DLR Projektträger

Bundesministerium für Bildung und Forschung

Leitfaden für die Erstellung von ausführlichen Projektskizzen / Anträgen für konfirmatorische präklinische Studien zur „Richtlinie zur Förderung von konfirmatorischen präklinischen Studien - Qualität in der Gesundheitsforschung -“

Aktualisiert 02.08.2019

Dieser Leitfaden stellt die Anforderungen für die Erstellung von beurteilungsfähigen Projekt-anträgen dar. Er ergänzt die am 27. Dezember 2018 im Bundesanzeiger veröffentlichte o. g. Förderrichtlinie des BMBF (https://www.gesundheitsforschung-bmbf.de/de/8344.php). Er soll offene Fragen im Vorfeld der Einreichung klären.

Projektanträge, die den Vorgaben der Förderrichtlinie und des folgenden Leitfadens nicht entsprechen, können ohne weitere Prüfung abgelehnt werden.

Es wird dringend empfohlen, zur Beratung mit dem DLR Projektträger Kontakt aufzunehmen. Ansprechpartnerinnen sind:

Dr. Marianne Kordel
Telefon: 0228-3821 1137; E-Mail: praeklinische-studien@dlr.de

Dr. Cosima Pfenninger
Telefon: 030-67055 9609; E-Mail: praeklinische-studien@dlr.de

Allgemeine Informationen

Es können beantragt werden:

Wissenschaftsinitiierte, prospektive, kontrollierte präklinische Studien zum Wirksamkeitsnachweis eines klinisch relevanten therapeutischen Ansatzes. Die Studien sollen möglichst als multizentrische Studien durchgeführt werden. Jede Studie muss eine konfirmatorische Zielsetzung aufweisen, um die in explorativen Studien erzielten Erkenntnisse zu validieren.

Entscheidungsverfahren

Konfirmatorische präklinische Studien (Modul 1)

Für konfirmatorische präklinische Studien werden zwei fachliche Begutachtungsschritte durchgeführt. Im ersten Schritt wurden unter Beteiligung eines unabhängigen, internationalen Begutachtungsgremiums Projekte ausgewählt, für die jetzt **ausführliche Vorhabenbeschreibungen (full proposals)** eingereicht werden können. Diese werden in einem zweiten fachlichen Begutachtungsschritt wiederum durch ein unabhängiges, internationales Begutachtungsgremium bewertet.

Formale Vorgaben für die Projektanträge

Einreichende, deren Skizzen im ersten Begutachtungsschritt positiv bewertet wurden, werden zur Vorlage von ausführlichen Vorhabenbeschreibungen eingeladen. **Gleichzeitig** soll der Formantrag eingereicht werden.

Es sind demzufolge folgende Unterlagen einzureichen:

- die **englischsprachige begutachtungsfähige ausführliche Vorhabenbeschreibung** (full proposal, s. unter 1.),
- der **Formantrag** (s. unter 2) bestehend aus:
  - dem förmlichen Förderantrag (AZA/AZAP/AZK),
  - einer deutschsprachigen Zusammenfassung mit detailliertem Arbeitsplan incl. vorhabenbezogener Ressourcenplanung (http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Ressourcenbezogener_Arbeitsplan.xlsx) und Meilensteinplanung und detailliertem Finanzierungsplan des Vorhabens,
  - einem ausführlichen Verwertungsplan mit einer Darstellung der Notwendigkeit der Zuwendung http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Verwertungsplan_und_Notwendigkeit_der_Zuwendung.pdf .

1. Erstellung und Einreichung der englischsprachigen begutachtungsfähigen ausführlichen Vorhabenbeschreibung

Im Sinne der Vergleichbarkeit sind dafür die Formatvorgaben des Leitfadens und die darin vorgegebene Gliederung verbindlich einzuhalten (s. Abschnitt „Template Full Application – Preclinical Confirmatory Study (Module 1), s.u.)“:
http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Template_Full_Poposal_Preclinical_Confirmatory_Study_2019.docx.

Die ausführlichen englischsprachigen Vorhabenbeschreibungen sind ausschließlich elektronisch bis zum 12.11.2019 als ein einzelnes pdf-Dokument über das Internetportal https://ptoutline.eu/app/praeklinstudien **einzureichen.** Eine Vorlage per E-Mail oder FAX ist nicht möglich. Im Rahmen der elektronischen Einreichung wird ein pdf-Dokument zur Authentifizierung der Einreichenden generiert („Projektblatt“). Der Ausdruck dieses Dokuments ist von der oder dem Projektverantwortlichen sowie dem beteiligten Biometriker bzw. Biometrikerin handschriftlich zu unterzeichnen und innerhalb von einer Woche nach Einreichungsfrist als Scan per E-Mail an die darauf angegebene Adresse zu senden.

