Institutional Review Board, Tata Memorial Centre (IRB, TMC)

Title: Initial Review of Submitted Protocol

SOP Code: SOP 04a/ V1	Date : 05/09/2012	Pages: 1 to 20

4a.1 Purpose

The IRB should review and must approve, every research study involving human participants and other forms of studies, before the research is initiated. The IRB should evaluate the scientific rationale, scope and, methodology, and the ethical aspects of the study. The committee should evaluate the possible risks to the participants with proper justification as well as the expected benefits to participants/community. The adequacy of documentation for ensuring privacy & confidentiality should also be reviewed.

The purpose of this Standard Operating Procedure (SOP) is to describe how the IRB members will review an initial submission of the research study for approval using the Assessment Form. The Assessment Form AX1-V1SOP04a/V1 is designed to standardize the review process and to facilitate reporting, recommendations and comments offered to each study.

4a.2 Scope

This SOP applies to the review and assessment of all studies submitted for initial review and approval of the IRB. The specific points/items in the Assessment Form must be adequately addressed in the protocol and/or protocol-related documents submitted for the review. Relevant comments made during discussion and deliberation about a study should be recorded in the minutes of the meeting. The decision reached by the IRB will be communicated to the PI.

4a.3 Categorization of protocols

The Member Secretary, IRB or secretariat shall screen the proposals for their completeness.
Depending on the risk involved in the research proposals, Member Secretary will categorise them into three types, viz.,

i. Initial review
ii. Expedited review
iii. Exemption from review

An investigator may categorize his/her protocol in to the above three types, providing justification for the same, and after filling up Standard Request Forms for Expedited Review AX1-V1/SOP04b/V1 (SOP 04b/V1) / Exemption from review AX1-V1/SOP04c/V1 (SOP 04c/V1). However the decision to accept the request for Exemption from review / Expedited Review will be made by the Member Secretary, IRB.

This SOP describes the process of initial review.

4a.4 Initial Review

All research studies presented with more than minimal risk and which do not qualify for

exemption or expedited review, or involve vulnerable populations and special groups, should be subjected to full board review.

While reviewing the research studies, the following situations should be carefully assessed against the existing facilities at the research site for risk/benefit analysis:

a. Collection of blood samples by finger prick, heel prick, ear prick, or venipuncture from (Refer APP6/V1) :-
   i. Healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week
   ii. From other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg whichever is lesser, is drawn in an 8 week period and not more than 2 times per week
   iii. From neonates depending on the haemodynamics, body weight of the baby and other purposes not more than 10% of blood is drawn within 48 – 72 hours. If more than this amount is to be drawn it becomes a risky condition requiring infusion/blood transfusion
   iv. Prospective collection of biological specimens for research purposes by non-invasive means.
   For instance:
      - skin appendages like hair and nail clippings in anon-disfiguring manner;
      - dental procedures - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supra and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
      - excreta and external secretions (including sweat);
      - uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue ;
      - mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings ;
      - sputum collected after saline mist nebulization and bronchial lavages.

b. Collection of data through non-invasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/ approved for marketing, for instance –
      - physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;
      - Weighing or Testing Sensory Acuity;
      - Magnetic Resonance Imaging;

- Electrocardiography, Echocardiography Electroencephalography, Thermography, detection of naturally occurring radioactivity, Electroretinography, Ultrasound, Diagnostic Infrared Imaging, Doppler Blood Flow and such alike;
- Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual;

c. Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes
d. Collection of data from voice, video, digital, or image recordings made for research purposes;
e. Research on individual or group characteristics or behaviour not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies;
f. Research involving collection and storage of genetic materials (Refer APP10/V1);
g. Research involving gene therapy and gene transfer protocols (Refer APP11/V1).

4a.5 Elements of Review

The primary task of the IRB is to review research proposals and their supporting documents with special attention to the scientific validity, informed consent and submission form for the suitability and feasibility of the study.

