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ethik-kommission
founded 1980
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Guideline for the review request form clinical study **Version 30.06.2003**

(this guideline should not be submitted with the review request form)

Every document can be submitted in German or English. The Informed Consent (IC) should be submitted in the national language as well as in German or English; if the study takes place in Germany, the IC has to be submitted in the German language.

General information concerning the review request form

The review request form clinical study Version 30.06.2003 is available as a PDF-file. Please fill in the given boxes accordingly. In case a box should not allow enough room for your text, please write your text onto an extra sheet of paper, indicate this sheet accordingly and enclose it with the review request form.

Specific information concerning the review request form

Title of the Study

The title should clearly inform about the type of study as well as the study's aim.

Study Code or Study Number

Code 1: The sponsor normally provides the study with a code or number. If a code is provided, please enter it into the box Code 1.
Code 2: If the sponsor commissions a contract research organisation, this organisation does normally assign the study with their own code or number. If a code is provided, please enter it into the box Code 2.

As this review request form consists of several pages, the code will be transfered automatically onto each page.

1. Data about the Persons in Charge

It is not necessary to mention sponsor and invoice recipient by name/title!
If several of the persons in charge are identical, it is possible to refer in the box name/title to a box that has already been filled in (e.g.: are the party requesting review and the principle investigator identical, it is possible to fill 1.2. name/ title with "see 1.1 *party requesting review*").

2. Documents Required for Review of the clinical study by the freiburg ethics commission international (feki).

For reasons of identification any document is normally provided with an indication. This may be a version and/or number and/or date. Please enter this kind of identification into the box version / number / date. e.g.: the review request form of the feki is indicated with Version 30.06.2003.

In the category e-mail / fax / post please mark the appropriate box with a cross [x] to show 1. the document is or was submitted and 2. the way chosen to submit the corresponding document. It is possible to submit a document per e-mail, fax and post - in that case all three boxes have to be marked with a cross.

The following documents are always obligatory for discussion, assessment and examination of the clinical study on human subjects:

- 2.2 Review Request Form
- 2.3 Study Protocol
- 2.4 Informed Consent (IC); both in the national language and in German.

2.1. Informal Letter

A short informal letter should be included.

2.2. Review Request Form

Please fill in the review request form with care, as this provides the first necessary information about the persons in charge and the submitted documents for the clincal study.

2.3. Study Protocol

The study protocol should be submitted as "final version" and already be signed by at least one person in charge.

The study protocol should contain a "protocol-synopsis", if not, a synopsis of the protocol should be submitted as a further document, for example in point 2.13.

A schedule of assessment is often helpful for studying the investigational protocol and should therefore be included in the protocol.

Example of a protocol-synopsis: see "attachment protocol-synopsis ".

Example of a table of contents of an investigational protocol: see "attachment investigational protocol".

2.4. Informed Consent

The legal aspects of clinical investigation show that every experiment with and on human subjects are permitted by criminal law, as long as the consequences of the experiment don't breach any criminal offence. Of course, one of the most essential conditions is the informed consent of the test subject; the IC is based on the right of self-determination ensured by constitutional law. The consent will only be effective and exclude illegality, when the test subject has understood the fundamental issues of character, meaning and possible consequences of the clinical investigation. The following basic principle is in force: Without an informed consent of the test subject/patient, any medical treatment is illegal, even though it is/was carried out proficiently and without faults.

The burden of proof for a sufficient information lies with the doctor/clinical investigator.

The written information serves as a guideline for the obligatory oral information given by the doctor/ clinical investigator.

Example for a table of contents (incl. standard sentences): see "attachment Informed Consent".

2.5. Investigator's Brochure / Product Information

The investigator's brochure or product information are documents the sponsor puts at the investigator's disposal. The sponsor is legally liable for the accuracy of the content. The investigator's brochure or product information enable the investigator to gain exact information about the test substance (e.g. description and name of test substance and/or test product, results of pharmacological- toxicological investigations, results of biological safety tests as well as technical safety, results of pre- clinical and clinical investigations, etc.).

2.6. Verification of Insurance Policy Covering Test Subjects

In case the sum insured for the individual test subject/patient exceeds the sum laid down by law of 500.000 Euro (in Germany), this sum insured should be recorded both in the study protocol and in the Informed Consent. The feki will check, whether the amount of the sum insured is adequate. Due to the fact that insurance companies often insist on awaiting the results of ethical review before handing out he verification of the insurance policy covering test subjects, it is possible to submit this verification later. However, the verification with the exact amount of the insurance for the individual test subject/patient stated has to be submitted to the feki before the start of the study.