2. Erstellung und Einreichung des Formantrags (förmlicher Förderantrag und ergänzende Unterlagen)

Der Formantrag ist **bis spätestens zum 03.12.2019, 12:00 Uhr (MEZ)** durch die Projektleitung elektronisch über das Internetportal von easy Online (https://foerderportal.bund.de/easyonline/reflink.jsf?m=KB-PRAEKLINISCHESTU&b=KB-

PRAEKLINISCHESTUD) zu erstellen. Bitte nehmen Sie hierzu Kontakt mit uns auf. Zusätzlich ist die umgehende Vorlage eines rechtsverbindlich unterschriebenen Formantrags auf dem Postweg erforderlich.
Bitte beachten Sie die „Hinweise und Checkliste zur Formantragstellung“ (http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Checkliste_zum_Erstellen_des_Formantrages.docx)
Im „Formularschrank“ des BMBF, der ebenfalls über das Förderportal des Bundes zu erreichen ist, finden Sie die Richtlinien für Zuwendungsanträge auf Ausgabenbasis / Kostenbasis sowie das Merkblatt Vorkalkulationen für Zuwendungen – Kostenbasis. Bitte vergewissern Sie sich, dass der Formantrag alle auf der Checkliste angegebenen Unterlagen enthält. Diese Unterlagen sind in deutscher Sprache vorzulegen. Bei Verbünden und multizentrischen Studien sind die förmlichen Förderanträge in Abstimmung mit der Verbund-/Studienkoordination von jedem Verbundpartner einzureichen. Dabei ist zu beachten, welche Einrichtungen antragsberechtigt sind (siehe Punkt 3 der Förderbekanntmachung).

Bei Fragen zum Formantrag ist Ihre Ansprechpartnerin:

Frau Heike Manns
Telefon: 0228-3821 1495;

E-Mail: Heike.Manns@DLR.de

Die o.g. Anlagen sind als Anlagen beizufügen.
Entscheidend für die Fristwahrung ist der auf elektronischem Wege über das Internet-Portal „easy Online“ verbindlich eingereichte Förderantrag mit allen ergänzenden Informationen. Eine Vorlage per E-Mail oder FAX ist nicht möglich. Aus der Vorlage des Förderantrags kann kein Rechtsanspruch auf Förderung abgeleitet werden.

Einreichungsprozess des Formantrags: Erstellen Sie die Endfassung des förmlichen Förderantrags und die oben genannten Anlagen. Bestätigen Sie in der Maske „Pflichtanlagen“, dass die Anlagen hinzugefügt werden. Dann gehen Sie im Internet-Portal easyonline auf den Menüpunkt **„Endfassung einreichen“**. Dort werden Sie durch den Einreichungs-Prozess geführt. In einem eigenen Schritt werden Sie aufgefordert die Pflichtanlagen zum Formantrag hochzuladen.

Allgemeine Hinweise

Die nachfolgenden Hinweise sind bei der Planung und Einreichung aller Projektskizzen und ausführlichen Vorhabenbeschreibungen zu beachten.

Die Antragstellenden sollen sich im Vorfeld vergewissern, ob bereits präklinische (konfirmatorische) Studien oder systematische Reviews zu der von ihnen geplanten Fragestellung existieren oder derzeit erstellt werden.

Wissenschaftliche Standards
Die Antragstellenden sind verpflichtet, nationale und internationale Standards zur Qualitätssicherung der präklinischen Forschung einzuhalten. Hierzu sind die nachfolgenden Dokumente in der jeweils geltenden Fassung zu berücksichtigen:

- Handreichung der Senatskommission für tierexperimentelle Forschung der DFG zur Planung und Beschreibung tierexperimenteller Forschungsprojekte[1]
- ARRIVE Guidelines[2]
- PREPARE Guidelines
- Leitlinie zur Guten Zellkulturpraxis (Good Cell Culture Practice, GCCP)

