

Preparation Instructions | Draft Proposal - Clinical Trial

1 Trial Synopsis

Applicant/ Coordinating investigator	Name, address, telephone, fax, e-mail In case of multiple applicants the principal investigator/coordinating investigator ¹ of the trial who will assume responsibility for conducting the clinical trial should be listed first.
Title of trial	The title of the trial (not exceeding 140 characters) should be as precise as possible. If funding is granted, this title will be used in the DFG's annual report. An acronym is optional.
Medical condition	The medical condition being studied (e.g. HIV/AIDS, cirrhosis of liver)
Objective(s)	What main research questions will be addressed? Specify clearly the primary hypotheses of the trial that determines sample size calculation.
Intervention(s)	Description of the experimental and the control treatments or interventions as well as dose and mode of application. For diagnostic tests or procedures the index test and the reference procedure (gold standard) should be described. Experimental intervention/index test: Control intervention/reference test: Follow-up per patient: Duration of intervention per patient:
Key inclusion and exclusion criteria	Key inclusion criteria: Key exclusion criteria:
Outcome(s)	Primary efficacy endpoint: Key secondary endpoint(s): Assessment of safety:
Trial type	E.g. randomised/non-randomised, type of masking (single, double, observer blind), type of controls (active/placebo), parallel group/cross-over, prognostic, diagnostic
Statistical analysis	Efficacy/test accuracy: Description of the primary efficacy/test accuracy analysis and population: Safety: Secondary endpoints:
Sample size	To be assessed for eligibility: (n =) To be assigned to the trial: (n =) To be analysed: (n =)
Trial duration	First patient in to last patient out (months): Duration of the entire trial (months): Recruitment period (months):
Participating centres	How many centres will be involved? (n)

2 The Medical Problem - need for a trial

What medical problem will be addressed? What is the novel aspect of the proposed trial? What main research questions are to be addressed? Put them in order, indicating major and minor motivations/starting hypotheses of the investigation planned.

Put your trial into perspective. This section should detail the background of the starting hypotheses and the feasibility of the trial. What trials have been conducted either by you or by others? What is the relevance of their results? Give references to any relevant systematic review(s)^{2, 3} and/or (your own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/series. State what your trial adds to the totality of evidence when your trial is added to previous work. Include a description of how you searched for the evidence (databases, search terms, limits) and how you assessed its quality - i.e. how you selected and how you combined the evidence. Note that proposals that fail to provide sufficient evidence cannot be funded.

How significant is the trial in terms of its potential impact on relieving the burden of disease and/or improving human health? What impact will the results have on clinical practice? How will the individual patient and the patient population benefit from the trial? How have patients or their respective organisations been involved in planning the trial? Describe any potential commercial interest of a company in the results of the trial or explain why no such interest exists. Please note that proposals for trials whose outcomes are of direct commercial interest to a company are not eligible for funding.

3 Justification of Design Aspects

Please provide justifications in addition to listing the respective parameters.

3.1 Control(s)/Comparator(s)

Justify the choice of control(s)/comparison(s): Is the use of placebos acceptable? Which trials establish efficacy and safety of the chosen control regimen? For diagnostic trials: What is the rationale for the units, cut-off and/or categories?

3.2 Inclusion and exclusion criteria

Justify the population to be studied and include reflections on generalisability and representativeness.

3.3 Outcome measures

Justify the endpoints chosen: Are there other trials that have used this endpoint? Are there any guidelines proposing this endpoint/these endpoints? Discuss the clinical relevance of the outcome measures for the target population or the individual patient. Have the measures been validated?

3.4 Methods against bias

Is randomisation feasible? What prognostic factors need to be regarded in the randomisation scheme and the analysis? What are the proposed practical arrangements for assigning participants to trial groups? Will trial site effects be considered in randomisation? Is blinding possible? If blinding is not possible, please explain why and give details of alternative methods to avoid biased assessment of results (e.g. blinded assessment of outcome). For diagnostic trials: Describe the training and expertise of persons executing and reading the index tests and the reference standards.

3.5 Proposed sample size/Power calculations

What is the proposed sample size and what is the justification for the assumptions underlying the power calculations? Include a comprehensible, checkable description of the power calculations and sample sizes detailing the outcome measures on which these have been based for both control and experimental groups; give event rates, means and medians, the software used for sample size calculation, etc., as appropriate. Justify the size of difference that the trial is powered to detect, or in case of a non-inferiority or equivalence study, the size of difference that the trial is powered to exclude. It is important that the sample size calculations take into account anticipated rates of non-compliance and losses to follow up.

3.6 Feasibility of recruitment

What is the evidence that the intended recruitment rate is achievable (e.g. pilot study)? Describe the data from which you have assessed the potential for recruiting the required number of suitable subjects.

4 Statistical Analysis

What is the proposed strategy of statistical analysis? What is the strategy for analysing the primary outcome? If interim analyses are planned, please specify. Are there any subgroup analyses? What are the methods for calculating test reproducibility in diagnostic trials?

5 Ethical Considerations

Discuss briefly the acceptability of the risk incurred by the individual participant versus the potential benefit for the participant/population concerned.

6 Trial Management

6.1 Key participants

Please indicate persons responsible for the design, management and analysis of the trial.

6.2 Time-schedule and milestones

Please give an clear overview about your work packages, including a time-schedule.

6.3 Trial expertise (your own project-related publications)

Please list your most significant publications that relate directly to the proposed project and document your preliminary work. This list serves as an important basis for assessing your proposal.

Please structure the list as follows:

(I) Articles which at the time of proposal submission have been published or officially accepted by publication outlets with scientific quality assurance, listed in standard format; and book publications. For works that have been accepted for publication but not yet published, the publisher's acknowledgement of acceptance has to be provided with the draft.

(II) Other publications

(III) Patents

a. Pending

b. Issued

Please note the maximum number of works you may list under (I) and (II) combined:

Single applicant: two publications per year of the funding period

Multiple applicants: three publications per year of the funding period

6.4 Supporting facilities

What trial-specific facilities and other resources are available for conducting the trial?

7 Budget Summary

Please give a rough estimate of the costs expected for the total duration of the trial.

8 Bibliography

In this bibliography, list only the works you cite in your presentation of the state of the art, the research objectives, and the work programme. This bibliography is not the list of your own project-relevant publications (see above).

Cited references within this guideline

1 "Investigator" as defined in the harmonized "Guideline for Good Clinical Practice" of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH GCP) (<http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf>). This definition should be used accordingly for non-drug trials/studies: (1.34 Investigator) "A person responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator." (1.19 Coordinating investigator) "An investigator assigned the responsibility for the coordination of investigators at different centers participating in a multicenter trial."

2 Checklists for review articles. Oxman AD. BMJ. 1994 Sep 10;309(6955):648-51.

3 Systematic literature reviews and meta-analyses: part 6 of a series on evaluation of scientific publications. Ressing M, Blettner M, Klug SJ. Dtsch Arztebl Int. 2009 Jul;106(27):456-63. doi: 10.3238/arztebl.2009.0456. Epub 2009 Jul 3. Review.

4 Putting research into context--revisited. Clark S, Horton R. Lancet. 2010 Jul 3;376(9734):10-1.

5 Assure that the biostatistician has the expertise to carry out clinical trials, e.g.: GMDS certificate, <http://www.gmds.de/organisation/zertifikate/zertifikate.php>; ICH guidance E9 "Statistical Principles of Clinical Trials".