DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

Clinical Research:

DZHK-associated Clinical Studies, Registries or Cohort Studies

CR.3-D

(without DZHK financing)

- Application preparation instructions for application template CR.2-D -

1. Please prepare your application in English not exceeding a maximum of 10 pages for the headings 1.-9. Structure your application using the headings listed below. Please do not erase any heading, rather answer 'not applicable'. Applications that do not meet the guideline will not be considered.

2. Please refer to the DZHK guideline 'DZHK-associated Clinical Studies' (CR.1-D) for study requirements.

3. Please use the application template CR.2-D (word file) for your application.

4. Proposals may be submitted any time.

5. Please submit one signed PDF file to clinicalstudies@dzhk.de.

1. Study synopsis

a) Applicant/ Coordinating investigator	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. First name, last name, academic title Institution and department (complete name) Postal address Telephone E-mail address
c) Title of study	The title of the trial should not exceed 140 characters and should be as precise as possible. In case of funding this title shall be quoted in the annual reports of the funding organisations. Please provide an acronym.
d) Medical condition	The medical condition being studied (e.g. asthma, myocardial infarction, depression).
e) Objectives	Which principal research questions are to be addressed? Specify clearly the primary hypothesis of the trial that determines sample size calculation. Name any secondary hypotheses.
f) Interventions	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.
i) Study type	e.g randomized/non-randomized, type of masking (single, double, observer blind), type of controls (active/placebo), parallel group/ cross-over, prognostic, diagnostic
m) Participating centres	To be involved (n): How many centres will be involved? Signed agreement to participate (n): How many centres have signed an agreement to participate? Please provide the full list under heading 6.2.

[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) ('Guideline for Good Clinical Practice'). 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 multicentre trial').

1.1. Summary

Give a summary of the main aspects of the project; it should not exceed 15 lines (max. 1,600 characters including blanks) and include information on the principal aspects e.g. goals, design, subjects, expected outcome of your project. It should be concise as well as comprehensible to a lay public. In case of DZHK-association this summary may be used for display on the DZHK Internet. Electronic search will be eased if you avoid abbreviations and include suitable key words.

1.2. Key words

1.3. Intervention scheme and trial flow

Describe the intervention scheme and additionally give a schematic diagram (flow chart) of design, procedures and stages.

1.4. Frequency and scope of study visits

What is the proposed frequency and scope of study visits and, if applicable, the duration of post-trial follow-up? Please give a schematic diagram additionally.

2. The medical problem

Which medical problem is to be addressed? What is the novel aspect of the proposed study? 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; substantiate your starting hypothesis. What is the rationale for the intervention? 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) and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/series. State what your study adds to the totality of evidence when your study 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.

2.2. Impact of the clinical study

What impact will the results have on clinical practice or understanding of the proposed intervention or underlying disease? Why is a trial needed now? How will a) the individual patient and b) society/science benefit from the trial? Detail potential economic impact.

3. Justification of design aspects

Please specify the respective parameters and provide justifications.

3.1. Controls/Comparators

Justify the choice of controls/comparisons: Is placebo acceptable? Is there a gold standard? 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 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

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? 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: what is 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 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? 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.

Trial sponsor (generally the coordinating PI's institution in an IIT)				
Key participants				
#	Name	Affiliation	Responsibility/Role	Signature
1			Principal/Coordinating investigator	
2			Trial statistician*	

* Please ensure 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'.

6.2. Supporting facilities

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

Trial supporting facilities (central laboratories, pharmacies etc.)			
#	Name	Affiliation	Responsibility/Role
Recruiting centres (please provide signatures on declaration of commitment)			
#	Name	Affiliation (only institution and city, no complete address)	Expected number of patients recruited for the complete trial
Total sum of recruited patients			Σ =

7. Financing

7.1. Financial summary

Indicate total duration of the trial, the period of time for which the project is funded and when funding begins. Please give a rough estimate of the costs expected for the total duration of the trial.

7.2. Outline of cost coverage

Please name all funding sources and the amount of money acquired. Is the trial co-financed by a company?

7.3. Intellectual property status

Please state whether the trial drug is covered by a patent and, if applicable, enter the date of patent expiry.

7.4. Commercial interest

Please 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 DZHK funding.

8. Match of DZHK and trial aims

8.1. Matching of scientific aims

Please describe briefly how your trials' aims match with the strategy and aims of the DZHK aims.

8.2. Advantages linked to the trials DZHK association for the DZHK

Please describe why the DZHK should be associated with your trial from the perspective of the DZHK.

8.3. Expectations related to DZHK-association of the trial

Please indicate your expectations from the DZHK with regard to the DZHK-association commitment.

8.4. Suggestions for merging the trial into DZHK infrastructure

Please provide your plan of how to fit your trial into the DZHK scientific infrastructure, e.g. do you plan to use the DZHK central data management, to submit your data to the Use & Access policy of the DZHK, to apply SOPs of the DZHK, etc.

9. Bibliography

Please list publications in the order of appearance in the text. Please list only publications you have cited. Please highlight your own project-relevant publications.