[1] https://www.dfg.de/download/pdf/dfg_im_profil/gremien/senat/tierexperimentelle_forschung/handreichung_sk_tierversuche.pdf
[2] https://www.biorxiv.org/content/biorxiv/early/2019/07/15/703181.full.pdf

Registrierung und Zugänglichkeit des Studienprotokolls sowie der Forschungsergebnisse

Eine (Prä-)Registrierung von präklinischen Studien erhöht die Transparenz über die durchgeführte Forschung und trägt zur Robustheit der Studien bei. Deshalb empfehlen wir die (Prä)-Registrierung der präklinischen Studien in geeigneten Registern. Die Registrierung soll nachgewiesen werden[3]. Auch das Studienprotokoll sollte dort hinterlegt werden. Falls dies nicht geplant wird, muss dies im Antrag begründet werden.

Die aus dem Forschungsvorhaben resultierenden Ergebnisse (auch die Null-Resultate) sollen möglichst bald (innerhalb von 1-2 Jahren) nach Beendigung der Studie veröffentlicht werden. Dies beinhaltet mindestens die Publikation der Ergebnisse auf einem wissenschaftlichen Kongress und die Publikation der Ergebnisse in einer einschlägigen wissenschaftlichen Fachzeitschrift. Die Veröffentlichung soll in einer wissenschaftlichen Zeitschrift so erfolgen, dass der Öffentlichkeit der unentgeltliche elektronische Zugriff (Open Access) auf den Beitrag möglich ist. Für eine Open Access Veröffentlichung der Vorhabenergebnisse können nur solche Zeitschriften ausgewählt werden, deren Beiträge unmittelbar nach Erscheinen über das Internet für Nutzer entgeltfrei zugänglich sind und die im jeweiligen Fach anerkannte, strenge Qualitätssicherungsverfahren anwenden. Publikationsgebühren für Open Access Publikationen sind während der Laufzeit der Vorhaben zuwendungsfähig.

Unter Punkt 11.E in der ausführlichen Vorhabenbeschreibung der konfirmatorischen präklinischen Studien ist zu beschreiben, wie, in welchem Umfang, in welcher Verarbeitungsstufe und in welchem zeitlichen Rahmen die Forschungsdaten zugänglich gemacht werden, um eine sinnvolle Nachnutzung durch Dritte zu ermöglichen (unter Wahrung der Rechte Dritter insbesondere Datenschutz, Urheberrecht). Für weitere Informationen s. https://www.dfg.de/download/pdf/foerderung/antragstellung/forschungsdaten/guidelines_research_data.pdf .

Merkblätter und Richtlinien des BMBF

Neben diesem Leitfaden gelten die entsprechenden Merkblätter und Richtlinien des BMBF, soweit in diesem Leitfaden nicht ausdrücklich andere Regelungen getroffen werden. Weiterführende Links für die Antragstellung finden Sie auf den Internetseiten des BMBF (www.foerderportal.bund.de). Die dort veröffentlichten Anforderungen /Informationen werden regelmäßig aktualisiert.

Weitere nützliche Arbeitshilfen sind zu finden in der QUEST-Toolbox[4] des Berliner Instituts für Gesundheitsforschung sowie in der Toolbox des Open Science Center der LMU München[5].

[3] Z.B. https://www.animalstudyregistry.org/ oder https://www.preclinicaltrials.eu/ ; oder https://cos.io/prereg/ . Präklinische konfirmatorische Studien können auch über die Formate verschiedener Journale (z.B. CORTEX: Preregistered Study) oder auch PeerJ, PlosOne, BioRxiv, oder ScienceOpen) registriert werden.
Systematische Reviews zu präklinischen Studien können z.B. bei http://syrf.org.uk/protocols/ oder bei https://www.crd.york.ac.uk/PROSPERO/#aboutregpage registriert werden.

[4] https://www.bihealth.org/en/research/quest-center/mission-approaches/open-science/quest-toolbox/

[5] https://www.osc.uni-muenchen.de/toolbox/index.html

Mustervorlagen und Erläuterungen zur Erstellung der Anlagen zum Formantrag

Mustervorlage Vorhabenbezogener Ressourcenplanung:
http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Ressourcenbezogener_Arbeitsplan.xlsx

Verwertung und Notwendigkeit der Zuwendung:
http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Verwertungsplan_und_Notwendigkeit_der_Zuwendung.pdf

Checkliste zum Erstellen des Formantrages:
http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Checkliste_zum_Erstellen_des_Formantrages.docx

Mustervorlage & Erläuterungen für ausführliche Vorhabenbeschreibungen für präklinische konfirmatorische Studien

Full Application – Preclinical Confirmatory Study (Module 1)

To ensure comparability of all submitted outline applications please prepare your application in English **not exceeding 20 pages for the headings 1.-10.** (DIN A4, at least 10 point Arial, margins of at least 2 cm and single-spaced lines). The number of pages includes cited literature.