The following will be considered as applicable:

4a.5.1 Scientific Design and Conduct of the Study

- Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
- Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
- Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well reasoned and appropriate to the aims of the project?
- Relevance of the work in the context of contemporary translation or clinical cancer research:
  * Does this study address an important research question or is it a predominantly service proposal?
  * If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
  * What will be effect of these studies on the concepts, methods, technologies,

treatments, services, or preventive interventions that drive this field?

- Appropriateness of the study design in relation to the objectives of the study;
- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- The justification for the use of control arms;
- Potential of the work that would be conducted to lead into a larger and high impact study;
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole;
- The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board;
- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward;
- The adequacy of the site, including the support staff, available facilities, and emergency procedures;
- Study Reporting and publication of the research.

4a.5.2 Care and Protection of Research Participants

- Required qualifications and experience of the investigators' for the proposed study;
- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;
- Plans to withdraw subjects from the study by the investigator ;
- Medical care to be provided to research participants during and after the course of the research;
- Adequacy of medical supervision and psycho-social support for the research participants;
- Steps to be taken if research participants voluntarily withdraw during the course of the research;
- Criteria for extended access to, the emergency use of, and/or the compassionate use of study products;
- Arrangements, if appropriate, for informing the research participant's general practitioner or family doctor, including procedures for seeking the participant's consent to do so;
- Description of any plans to make the study product available to the research participants following the research and description of any financial costs to research participants (Refer APP3/V1);
- Rewards and compensations for research participants (including money, services, and/or gifts);
- Provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research (Refer APP4/V3) as per institutional policy/ICMR guidelines/existing national legislation(CDSCO, DCGI).

- Insurance and indemnity arrangements.

4a.5.3 Protection of Research Participant Confidentiality

- A description of the persons who will have access to personal data of the research participants, including medical records and biological samples;
- Measures taken to ensure the confidentiality and security of personal information concerning research participants.

4a.5.4 Informed Consent/ Consent Process

- Essential Elements:

1. Statement that the study involves research and explanation of the purpose of the research
2. Expected duration of the Subject's participation
3. Description of the procedures to be followed, including all invasive procedures
4. Description of any reasonably foreseeable risks or discomforts to the Subject
5. 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.
6. Disclosure of specific appropriate alternative procedures or therapies available to the Subject.
7. 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
8. Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)
9. Compensation and/or treatment(s) available to the Subject in the event of a trial-related injury
10. An explanation about whom to contact for trial related queries in the event of any injury and rights of Subjects
11. The anticipated prorated payment, if any, to the Subject for participating in the trial
12. Subject's responsibilities on participation in the trial
13. 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
14. Any other pertinent information

- 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 participation 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 fetus, if the Subject is or may become pregnant), which are currently unforeseeable.
f. Approximate number of Subjects enrolled in the study

- A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent (Refer APP7/V1 & APP8/V1)

- Adequacy, completeness and comprehension of written and oral information to be given to the research participants, and, when appropriate, their Legally Acceptable Representative(s) (LAR) (Refer APP5/V1);

- Clear justification for the intention to include research participants who cannot consent, and a full account of arrangements made to obtain their consent /authorisation/consent of LAR;

- Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being;

- Provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

4a.5.5 Community Considerations

- Impact and relevance of the research to the local community and the concerned communities from which the research participants are drawn;
- Steps taken to consult with the concerned communities during the course of designing the research;
- Influence of the community on the consent of individuals;
- Proposed community consultation during the course of the research;
- Extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;
- a description of the availability and affordability of any successful study product to

the concerned communities following the research;
- the manner in which the results of the research will be made available to the research participants and the concerned communities.

4a.5.6 Recruitment of Research Participants

- The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity) (Refer APP2/V1);
- the means by which initial contact and recruitment is to be conducted;
- the means by which full information is to be conveyed to potential research participants or their representatives;
- inclusion criteria for research participants;
- exclusion criteria for research participants;
- students or staff recruitment in research (Ref. APP1/V1);
- healthy volunteers.

4a.6 Responsibility

The IRB Secretariat is responsible for receiving, verifying, and managing the hard copies of the received submission. In addition, the Secretariat should create a study specific file, distribute the packages and study assessment forms to the IRB members for review, and communicate the review results to the investigators.

