

## **ADDENDUM To Standard Operating Procedure (SOP) for Institutional Ethics Committee for Human Research at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow**

Clinical trials are generally classified into Phases I to IV. It is not possible to draw distinct lines between the phases, and diverging opinions about details and methodology to exist. Description (in brief) of the individual phases, based on their purposes as related to clinical development of pharmaceutical products, are given below:

### **a) Phase I**

These are the first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans.

### **b) Phase II**

The purpose of these therapeutic pilot studies is to demonstrate activity and to assess short-term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. The trials are performed in a limited number of subjects and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. This phase also aims at the determination of appropriate dose ranges/regimens and (if possible) clarification of dose/response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

### **c) Phase III**

Trials in larger ( and possibly varied) patient groups with the purpose of determining the short-and long-term safety/efficacy balance of formulation(s) of the active ingredient, as well as to assess its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g. clinically-relevant drug interactions, factors leading to differences in effect such as age, etc.). The design of trials should preferably be randomized double-blind, but other designs may be acceptable, e.g. long-term safety studies. Generally, the circumstances of the trials should be as close as possible to normal conditions of use.

### **d) Phase IV**

Studies performed after marketing of the pharmaceutical product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of post-marketing surveillance, assessment of therapeutic value of treatment strategies. Although methods may differ, phase IV studies should use the same scientific and ethical standards as applied in premarketing studies. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new pharmaceutical products.

The sponsor is responsible for providing the investigational and comparator (if any) products, as well as appropriate information to support the safe use of those products. In addition, the sponsor is responsible for ensuring that the trial is conducted in accordance with sound scientific principles and good clinical practice standards by selecting qualified investigators, providing a protocol and ensuring protocol compliance, establishing the distribution of trial-related responsibilities, and providing procedures and staff for management of the clinical trial, recordkeeping and handling data, monitoring, and quality assurance. The sponsor is also ultimately responsible for ensuring compliance with applicable legal, ethical, and regulatory requirements (although local regulations may designate certain required activities as investigator responsibilities), and for providing compensation and indemnity for trial-related injury according to local laws and regulations.

## **Agreement of Principal Investigator with the sponsor of the Trial**

The sponsor has certain responsibilities and there is a need for an agreement between principal investigator and sponsor of the study. The following may be considered as guideline for studies to be undertaken at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow.

### **Delegation of Responsibilities to CRO**

The sponsor may transfer all or any trial related responsibilities to a scientific body/CRO and this should be clearly stated.

### **Investigator and site selection**

Sponsor should state that investigator has been selected taking into consideration the qualification, experience, availability for the duration of the study, and facilities at the trial site. The trial site should have adequate facilities including laboratories, equipment and sufficient medical, paramedical and administrative staff to support the trial. The laboratory assays should be performed in accordance to Good Laboratory Practice (GLP).

### **Supply of investigational and comparator product**

Sponsor should undertake the responsibility of providing the investigational and comparator (if any) products as well as the appropriate information for safe use of the product. The sponsor must bring any new relevant new information to the attention of investigator.

### **Delegation of responsibilities to the investigator**

The sponsor should delegate the responsibilities to the investigator for conducting of clinical trial, data processing, breaking of code, statistical handling, preparation of trial reports and submission of trial materials to institutional ethics committee, regulatory authorities (if required) and others (for audit, monitor and inspection).

**Quality assurance**

The sponsor should establish system of quality assurance (including independent auditing) to ensure that the conduct of trial and generation, documentation and reporting of data comply with the protocol, Good Clinical Practice standards and applicable regulatory requirements.

**Compensation and indemnity**

There should be adequate compensation/treatment to subjects in the event of trial related injury or death and provide indemnity (legal & financial coverage) for the investigator except for claims resulting from malpractice and negligence.

**Final report**

A copy of trial report prepared by the sponsor should be submitted to the institutional ethics committee in order to inform the IEC of the participating centre regarding final outcome after completion of the study.