Structure your application using the headings listed below. **Make an entry under each heading /subheading. It is important that you are as explicit and precise as possible.**

Scanned signatures of the principle/coordinating investigator and the study statistician are mandatory in appendix 2 "Declaration by partners involved in the study".

Additionally three appendices are to be submitted: 1. Search Strategy, 2. Declaration by partners involved in the study, 3. CVs of major participants.
Do not submit any other appendices.

Please pay attention to the **reviewers´ recommendations** to your outline proposals as well as to the **glossary** provided (*http://www.dlr.de/pt/Portaldata/45/Resources/Dokumente/GF/Glossary_Preclinical_Confirmatory_Studies_and_Systematic_Reviews.pdf*).

Text in italic in this template hints to the expected information to be given by the applicants and should be replaced.

STUDY SYNOPSIS[6]

APPLICANT / RESPONSIBLE INVESTIGATOR	*Name, institution and department, address, telephone, fax, e-mail*
PARTICIPATING LABS OTHER CONTRIBUTORS	*Name, institution and department, address, telephone, fax, e-mail*
TITLE OF STUDY	*Descriptive title identifying the study design, animals/cells/or other, and interventions. In case of funding this title shall be quoted in the annual reports of the BMBF.*
ACRONYM	*Acronym (max. 25 characters)*
MEDICAL CONDITION	*Please describe the medical condition addressed*
OBJECTIVE(S)	*Which hypotheses are to be tested? Which principal research questions are to be addressed? Clearly specify the primary objective of the study determining the sample size calculation. Specify any secondary objectives.*
MODEL/SETTING	*Which models / samples (animals, probes/samples of humans, cell cultures etc.) are to be used, e.g. species, strain, source, sex, age (developmental stage), genetic modification, weight; cell line, authentication and characterization, age and sex of donor, nature of tissue specimen, storage and banking.*
INTERVENTION	*Brief description of the experimental and the control treatments or interventions as well as dose and mode of application.*

[6] *In preparation of the application the following information related to study design is worth noting:*
https://www.nc3rs.org.uk/experimental-design
https://www.nc3rs.org.uk/experimental-design-assistant-eda
https://www.nc3rs.org.uk/arrive-guidelines
http://journals.sagepub.com/doi/10.1177/0023677217724823
https://www.dfg.de/download/pdf/dfg_im_profil/gremien/senat/tierexperimentelle_forschung/handreichung_sk_tierversuche.pdf

	• *Experimental Intervention* • *Control intervention (pos. / neg.):* • *Duration of intervention:* • *Follow-up:*
ETHICAL STATEMENT	*Discuss briefly the acceptability of the harm incurred by the animals versus the potential benefit for the patients*
STUDY DESIGN	*Please provide:* • *Experimental and control groups* • *Key inclusion and exclusion criteria* • *Consideration of external validity: age, sex of animals or samples, comorbidities, lab variety (number of labs participating in the study)* • *Outcome: define the primary endpoint; key secondary endpoint(s)* • *Methods to reduce risk of bias: e.g. randomization and blinding* • *Parallel groups / crossover design*
EXPERIMENTAL PROCEDURES	*Briefly outline the experimental procedures to be carried out.*
STATISTICAL ANALYSIS	• *Brief outline of the statistical analyses including handling of missing data or clustering/hierarchical structures within the data* • *Assumed effect sizes (should be justified by effect sizes from previous studies)* • *Description of the primary efficacy analysis and population*
SAMPLE SIZE CALCULATION	• *Experimental unit* • *Sample size calculation used (considering the rationale for the chosen effect size and statistical power. The power must be 90 % or higher for all tests. The power analysis must be based on the lowest available or meaningful estimate of the effect size).* • *Total number of animals / cell culture / samples to be used in each experiment* • *Number of animals / cell culture / samples in each experimental group* • *Total number of animals / cell culture / samples to be analyzed* • *Statistical methods to be used*
STUDY DURATION	• *Time for preparation of the study (months):* • *Time for the study (months):* • *Time for data clearance and analysis (months):* • *Duration of the entire study (months):*
QUALITY CONTROL	• *Precautions to secure validity of test procedures (also across labs), authentication of biological resources (animals, cells, antibodies, media etc.), skills needed, standardized protocols, data management, (pre)registration, reporting guidelines*
DATA MANAGEMENT PLAN	*Please describe shortly what measures will be taken to ensure data management, maintenance and long-term accessibility of your results for future updates and reuse.*
REGISTRATION NUMBER[7]	
DATE AND LOCATION OF PROTOCOL REGISTRATION[7]	