IRB members are responsible for receiving, verifying, and reviewing the research protocols.

4a.7 Detailed instructions

Only investigator initiated trials/studies seeking intramural grants are sent prior to the meeting for external review. Project is scored by the reviewer (Reviewer Assessment Form AX2-V1/SOP04a/V1). The external scores will be considered for granting intramural funds. The external reviewer comments if received on time will be considered during the IRB discussion. However pharma-sponsored studies and investigator initiated studies requiring no intramural funds/extramural studies will be tabled in the IRB meeting without any prior external review.

Distribution of the project documents

- The distribution of the project documents for IRB review will be as follows:
  - For investigator initiated studies, soft copy on a CD to all members;
  - For Pharma funded projects printed/hard copies only to the Member Secretary and the lead discussant/s; soft copy to the remaining members.

Assigning Lead discussants

- The Member Secretary, IRB will assign lead discussants to each research

study for scientific, ethical and statistical review. The lead discussants will be members of the IRB and will have to present a detailed relevant review of the assigned study.

- The lead discussants/Primary Reviewers will present the research study at a regular full board or expedited review subcommittee or special meeting of the IRB. The Investigator may be called for any questions or clarification required by the board members

  - The lead discussant is informed no less than 7 days prior to the meeting through the agenda. In case the lead discussant is not in a position to review due to some reason, he/she should inform the Member Secretary, IRB at the earliest, so that the research study can be assigned to another member.
  - In the event of his/her absence, a lead discussant can send written comments on the research protocols to the Member Secretary, which will be tabled and discussed during the meeting. However, a final decision on the research protocol will be arrived at, by a broad consensus at the end of discussion among attending members and not solely based on written comments.
  - It is the responsibility of the assigned lead discussant/s to review the research protocols assigned to them thoroughly and communicate their observations, comments and decisions to the IRB during the meeting. The lead discussant/s should return the research protocols and relevant documents to the secretariat on the day of the meeting.

- The Member Secretary can invite an independent consultant (if necessary) for comments during the full board meeting.

Responsibilities of IRB members

- Check the contents of the packages.
- Sign and date an acknowledgement form / receipt upon receiving the packages.
- Return the acknowledgement form/ receipt back to the delivery person /IRB Secretariat.
- Check the meeting date to see if he/she is available to attend the meeting.
- Identify the project assigned for review.
- Notify the IRB Secretariat 3 days prior to the convened IRB meeting regarding the missing documents, if any.
- The members must return the packages including CD to the IRB Secretariat on the day of the scheduled meeting. In case an IRB member is not in a position to attend the scheduled meeting, the responsibility of returning the packages would be that of the respective IRB member.

4a.8 Review the Protocol:

Review all elements as per section 4.3, 4.4, 4.5. The protocol will be reviewed by each member as per guidelines to review a study protocol described in AX1-V1SOP04/V1

4a.9 Use of study assessment forms and reviewer assessment form

It is the responsibility of the IRB members to use assessment form as a checklist while reviewing each research protocol. The duly filled, signed and dated assessment forms may be returned along with the research protocols to the Secretariat one day prior to the meeting. The assessment form is designed to standardize the review process. The study assessment form (AX1-V1SOP04a/V1) helps to ensure that all elements of research study are reviewed and are accordingly documented during the discussion / meeting.

IRB members having expertise in the study should also score the studies seeking intramural funds as per Reviewer Assessment Form (AX2-V1SOP04a/V1)

Note: **The completed assessment form is the official record of the decision reached by the IRB for the specific protocol**

4a.9.1 Collection of the assessment reports

The IRB Secretariat will collect the Assessment Forms AX1-V1SOP04a/V1 and the comments from each reviewer and file them in the original set of the study file.

