Aktualisierte Version vom 11. März 2019

DLR Projektträger

Bundesministerium für Bildung und Forschung

Leitfaden für die Erstellung von Projektskizzen zur Förderrichtlinie „Interdisziplinäre Forschungsverbünde zu muskuloskelettalen Erkrankungen“

vom 19.12.2018

Dieser Leitfaden stellt die Anforderungen für die Erstellung von beurteilungsfähigen Projektanträgen (in der Förderrichtlinie als „Projektskizze“ bezeichnet) dar. Er ergänzt die am 8. Januar 2019 im Bundesanzeiger veröffentlichte o.g. Förderrichtlinie des BMBF (https://www.gesundheitsforschung-bmbf.de/de/8360.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:

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Allgemeine Informationen

Gefördert werden können interdisziplinäre Verbundprojekte:

- die Querschnittsthemen bearbeiten, die verschiedene muskuloskelettale Krankheitsbilder gemeinsam betreffen und deren interdisziplinäre Bearbeitung neuen Erkenntnisgewinn verspricht sowie neue Forschungs- und Behandlungsansätze ermöglicht;
- die einen gemeinsamen inhaltlichen und/oder methodischen Fokus aufweisen;
- die alle notwendigen Kompetenzen zur gemeinsamen Erforschung krankheitsübergreifender Querschnittsthemen bei muskuloskelettalen Erkrankungen bündeln;
- die ein besonderes Augenmerk auf die Translation der Forschungsergebnisse in die klinische Praxis legen;

- die sich aus Arbeitsgruppen aus universitären, außeruniversitären und ggf. industriellen Forschungseinrichtungen auf regionaler oder überregionaler Ebene zusammensetzen und Patientinnen und Patienten oder ihre Vertretungen einbinden;
- die aus (in der Regel) nicht mehr als fünf bis acht Teilprojekten und maximal 10 Arbeitsgruppen bestehen. Die einzelnen Teilprojekte sollten dabei, wenn möglich, interdisziplinär angelegt sein.

Wo immer möglich und sinnvoll, ist die gezielte Nutzung der in dem bereits existierenden Forschungsnetz zu muskuloskelettalen Erkrankungen (https://www.gesundheitsforschung-bmbf.de/de/forschungsnetz-muskuloskelettale-erkrankungen.php) erzielten Ergebnisse und etablierten Strukturen sowie von weiteren bereits vorhandenen Datensätzen, Patientenregistern, Kohorten und Materialsammlungen für die Bearbeitung der Forschungsfragen vorzusehen. Es ist ausdrücklich erwünscht, dass sich auch Forschungsgruppen außerhalb des zuvor geförderten Forschungsnetzes beteiligen.

Nicht gefördert werden können:

- Einzelvorhaben ohne Zugehörigkeit zu einem Forschungsverbund;
- Verbünde, die ausschließlich Grundlagenforschung betreiben;
- Verbünde, die sich mit nur einem Krankheitsbild beschäftigen;
- Verbünde, die die Neuanlage von Forschungsinfrastrukturen wie z. B. Register, Kohorten, Materialbanken usw. planen.

Einreichungsverfahren und formale Vorgaben für die Projektanträge

Der einzureichende Antrag (in der Förderrichtlinie als „Projektskizze“ bezeichnet) soll entsprechend der Mustervorlagen und den weiteren Angaben in diesem Leitfaden **in einer Datei** erstellt werden. Der Projektantrag ist durch den Verbundkoordinierenden im pdf-Format elektronisch über das Internetportal von easy Online (https://foerderportal.bund.de/easyonline/reflink.jsf?m=EC-MUSKULOSKELETTALE&b=EC1MUSKULOSKELET2019&t=SKI) einzureichen. Bitte folgen Sie dazu den Anweisungen des Portals.

Die verbindliche Einreichung des Antrags muss bis spätestens zum **11. April 2019, 23:59 Uhr (MESZ)** elektronisch erfolgt sein. Damit die Online-Version Bestandskraft erlangt, muss der Antrag in Papierform doppelseitig gedruckt und gebunden in einfacher Ausfertigung zusammen mit einem Anschreiben/Vorblatt, auf dem alle am Verbund beteiligten Projektpartnerinnen und -partner mittels Unterschrift die Kenntnisnahme sowie die Richtigkeit der in dem Projektantrag gemachten Angaben bestätigen, **spätestens zwei Wochen nach Ende der elektronischen Einreichungsfrist** beim Projektträger eingereicht werden:

DLR Projektträger
- Gesundheit -
Stichwort „Muskuloskelettale Erkrankungen“
Heinrich-Konen-Straße 1
53227 Bonn

Entscheidend für die Fristwahrung ist der auf elektronischem Wege im Internet-Portal verbindlich eingereichte Antrag. Zusendungen per E-Mail oder Fax werden nicht berücksichtigt. Aus der Vorlage des Förderantrags kann kein Rechtsanspruch auf Förderung abgeleitet werden.

