14 Ethics

To carry out a clinical trial, the fundamentals of ethics must be strictly in compliance. An independent Ethics Committee (IEC) at the study site controls these adherences. The IEC is a consortium of physicians, scientists and non-medical members from the study site or local community. Their responsibilities are to protect the rights, the safety and the well-being of all clinical trial participants at their institution.

Before the implementation of a clinical trial, the IEC has to give a favourable vote; otherwise, the trial cannot begin.

Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and be consistent with GCP and the applicable regulatory requirement(s).

Regulatory Reference

- ! ICH GCP Guideline, Chapters 3, 4.4
- ! Declaration of Helsinki
- ! EU Directive 2001/20/EC, Art. 3.2(a), Art. 6

Responsibilities

Required Documents

To get a positive vote from the IEC, submit the following documents:

- Trial protocol(s)/amendment(s)
- Written informed consent form(s) and consent from updates
- Subject recruitment procedures (e.g. advertisement)
- Written information to be provided to participants
- The IB, if available
- Available safety information
- Information about payments and compensation available to participants
- The sponsor-investigator's current curriculum vitae and/or other documentation evidencing qualifications
- The suitability of the sponsor-investigator and supporting staff
- The quality of the facilities
- The adequacy and completeness of the written information to be given and the procedure to be followed for the purpose of obtaining informed consent and the justification for the research on persons incapable of giving informed consent as regards the specific restrictions laid down in Article 3 of the EU Directive 2001/20/EC
- Provision for indemnity or compensation in the event of injury or death attributable to a clinical trial
- Any insurance or indemnity to cover the liability of the sponsor-investigator
- The amounts and, where appropriate, the arrangements for rewarding or compensating sponsor-investigator's and trial participants and the relevant aspects of any agreement between the sponsor-investigator and the trial site
- The arrangement for the recruitment of participants
- Any other documents that the IEC may need to fulfil its responsibilities

see 11
Investigator's Brochure/Summary of Product Characteristics

Responsibilities of the Independent Ethics Committee (IEC)

As the IEC is responsible for the protection of the rights, the safety and the well-being of the trial participants, all documents will be put to the 'acid test'. A clinical trial may be initiated only if the IEC and/or the competent authority come to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.

The sponsor-investigator should know that the IEC is required to monitor or control the trial at regular intervals to ensure that there is an appropriate benefit/risk for the trial participants.

The IEC can demand that the sponsor-investigator must deliver more information to the trial participants if any new information advances the rights, the safety and/or the well-being of the trial participants substantially.

This committee also would review any disbursement amounts and method of payment to avoid that the payment serves as an enticement.

see 10 Informed Consent

This information has to be written down in the Informed Consent.

Respites of the Evaluation/Application

Within **60 days** from the date of the receipt, the IEC is required to decide whether a favourable vote can be given and the study can be authorized to start.

If medical products for gene therapy or somatic therapy, or medical products containing genetically modified organisms are tested, an extension of **30 days** is permitted.

Furthermore, the authorization period can be **extended another 90 days** in the event of a consultation of a group or a committee in accordance with regulations and procedures of the Member States.

In the case of xenogenic cell therapy, there are no time limits to the authorization period.

The Member States are allowed to shorten the 60-day period on their own. If the sponsor-investigator has any amendments, the IEC has **35 days** from the date of the receipt of the proposed amendments to give an opinion.

Advice – Hints and Tips

- The Informed Consent of trial participants should be revised when important new information becomes available. All revisions to the Informed Consent Form and any written information provided to the study participants should also receive the IEC's favourable opinion in advance of use. The trial participants should be informed as quickly as possible.
- The protection of the trial participants have to be justified by reference to the toxicological investigations before the trial starts.

The International Code of Medical Ethics declares that, 'A physician shall act in the patient's best interest when providing medical care'.

According to this declaration, the sponsor-investigator has to ensure that during the trial, any necessary amendment to the protocol is made and that the rights, the safety and the well-being of all trial participants are protected at all times.

Regulatory Reference

- ICH GCP Guideline, Chapters 4.11, 4.12, 4.4.2, 4.4.3, 5.11, 5.17.1, 5.21
- Declaration of Helsinki
- EU Directive 2001/20/EC, Art. 6, Art. 9, Art. 10.1, Art. 10.2, Art. 16.3, Art. 17

Responsibilities

Amendment to the Study Protocol

If there are significant or substantial amendments, which refer to the safety of the trial participants or can change the interpretation of the scientific documents in support of the conduct of the trial or are substantial in any other way, the sponsor-investigator should inform the competent authorities and the IEC concerning the reasons for and content of these amendments in accordance with Articles 6 and 9 of the EU Directive 2001/20/EC.

After receiving the suggested change, the IEC has to approve the amendments according to the rights, the safety and the well-being of the trial participants. The IEC should give a statement within **35 days** after receipt.

In case of an unfavourable statement, the sponsor-investigator is not allowed to change the protocol; he/she may attempt to re-apply for an amendment until successful, however, this may affect the timelines of the study.

If the statement is positive and none of the competent authorities has doubts regarding the amendments, the sponsor-investigator is able to continue the trial after the adaption of the proposed amendment to the protocol.

AEs, SAEs and SUSARs

In case of death of a trial participant, the sponsor-investigator is required to notify the IEC and should provide additional information.

The sponsor-investigator must care that all important information about SAEs and SUSARs, which could lead to or where leading to death, should be documented and redirected to the competent authorities and the IEC as quickly as possible, **7 days** at most, after the sponsor-investigator is aware of the event. Subsequently, the sponsor-investigator has **8 days** to submit any missing information.

see 11 Investigator's Brochure/Summary of Product Characteristics

All other SAEs and SUSARs should be referred to the competent authorities and the IEC as soon as possible, **15 days at most**, after the time of occurrence.

Once a year during the conduct of the trial, the sponsor-investigator must submit a list/schedule of all SAEs and SUSARs that have occurred during the trial to the competent authorities and the IEC. At a minimum, the sponsor-investigator must produce a report about all the trial participants' safety.

After a study is closed, the authors, editors and publishers have ethical obligations with regard to the publication of the results of the research.

Regulatory Reference

- ICH GCP Guideline, Chapter 4.13
- Declaration of Helsinki
- EU Directive 2001/20/EC, Art. 10.3
- EU Directive 2005/28/EC, Chapter 2, Art. 6.2

Responsibilities

see 8 EudraCT

Within 90 days after the end of the trial, the sponsor-investigator should inform the competent authorities and the IEC that the trial is completed.

In the case of an early termination, the sponsor-investigator has only 15 days to inform the competent authorities and the IEC, and must also explain the reasons for termination.

Advice – Hints and Tips

Please note: after a study has ended, the IEC is required to store the essential documents of all clinical trials for a period of at least 3 years. If there are special requirements, they have to store the documents according to their own standard operating procedures.