DLR Projektträger

Bundesministerium für Bildung und Forschung

Leitfaden für die Erstellung von Projektskizzen zur „Richtlinie zur Förderung von präklinischen konfirmatorischen Studien und systematischen Reviews“

vom 20.07.2022

Inhaltsverzeichnis

Dieser Leitfaden stellt die Anforderungen für die Erstellung von beurteilungsfähigen Projektskizzen dar. Er ergänzt die am 20. Juli 2022 im Bundesanzeiger veröffentlichte o. g. Förderrichtlinie des BMBF (https://www.gesundheitsforschung-bmbf.de/de/14868.php).

Projektskizzen, 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. Ansprechpersonen sind:

Dr. Marianne Kordel
Dr. Cosima Pfenninger
Dr. Patricia Ruiz Noppinger

Telefon: 0228-3821-1700

E-Mail: praeklinische-studien@dlr.de

1. Allgemeine Informationen

Es können beantragt werden:

- **Wissenschaftsinitiierte, prospektive, kontrollierte, präklinische Studien** zum Wirksamkeitsnachweis eines klinisch relevanten therapeutischen Ansatzes (Modul 1). Jede Studie muss eine konfirmatorische Zielsetzung aufweisen, um die in explorativen Studien erzielten Erkenntnisse zu validieren. Die Studien müssen in einem laborübergreifenden Ansatz als multizentrische Studien durchgeführt werden. Die präklinischen Studien können in der Regel für einen Zeitraum von zwei bis drei Jahren gefördert werden.
- **Systematische Reviews und Metaanalysen von präklinischen Studien** nach internationalen Standards (Modul 2). Die systematischen Reviews können in der Regel für einen Zeitraum von bis zu zwei Jahren gefördert werden.

Näheres regelt die o.g. Förderrichtlinie.

Es wird eine virtuelle Informationsveranstaltung angeboten:
https://projekttraeger.dlr.de/media/gesundheit/GF/Infos_Informationsveranstaltung.pdf

2. Antrags- und Entscheidungsverfahren

a. Präklinische konfirmatorische Studien (Modul 1)

Für die präklinischen konfirmatorischen Studien sind zwei fachliche Begutachtungsschritte vorgesehen. Zunächst sind **kurze, englischsprachige Projektskizzen (Kurzskizzen)** einzureichen, die von einem unabhängigen, internationalen Begutachtungsgremium geprüft werden. In diesem ersten Begutachtungsschritt werden die Anträge nach den folgenden Kriterien bewertet:

- Erfüllung des Gegenstands der Förderung und der Zuwendungsvoraussetzungen;
- klinische Relevanz der Fragestellung;
- Translationsrelevanz und Erfolgsaussichten des Projekts;
- wissenschaftliche und methodische Qualität der vorliegenden Evidenz aus den Vorarbeiten (u. a. aus einer explorativen Studie);
- wissenschaftliche Exzellenz und methodische Qualität der konfirmatorischen präklinischen Studie;
- Expertise des Projektteams.

Für den ersten Schritt sind **Kurzskizzen (engl.: outline applications)**

bis spätestens zum 19. Oktober 2022, 16:00 Uhr (MESZ)

über das folgende Portal einzureichen:

https://foerderportal.bund.de/easyonline/reflink.jsf?m=KC1PRAEKLINSTUDIEN&b=KC1KON-PRAESTUDSKIZZE&t=SKI

Eine Vorlage per E-Mail oder FAX ist nicht möglich.

Die Kurzskizze ist ausschließlich in elektronischer Form vorzulegen. Eine postalische Übersendung des Antrags ist nicht notwendig.

Der/die Verbundkoordinator/in reicht für den Forschungsverbund eine gemeinsame Kurzskizze ein. Diese besteht aus den folgenden Teilen:
Englischsprachige Projektbeschreibung und drei Annexe. Hierzu nutzen Sie bitte zwingend die vorgegebene **Mustervorlage** in diesem Leitfaden unter Punkt 3. Bitte beachten Sie, dass in Annex 3 die händischen Unterschriften der koordinierenden Person, der PIs der weiteren teilnehmenden Labore und des Statistikers/der Statistikerin erforderlich sind. Alle Unterlagen (Projektbeschreibung, Annexe) sind in einem pdf-Dokument zusammenzufassen und im oben angegebenen Portal hochzuladen.