[7] can be given later,
(Pre-)registration is highly recommended and can be done in: e.g. “Animal Study Registry” (https://www.animalstudyregistry.org) or
“International register of preclinical trial protocols” (https://preclinicaltrials.eu/)

Below, please substantiate:

0. RESPONSE TO REVIEWERS´ COMMENTS

Please summarize in English the recommendations given to your outline application. Please respond with a short point-by-point reply separately to each recommendation (2 pages max.). Where necessary, refer to changes made in this full application.

1. SUMMARY

1.1 SUMMARY

Give a summary of the main aspects of the project; (max. 1600 characters incl. blanks).

1.2 KEY WORDS

Give max. 5 key words which apply to the planned study.

2. RELEVANCE

Which medical condition is to be addressed? Which principal research questions are to be addressed? How will your study affect the translational process?

2.1 IMPACT OF THE STUDY

Please describe possible results of the planned study. Please describe the relevance of these for the clinical problem.

Novelty: Which therapy options are available for treatment of the disease? What is the novel aspect of the proposed study? This can include aspects of the original study that forms the basis of the confirmatory study.

2.2 EXPLOITATION OF RESULTS

How will your results facilitate translation of the initial findings into improved therapies or diagnostics? What will be the next steps? In case new evidence will be generated that goes beyond a confirmation, please describe. Please state how the expected results will inform the decision to start clinical (human) trials.

3. SCIENTIFIC PREMISE / PREVIOUS RESULTS

This section should detail the background of the starting hypotheses of the study.

3.1. SCIENTIFIC PREMISE

Please provide the scientific premises to understand the motivation and context for the study: Please describe how the existing literature was reviewed, and provide your search strategy[8] in the appendix.

3.2 PREVIOUS (OWN) RESULTS DIRECTLY RELATED TO THE PLANNED STUDY

Please describe previous results, e.g. explorative studies, triangulation, others. If they are published please provide the references.

Which is the central finding that is to be confirmed?

Also give evidence why a confirmatory study is justifiable at this stage (e.g. what evidence does exist to show a treatment effect).

[8] *Guidance concerning search techniques can be found at the following address: http://syrf.org.uk/systematic-review/step-3-search-strategy or in the following publication: Leenaars et al. (2011) 'A step-by-step guide to systematically identify all relevant animal studies' Laboratory Animals 2012; 46: 24–31. DOI: 10.1258/la.2011.011087*

4. MODEL, HOUSING AND HUSBANDRY

4.1. RELEVANCE OF THE MODEL

Which model/models is/are to be used: Please provide details for animal species / cell model, strain, sex, age (developmental stage), weight. Provide source of animals or cells, international nomenclature, genetic modification status, genotype, health/immune status, drug or test naive; cell line, authentication and characterization, age and sex of donor, nature of tissue specimen, storage and banking.

Please provide sound scientific reasoning how and why the chosen model can address the scientific objectives and the study´s relevance to human biology. Is the (animal) model different from the previous/to be confirmed studies? If yes, why?

In case animal studies are planned please also explain: Why are there no suitable non-animal alternatives?

4.2. HOUSING AND HUSBANDRY

Please describe animal husbandry, caging and housing (e.g. type of facility, current microbiological status of the facility, whether a health surveillance program is established, temperature, light/dark cycle, type of cage, number of animals per cage, food, water, bedding, enrichment).

5. STUDY DESIGN

Please **substantiate** and do not only list the respective information.

5.1 THE NUMBER OF EXPERIMENTAL GROUPS AND DESIGN

Please describe

5.2 CONTROL(S) / COMPARATOR(S)

Give details and justify the choice of control(s) / comparison(s). Which studies establish efficacy of the chosen positive control regimen? Highlight and justify controls added in the confirmatory study compared to the original study.

