff, Sponsor/ designates, Central laboratory etc.).

8. Introduction: A brief description of the device development rationale should be given here.

9. Study Objective: A statement describing the overall purpose of the study and the primary and secondary objectives to be achieved should be mentioned here.

10. Investigational Plan: This section should describe the overall trial design, the Subject selection criteria, the treatment procedures, inding / randomization techniques if any, allowed/ disallowed concomitant treatment, the efficacy and safety criteria assessed, the data quality assurance procedures and the statistical methods planned for the analysis of the data obtained.

11. Trial Subjects: A clear accounting of all trial Subjects who entered the study will be given here. Mention should also be made of all cases that were dropouts or protocol deviations. Enumerate the patients screened, randomised, and prematurely discontinued. State reasons for premature discontinuation of subjects in each applicable case.

12. Efficacy evaluation: The results of evaluation of all the efficacy variables will be described in this section with appropriate tabular and graphical representation. A brief description of the demographic characteristics of the trial patients should also be provided along with a listing of patients and observations excluded from efficacy analysis.

13. Safety Evaluation:

This section should include the complete list

13.1 all serious adverse events, whether expected or unexpected and

13.2 unexpected advese events whether serious or not (compiled from data received as per Annexure VI).

The comparison of adverse events across study groups may be presented in a tabular or graphical form. This section should also give a brief narrative of all important events considered related to the investigational product.

14. Discussion and overall Conclusion: Discussion of the important conclusions derived from the trial and scope for further development.

15. List of References:

16. Appendices: List of Appendices to the Clinical Trial Report

a. Protocol and amendments
b. Specimen of Case Record Form
c. Investigators' name(s) with contact addresses, phone, e-mail etc.

d. Patient data listings
e. List of trial participants treated with investigational product
f. Discontinued participants
g. Protocol deviations
h. CRFs of cases involving death and life threatening adverse event cases
i. Publications from the trial
j. Important publications referenced in the study
k. Audit certificate, if available
l. Investigator's certificate that he/she has read the report and that the report accurately describes the conduct and the results of the study.