Antragstellende, deren Kurzskizzen im ersten Begutachtungsschritt positiv bewertet wurden, werden schriftlich zur Vorlage von **ausführlichen, englischsprachige Projektskizzen (engl.: full proposals)** aufgefordert. Diese werden in einem zweiten fachlichen Begutachtungsschritt wiederum durch ein unabhängiges, internationales Begutachtungsgremium bewertet.

Für die im zweiten Schritt zu erstellenden **ausführlichen Projektskizzen** werden die entsprechenden Vorgaben und Informationen zu einem späteren Zeitpunkt zur Verfügung gestellt.

b. Systematische Reviews (Modul 2)

Für präklinische systematische Reviews ist nur ein fachlicher Begutachtungsschritt vorgesehen.

Die **Projektskizzen (full proposals) sind**

bis spätestens zum 19. Oktober 2022, 16:00 Uhr (MESZ)

über das folgende Portal einzureichen:

https://foerderportal.bund.de/easyonline/reflink.jsf?m=KC1PRAEKLINSTUDIEN&b=KC1KON-PRAESTUDSKIZZE&t=SKI

Eine Vorlage per E-Mail oder FAX ist nicht möglich.

Die Projektskizze ist ausschließlich in elektronischer Form vorzulegen. Eine postalische Übersendung des Antrags ist nicht notwendig.

Die Projektskizze besteht aus den folgenden Teilen:
Englischsprachige Projektbeschreibung und drei Annexe. Hierzu nutzen Sie bitte zwingend die vorgegebene **Mustervorlage** in diesem Leitfaden unter Punkt 3. Bitte beachten Sie, dass in Annex 3 die händischen Unterschriften der antragstellenden/koordinierenden Person und ggf. des Statistikers/der Statistikerin erforderlich sind. Alle Unterlagen (Projektbeschreibung, Annexe) sind in einem pdf-Dokument zusammenzufassen und im oben angegebenen Portal hochzuladen.

Anschließend werden die englischsprachigen Projektskizzen durch unabhängige, internationale Begutachtende bewertet.

Antragstellende, deren Skizzen durch dieses Gremium positiv bewertet werden, werden schriftlich zur Vorlage von **Formanträgen** aufgefordert.

3. Mustervorlagen und Erläuterungen

Die Unterlagen müssen selbsterklärend und aussagekräftig sein. Sie sollen alle notwendigen Informationen enthalten, um dem Kreis begutachtender Personen eine abschließende fachliche Stellungnahme zu erlauben.

Im Sinne der Vergleichbarkeit aller eingereichten Projektskizzen sind die Formatvorgaben dieses Leitfadens verbindlich einzuhalten. Bitte benutzen Sie unbedingt die folgenden verlinkten **Mustervorlagen:**

1. Outline Application – Preclinical Confirmatory Study (Module 1): **Link**
2. Full Proposal - Preclinical Systematic Review (Module 2): **Link**

Die Mustervorlagen sind auch unter Punkt 4 und 5 in diesem Leitfaden aufgeführt. Die in den Mustervorlagen **vorgegebenen Gliederungen sind verbindlich**. Die vorhandenen Eintragungen in kursiver Schrift sind als Hinweise für die Erstellung der Projektskizze gedacht und vor dem Einreichen zu löschen.

Die nachfolgenden Hinweise sind bei der Planung und Einreichung der Skizze zu beachten.

Die Antragstellenden sind verpflichtet nationale und internationale Standards zur Qualitätssicherung der präklinischen Forschung einzuhalten.

