Application for a Clinical Trial within Modules 1 and 2

This template may be used for stand-alone research project or for research projects within a consortium.

*The length of the - excluding the appendix – should not exceed 20 pages. Please do not change the formatting of the document or single paragraphs. When filling out the templates, please note that the entries in italics are intended as information for the application and must be deleted before submitting the application. Please make an entry for each heading. Please prepare your application in English (DIN A4, 11 point Arial and 9 point Arial for the synopsis and references, margins of at least 2 cm and single-spaced lines).*

|  |  |
| --- | --- |
| **PRINCIPAL INVESTIGATOR OF THE TRIAL**[[1]](#footnote-1) | *In case of multiple applicants the principal investigator / coordinating investigator 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 * Fax * E-mail address |
| **Subtype of Covid-19** | *Please specify (if applicable) which subtype/course of condition your trial is aiming at (e.g. severe, asymptomatic, moderate form)* |
| **TITLE OF STUDY AND ACRONYM** | *Descriptive title identifying the study design, population, and interventions. In case of funding this title shall be quoted in the annual reports of the BMBF.* |
| **OBJECTIVE(S)** | *Which principal research questions are to be addressed? Specify clearly the primary hypothesis of the trial that determines sample size calculation.* |
| **INTERVENTION(S)** | *Brief description of the experimental and the control treatments or interventions as well as dose and mode of application.*  Experimental intervention:  Control intervention:  Duration of intervention per patient:  Follow-up per patient:  Accompanying measures: *(e.g. pharmacokinetic analyses)* |
| **KEY INCLUSION AND EXCLUSION CRITERIA** | Key inclusion criteria:  Key exclusion criteria: |
| **OUTCOME(S)** | Primary efficacy endpoint(s): *(e.g. for dose finding and/or for assessment of activity)*  Key secondary endpoint(s):  Assessment of safety: |
| **STUDY TYPE** | *e.g. randomized / non-randomized, type of masking (single, double, observer blind), type of controls (active / placebo), parallel group / cross-over* |
| **STATISTICAL ANALYSIS** | Efficacy:  Description of the primary efficacy analysis and population:  Safety:  Secondary endpoints: |
| **SAMPLE SIZE** | To be assessed for eligibility (n = …)  To be allocated to trial (n = …)  To be analysed (n = …) |
| **TRIAL DURATION** | Time for preparation of the trial (months):  Recruitment period (months):  First patient in to last patient out (months):  Time for data clearance and analysis (months):  Duration of the entire trial (months): |
| **PARTICIPATING CENTERS** | To be involved (n): How many centres will be involved? *if applicable*  Signed agreement to participate (n)*: How many centres have signed an agreement to participate? Full list under point 12.* |
| **SUMMARY** | *Please summarize your proposal in a max. of 300 words.* |

1 Innovation and Relevance of the Project

***1.1 Objectives/Research Goals***

*What is the objective? Which results are to be expected?*

***1.2 Evidence***

*Set your trial into perspective; substantiate your starting hypothesis. What is the rationale for the intervention? Please describe the existing evidence to support the trial (e.g. proof of principle in a disease specific animal model, relevant systematic review(s) and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/series).*

**Please note:** *Prerequisite for funding of early clinical trials is the provision of relevant and reliable data concerning the potential clinical efficacy of the therapeutic approach in the respective disease area. Therefore, please describe in detail the strengths and weaknesses in the stringency of the previous research and provide evidence for your previous results.*

***1.3 Safety***

*Please provide reliable data on safety and tolerability of the therapy.*

***1.4 Novel aspects and future impact***

*What is the novel aspect of the proposed therapy? Describe the innovative approach, development stage of therapeutic concept, prior art/comparison with existing therapies, innovative character. Specify the clinical impact and the therapeutic benefit. What will be the improvement for the patients? Why are the results of the trial important?*

*Reflect on the socioeconomic impact of the trial (e.g. potential cost reductions for health care, prospective pricing).*

***1.5 Subsequent Trial(s)***

*What would be the information gained for a subsequent trial? Define criteria that need to be fulfilled for transferring the proposed approach to a subsequent trial or for dismissing the proposed interventional approach.*

