Guidelines for Reviewers
Clinical Trial Proposals
1 General Information for Reviewers

As a rule, each proposal submitted to this programme is evaluated by at least two, usually three independent reviewers. The "Clinical Trials" review panel takes these written reviews into consideration when making an award recommendation. All documentation is then sent to the Joint Committee, which makes the final funding decision. All reviewers participating in the process will be informed of the final decision.

The DFG endeavours to identify reviewers who have extensive knowledge in the field but who are not linked to the applicants through collaboration, direct competition or in other ways. Please examine whether circumstances exist that could be interpreted as your having a conflict of interest. If for any reason you do not feel able to carry out the review, please return the proposal as quickly as possible. In this case we would be grateful if you could assist us by suggesting other possible reviewers. If you have any questions about the proposal, please contact the DFG only (do not contact the applicant or any third person). When preparing your review please consider that the DFG Head Office may forward your comments on the proposal to the applicant in an anonymous form.

2 The Clinical Trials Programme

The programme’s objective is to significantly improve investigator-initiated trials in Germany and to increase the ability of German university clinics to design and conduct internationally competitive trials. The funding programme is focused on scientifically excellent interventional, prospective and confirmatory multicentric interventional trials. These trials include therapeutic trials, such as pharmacological, diagnostic and prognostic trials, provided these test defined therapeutic approaches, procedures or markers. Non-interventional studies or early phase, exploratory studies such as proof-of-concept studies cannot be funded in this programme.

Gender and age-group aspects should be taken into account in all trials. Trials will not be considered for funding if companies have immediate commercial interests in the results. Applicants must have completed appropriate preliminary work relevant to the clinical trial. All trials funded within this programme must comply with international standards (Good Clinical Practice (ICH-GCP), Declaration of Helsinki, CONSORT Statement).
Proposals with an initial funding duration of three years may be submitted. A renewal proposal can be submitted after the initial three-year period to enable longer studies. Only expenditures incurred by the trial itself can be funded, e.g. staff, consumables, monitoring (audits may be initiated by the funding organisations), travel and expense allowances for participating advisory boards, travel allowances, insurance coverage, registrations fees, specific tests and analyses, and expenses resulting from collaboration with trial centres abroad.

The proposal process consists of two stages, draft proposals and full proposals.

3 Information on the Review Process - Draft proposals

First, a draft proposal must be submitted. It must be drawn up in accordance with a template provided by the DFG and signed by the principal investigator and the responsible biostatistician. Draft proposals that do not comply with these rules will not be considered.

3.1 Clinical evaluation

In order to assess the draft proposal, the following questions should be addressed and scored (with “1” being the lowest score and “6” being the highest score):

Starting hypotheses
- How clearly is the existing evidence described and discussed?
- How convincingly does the evidence presented support the trial rationale?
- How justifiable is a confirmatory trial at this stage?
- How well founded is the estimated effect size?
- In a diagnostic trial: Is the gold standard well chosen?
- In a diagnostic/prognostic trial: Is there a clear concept for clinical or epidemiological action/further steps in research?

Innovation and relevance of the trial
- How significant is the trial in terms of its potential impact of relieving the burden of disease and/or improving human health?
- How novel is the question it addresses?

Design aspects
- How suitable are the control(s)/comparator(s)?
How clinically relevant are the clinical outcome measures?
How feasible is the trial?

Qualifications of applicant(s)/trial management
- How qualified is the team of investigators to conduct the trial?

Commercial exploitation
- Could a company have a substantial economic benefit from the potential trial results?

3.2 Biostatistical evaluation

In order to assess the draft proposal, the following questions should be addressed and scored (with “1” being the lowest score and “3” being the highest score):

Hypothesis
- Is the hypothesis of this trial precise enough?
- Is the primary hypothesis in line with the design of the trial?
- In an active controlled trial: Is the assumption about the efficacy of the comparator substantiated?
- In a diagnostic trial: Are the measures (such as sens, spec, PPV and NPV) and their relative importance consistent with the intention of the research question?
- In a prognostic trial: Is the target and study population adequate (internal and external validity)? Are the clinical or epidemiological consequences of prognosis adequately discussed?

