

I. Outline Clinical Trials Application

FUNDING MEASURE: Please indicate the funding measure you apply for

Please prepare your application in English not exceeding 6 pages (DIN A4, at least 10 point Arial). Make an entry under every heading/subheading. Signatures of principal/coordinating investigator and responsible biostatistician are mandatory.

Note: Applications that fail to comply with these requirements will be considered incomplete and will constitute grounds to reject the application outline without peer review.

1. STUDY SYNOPSIS

APPLICANT / COORDINATING INVESTIGATOR	Name, address, telephone, fax, e-mail <i>In case of multiple applicants the principal investigator / coordinating investigator¹ of the trial who will assume responsibility for conducting the clinical trial, should be listed first.</i>
TITLE OF STUDY	<i>The title of the trial (not exceeding 140 characters) should be as precise as possible. In case of funding this title shall be quoted in the annual reports of the funding organisations. Acronym is optional.</i>
CONDITION/TOPIC	<i>The medical condition being studied (e.g. Parkinson, depression, asthma)</i>
OBJECTIVE(S)	<i>Which principal research questions are to be addressed? Specify clearly the primary hypotheses of the trial that determine sample size calculation.</i>
INTERVENTION (S)	<i>Description of the experimental and the control treatments or interventions as well as dose and mode of application. For diagnostic tests or procedures the experimental test and the gold-standard or reference procedure should be described.</i> <u>Experimental intervention:</u> <u>Control intervention:</u> <u>Duration of intervention per patient/subject:</u>
KEY INCLUSION AND EXCLUSION CRITERIA	<u>Key inclusion criteria:</u> <u>Key exclusion criteria:</u>
OUTCOME(S)	<u>Primary efficacy endpoint:</u> <u>Key secondary endpoint(s):</u> <u>Assessment of safety:</u>
STUDY TYPE	<i>e.g. randomized / non-randomized, type of masking (single, double, observer blind), type of controls (active / placebo), parallel group / cross-over</i>

¹ "Investigator" as defined in the harmonised "Guideline for Good Clinical Practice" of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH GCP) (<http://www.emea.eu.int>). 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 centres participating in a multicenter trial."

STATISTICAL ANALYSIS	<u>Efficacy:</u> <u>description of the primary efficacy analysis and population:</u> <u>Safety:</u> <u>Secondary endpoints:</u>
SAMPLE SIZE	<u>To be assessed for eligibility (n = ...)</u> <u>To be allocated to trial (n = ...)</u> <u>To be analysed (n = ...)</u>
TRIAL DURATION	<u>First patient/subject in to last patient/subject out:</u> <u>Duration of the entire trial:</u>
PARTICIPATING CENTERS	<i>How many centres will be involved?</i>
PREVIOUS DFG / BMBF PROJECT NUMBER	<i>If applicable, the DFG/BMBF code number of the latest application or of any previous application(s) for project-funding concerning this trial.</i>

2. THE MEDICAL PROBLEM

Which medical problem is to be addressed? What is the novel aspect of the proposed trial? Which principal research questions are to be addressed? Bring them into order indicating major and minor motivations/starting hypotheses of the investigation planned.

2.1 EVIDENCE

Set your trial into perspective. Which 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 and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/series. If you believe that no relevant previous trials have been done, give details of your search strategy for existing information. This should both detail the background of the starting hypotheses and the feasibility of the trial.

2.2 THE NEED FOR A TRIAL

What impact will the results have on clinical practice or understanding of the proposed intervention or underlying disease?

3. JUSTIFICATION OF DESIGN ASPECTS

3.1 CONTROL(S) / COMPARATOR(S)

Justify the choice of control(s)/comparison(s): Is placebo acceptable? Which trials establish efficacy and safety of the chosen control regimen?

3.2 INCLUSION/EXCLUSION CRITERIA

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

3.3 OUTCOME MEASURES

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

3.4 METHODS AGAINST BIAS

² For definition of a systematic review, see Oxman, AD (1994). Checklists for review articles, BMJ; 309; 648-51.

Is randomisation feasible? Which prognostic factors need to be regarded in the randomisation scheme and the analysis? What are the proposed practical arrangements for allocating participants to trial groups?

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).

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, 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 from what data you assessed the potential for recruiting the required number of suitable subjects.

4. STATISTICAL ANALYSES

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?

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 TRIALS EXPERTISE

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

#	Name	Affiliation	Responsibility / Role	Signature
			Principal/Coordinating Investigator	
			Trial Statistician ³	
			

Please indicate trials expertise of all above-mentioned participants by citing relevant publications and/or specifying major role in ongoing trial(s) (to be identified; max. 5 publications of the last 5 years). Ensure that the team of investigators has the necessary range of disciplines and expertise to carry out the study.

6.2 TRIAL-SUPPORTING FACILITIES

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

7. FINANCIAL SUMMARY

³ Assure that the biostatistician has the expertise to carry out clinical trials, e.g.: GMDS certificate, <http://www.gmds.de/texte/zertifikate-weiteres.html>; ICH guidance E9 "Statistical Principles of Clinical Trials"

Please give a rough estimation of the costs expected for the first 3 years and the total duration of the trial.

Item	Year 1-3	Total period ... years
Clinical Project Management		
Project Management: Trial Design and Preparation (e.g. Statistical Planning, Protocol, Case Report Form (CRF), Informed Consent, CRF printing)	€	€
Case Payment	€	€
Data management, IT (e.g. Database Set-up and Validation Data Entry, Coding, Query Management)	€	€
Biometry	€	€
Quality Assurance (e.g. on-site Monitoring, Data Monitoring and Safety Committee)	€	€
Travel (e.g. Trial Committees, Meetings)	€	€
Reference Centres	€	€
Materials	€	€
Trial Drug	€	€
Fees, Insurance	€	€
TOTAL	€	€

Please indicate any co-financing of the trial by industry.