Bei Anträgen für präklinische konfirmatorische Studien sind die folgenden Standards in der jeweils geltenden Fassung zu berücksichtigen:

- PREPARE Guideline: https://journals.sagepub.com/doi/pdf/10.1177/0023677217724823
- Leitlinien zur Guten Zellkulturpraxis (Good Cell Culture Practice, GCCP, z. B. https://www.altex.org/index.php/altex/article/view/2376/2327)
- ARRIVE Guideline als Publikationsleitlinie: https://arriveguidelines.org/

Zusätzlich ist diese Handreichung zu beachten:

- Handreichung DECIDE

Bei Anträgen für präklinische systematische Reviews sollen die Werkzeuge und Hinweise unter

- Handreichung DECIDE
- https://www.camarades.de/
- https://syrf.org.uk/

berücksichtigt werden. Die Antragstellenden sollen sich außerdem im Vorfeld vergewissern, ob bereits systematische Reviews zu der von ihnen geplanten Fragestellung existieren oder derzeit erstellt werden. Als Publikationsleitlinie sind die PRISMA-Leitlinie und ggf. relevante Updates dazu zu beachten: http://prisma-statement.org/.

Die Protokolle der konfirmatorischen präklinischen Studien sowie der systematischen Reviews sollen in geeigneten Registern (z.B. https://www.animalstudyregistry.org/asr_web/index.action; https://preclinicaltrials.eu; https://osf.io/prereg/ bzw. https://library.cumc.columbia.edu/insight/prospero-registry-systematic-review-protocols) vor Beginn der Projektarbeiten registriert und ggf. publiziert werden.

4. Outline Application – Preclinical Confirmatory Study (Module 1)

To ensure comparability of all submitted outline applications please prepare your application in English ***not exceeding 8 pages*** *(DIN A4, at least 11 point Arial and 10 point Arial for the synopsis and references, margins of at least 2 cm and single-spaced lines).*

Structure your application using the headings listed below. Make an entry under each heading/subheading. Please replace the italicized text with your information.[1]

Additionally, 3 appendices are to be submitted (one page each). Appendix 3: ***Signatures*** *of the coordinator, PIs and statistician to confirm that the information and data given in the outline application are correct.* ***Do not*** *submit any other appendices.*

STUDY SYNOPSIS

COORDINATING INVESTIGATOR	*Name, address, telephone, e-mail*
PARTICIPATING LABS	*To be involved (n):* *Name of PI, Affiliation, City*
TITLE OF STUDY	*Descriptive title, max. 140 characters. In case of funding this title shall be quoted in the annual reports of the BMBF.*
ACRONYM	*Derived from the title, max. 40 characters*
TIME SCALE	*Duration of the entire study (months)*
BUDGET APPLIED FOR	*Please give the total amount for the consortium*
MEDICAL FIELD	*Please name the medical field(s) the study addresses*
MEDICAL CONDITION	*Please describe the medical condition addressed*
OBJECTIVE(S)	*Which hypothesis is to be tested? Specify the primary objective of the study that determines sample size calculation. Specify any secondary objectives.*
MODEL/SETTING	*Animals/strain, probes/samples of humans, cultured cells, etc. to be used*
INTERVENTION	*Please describe shortly:* *Intervention:* *Control intervention (pos./neg.):*
STUDY DESIGN	*Please provide:* • *Number of experimental and control groups* • *Key inclusion and exclusion criteria* • *Consideration of external validity: age, sex of animals or samples, comorbidities* • *Outcome: define the primary efficacy endpoint; key secondary endpoint(s)* • *Methods to reduce risk of bias: randomization and blinding*
STATISTICAL PLANNING AND ANALYSIS	• *Shorty outline the sample size calculation (including rationale for the chosen effect size and statistical power). Motivate this by effect sizes from previous studies.* • *Indicate the total number of animals / cultured cells / samples to be used in each experiment, and the number of animals / cultured cells / samples in each experimental group* • *Shortly outline the statistical methods to be used for each analysis*

[1] *In preparation of the application the following information related to study design is worth noting:*
Handreichung DECIDE
https://www.nc3rs.org.uk/our-portfolio/experimental-design-assistant-eda
https://journals.sagepub.com/doi/10.1177/0023677217724823
https://www.nc3rs.org.uk/arrive-guidelines

