Chapter 6
Preparation of Ethics Committee (IRB) Proposal

The ethics committee is responsible for reviewing a number of trial-related documents and giving their approval (or in some cases favourable opinion) before a study starts. Usually, the local IEC (or IRB in some countries) must be consulted [1].

6.1 ICH GCP Requirements for the Composition of the Ethics Committee (IRB)

- 'A reasonable number of members who collectively have the qualifications and experience to review and evaluate the science, medical aspects and ethics of the proposed trial'
- 'At least five members'
- 'At least one member whose primary interest is non-scientific (lay member)'
- 'At least one member who is independent of the trial site'

Only members who are independent of the investigator can vote or provide an opinion [1].

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At the time of writing, a new European Directive, if implemented, will control the constitution and working practices of ethics committees in Europe, similar to regulations in the USA. Until this time, investigators and sponsors have to deal with largely inefficient ethics committees, and the investigators should ensure that their local ethics committee fulfils the ICH GCP requirements [1].

6.2 What Documents Must Be Submitted to the Ethics Committee (IRB)?

Although there is currently a great diversity of documentation requested by ethics committees (IRBs), the ICH GCP guidelines are quite specific about the documents that need to be submitted. The investigator should make sure that final versions of the following documents are obtained from the sponsor and sent to the ethics committee (IRB) for review [1]:

- Trial protocol (and any amendments)
- Consent form and subject information sheets
- Subject recruitment procedures (e.g. advertisements)
- Investigator's brochure and any available safety information
- Information about payments and compensation available to subjects
- Investigator's current curriculum vitae
- Any other documents specifically requested by the ethics committee (IRB)

The investigator should never submit a draft document to the ethics committee (IRB) to speed up this rate-limiting step.

It is important to obtain a letter from the ethics committee (IRB) confirming that they have reviewed the above documents (adding the dates and versions seen) and have given their

approval or favourable opinion (or else reasons for disapproval). The letter should also give details about the date of the meeting and, if possible, a list of members who attended the meeting. This letter should be given to the trial monitor and a copy retained in the investigator's study file.

Many ethics committees (IRBs) fail to provide adequate documentation. To overcome this problem, it might be necessary to ask the sponsor to prepare a pro forma letter, which the ethics committee (IRB) can sign; this ensures that all necessary information has been included, and the appropriate GCP requirements have been fulfilled.

In some cases, the chairman of the ethics committee might inform the investigator that the study is acceptable and may be started. This is an unacceptable practice; ethics committee approval is valid only if a quorum of members has given approval, and their verdict has been received in writing [1].

6.3 Communication with an IRB/IEC

1. 'Before initiating a trial, the investigator/institution should have written and dated approval/favourable opinion from the IRB/IEC for the trial protocol, written ICFs, consent form updates, subject recruitment procedures (e.g. advertisements), and any other written information that is to be provided to subjects'.
2. 'As part of the investigator's/institution's written application to the IRB/IEC, the investigator/institution should provide the IRB/IEC with a current copy of the investigator's brochure. If the investigator's brochure is updated during the trial, the investigator/institution should supply a copy of the updated investigator's brochure to the IRB/IEC'.
3. 'During the trial the investigator/institution should provide to the IRB/IEC all documents subject to its review' [2, 3].

6.4 Compliance with Protocol

1. 'The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies), which was given approval/favourable opinion by the IRB/IEC. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm their agreement'.
2. 'The investigator should not implement any deviation from, or changes to, the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g. change of monitor(s), change of telephone number(s))'.
3. 'The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol'.
4. 'The investigator may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB/IEC approval/favourable opinion. As soon as possible, the implemented deviation or change, the reasons for it and, if appropriate, the proposed protocol amendment(s) should be submitted':

   (a) 'To the IRB/IEC for review and approval/favourable opinion'
   (b) 'To the sponsor for agreement and, if required'
   (c) 'To the regulatory authority(ies)' [2, 3]

References

1. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). ICH, April 1996.
2. Hutchinson D. The Trial Investigator's GCP handbook: a practical guide to ICH requirements. Brookwood Medical Publications Ltd.; Surrey, UK, 1997.
3. ICH Harmonised Tripartite Guideline for good clinical practice. Second publication, Brookwood Medical Publications Ltd.; 1997.