5.3 INCLUSION / EXCLUSION CRITERIA

Describe and justify the population to be studied; include reflections on generalisability and representativeness (external validity: age, sex, comorbidities, lab variety). Please also explain how many laboratories will be involved and how the study will be carried out across these laboratories. How will intra- and inter-laboratory variation be taken into account?

5.4 OUTCOME MEASURES

Justify the endpoints chosen (primary, secondary): Why are the chosen endpoints relevant? Are there other studies that have utilized these endpoints?

5.5 METHODS TO REDUCE RISK OF BIAS

Describe possible risk of bias in your methods, conduct and analysis of your proposed study. Address risk of reporting bias, too.

Please describe explicitly e.g.

- *Procedures for randomization and blinding: Please detail your description how blinding and randomization will be performed.*
- *Outlier criteria: Please describe predefined outlier criteria that would lead to exclusion of animals or data points.*
- *Use of reporting guidelines*
- *Reporting of all results*

If randomization or blinding is not possible please explain why and give details of alternative methods to avoid biased assessment of results.

6. INTERVENTION AND EXPERIMENTAL PROCEDURES

6.1 INTERVENTION(S)

For each study group including controls, please describe[9] and give rationale

- *How the interventions / procedures are to be carried out. Give details on e.g. drug formulation and dose, availability of the drug formulation, site and route of administration, surgical procedure, anaesthesia, provide details of specialist equipment to be used and suppliers*
- *When: e.g. time of day*
- *Where: e.g. lab, cage*
- *By whom*

Illustrate your intervention scheme graphically.

7. SAMPLE SIZE CALCULATIONS AND STATISTICAL ANALYSIS

7.1 PROPOSED SAMPLE SIZE / POWER CALCULATIONS

Please substantiate: *What is the experimental unit of your study (see glossary)? Clearly outline independence / dependence of experimental units (and nesting, if applicable). What is the proposed sample size? This should be deduced from the previous study that is to be confirmed. What is the minimum clinically relevant effect size based on the previous results that is used for the sample size calculation of this confirmatory study? (Data need to be publicly available. If not, confidential reports summarizing the data have to be submitted with the application.) The minimum power for the confirmatory study should be > 90 %, an alpha level of 0.05 should be used. 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, as appropriate. It is important that the sample size calculations take into account anticipated rates of losses. Please also mention the software used. In case of complex calculations, details on the methods (including references) should be provided.*

7.2. FEASIBILITY

What is the evidence that the intended sample size is achievable?
Comment on the access to animals / cells / samples in labs of partner institutions, the capacity, and their willingness to cooperate in the study. Please provide declarations of intent for cooperating partner institutions (Appendix 2).
Please specify and justify how the experimental units will be distributed across the labs of the partner institutions (multi-centre study).

International collaborations
If the proposed study includes foreign centres or collaboration with organizations in other countries please give full details of funding arrangements agreed or under consideration.

7.3. STATISTICAL ANALYSIS

What is the 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? How will missing data and subjects withdrawn from the study be handled statistically? How will nesting / clustering, if applicable, be dealt with statistically? How is the multi-centre structure reflected in the analysis strategy?

How does the analysis parallel / deviate analysis strategies from the studies that are to be confirmed?

8. ETHICAL CONSIDERATIONS

If applicable:

Discuss the acceptability of the harm incurred by the animals versus the potential benefit for the patients.

In case your study will be recommended for funding you will be obliged to provide the approval of the respective regulation office for animal studies before the start of the study.

[9] *You may find recommendations for a description in the TIDieR checklist and guide*.

9. QUALITY CONTROL AND STUDY MANAGEMENT

9.1 QUALITY ASSURANCE / MONITORING

What are the measures for quality assurance? Which institution will be responsible? Which SOPs will be set up / utilized? How will monitoring be conducted? Which precautions will be planned to secure validity of test procedures (also across labs), authentication of biological resources (animals, cells, antibodies, media etc.), skills needed, standardized protocols, (pre-) registration of the study and study protocol.

9.2. MANAGEMENT STRUCTURE AND PROCEDURES

Describe the roles and responsibilities of the partners of the study (e.g. principal / coordinating investigator, statistics, performance of the study and adherence to the protocol, quality control (checking that data are correct)). Please also state how the independence of study analysis from the previous study which is to be confirmed can be secured.

10. TIME FLOW AND MILESTONES

Describe the proposed time flow with all relevant steps including milestones. Please provide a diagram reflecting preparation (including study protocol, submission to authorities, SOPs, initiation of labs), execution of study, data base cleaning, data analysis.