Graphic study overview: *Please illustrate the study graphically with a flow chart in appendix 1 including at least the aspects: objective, setting, intervention and study design (e. g. using the experimental design assistant EDA, https://eda.nc3rs.org.uk). Illustrate also the timeline of the study.*

Below, please substantiate and justify:

1. RELEVANCE

Clinical Relevance and Novelty

- *Which medical condition is to be addressed?*
- *Which therapy options are available for treatment of the disease?*
- *Which principal research questions are to be addressed?*
- *What is the novel aspect and relevance for the treatment of the disease of the proposed study?*

Impact of the study

- *Please describe possible results and impact of the planned study.*
- *What will be the next steps?*

2. SCIENTIFIC PREMISE / PREVIOUS RESULTS

This section should detail the background of the study hypothesis.

Scientific premise:
Please provide the scientific premises to understand the motivation and context for the study:

- *Please describe how the existing literature was systematically reviewed to avoid duplication of research. Provide your search strategy (data bases, search terms, operators, filters; time period covered; date of search) and results.*
- *A full electronic search strategy exemplary for one database, including any limits used, has to be presented in appendix 2 (max. one page). Guidance concerning search techniques can be found at the following address:* https://www.camarades.de/systematic-search.html

Previous (own) results directly related to the planned study:

- *Please describe previous results, e.g. explorative studies, triangulation, within-lab replication, 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.*
- *Describe and justify deviations between your previous study and the planned confirmatory study.*

It is strongly recommended *to check the minimum requirements to start a confirmatory study in the guidance document of the DECIDE project (Handreichung).*

Please note:
The experimental design of the confirmatory study should reflect the initial design of the exploratory study. Crucial factors like primary outcome, essential methods, and model should stay constant between exploratory and confirmatory phase. Deviations need to be spelled out, motivated, and strengthen validity. To strengthen validity, limited extensions are possible. That is, a confirmation is not necessarily a direct replication of the initial experiment. It is rather a test of the underlying knowledge claim and should enable decisions for future steps and translation into clinical contexts. For deviations regarding the number of experimental units see statistical analysis and planning in the guidance document of the DECIDE project (Handreichung).

3. RELEVANCE OF THE MODEL

Which model is to be used? Please provide details for animal species and strain / cell model, source of animals or cells, age and sex.

Please provide sound scientific reasoning why the chosen model can address the scientific objectives and its relevance to the human disease. Please also state limitations of the model.

In case animal studies are planned please explain:

- *why there are no realistic non-animal alternatives*
- *Is the (animal)model different from the previous/to be confirmed studies? If yes, why?*

4. STUDY DESIGN

Please provide justifications and do not only list the respective information.

4.1 CONTROL(S) / COMPARATOR(S)

Justify the choice of control(s) / comparison(s). Which studies establish efficacy of the chosen positive control regimen?

4.2 INCLUSION / EXCLUSION CRITERIA

Justify the inclusion and exclusion criteria, the population to be studied, include reflections on generalizability and representativeness (external validity, age, sex, comorbidities).

4.3 INTERVENTION(S)

Justify the choice of your planned intervention(s)/treatment(s).

Define the primary outcome. It should be the same (or similar) as in the exploratory study. Secondary outcome measures can serve as supporting evidence.
Justify the endpoints chosen (primary, secondary): Why are the chosen endpoints relevant? Are there other studies that have utilized these endpoints?

4.4 METHODS TO REDUCE RISK OF BIAS

Describe your strategy to handle possible risk of bias in your methods, conduct and analysis of your proposed study.

Describe:

- *Method for randomization*
- *Procedures for blinding*

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

5. STATISTICS

5.1 PROPOSED SAMPLE SIZE / POWER CALCULATIONS

Justify:

- *What is the experimental unit of your study (see glossary)? Clearly outline independence / dependence of experimental units (and nesting, if applicable).*
- *What is the minimum clinically relevant effect size based on the previous results that is planned to be achieved with this confirmatory study?*
- *What is the proposed sample size? It must be based on the experimental unit. Sample size estimation needs to account for larger biological variability in the results in the confirmatory compared to the exploratory experiments. The minimum power for the confirmatory study should be 80%. Include a comprehensible, checkable description of the power calculations and sample sizes detailing the primary outcome measure on which these have been based for both control and experimental groups, as*

appropriate. It is important that the sample size calculations will take into account anticipated rates of losses.