4a.10 At IRB meeting

The details of the review procedures and communication of the decision is described in detail in SOP05/V1

References

1. World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000) Retrieved from- *www.who.int/tdr/publications/publications/*accessed 14th September 2008
2. International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 Retrieved from- *http://www.ich.org/LOB/media/MEDIA482.pdf* accessed 14th September 2008
3. Cavazos N., Forster D., and Bowen A.J., Ethical Concerns in Placebo-controlled studies: An Analytical Approach, Drug Information Journal 36(2) 2002: pgs 249-259, via WIRB documents
4. Draft Guidelines for Compensation to Participants for Research Related Injury in India. http://icmr.nic.in/guidelines.htm

Glossary

Document: Document may be in any form, e.g., paper, electronic mail (e-mail), faxes, audio or video tape, etc.

Expedited review/meeting: A review process by only member secretaries of both the IRBs or IRB subcommittee, who then report the decision to the full board in a formal meeting. An expedited review is an accelerated review for minor changes to the approved protocol, research proposal with minimal risk and documents of minor nature.

Extramural : The studies funded by external sources

Full Board/ Regular Review: Review of initial, resubmitted, continuing review, amendments of protocols and or ICFs and any other documents which are tabled in a formally convened meeting of the full IRB committee for detailed discussion and decisions.

Initial Review: The first time review of the protocol done by one or two individual reviewers/lead discussants (IRB members) during the formally convened full board IRB meeting.

Intramural- The studies funded by the institution

Pre-clinical study: Animal and *in vitro* studies providing information on possible toxicities

and mechanisms of action, and starting doses for human studies.

Phase I studies: Initial introduction of an investigational new drug (IND) into humans, studies designed to determine the metabolism and pharmacological actions of drugs in humans, and studies designed to assess the side effects associated with increasing doses .

Phase II study: A study of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

Phase III study: A study expands controlled and uncontrolled trials performed after preliminary evidence suggesting effectiveness of the drug has been obtained. They are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling

Phase IV study: A study that seeks to expand an approved medication's use into a new population, new indication, or new dose.

Study Assessment Form: An official record that documents the protocol review process.

Reviewer Assessment Form: An official record that documents the scoring of the protocol.

Vulnerable subjects: A vulnerable category of subjects includes children, prisoners, pregnant women, handicapped or mentally disabled persons, refugees, displaced persons and economically or educationally disadvantaged persons, who are likely to be vulnerable to coercion or undue influence.

Annexure

AX1-V1/SOP04a/V1

Study Assessment Form to be used at the IRB meeting.

Page 1 of 5

Study Assessment Form

Protocol Number :		Date (DD/MM/YY):	
Protocol Title :			
Principal Investigators:		MMC Registration No.	
Institute:		Contact No.	
Co – investigator(s):		Contact No.	
Delineation of responsibilities of investigators:			
Total No. of Participants:		No. of Study site/s:	
Funding Agency:		Contact No.	
Duration of the Study:		Status:	☐ New ☐ Revised ☐ Amended
Reviewer's name :		Contact No.	
Type of the Study :	☐ Intervention ☐ Epidemiology ☐ Observational ☐ Document based ☐ Individual based ☐ Genetic ☐ Social Survey ☐ Others, specify……		
Review Status:	☐ Regular ☐ Expedited ☐ Emergency		
Description of the Study in brief: Mark whatever applied to the study. ☐ Randomized ☐ Stratified Randomized ☐ Open-labeled			

☐ Double blinded	☐ Placebo controlled	☐ Treatment controlled
☐ Cross-over	☐ Parallel	☐ Interim Analysis
☐ Multicenter study	☐ Screening	☐ Descriptive
☐ Use of Tissue samples	☐ Use of Blood samples	☐ Use of genetic materials

Brief the study design and the statistics used:

Study Objectives:
Please see my attached comments in a separate sheet
……
……
……
……
……

Mark and comment on whatever items applicable to the study

1	Objectives of the Study ☐ clear ☐ unclear	What should be improved?
2	Need for Human Participants ☐ Yes ☐ No	Comment:
3	Methodology: ☐ clear ☐ unclear	What should be improved?
4	Background Information and Data ☐ sufficient ☐ insufficient	Comment:
5	Risks and Benefits Assessment ☐ acceptable ☐ unacceptable	Comment:
6	Inclusion Criteria ☐ appropriate ☐ inappropriate	Comment:
7	Exclusion Criteria ☐ appropriate ☐ inappropriate	Comment:
8	Discontinuation and Withdrawal Criteria ☐ appropriate ☐ inappropriate	Comment:
9	Involvement of Vulnerable Participants ☐ Yes ☐ No	Comment:
10	Voluntary, Non-Coercive Recruitment of	Comment:

	Participants ☐ Yes ☐ No	
11	Sufficient number of participants? ☐ Yes ☐ No	Comment:
12	Control Arms (placebo, if any) ☐ Yes ☐ No	Comment:
13	Are qualifications and experience of the Participating Investigators appropriate? ☐ Yes ☐ No	Comment:
14	Disclosure or Declaration of Potential Conflicts of Interest ☐ Yes ☐ No	Comment:
15	Facilities and infrastructure of Participating Sites ☐ Appropriate ☐ Inappropriate	Comment:
16	Community Consultation ☐ Yes ☐ No	Comment:
17	Involvement of Local Researchers and Institution in the Protocol Design, Analysis and Publication of Results ☐ Yes ☐ No	Comment:
18	Contribution to Development of Local Capacity for Research and Treatment ☐ Yes ☐ No	Comment:
19	Benefit to Local Communities ☐ Yes ☐ No	Comment:
20	Availability of similar Study / Results ☐ Yes ☐ No	Comment:
21	Are blood/tissue samples sent abroad? ☐ Yes ☐ No	Comment:

22	Are procedures for obtaining Informed Consent appropriate? ☐ Yes ☐ No	Comment:
23	Contents of the Informed Consent Document ☐ clear ☐ unclear	Comment:
24	Language of the Informed Consent Document ☐ clear ☐ unclear	Comment:
25	Contact Persons for Participants mentioned? ☐ Yes ☐ No	Comment:
26	Privacy & Confidentiality ensured? ☐ Yes ☐ No	Comment:
27	Inducement for Participation ☐ Unlikely ☐ Likely	Comment:
28	Provision for Medical / Psychosocial Support ☐ appropriate ☐ inappropriate	Comment:
29	Provision for Treatment of Study-Related Injuries ☐ appropriate ☐ inappropriate	Comment:
30	Provision for Compensation ☐ appropriate ☐ inappropriate	Comment:
31	Provision for post-trial access ☐ appropriate ☐ inappropriate	Comment:

Assessment Report

Review Date (DD/MM/YYYY): Protocol number:

Protocol Title :		
Elements Reviewed	☐ Attached	☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:	
DECISION :	☐ Approved ☐ Approved with Recommendation ☐ Resubmission ☐ Disapproved	
Comment:		
Signature :		Date:

AX2-V1/SOP04a/V1

Reviewer's Comments and Score
Tata Memorial Centre (TMH/ACTREC)
Assessment Form

TMH Project No. -

Principal Investigator-

Review Criteria	*Max. Marks*	Reviewer's Score	IRB Committee Score
Innovation: Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?	30		
Relevance of the work in the context of contemporary Translation or clinical cancer research: * Does this study address an important research question or is it a predominantly service proposal? * If the aims of the application are achieved, how will scientific knowledge or clinical practice are advanced? * What will be effect of these studies be on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?	20		
Appropriateness of study design, work plan & structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods & analyses adequately developed, well integrated, well reasoned & appropriate to the aims of the project?	20		

Potential of the work that would be conducted through research grant to lead into a larger and high impact study	20		
Investigator's capability, availability of Infrastructure & scientific environment to conduct the study within the time frame and carry it forward	10		
Total	100		