11. DATA MANAGEMENT PLAN, DATA SHARING, DISSEMINATION OF RESULTS

The data management plan (DMP) is intended to be a living document in which information can be made available on a finer level of granularity through updates as the implementation of the project progresses and when significant changes occur. Therefore, DMPs should have a clear version number and include a timetable for updates.

Clearly describe your data management plan (DMP) which has to ensure data management, maintenance and long-term accessibility for future reuse of your results (also by third parties, taking into account privacy rules and proprietary data)[10]. Also mention at which stage data sharing will be envisaged. To ensure that your research data are soundly managed please follow the principles of FAIR data[11]. Please use existing international standards and data repositories which allow publishing of FAIR data and are non-commercial. Data management costs are eligible for funding during the period of funding.

Version No.:

Date of Update:

A	**General information**	
A.1	Acronym	
A.2.	Responsibilites: • data management • metadata creation • data security • quality assurance of data	*Apart from the PI: who is responsible*
A.3.	DM support office:	*Is there a DM support office in your institution?* ☐ Yes ☐ No *If yes, have you contacted it for support?*
B	**Description of data set**	
B.1.	Data to be collected / generated:	*Describe the data that will be collected / generated within the project.*
B.2	Type and format of data:	*Specify the type, and format of the data.*

[10] The following information may be worth noting: Horizon 2020 DMP https://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/oa_pilot/h2020-hi-oa-data-mgt_en.pdf

[11] http://www.forschungsdaten.org/index.php/FAIR_data_principles

C	**Data storage**	
	During the research	
C.1	Volume of data and site of storage:	*What is the volume of the data and where will the data be stored?*
C.2	Storage capacity during the project	*Is there sufficient storage capacity during the project?* ☐ Yes ☐ No
	Data back-up and responsibility:	*Will the data be backed-up regularly during the project?* ☐ Yes ☐ No *Who is responsible for this?*
	After the research	
C.3	Trusted Repository and FAIR principles:	*Specify in which trusted repository the data will be stored after the project*[12]*.* *If the data will not be stored in a trusted repository: how will the data be made* *- findable,* *- accessible and* *- reusable?*
C.4	Persistent identifier:	*Will a persistent identifier be used to make the data findable?* ☐ Yes ☐ No
C.5	Storage of confidential, privacy-sensitive or competition-sensitive data[13]:	*How will confidential, privacy-sensitive or competition-sensitive data be stored?*
C.6	Duration of archiving:	*For how long will the data be archived?*
D	**Standards and metadata**	
D.1	Documentation of data: Metadata standard:	*How will the data be documented?* *What metadata standard will be used to make the data accessible and reusable? If no standard exists please outline how a suitable metadata structure will be developed.*
E	**Making data available**	
E.1	Availability / reuse of the data:	*Are the data available for reuse after the project?* ☐ Yes, immediately after the project ☐ Yes, after ....months/years ☐ No *If not, please explain why the data are not suitable and/or available for reuse.*
E.2	Limited availability of data?	*If data are only made available after a certain period then please state the reason for this.* *If part of the data cannot be made (directly) available then please state the part concerned.*
E.3	Conditions for the reuse of the data:	*Please specify:* *If so, are these conditions defined in a consortium agreement?*

[12] See for example: https://www.denbi.de or https://www.publisso.de/open-access-publizieren/forschungsdaten/forschungsdatenrepositorien/

[13] This section MUST be completed if your research data includes personal data relating to human participants in research. For other research, the safeguarding and security of data should also be considered. Please note this section concerns protecting the data, not the patients.

12 FINANCIAL DETAILS OF THE STUDY

12.1. COMMERCIAL INTEREST

Please describe any potential commercial interest of a company in the results of the study. Please pay particular attention to “Freedom to operate” concerning exploitation of the results of the study.

12.2. FINANCIAL SUMMARY

Indicate total duration of the study, the period of time for which funding is requested and when funding should begin. Funding will be granted for up to 3 years.

The overall expenditure should be summarized in the table below (maximum 1 page). Indicate amounts in € in the column “Total (€)”. Please provide man months for staff and € for all other expenditures.

Keep in mind that this financial summary serves as an overview of the funds you apply for and must not exceed 1 page. For creation of the financial summary you must use the template table on the next page of this document.