Design aspects
- Can the trial design adequately answer the question posed?

Randomisation
- How appropriate are the proposed methods for assigning participants to trial groups?

Sample size calculation
- How convincing are the assumptions (assumed differences, etc.) underlying the sample size calculations?
- Are references given to substantiate these assumptions?

Analysis
- Is the primary analysis population specified and appropriate?
- How adequate is the proposed strategy of statistical analysis?
Each draft proposal is assessed by two clinical as well as one statistical reviewer, giving an overall score. Constructive and concise feedback to applicants is also requested. Fundamental and irreparable flaws in concept and design should be reflected in lower scores. The assessment forms and the overall score assist the review panel to come to a final recommendation for each draft proposal during the review session. As the aim of the meeting is to identify the very best trials to be taken to the full proposal stage, rigorous scoring is expected. All drafts are considered to be in full competition to each other, regardless of discipline. Thus, reviewers are asked to identify those projects that are of high scientific interest and for which a high clinical impact can be assumed. All other projects should be denied.

4 Information on the Review Process - Full Proposals

If evaluated positively, applicants will be invited to submit a full proposal in accordance with a prescribed template. The proposal should be detailed yet not exceed a specified number of pages. Full proposals are considered by external reviewers and subsequently by the “Clinical Trials” review panel in full competition to each other, regardless of discipline.

4.1 External Reviewers

Each proposal is submitted to three independent external reviewers (clinical experts in the specific field, who are usually not members of the panel, and to one biostatistician). The written review will ideally be limited to 1-2 pages, as appropriate for the complexity of the proposal. A clear recommendation as to whether the project should be funded should be provided. The funding recommendation should always be based on whether reviewers think it is worth carrying out the research. The criteria that reviewers are asked to consider when assessing the full proposal can be found below.

4.2 “Clinical Trials” review panel

Panel members will discuss the proposals taking into consideration the written statements of the external reviewers. Each proposal is presented by two panel members serving as “rapporteurs”. The panel’s discussion will identify the most excellent and most important trials by asking:

- How important are the questions, or gaps in knowledge, that are being addressed?
- What is new about the research question being addressed?
- Is the clinical impact high?
- Will the trial make a significant difference in patient care in the immediate future?
- Is the trial internationally competitive?
- Is the trial feasible?

5 Criteria for the Assessment of Clinical Trials – Full proposals

5.1 Clinical evaluation

Starting hypotheses
- Is the general evidence in the proposal
  - clearly established by providing and discussing published or the investigators’ own data,
  - convincingly in support of the trial rationale?

- Is the effect size of the experimental intervention
  - supported by providing and critically evaluating published or the investigators’ own data,
  - of significant clinical relevance for the patient?

- In a diagnostic/prognostic trial:
  - Is the gold standard well chosen?
  - Is there a clear concept for clinical or epidemiological action/further steps in research?

Significance of the topic/ethical considerations
- How novel is the question the trial addresses?
- How significant is the trial in terms of its potential impact of relieving the burden of disease and/or improving human health?
- Is the trial ethically acceptable?

Design aspects
- How appropriate are control(s)/ comparator(s), inclusion/exclusion criteria (generalisability and representativeness), outcome measures, methods against bias, sample size, power calculations, and statistical analyses? Are they relevant for the patient population addressed?
- Are the interventions feasible? Are the trial drugs or medicinal products available? Are the training and quality control measures for complex interventions or complex outcome assessments adequate?
- How feasible are recruitment rates? Are the enrolment, the potential drop-out rates and the compliance of patients adequately assessed?
Qualifications of applicant(s)/trial management

- Does the proposed team of investigators possess the necessary range of expertise and documented experience to successfully carry out the proposed trial?
- Is the trial coordination convincing? Are advisory bodies necessary and adequately defined?

Commercial exploitation

- Could a company have a substantial economic benefit from the potential trial results?