***1.6 Patient involvement***

*Please describe how patient involvement is implemented in the planning, conduct and exploitation of results of the trial. Patient involvement can be implemented in different stages of the trial and to a different extent. Please describe your concept for patient involvement.*

2 Exploitation concept

*Funding is provided in order to accelerate the clinical development and the transfer into clinical practice of new therapies which are of high medical relevance for COVID-19. The following list points out essential features which need to be adjusted according to the development status of your project.*

***2.1 Intellectual property rights***

*Please describe the existing freedom to operate of the academic study sponsor in respect to patent and exploitation strategy.*

***2.2 Assessment of regulatory aspects***

*Assess the regulatory aspects of your scientific and clinical activities. Describe how regulatory knowledge is represented in your project. Are industrial partners involved who may pursue authorization of the new therapeutic concept, if necessary? Have meetings with regulatory authorities already taken place? Please summarize briefly the results of these meeting(s).*

***2.3 Next Steps/Milestones***

*Present necessary next steps and major planned milestones until market entry or introduction into medical practice.*

***2.4 Expertise for exploitation***

*Describe skills and expertise of the members of the management team to promote the therapeutic approach and to drive into medical practice. Outline involvement of experts with respect to advice on industrial standards, regulatory aspects, and cooperation with industrial partners.*

3 Intervention and Design Aspects

***3.1 Intervention Scheme / Trial Flow***

*Describe the intervention scheme in depth and give a schematic diagram (flow chart) of design, illustrating interventions, procedures and stages. Recommendations for a complete description you may find in the TIDieR checklist and guide.*

***3.2 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 also give a table with time-points of visits and procedures per time-point. Specify items to be recorded on CRF per procedure.*

*3.3 Control(s) / comparator(s)*

*Justify the choice of control(s) / comparison(s): Is placebo acceptable? Is there a gold standard? Which previous (animal) studies established efficacy and safety of the chosen control regimen?*

***3.4 Dose, Mode and Scheme of Intervention***

*Justify the dose (finding), the mode and the scheme of the intervention. How does the intervention compare to other interventions for the same condition? Will the trial drugs be readily available for the trial?*

*3.5 Additional Treatments*

*Please describe the medication(s) / treatment(s) permitted (including rescue medication) and not permitted before and / or during the trial, if applicable.*

*3.6 Inclusion / exclusion criteria*

*Justify the population to be studied, include reflections on generalisability and representativeness, specifically with regard to gender and age.*

*3.7 Outcome measures*

*Justify the endpoints chosen: Are there other trials that have utilized this endpoint? Are there any guidelines proposing this endpoint / these endpoints? Patient-relevant endpoints have to be prioritized, if possible. Discuss the clinical relevance and as well the relevance for the patient of the outcome measures for the target population or the patient. Have the measures been validated? Justify appropriateness and limitations of composite endpoints, if applicable.*

Determination of primary and secondary measures

*How will primary and secondary endpoints be derived from actual measurements, e.g. how is the figure used in the statistical test calculated from the variables initially measured in the subjects?*

*3.8 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).*

*3.9 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. Give evidence / references for the estimated effect size.*

*If the proposed sample size is not based on statistical calculation, please justify why another approach has been chosen and why the proposed sample size will be adequate to answer the objective of the trial.*

*Sample size calculations need to take into account anticipated rates of non-compliance and losses to follow up.*

Compliance / Rate of loss to follow up

*Provide details for assumptions on compliance issues. On what evidence are the compliance figures based?*

*What is the assumed rate of loss to follow up? On what evidence is the loss to follow up rate based? How will losses to follow up or non-compliance be handled in the statistical analysis?*

*3.10 Feasibility of Recruitment*

*What is the evidence that the intended recruitment rate is achievable (i.e. available pilot data, access to patients etc. ?*

International collaborations

If the proposed trial includes foreign centres or collaboration with organisations in other countries, please give full details of funding arrangements agreed or under consideration.