Financial Table – "Title of study"

Task	Institution	Personnel			Consumables €	Study drug €	Equipment €	Commissions €	Travel		Publication costs €	Other €	Overheads €[2]	**Total funding requested €[3,4]**
		Number of Sci, Grad, Eng, T, O[1]	No. of months	€					No. of meetings	€				
1. e.g. PI, Project planning and management	e.g. University of…				*e.g. lab expenses*		*> 410 €*	*incl. 19 tax*			*Ressources for open access publications only*	*e.g. animal costs, data management*		
2. Project partner 1	e.g. University of ….													
3.Project partner 2	e.g. Institute of ….													
4. e.g. Study statistician, independent analysis	e.g. University of…													
5..e.g. Data handling and management	e.g. University of ….													
6.e.g. Quality assurance / Monitoring	e.g. …. GmbH													
Requested Budget (Sum)														

[1]Sci = Scientist, Grad = Graduate student, Eng = Engineer, T = Technician, O = Other; Please calculate your local institutional salaries.
[2]Overhead = Gemeinkosten, 20% Projektpauschale
[3]Please calculate requested amount according to funding rate: generally up to 100% of total costs for academia and generally up to 50% of total costs for industry (plus bonuses for KMU, if applicable).
[4]Please summarize for each institution

12.3 EQUIPMENT

Please list all requested research equipment. Explain why the equipment is essential to the project. Note that equipment commonly in use at the research institution (Grundausstattung) cannot be granted.

12.4 CO-FINANCING BY INDUSTRY AND / OR OTHER THIRD PARTIES

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

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

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

- Describe the type and volume of support (including any services or consumables provided free of charge, e.g. drugs for the study).
- Indicate the amount of support to be provided and assure in writing that the third party will render these services, stating their terms and conditions, if any.
- Assure that the coordinating investigator is independent, in particular with regard to the analysis of the study and the publication of its results. A statement giving such assurances will be demanded by the BMBF after the review process is finished.

Please do not make any 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 must be concluded between all those playing a part in the conduct of the study before start of the study.

12.5 OTHER FUNDING

In case you have already submitted the same request for financial support or parts hereof to other institutions or the BMBF, please mention this here. Indicate those third parties which will provide funds, free services or consumables such as study medication.

If this is not the case please declare:

"A request for funding this project has not been submitted to any other addressee. In case I submit such a request I will inform the Federal Ministry of Education and Research immediately".

13. REFERENCES

APPENDICES

1. SEARCH STRATEGY

To substantiate the evidence presented in section 3.1, please present the full search strategy for one electronic database (e.g. MEDLINE) including any limits used such that it could be repeated. Indicate filters used (data bases, search terms, operators, filters; time period covered; date of search, results; max. one page). Present the search strategy only, do not provide further explanations. The narrative of the results is to be presented under section 3. The following information is worth noting: http://syrf.org.uk/systematic-review/step-3-search-strategy/ or Leenaars et al. (2011) 'A step-by-step guide to systematically identify all relevant animal studies' Laboratory Animals 2012; 46: 24–31. DOI: 10.1258/la.2011.011087

2. DECLARATIONS OF PARTNERS INVOLVED IN THE STUDY

The signatures for the participating laboratories indicate that the signees agree to participate in the above-named preclinical study and support the study by examining animals / cell cultures.
With the signature the partners declare that any conflict of interest with respect to private, economical or financial aspects with regard to the preclinical study as well as patents, whether planned, pending or issued, broadly relevant to the work, are laid open.

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

Study Management					
#	Name	Affiliation	Responsibility / Role		Signature
Study statistician[+]					
#	Name	Affiliation	Responsibility / Role		Signature
			……		
Data Management					
#	Name	Affiliation	Responsibility / Role		Signature
Participating Laboratories					
#	Name	Affiliation	Responsibility / Role	No. of animals / cell entities to be provided to the study	Signature
Supporting Facilities					
#	Name	Affiliation	Responsibility / Role		Signature

[+] The study statistician needs to be qualified. In the CV, evidence should be provided, e.g. certificate of GMDS / IBS-DR.

3. CVs OF MAJOR PARTICIPANTS

Indicate the preclinical study expertise of all above-mentioned participants. Include tabular scientific CVs (max. one page) for academic members of the study team playing a leading role (i.e. principle investigator, co-applicants, study statistician, data manager, not all collaborating partners at all sites) including a list of a maximum of 5 publications of the last 5 years (related to the planned study).