2.7. Pinciple Investigator's CV

The CV serves as proof for the principle investigator's scientific qualification and necessary two-year experience in clinical studies.

2.8. Confidentiality Statement

Free formulation is possible. A feki-member in charge will countersign this statement; the statement shall confirm that the submitted documents for the clinical study will be treated confidentially by the feki and their members and will not be passed on to a third party.

2.9. Copy of CE-Certificate (applies only to medical devices)

Please submit if available. Please inform, whether the CE-Certificate meets the requirements being applied in the clinical study.

2.10. Case Report Form (CRF)

Delayed submission is possible. Often, the results of ethical review are being awaited before completing the final version of the CRF. The document, however, has to be submitted to the feki before starting the study.

2.11. Information Concerning Test Subject Recruitment

If a test subject/patient recruitment takes place, for example via newspaper advertisement, this kind of advertisement (form and content of advert) should be submitted to the feki for assessment.

2.12. Information Concerning the Qualification of the Study Centre

A short description of the study centre should be provided to confirm that investigator and staff are able to conduct the study properly with the equipment available. Please also inform the feki whether it is possible in the study centre to take all necessary emergency measures concerning the clinical study. Only to be submitted, if the centre is not yet known by the feki.

2.13 Further Documents

Further documents could be: synopsis of the protocol, literature, amendment, etc.
Please list accordingly.

3. Details Concerning Test Substance and/or Test Product

Please fill in accordingly.

4. Details Concerning the Clinical Study

Please fill in accordingly.

5. Details Concerning Study Centres

Please fill in accordingly. It is possible to refer to the study protocol, if mentioned there. If at a later time further study centres will be included, a notification in the form of an amendment should be sent to the feki.

6. List of Existing Votes from Other Ethics Commissions

The VGH BW has pronounced in its verdict, dated September 9, 2002 <AZ 9 S 2506/01>:

> "A doctor who is a member of the defendants (*here: Landesärztekammer [State Medical Board of Registration])* does not need an additional vote of the ethics commission of the defendants for participating in a clinical investigation of a medical product on human subjects, if an approved vote of the plaintiff (*here: freiburg ethics commission international*) does exist."

This is a clear verdict. Any statement to the contrary equals an offence. In the whole of Germany the verdict is in force. This means that with existing vote from the feki (also for a multicenter study) no further vote is necessary: neither from an ethics commission being under public law, nor due to the Medical Association's professional code of conduct for doctors or any other regulation.

If nevertheless votes from other ethics commissions exist, please fill in the box accordingly.

7. Further Informal Commentary

When required, please fill in accordingly.

Attachment: **Protocol-Synopsis**

Example for a table of contents of a protocol-synopsis:
Of course, the table of contents of a protocol-synopsis depends on the content of the planned study; points may be added or omitted.

Study Title	
Study Drug / Device	
Study Rational	
Indication	
Study Objective	
Study Design	
Study Duration	
Target Population Inclusion criteria: Exclusion criteria:	
Planned Number of Subjects	
Primary Objectives	
Secondary Objectives	
Procedure	
Risk Benefit Analysis	
Investigational Sites and / or Contract Research Organisation	
Sponsor	

Attachment: **Study Protocol**

The study protocol should be provided with a study number or protocol number and/or version and/or date.

The given example of a table of contents of a study protocol is only meant for assistance; each sponsor/clinical investigator structures the table of contents in their own style.
Of course, the table of contents of a study protocol depends on the planned clinical study. Major variations are therefore possible (points may be added or omitted); the points recorded here can be amplified with sub-sections.

Table of Contents
List of Abbreviations

Persons in Charge and Signatures

Study Synopsis

Introduction with Scientific Background
Study Objective
Study Design
Objective Parameter
Test Subject/Patient Recruitment
Test Substance/ Test Product
Application of Test Substance/ Test Product
Accompanying Aplication
Study Procedure and Course of Study
Schedule of Assessment
Benefit-Risk Ratio and Precautionary Measures
Control Committee
Biometrics
Ethical and Legal Aspects
Publications
Literature

Attachment: **Informed Consent**

The Informed Consent (IC) should be provided with the protocol number of the planned clinical study and with a date. The language used should be readily comprehensible; foreign words should be avoided where possible or paraphrased. The language should be the national language of the test subjects/patients (the feki does only assess German or English IC's; for IC's in other languages the feki asks for an authorised translation into German or English).