*3.11 Stopping rules*

Please specify the “stopping rules” or “discontinuation criteria”

*a) for the individual patient,*

*b) for participating centers which fail to include the estimated number of patients (if applicable) and*

*c) for the whole trial.*

4 Statistical Analysis

*What is the proposed strategy of statistical analysis? What is the strategy for analysing the primary outcome? If applicable, how will multiple primary endpoints be analysed statistically? If interim analyses are planned, please specify. Are there any subgroup analyses? Discuss the robustness of your results e.g. with respect to unavoidable incomplete or missing data.*

5 Ethical Considerations

*Give a description of ethical considerations relating to the trial (assessment of risks and benefits, care and protection for research participants, protection of research participants’ confidentiality, informed consent process).*

6 Strategies for Data Storage, Handling and the Dissemination of Results

*Describe how data will be collected / generated and how consistency and quality of data will be controlled and documented. Describe how data will be stored, backed-up, managed and curated in the short to medium term. Specify any community agreed or other formal data standard used.*

*Which metadata is produced about the data generated from the research to enable research data to be used by others outside of your own team (taking into account privacy rules and proprietary data), e.g. documentation of methods used to generate the data, analytical and procedural information, provenance of data and their coding, detailed descriptions for variables, records etc.? Provide plans and place for long-term storage and preservation. Please use existing standards and data repositories where appropriate. Further information can be found under:*

<http://www.dfg.de/download/pdf/foerderung/antragstellung/forschungsdaten/guidelines_research_data.pdf>.

*Please provide a data sharing statement, which includes answers to the following questions: Will individual deidentified participant data (including data dictionaries) be shared at all? What data in particular will be shared? Will additional, related documents be available (e.g., study protocol, statistical analysis plan, etc.)? When will the data become available and for how long? By what access criteria will the data be shared (including with whom, for what types of analyses, and by what mechanism)? Further information on the data sharing statement can be found under* <https://www.nejm.org/doi/full/10.1056/NEJMe1705439>.

*Discuss the dissemination of results of the project, especially beyond regular journal publication. Please state your willingness to share relevant research and project data with other international funding organisations using GloPID-R. Please also indicate which parts of your research contain IP-relevant details and should therefore not be shared.*

7 Quality Assurance and Safety

***7.1 Quality assurance / monitoring***

*What are the proposed measures for quality assurance? Which institution will perform the monitoring? Which SOPs will be utilized? Describe and justify the monitoring strategy (percentage of source data verification, number of monitor visits per trial site).*

***7.2 Safety/ Pharmacovigilance***

*Describe and justify briefly the proposed strategy for the assessment of patients’ safety in the trial (monitoring of adverse events, documentation, reporting procedures, etc).*

8 Project Organisation and Management Structure

***8.1 Cooperation***

*Which structure is available, respectively will be implemented for an efficient cooperation within the project? How will the project be managed? What are the contributions of the individual partners?*

***8.2 Work Programme***

*Give a short overview of the work programme and the work packages planned with references to section 11. Indicate which tasks will be taken over by whom in the different work packages. Describe the methods you intend to apply.*

***8.3 Compliance with GLP and GMP***

*Please indicate how the research will be conducted in compliance with the requirements of GLP (good laboratory practice) and GMP (good manufacturing practice) standards where required.*

***8.4 Infrastructures***

*Please describe the facilities available to conduct the clinical trial (e.g. early clinical trial units, GMP facilities, if applicable).*

***8.5 Management Structure and Procedures***

*Arrangements for the management of the trials will vary according to the nature of the study proposed. However, all should include an element of expert advice and monitoring, that is* ***entirely independent*** *of the principal / coordinating investigator and the medical institutions involved. This will normally take the form of a scientific advisory board / trial steering committee (TSC) and / or an independent DSMB.*

*It is recognised that these arrangements may not always be appropriate and the committees needed may vary according to the nature of the study. Thus, the arrangements for supervision should be detailed and justified. The role of these committees can comprise to monitor and supervise the progress of the trial (including the safety data and the critical efficacy endpoints at intervals), to review relevant information from other sources, to ensure adherence to protocol, to consider interim analyses, to advise whether to continue, modify or stop a trial and provide the funding agency with information and advice.*

*Applicants should submit their proposed arrangements for overseeing of the trial and a suggested* ***membership*** *for the committee(s). A minimum of three members should be listed under section 11.*