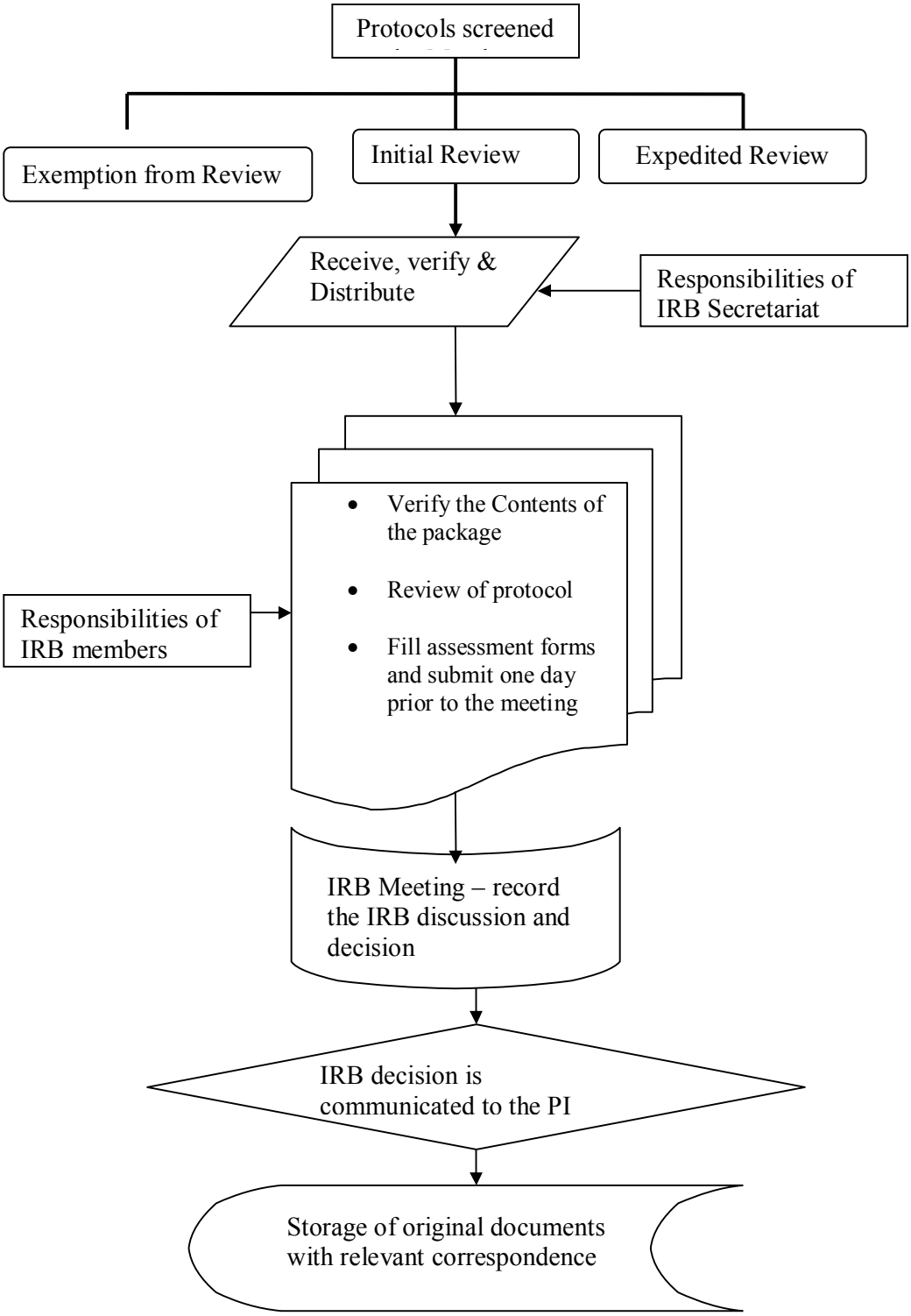
Comments or suggestions if any (Attach extra sheets, if necessary):

Is there any conflict of interest (scientific, service or financial) between you and that of the Investigators?

N	Y

Reviewer's Signature & Name (below the line please): Date:

Flow Chart


Protocols screened
Exemption from Review
Initial Review
Expedited Review
Receive, verify & Distribute
Responsibilities of IRB Secretariat
Verify the Contents of the package
Review of protocol
Fill assessment forms and submit one day prior to the meeting
Responsibilities of IRB members
IRB Meeting – record the IRB discussion and decision
IRB decision is communicated to the PI
Storage of original documents with relevant correspondence