Of course, the table of contents of the Informed Consent depends on the content of the planned clinical study; points may be added or omitted.

Regarding the content, the written information should be in accordance with the following points:

- Title of the study
- Introduction with general information about the clinical investigation
- Purpose and aim of the clinical investigation
- Information about test-substance and/or test product
- Requirements for participation
    - Inclusion criteria and exclusion criteria
    - Voluntary nature of participation
    - Early withdrawal from participation
- Course of clinical investigation
- Possible risks, trouble and side effects
- Possible benefit gained by participation
- Other forms of treatment or alternative procedures
- Insurance cover; in this context following points should be stated:
    - Name and address of insurance company
    - If the study takes place in Germany, a German address has to be provided
    - Amount of the sum insured (only when exceeding 500.000 Euro)
    - Obligations of the insurance company as detailed below

    a. *Except in cases of emergency, the patient/trial subject is to undergo other medical treatment only after consulting with the study investigator. The study investigator is to be informed without delay of any emergency treatment.*
    (Während der Dauer der klinischen Prüfung dürfen Sie sich einer anderen medizinischen Behandlung – außer im medizinischen Notfall – nur im Einvernehmen mit dem klinischen Prüfer unterziehen. Der klinische Prüfer ist unverzüglich von einer Notfallbehandlung zu unterrichten.)
    b. *Any injury that may have arisen as a result of participation in the clinical study is to be reported to the insurer without delay. This report may be relayed via the study investigator.*
    (Während der Dauer der klinischen Prüfung dürfen Sie sich einer anderen medizinischen Behandlung – außer im medizinischen Notfall – nur im Einvernehmen mit dem klinischen Prüfer unterziehen. Der klinische Prüfer ist unverzüglich von einer Notfallbehandlung zu unterrichten.)

- Test subject/patient's fee, only if payment of a fee for the clinical study is offered
- Confidentiality
- Name and telephone number of the clinical investigator and further contact

Regarding the content, the written consent should equal the following points or text passages:
(for Germany please consider: MPG § 20 paragraph 1 No.2 and paragraph 2 and AMG § 40 paragraph 1 No. 2 and paragraph 2)

- I have received written information about the clinical study and had sufficient time to read through it. I have also received extensive oral information about character, meaning and consequences of the clinical investigation by… (name of clinical investigator, who has to be a doctor in Germany); in particular about study target, implementation, benefits, risks, insurance cover including their obligations. All my questions were answered comprehensibly and at the moment I have no further questions. I know questions can be asked at any time during and after the clinical investigation.

- I voluntarily give my consent to the clinical study. I know I can withdraw my consent at any time and know my treatment will not be compromised after doing so.

- I agree to the recording of my data within the framework of the clinical study. I also agree that my data can be passed on in anonymous form to authorized specialists to be used for data processing and scientific analysis as well as to the appropriate authorities for review.

- Concerning Studies of Medical Devices (compare 2. ÄndG-MPG § 20 Abs. 1 no.2)
  Please include the following passage in the written consent:
  "I declare that I give my consent to the recording of my medical data within the framework of the clinical investigation and I agree that representatives of the client or of the appropriate authority can look at the data for investigational purposes."
  „Ich erkläre zugleich, dass ich mit der im Rahmen der klinischen Prüfung erfolgenden Aufzeichnung von Gesundheitsdaten und mit der Einsichtnahme zu Prüfungszwecken durch Beauftragte des Auftraggebers oder der zuständigen Behörde einverstanden bin."

- Concerning Drug Studies
  I permit that official representatives of the client of this clinical study while being bound to imposed confidentiality look at my personal medical file at the location of the clinical study. This will be done to ensure that all data taken in this study is correctly and comprehensively captured.

- Finally, I also give my consent to the scientific publication of the results of research while adhering to the regulations of data protection.

- If the study takes place in several countries, I likewise agree that my personal study data may be viewed by the appropriate foreign authorities.

- Signatures of the informing doctor and test subject/patient with location and date