***8.6 Scientific Discipline and Previous Work***

*Please name your discipline and your special field of work. Describe the major findings of your previous work. Specify your most relevant five publications and indicate the public access links if possible. Ensure that the team of investigators has the necessary range of disciplines and expertise to carry out the study.*

9 References

*For your references please use the Vancouver style (Further information: International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts submitted to Biomedical Journals. NEJM 1997;336:309-15).*

10 Project Timeline Flow

*As funding by BMBF will critically depend on the project progression according to milestones, please provide a diagram reflecting pre-clinical work packages, GMP production (if applicable), study preparation, pre-study-visits and initiation of centres, recruitment, follow-up and data cleaning/analysis (one page max.).*

11 List of Participants

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Trial Sponsor** | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | |
| **Trial Management** | | | | | | | | | | | | | | | | |
| # | Name | | Affiliation | | | Responsibility/Role | | | | | | | Scanned signature | | | |
|  |  | |  | | |  | | | | | | |  | | | |
|  |  | |  | | |  | | | | | | |  | | | |
| **Trial statistician *(It is mandatory that a trial statistician is included!)*** | | | | | | | | | | | | | | | | |
| # | Name | | Affiliation | | | | | | | | | | Scanned signature | | | |
|  |  | |  | | | | | | | | | |  | | | |
| **Other major participants** | | | | | | | | | | | | | | | | |
| # | Name | | Affiliation | | Responsibility/Role | | | | | | | Scanned signature | | | | |
|  |  | |  | |  | | | | | | |  | | | | |
| **Subcontractors** | | | | | | | | | | | | | | | | |
| # | Name | | Affiliation | | Responsibility/Role | | | | | | | | | | | |
|  |  | |  | |  | | | | | | | | | | | |
| **Trial Supporting facilities** *(reference 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)* | | | | | No. of patients with condition relevant to the trial seen in the last 12 months | | No. of these patients fulfilling the inclusion criteria | | | No. of these patients which would approx. agree to participate in the trial per year | Expected no. of patients recruited for the complete trial | Source of these figures |
|  |  | | |  | | | | |  | |  | | |  |  |  |
|  |  | | |  | | | | |  | |  | | |  |  |  |
| **Total sum of recruited patients** | | | | | | | | Σ = | | | | | | | | |
| **Data Safety and Monitoring Board (DSMB)** | | | | | | | | | | | | | | | | |
| # | Name | | Affiliation *(only institution and city, no complete address)* | | | | | | | | | | | | | |
|  |  | |  | | | | | | | | | | | | | |
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|  |  | |  | | | | | | | | | | | | | |
| **Other participating groups / bodies** *(e.g. steering committee in international trials)* | | | | | | | | | | | | | | | | |
| # | | Name | | | | | Affiliation | | | Responsibility/Role | | | | | | |
|  | |  | | | | |  | | |  | | | | | | | |

*Include a tabular scientific CV (****two pages****) for the principal/ coordinating investigator. Include also tabular scientific CVs (****one page****) for other participants playing a leading role in section 14 (not separately in the appendix). Please see section 14 for details.*

*Recruiting centres must detail their commitment on a separate sheet (cf. appendix) as provided by the funding agency.*

*A final version of the trial protocol has to be submitted to the funding agency together with the statement by the ethics committee after the review process. While funding for a preparatory phase might be provided upon the general funding decision, funding of the actual trial can only be provided if all necessary formal and legal requirements are met.*

12 Information on Financial Aspects

Funds can only be granted for research activities. Do not include patient care costs.