5.2 STATISTICAL ANALYSIS

Please describe:

- *What is the strategy of statistical analysis? What is the strategy for analyzing the primary outcome? Are there any subgroup analyses?*
- *How does the analysis parallel/deviate analysis strategies from the studies that are to be confirmed?*

Please explain: how will you define if the confirmation of your study has been successful or not?

6. QUALITY CONTROL

Please describe shortly the strategy for harmonization of protocols as well as trainings between different labs.

Comment on the precautions 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, independence of data analysis and monitoring.

Please keep in mind and plan accordingly: in the full proposal stage you will have to give details on data management, maintenance and long-term accessibility for future reuse of your results (also by third parties, respecting privacy rules and proprietary data).
To ensure that your research data are soundly managed please follow the principle of FAIR data[2]. Please use existing standards and data repositories.

7. ETHICAL CONSIDERATIONS

If applicable:

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

8. STUDY MANAGEMENT

8.1 MAJOR PARTICIPANTS

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

#	Name	Affiliation	Responsibility/Role
			Principal/Coordinating Investigator
			Participating lab
			Statistician (study planning and analysis)
			Data management
			……

8.2 STUDY EXPERTISE

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

9. REFERENCES

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

10. FINANCIAL SUMMARY

Please give a rough estimation of the costs expected for the total duration of the study showing the overall financial structure of the project. Please make sure that all overhead costs (e.g., "Projektpauschale" for universities and university clinics) are properly considered. Inclusion of overhead costs must be clearly visible. In addition, also consider the added value tax (Mehrwertsteuer) for commissions, if applicable. An additional justification of the costs is not required at this stage.

Item	**Costs (€)**
Personnel (position, task)	
e.g. PI / Project Management	
Scientists (e.g. study design, study execution, biostatistical planning and analysis, documentation and data management, quality assurance, cooperation with the accompanying research project)	
Technicians	
Materials (e.g. consumables, lab expenses)	
Equipment (> 410 €)	
Commissions (incl. 19 % tax)	
Travel (e.g. lab visits, meetings)	
Other (e.g. animal costs)	
Total Budget	
Institutional Overhead*: e.g. 20% "Projektpauschale" for universities / university clinics*	
Requested Budget (Sum)	

APPENDICES

The following documents (each NOT exceeding one page) have to be submitted with the outline application. The appendices are to complement the information given in the respective sections.

1. STUDY OVERVIEW

Please provide a flow chart of the planned study to complement the information given in the study synopsis (e.g. using EDA, see above)

2. SEARCH STRATEGY

To substantiate the scientific premise presented in section 2, please present the full search strategy for the electronic database including any limits used, such that it could be repeated. Indicate filters used. Present the search strategy only, do not provide further explanations. The narrative of the results is to be presented under section 2. For guidance refer to http://syrf.org.uk/

3. SIGNATURES

Project title and acronym:

Function	Name	Institution/Department	Signature*
Coordinator			
Statistician			
Partnering lab PI			

*I herewith confirm that all information and data given in the outline application are known to me and correct.

5. Full Proposal - Preclinical Systematic Review (Module 2)

To ensure comparability of all submitted proposals please prepare your proposal in English ***not exceeding 12 pages*** *(DIN A4, at least 10 point Arial for the table and 11 point Arial for any remaining text, margins of at least 2 cm and single-spaced lines).*

Structure your proposal using the headings listed below. Make an entry under each heading/subheading.[3]

Additionally, 3 appendices are to be submitted. Do not submit any other appendices.