5.2 Biostatistical evaluation

Trial design

- Is the trial design adequate to answer the proposed question?

Hypothesis

- Is the hypothesis of this trial precise enough?
- Is the primary hypothesis in line with the design of the trial?
- In an active controlled trial: Is the assumption about the efficacy of the comparator substantiated?
- In a diagnostic trial: Are the measures (such as sens, spec, PPV and NPV) and their relative importance consistent with the intention of the research question?
- In a prognostic trial: Are the target and trial population adequate (internal and external validity)? Are the clinical or epidemiological consequences of prognosis adequately discussed?

Randomisation

- Is randomisation stratified for important prognostic factors? Is the number of strata acceptable?

Sample size calculation

- Are references given from which the assumptions underlying the sample size calculation can be verified?
- Is there a discussion about the impact of non-compliance and missing values on the sample size?

Analysis

- Is the primary analysis population specified and appropriate?
- How adequate is the proposed strategy of statistical analysis? Is the randomisation scheme reflected in the analysis?
- If a substantial amount of missing values can be expected: Is there a discussion regarding which analysis strategy is conservative?
Funding recommendation/comments
Please give a clear funding recommendation of whether to fund (at high, medium, or low priority) or reject the proposal. Also give comments for the applicants if you feel that this might be helpful.

6 Confidentiality

All proposals and correspondence forwarded to you, the reviews, and the identity of the reviewers and members of review boards participating in the evaluation must be treated confidentially. They must not be revealed to third parties. Therefore, the responsibilities of a reviewer may only be undertaken personally and may not be delegated to third parties. The scientific content of the proposal may not be exploited for personal or other scientific purposes. Furthermore, we ask that you do not identify yourself as a reviewer to the applicant or to any third party.

7 Conflicts of Interest

At each stage of the proposal process, the DFG Head Office examines whether or not a conflict of interest exists. A conflict of interest is given if you are directly affected by the subject matter of the funding project or there is another reason sufficient to raise doubts about the impartiality of your specialist evaluations. Before submitting your written review or prior to participating in a review session, please inform us whether circumstances exist that could be interpreted as a conflict of interest. Please inform us of any possible reservations so that the DFG Head Office and you together can determine whether your participation in a particular review process is appropriate. The mere appearance of a conflict of interest means that you will not be able to participate in this particular review process. You may not submit an evaluation in the written process. As a member of a review panel, we ask that you leave the conference room before the oral consultations about the proposal in question begin. During a final review of several proposals, you will abstain from voting on the proposal in which you might have a conflict of interest.

Conflicts of interest may include the following:
- Personal relationships, personal ties or conflicts
- Close scientific collaboration, e.g. implementation of joint projects or joint publications within the past 3 years
- Direct scientific competition with personal projects or plans
- Close proximity, e.g. member of the same scientific institution or impending move of the reviewer to the institution of the applicant or vice versa
- Teacher/student relationship, unless there has been independent scientific activity for more than 10 years
- Dependent employment relationship during the past 3 years
- Participation in ongoing or just previously concluded professorial appointment proceedings
- Current or previous activity in advisory bodies at the applicant's institution, e.g. scientific advisory boards
- Participation in mutual review processes, also outside of the DFG process, within the past 12 months
- Personal economic interests in the funding decision
- Competitive relationship or common economic interests, e.g. common business management

8 Obligation to Follow Rules of Good Scientific Practice

The rules of good scientific practice also apply to reviewers. A violation of these rules can exist if in a scientific context false information is provided intentionally or with gross negligence, the intellectual property of others is infringed upon or the research activity of others is impaired in some other manner. Violations may also occur in cases of non-compliance with sections 6 and 7. The circumstances of the individual case are decisive.

Depending on the type and severity of the determined misconduct, the DFG may impose one or more sanctions. These may range from a written reprimand to the loss of eligibility to submit proposals to the DFG for one to eight years or the exclusion from serving as a reviewer or in statutory bodies of the DFG as well as the disqualification of the active and passive right to vote for statutory bodies of the DFG.