12.1 Financial Summary

*Please fill out the financial summary below.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Organizational Segment** | **Institution/ Participant / Trial Site** | **No of items/ Kind of equipment / Explanation** | **Qualification of staff** | **TV-ÖD**  **TV-L**  **TV-Ä** | **Total months** | **Mittel in Euro** |
| 1 | **Clinical Project Management** |  |  |  |  |  |  |
| 2 | **Project Management** |  |  |  |  |  |  |
| 4 | **Data Management** |  |  |  |  |  |  |
| 5 | **Biometry** |  |  |  |  |  |  |
| 6 | **Quality Assurance / Monitoring** |  |  |  |  |  |  |
| 7 | **Safety / Pharmaco-vigilance** |  |  |  |  |  |  |
| 8 | **Trial Committees** |  |  |  |  |  |  |
| 9 | **Meetings / Travel** |  |  |  |  |  |  |
|  |
| 10 | **Case Payment** |  |  |  |  |  |  |
| 11 | **Reference Centers** |  |  |  |  |  |  |
| 12 | **Materials** |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| 13 | **Trial Drug** |  |  |  |  |  |  |
| 14 | **Insurance** |  |  |  |  |  |  |
| 15 | **Fees** |  |  |  |  |  |  |
| 16 | **Equipment** |  |  |  |  |  |  |
| 17 | **Publications** |  |  |  |  |  |  |
| 18 | **Other** |  |  |  |  |  |  |
|  | **TOTAL (without overhead / „Projektpauschale“)** | | |  |  |  |  |

*12.2 Co-financing by industry or other parties is possible if*

Co-financing by industry or other third parties is possible if

* the independence of investigators is ensured and
* if terms and conditions of the financial commitment are disclosed.

If co-financing is intended, please describe the type and volume of the intended co-financing, indicating the respective company or other third party.

**Please don’t make any legally binding agreements before notion of award has been made; please contact the project management agency (DLR-PT) first!** Appropriate agreements on intellectual property, confidentiality, publication of results, property rights should be concluded between all those playing a leading part in the conduct of the trial.

**12.3 Other Funding**

*In case you have already submitted parts of the same request to other institutions or the BMBF, please mention this here. Indicate other sources which will provide funds, free services or consumables.*

*If this is not the case, please declare: "A request for funding of this project has not been submitted to any other addressee. In case I submit such a request I will inform the DLR Projektträger immediately.”*

13 CVs of Major Participants

***13.1 Principal / Coordinating Investigator***

*Include a tabular scientific CV (max. two pages) for the principal / coordinating investigator containing a list of the last five clinical trials by him/her and their reporting status with regard to registration of the trial, publication of the trial protocol and of major results. Explain where trials have remained unreported.*

***13.2 Other participants with Leading Role***

*Include tabular scientific CVs (one page) for other participants playing a leading role (e.g. co-applicants, members of trial management, trial statistician; not all collaborating partners at all trial centres) including a list of a maximum of 5 publications on the most relevant projects related to this project’s topic by him/her that have appeared during the last five years.*

# APPENDIX

Declarations of commitment of participating centres

*Please use the template provided to declare the commitment of each participating center (including the center of the principal investigator). The template is to be signed personally by the investigator at the respective site (as named in the list of participants involved in the trail; see heading 11 of the proposal). Do not submit facsimiles.*

|  |  |
| --- | --- |
| Name of investigator: |  |
| Institution: |  |

**Information on the clinical trial** *(according to the proposal)1*

|  |  |
| --- | --- |
| Trial title: |  |
| Inclusion criteria: |  |
| Exclusion criteria: |  |
| recruitment period (months): |  |

**Strategy for the determination of recruitment figures**

|  |  |
| --- | --- |
| How many patients with the condition speci­fied above have you seen in your institution during the last 3 months? |  |
| How many patients do you estimate to see in the course of the next year |  |
| How many of these patients would fulfil the inclusion criteria of the above mentioned trial? |  |
| How many of these patients would approximately agree to participate in the above named clinical trial per year? |  |
| How many patients will approximately be recruited during the entire trial? |  |

|  |
| --- |
| Which source/assumptions did you use for the estimation of potential participants in the above named clinical trial?  Individual estimation  Hospital data management system  Patient registry  Others  If others: please specify |

|  |  |
| --- | --- |
| Are there any other ongoing clinical trials/ projects competing for the same patients? | yes  no |
| If yes: How will this affect recruitment for the above-named clinical trial? | |

**Commitment to participate**

I hereby agree to participate in the above-named clinical trial and support the trial by recruiting patients.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date / Signature 2

1 Delete italic text at completion of the template.

2 Note: This document is to be signed personally by the investigator at the respective site (as named in the list of participants involved in the trial; see 11. in the proposal), do not submit facsimiles.

1. Zur Definition des "Investigator" siehe “Guideline for Good Clinical Practice” der International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH GCP) (<http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf>). [↑](#footnote-ref-1)