The signature of the applicant/coordinator in appendix 3 is mandatory. *Please ensure that the team of participating investigators has the necessary range of disciplines and expertise to carry out the systematic review.*

SYSTEMATIC REVIEW PROTOCOL (based on: SR Protocol Format)

Item #	Section / Item	Description
	A. General	
1	Title of the review	
2	Applicant/Coordinator (name, affiliation)	
3	Other contributors (names, affiliations)	
4	Conflicts of interest	
	B. Objectives	
	Background	
5	What is already known about this disease, models of the disease, intervention? Did you search for already existing systematic reviews in your field of interest?	
	Need for the systematic review	
6	Why is it important to do this systematic review? What is the novel aspect of this review? What is the relevance of the results? Discuss potential impact and relevance for translational aspects.	
	Research question	
7	Specify the disease/health problem/indication areas of interest	
8	Specify the population/species/cell culture/ etc. studied	
9	Specify the intervention/exposure	

[3] In preparation of the proposal the following information related to systematic reviews is **strongly recommended**: Handreichung DECIDE; http://syrf.org.uk or: https://www.camarades.de/ or tools and guidelines of RadboudUMC Meta Research Team. Please use analogous strategies for in vitro studies.

10	Specify the control population	
11	Specify the outcome measures	
12	State your research question (based on items 7-12)	
	C. Methods	
	Search strategy and study identification	
13	Identify literature databases to search (e.g. Pubmed, Embase, Web of science)	☐ MEDLINE via PubMed ☐ Web of Science ☐ SCOPUS ☐ EMBASE ☐ Other, namely: ☐ Specific journal(s), namely:
14	Define electronic search strategies (e.g. use the step by step search guide[4] and animal search filters[5], [6] or analogous strategies for in vitro studies)	*Please add a supplementary file containing your search strategy (appendix 1)*
15	Identify other sources for study identification	☐ Reference lists of included studies ☐ Books ☐ Reference lists of relevant reviews ☐ Conference proceedings, namely: ☐ Contacting authors, organizations, namely: ☐ Other, namely:
16	Define search strategy for these other sources	
	Study selection	
17	Define screening phases (e.g. pre-screening based on title/abstract, full text screening, both)	
18	Specify (a) the number of reviewers per screening phase and (b) how discrepancies will be resolved	
19	*Define all inclusion and exclusion criteria based on:*	
20	Type of study (design)	Inclusion criteria: Exclusion criteria:
21	Type of animals/cells/population (e.g. age, gender, disease model)	Inclusion criteria: Exclusion criteria:
22	Type of intervention (e.g. dosage, timing, frequency)	Inclusion criteria: Exclusion criteria:
23	Outcome measures/effect	Inclusion criteria: Exclusion criteria:
24	Language restrictions	Inclusion criteria: Exclusion criteria:
25	Publication date restrictions	Inclusion criteria: Exclusion criteria:
26	Other	Inclusion criteria: Exclusion criteria:

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265183/pdf/LA-11-087.pdf
[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104815/pdf/LA-09-117.pdf
[6] http://journals.sagepub.com/doi/pdf/10.1177/0023677213494374

27	Sort and prioritize your exclusion criteria per selection phase	Selection phase: 1. 2. etc. Selection phase: 1. 2. etc.
	Study characteristics to be extracted (for assessment of external validity, reporting quality)	
28	Study ID (e.g. authors, year)	
29	Study design characteristics (e.g. experimental groups, number of animals/samples)	
30	(Animal) model characteristics (e.g. species, gender, disease induction)	
31	Intervention characteristics (e.g. intervention, timing, duration)	
32	Outcome measures	
33	Other (e.g. drop outs)	
	Assessment risk of bias (internal validity) or study quality assessment[7]	
34	Specify (a) the number of reviewers assessing the risk of bias/study quality in each study and (b) how discrepancies will be resolved	
35	Define criteria to assess (a) the internal validity of included studies (e.g. selection, performance, detection and attrition bias) and/or (b) other study quality measures (e.g. reporting quality, power)	☐ By use of SYRCLE's Risk of Bias tool[8] ☐ By use of SYRCLE's Risk of Bias tool, adapted as follows: ☐ By use of CAMARADES' study quality checklist, e.g.[9] ☐ By use of CAMARADES' study quality checklist, adapted as follows: ☐ Other criteria, namely:
	Collection of outcome data	
36	For each outcome measure, define the type of data to be extracted (e.g. continuous/dichotomous, unit of Measurement)	
37	Methods for data extraction/retrieval (e.g. first extraction from graphs using a digital screen ruler, then contacting authors)	
38	Specify (a) number of reviewers extracting data and (b) how discrepancies will be resolved	
	Data synthesis and statistical analysis plan	
39	Specify (per outcome measure) how you are planning to combine/compare the data (e.g. descriptive	.

