

## AX12-V6.1/SOP 03/V6.1

### **Instructions for Submission of Projects for Institutional Ethics Committee Approval**

The latest version of IEC documents can be accessed ONLINE @TMC website- [tmc.gov.in/actrec.gov.in](http://tmc.gov.in/actrec.gov.in)

- ❖ All IRB submissions should be made via online IEC portal <https://www.iecportal.org/login.php>. Please refer to the online demo videos on the portal for completing the applications.
- ❖ Kindly refer to the checklist of documents to be submitted to IEC. All documents listed may not be applicable to your project.
- ❖ A brief description of study designs is provided along with the document checklist for your assistance.
- ❖ The checklist of documents, study design and this instruction page is for your reference and should not be submitted at the time of IEC submission of your study.
- ❖ The IEC will process all study related documentary submissions within 48 hours of submission of documents to the IEC office.

### **Initial Review of Projects**

#### **Instructions for filling the IEC submission form.**

1. IEC submission form has 4 sections- A, B, C and D
2. All sections should be completely filled.
3. Questions not relevant to your study should be filled as NA.
4. **Do not alter or remove the version no and date reflecting in header of IEC submission form.**
5. Do not make any formatting changes in the IEC submission form.
6. **The title of the study should be same in all four sections of the Project Submission Form.**
7. All 4 sections should be signed and dated by the Principal Investigator.
8. The signatures of your DMG Convener (if applicable) and Head of Department should be obtained before submission of hard copy of the IEC form to IEC.

### **After initial review of projects**

After review of project by IEC, your study may attain any one of the following statuses:

**A) Approved-**Your study is scientifically and ethically sound and you may initiate the study subject to terms indicated in the final approval letter.

**B) Revisions with minor modifications-** Implies that your study may be approved once all the queries/recommendations of IEC are addressed satisfactorily. The revisions will not be taken up for full board and would be reviewed by Member Secretary the respective lead discussant on behalf of the full board. However, in some cases may be referred for a full board review.

**C) Revisions with major modifications for resubmission-**The study design and/or ethical aspect of the study is not satisfactory and would require extensive revision and would be re reviewed during full board Ethics Committee Meeting.

**D) Not Approved-** The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the IEC Secretariat within 21 working days.

If your project, after initial review attains the status **B** or **C**, the following documents are to be submitted to IEC:

- 1) IEC form for re-review of projects **AX11-V6.1/SOP 03/V6.1**
- 2) Response letter, if applicable
- 3) Supporting documents such as modified protocols, CRFs, ICFs and any other documents if applicable and any other documents

**You do not** have to submit the IEC PROJECT SUBMISSIONFORM which was submitted at the time of initial review.

**The checklist of document provided to you lists out the mandatory documents to be submitted at the time of initial review. Instruction/template to develop them is provided below**

#### **General information**

- Protocol, CRF, ICF, should bear Project title, page number, **version no. & date** (not to be confused with the version no. and date present in the TMC-IEC submission form. You may refer to the CRS SOP for developing protocol.
- **The vernacular versions of ICF (Hindi, Marathi and any other language) should be submitted in .pdf format.**
- The ICF template provided by IEC is a reference document to assist in developing an effective informed consent document. However, the Principal Investigator may develop a customized ICF to suit the protocol requirement while addressing all key points.
- Kindly ensure that the study rationale and procedures described in the ICF is not a mere replica of the protocol. The ICFs should be written in a simple, non-technical style keeping in mind the educational and socio-economic background of the TMC patient population. Similarly, the child information sheet should be simple. It should be developed keeping in mind, the age group being addressed. Parent Information Sheet and consent form should be submitted in case of minors.
- In case of collaborative studies, kindly provide a draft MOU, CTA, MTA along with institutional legal advisor's comments whichever is applicable.
- Find below a brief definition of the study designs presented in the IEC Project Submission Form. In case, your study is based on a study design which is not mentioned in Section C of the IEC form, please specify the same while filling up the IEC Submission Form.

## Appendix-Study Designs

### **Randomized Controlled Trial:**

In a **randomized controlled trial**, participants are assigned to treatment conditions at random (i.e., they have an equal probability of being assigned to any group). Procedures are controlled to ensure that all participants in all study groups are treated the same except for the factor that is unique to their group. The unique factor is the type of intervention they receive. The **primary goal** of conducting an RCT is to test whether an intervention works by comparing it to a control condition, usually either no intervention or an alternative intervention. **Secondary goals** may include: identify factors that influence the effects of the intervention (i.e., moderators), understand the processes through which an intervention influences change (i.e., mediators or change mechanisms that bring about the intervention effect)

**In double-blinding**, neither the participants nor the investigator knows the participants' treatment assignment. In placebo-controlled trials, Masking can be improved by using an active placebo that has the same side effects as the drug but lacks its therapeutic effects.

**Partial Blinding:** Double-blinding is rarely possible in trials of behavioral treatment. It is usually obvious to participants which treatment they are receiving. Also, the treatment assignment is known by any research staff who delivers the treatment. However, the staff that assesses the study outcome can and should be kept blind to the patient's treatment condition. Special care is needed to prevent staff and study participants from unblinding the outcome assessor.

**Single-blind:** Term used to describe a study in which either the investigator or the participant, but not both of them, is unaware of the nature of the treatment the participant is receiving.

**Non-blinded trial or Open-label trial:** is a type of clinical trial in which both the researchers and participants know which treatment is being administered.

