**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.[[1]](#footnote-1)*

*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](https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fwww.radboudumc.nl%2Fgetmedia%2F852effde-161f-4ac5-9e3f-de8933f7cb26%2FSR-protocol-format-(fillable-version).aspx&wdOrigin=BROWSELINK))

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Item**  **#** | **Section / Item** | | **Description** | |
|  | **A. General** | |  | |
| 1 | Title of the review | |  | |
| 2 | Applicant/Coordinator (name, affiliation) | |  | |
| 3 | Other contributors (names, affilia- tions) | |  | |
| 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 sys- tematic 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 prob- lem/indication areas of interest |  | | |
| 8 | Specify the population/species/cell culture/ etc. studied |  | | |
| 9 | Specify the intervention/exposure |  | | |
| 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[[2]](#footnote-2) and animal search filters[[3]](#footnote-3), [[4]](#footnote-4)  or analogous strategies for in vitro studies) | *Please add a supplementary file containing your search strategy (appendix 1)* | | |
| 15 | Identify other sources for study iden- tification | 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: |
| 27 | Sort and prioritize your exclusion | | | Selection phase: |
| criteria per 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[[5]](#footnote-5)** | | | |
| 34 | Specify   1. the number of reviewers as- sessing the risk of bias/study quality in each study and 2. how discrepancies will be re- solved | | |  |
| 35 | Define criteria to assess   1. the internal validity of included studies (e.g. selection, perfor- mance, detection and attrition bias) and/or 2. other study quality measures (e.g. reporting quality, power) | | | By use of [SYRCLE's Risk of Bias tool[[6]](#footnote-6)](http://www.biomedcentral.com/1471-2288/14/43/abstract)  By use of SYRCLE’s Risk of Bias tool, adapted as follows:  By use of [CAMARADES' study quality checklist, e.g.[[7]](#footnote-7)](http://www.ncbi.nlm.nih.gov/pubmed/15060322)  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   1. number of reviewers extracting data and 2. how discrepancies will be re- solved | | |  |
|  | **Data synthesis and statistical analysis plan** | | | |
| 39 | Specify (per outcome measure) how you are planning to combine/compare the data (e.g. descriptive 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. I2, Q) | | |  |
| 44 | Which study characteristics will be examined as potential source of heterogeneity (subgroup analysis) | | |  |
| 45 | Any sensitivity analyses you pro- pose to perform | | |  |
| 46 | Other details meta-analysis (e.g. correction for multiple testing, cor- rection for multiple use of control group) | | |  |
| 47 | The method for assessment of pub- lication bias | | |  |
|  | **D. Strategies for data management, data sharing and dissemination of results[[8]](#footnote-8)** | | | |
| 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* |
|  |  |  | *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.*

|  |  |  |  |
| --- | --- | --- | --- |
| **Itema** | **Costs** | **Number** | **Sum in €** |
| *Staff:* *qualification, tasks* | *salary groupb* | *Number and man months* |  |
| *Consumablesc:* *detail* |  |  |  |
| *Traveld:* | *1.500* |  |  |
| *Commissions (incl. 19 % tax):* *detail* |  |  |  |
| *Other: detail* |  |  |  |
| **Budget requestede** |  | |  |
| **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**

### Search Strategy

*Provide a sketch of your search strategy (max. one page).*

### 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.*

### 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.

1. In preparation of the proposal the following information related to systematic reviews is **strongly recommended**: [Handreichung DECIDE](https://www.bihealth.org/fileadmin/QUEST/Publikationen/Bericht/DECIDE_Guidance_for_planning_and_conducting_confirmatory_preclinical_studies_and_systematic_reviews.pdf); http://syrf.org.uk or: <https://www.camarades.de/> or [tools and guidelines of RadboudUMC Meta Research Team](https://www.radboudumc.nl/en/research/departments/anesthesiology/meta-research-team). Please use analogous strategies for in vitro studies. [↑](#footnote-ref-1)
2. https[://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265183/pdf/LA-11-087.pdf](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265183/pdf/LA-11-087.pdf) [↑](#footnote-ref-2)
3. https[://w](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104815/pdf/LA-09-117.pdf)ww.[ncbi.nlm.nih.gov/pmc/articles/PMC3104815/pdf/LA-09-117.pdf](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104815/pdf/LA-09-117.pdf) [↑](#footnote-ref-3)
4. <http://journals.sagepub.com/doi/pdf/10.1177/0023677213494374> [↑](#footnote-ref-4)
5. [https://bmcmedresmethodol.biomedcentral.com/track/pdf/10.1186/1471-2288-14-](https://bmcmedresmethodol.biomedcentral.com/track/pdf/10.1186/1471-2288-14-43?site=bmcmedresmethodol.biomedcentral.com)  [43?site=bmcmedresmethodol.biomedcentral.com](https://bmcmedresmethodol.biomedcentral.com/track/pdf/10.1186/1471-2288-14-43?site=bmcmedresmethodol.biomedcentral.com) [↑](#footnote-ref-5)
6. <https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-14-43> [↑](#footnote-ref-6)
7. <https://www.ncbi.nlm.nih.gov/pubmed/15060322> [↑](#footnote-ref-7)
8. For reporting the results of systematic reviews please follow the Prisma reporting guideline <https://pubmed.ncbi.nlm.nih.gov/33789819/> and make use of the information given here: <https://www.camarades.de/publication.html> [↑](#footnote-ref-8)