[7] https://bmcmedresmethodol.biomedcentral.com/track/pdf/10.1186/1471-2288-14- 43?site=bmcmedresmethodol.biomedcentral.com
[8] https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-14-43
[9] https://www.ncbi.nlm.nih.gov/pubmed/15060322

	summary, meta-analysis)	
40	Specify (per outcome measure) how it will be decided whether a meta-analysis will be performed	
	If a meta-analysis seems feasible/sensible, specify (for each measure):	
41	The effect measure to be used (e.g. mean difference, standardized mean difference, risk ratio, odds ratio)	
42	The statistical model of analysis (e.g. random or fixed effects model)	
43	The statistical methods to assess heterogeneity (e.g. I^2, Q)	
44	Which study characteristics will be examined as potential source of heterogeneity (subgroup analysis)	
45	Any sensitivity analyses you propose to perform	
46	Other details meta-analysis (e.g. correction for multiple testing, correction for multiple use of control group)	
47	The method for assessment of publication bias	
	D. Strategies for data management, data sharing and dissemination of results[10]	
48	The protocol should be registered (PROSPERO) and/or published. What will be your strategies for the dissemination of results especially beyond regular journal publication? Indicate how the expected results of the systematic review will be used.	
49	Specify which systematic review data management system will be used, i.e. not Excel Describe what measures will be taken to ensure maintenance and long-term accessibility of your results for future updates and reuse (also by third parties). Please adhere to FAIR data principles.	
50	Specify how, where and when data and code will be made freely available (expectation that these will be shared without restriction unless expressly justified).	
51	Specify what reporting guidelines will be used for any publications	

E. Expertise of applicants

#	Name	Affiliation	Role
			e. g. Expertise with the experimental model

[10] For reporting the results of systematic reviews please follow the Prisma reporting guideline http://prisma-statement.org/ and make use of the information given here: https://www.camarades.de/publication.html

			e. g. Methodological expertise: systematic review
			e. g. Information specialist (e.g. librarian)
			e.g. statistician

Please provide your references in appendix 2.

F. Financial and Time Plan

Duration:

Financial plan:
Please calculate specifically and give all requested details.

The expenses should be summarized in the table below. Please also justify your expenses.

Item[a]	**Costs**	**Number**	**Sum in €**
Staff: qualification, tasks	*salary group*[b]	*Number and man months*	
Consumables[c]*: detail*			
Travel[d]*:*	*1.500*		
Commissions (incl. 19 % tax): detail			
Other: detail			
Budget requested[e]			
Institutional Overhead *(e.g. 20 % Projektpauschale for universities / university clinics)*			
Total requested budget			

[a] *Delete / add lines as needed*
[b] *Please calculate your local institutional salaries*
[c] *Publication costs can only be funded if an open access publication is planned with the funding period.*
[d] *Travel expenses can be applied for as flat rate: 1.500 € per full position of academic personnel (scientist or PhD student=1 position) per year*
[e] *Please calculate requested amount (funding rate for academia generally up to 100% of total costs)*

Time plan / Milestones	

APPENDICES

1. Search Strategy
Provide a sketch of your search strategy (max. one page).

2. References
Please indicate review/meta-analysis expertise of all above-mentioned participants by citing relevant publications and/or specifying major role in past/ongoing review(s) (max. 5

publications of the last 5 years per person). Ensure that the team of investigators has the necessary expertise to carry out the review/meta-analysis.

3. Signatures

Project title and acronym:

Function	Name	Institution/Department	Date, Signature*
Applicant/Coordinator			
Statistician (if applicable)			

*I herewith confirm that all information and data given in the proposal are known to me and correct.