**Adaptive design** is a trial design that allows modifications to some aspects of the trial after its initiation without undermining the validity and integrity of the trial. Adaptive design makes it possible to discover and rectify inappropriate assumptions in trial designs, lower development costs and reduce the time to market. An adaptive clinical trial evaluates patients' reactions to a drug beginning early in a clinical trial and modifies the trial in accord with those findings. The adaptation process continues throughout the trial. Modifications may include dosage, sample size, drug undergoing trial, patient selection criteria etc. In some cases, trials have become an ongoing process that regularly adds and drops therapies and patient groups as more information is gained. The aim is to more quickly identify drugs that have a therapeutic effect and to zero in on patient populations for whom the drug is appropriate. A key modification is to adjust dosing levels.

**Quasi-experiment or Nonrandomized clinical trials** arise from situations in which it is impossible or difficult to assign subjects to treatment by chance. A quasi-experiment is an empirical study used to estimate the causal impact of an intervention on its target population.

Quasi-experimental research shares similarities with or randomized controlled trial, but they specifically lack the element of random assignment to treatment or control.

**Interrupted time series study** a study that uses observations at multiple time points before and after an intervention (the 'interruption'). The design attempts to detect whether the intervention has had an effect significantly greater than any underlying trend over time.

**Cohort study:** For research purposes, a cohort is any group of people who are linked in some way and followed over time. Researchers observe what happens to one group that's been exposed to a particular variable — for example, the effect of company downsizing on the health of office workers. This group is then compared to a similar group that hasn't been exposed to the variable.

**Prospective cohort study:** A prospective study watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort of participants and watching them over a long period. Prospective studies are carried out from the present time into the future. Because prospective studies are designed with specific data collection methods, it has the advantage of being tailored to collect specific exposure data and may be more complete. The disadvantage of a prospective cohort study may be the long follow-up period while waiting for events or diseases to occur. Thus, this study design is inefficient for investigating diseases with long latency periods and is vulnerable to a high loss to follow-up rate.

**Retrospective cohort study:** Retrospective cohort studies, also known as historical cohort studies, are carried out at the present time and look to the past to examine medical events or outcomes. In other words, a cohort of participants selected based on exposure status is chosen at the present time, and outcome data (i.e. disease status, event status), which was measured in the past, are reconstructed for analysis. The primary disadvantage of this study design is the limited control the investigator has over data collection. The existing data may be incomplete, inaccurate, or inconsistently measured between participants.<sup>2</sup> However, because of the immediate availability of the data; this study design is comparatively less costly and shorter than prospective cohort studies.

**Case control study:** Here researchers use existing records to identify people with a certain health problem ("cases") and a similar group without the problem ("controls"). Example: To learn whether a certain drug causes birth defects, one might collect data about children with defects (cases) and about those without defects (controls). The data are compared to see whether cases are more likely than controls to have mothers who took the drug during pregnancy.

**Nested Case control study:** A nested-case control study depends on the pre-existence of a cohort that has been followed over time. This cohort, at its inception or during the course of follow-up, has had exposure information and/or biospecimens collected of interest to the investigator. The investigator identifies cases of disease that occurred in the cohort during the follow-up period. The investigator also identifies disease-free individuals within the cohort to serve as controls. Using previously collected data and obtaining additional measurements of exposures from available biospecimens the investigator compares the exposure frequencies

in cases and controls as in a non-nested case-control study. Nested case-control studies are carried out when it is either too costly or not feasible to perform additional biospecimen analyses on an entire cohort.

**Cross-sectional study** -examines the relationship between diseases (or other health related state) and other variables of interest as they exist in a defined population at a single point in time or over a short period of time (e.g. calendar year). Cross-sectional studies can be thought of as providing a snapshot of the frequency of a disease or other health related characteristics (e.g. exposure variables) in a population at a given point in time. Cross-sectional studies may be descriptive or analytical in nature.

1. **Descriptive Cross-sectional study** -A cross-sectional survey may be purely descriptive and used to assess the burden of a particular disease in a defined population.
2. **Analytical cross-sectional surveys** - Used to investigate the association between a putative risk factor and a health outcome In a cross-sectional survey the risk factors and outcome are measured simultaneously, and therefore it may be difficult to determine whether the exposure proceeded or followed the disease.

**A longitudinal survey** is an epidemiologic study that follows a population forward over time, evaluating the effects of one or more variables on a process is a correlation research study that involves repeated observations of the same variables over long periods of time.

#### **Feasibility study:**

Feasibility studies are pieces of research done before a main study in order to answer the question “Can this study be done?” They are used to estimate important parameters that are needed to design the main study. For instance:

1. Standard deviation of the outcome measure, which is needed in some cases to estimate sample size;
2. Willingness of participants to be randomized;
3. Willingness of clinicians to recruit participants;
4. Number of eligible patients; carers or other appropriate participants;
5. Characteristics of the proposed outcome measure and in some cases feasibility studies might involve designing a suitable outcome measure;
6. Follow-up rates, response rates to questionnaires, adherence/compliance rates, ICCs in cluster trials, etc. o availability of data needed or the usefulness and limitations of a particular database; and
7. Time needed to collect and analyze data.

**Pilot Study-** is a version of the main study that is run in miniature to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure recruitment, randomization, treatment, and follow-up assessments all run smoothly. It will therefore resemble the main study in many respects, including an assessment of the primary outcome. In some cases, this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or at the end of the pilot study the data may be analyzed and set aside, a so-called external pilot. Also referred to as exploratory trials.

**Pivotal Study-** Usually a phase III study which presents the data that the FDA uses to decide whether or not to approve a drug. A pivotal study will generally be well-controlled, randomized, of adequate size, and whenever possible, double-blind. Also referred to as confirmatory trials.