Der Antrag ist in englischer Sprache nach den Vorgaben des Leitfadens (DIN-A4-Format, Arial 11 Punkt, einzeilig, Ränder jeweils 2,0 cm) abzufassen. Neben der maximal 10-seitigen Darstellung des Verbundes ergibt sich die maximale Gesamtseitenzahl des Antrages aus Art und Anzahl der Teilprojekte. Der Antrag soll alle Informationen beinhalten, die für ein sachgerechtes Urteil hinsichtlich des interdisziplinären Verbundprojekts erforderlich sind. Der Antrag muss aus sich heraus, ohne Lektüre der zitierten Literatur, verständlich sein und eine Beurteilung ohne weitere Informationen/Recherche zulassen.

Gliederungsschema für die Beantragung eines interdisziplinären Forschungsverbundes

Als Hilfestellung für die Antragstellung ist die vorgegebene Antragsgliederung bereits in Englisch formuliert. Die Ausgestaltung muss der unten aufgeführten Antragsgliederung (**"Guideline for Project Application"**) entsprechen. Der Umfang soll **10 Seiten für das übergeordnete Verbundkonzept** (1) **und 5 Seiten pro geplantem Teilprojekt** (2) nicht überschreiten. Im Falle der Beantragung einer klinischen Studie (3) oder einer Tierstudie (4) sind für diese Teilprojekte **zusätzlich** die dafür vorgesehenen spezifischen Vorlagen zu benutzen. Diese dürfen **7 Seiten** nicht überschreiten (DIN-A4 Format, Arial 11 Punkt, 1-zeilig, Ränder jeweils 2 cm).

Bitte nutzen Sie unbedingt die für das jeweilige Teilprojekt passende Mustervorlage, die darin jeweils vorgegebene Gliederung ist verbindlich. Die vorhandenen Eintragungen in kursiver Schrift sind als Hinweise für die Erstellung der Projektanträge gedacht und sind vor dem Einreichen zu löschen. Bitte nehmen Sie zu jedem Punkt Stellung; sollte ein Punkt nicht zutreffen, kommentieren Sie dies entsprechend.

Die folgenden Mustervorlagen stehen zur Verfügung:

- Darstellung des Verbundes/Konsortiums (**max. 10 Seiten**),
- Mustervorlage für ein Teilprojekt (**max. 5 Seiten**),
- zusätzliche Mustervorlage für eine klinische Studie (**max. 7 Seiten**),
- zusätzliche Mustervorlage für eine Tierstudie (**max. 7 Seiten**)

Alle Informationen zur inhaltlichen Ausrichtung der Fördermaßnahme, den Voraussetzungen für eine Förderung sowie den Kriterien der Begutachtung finden sich in den „Richtlinien zur Förderung von interdisziplinären Forschungsverbünden zu muskuloskelettalen Erkrankungen“. Das Konzept soll in knapper, aussagekräftiger Form beschrieben werden.

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

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.

Wissenschaftliche Standards

Die Antragstellenden sind verpflichtet, nationale und internationale Standards zur Qualitätssicherung der präklinischen und klinischen Forschung einzuhalten. Dies gilt insbesondere für Biomaterialbanken, Patientenregister, IT-Vernetzung, Tierstudien und klinische Studien. Hierzu sind die nachfolgenden Dokumente in der jeweils geltenden Fassung zu berücksichtigen:

- ARRIVE Guidelines[1] (Tierstudien/-versuche)
- Leitlinie zur Guten Zellkulturpraxis (Good Cell Culture Practice, GCCP)[2]
- Deklaration von Helsinki[3]
- ICH-Leitlinie zur Guten Klinischen Praxis (ICH-GCP)[4]
- EU-Richtlinie 2005/28/EG, EU-Verordnung Nr. 536/2014[5],
- CONSORT- und STARD-Statements[6]

Die Registrierung von klinischen Studien in einem nationalen oder internationalen Studienregister ist vorzusehen und bei Beginn der Studie nachzuweisen. Daneben wird die Registrierung von präklinischen konfirmatorischen Studien in geeigneten Registern empfohlen[7].

Zugänglichkeit und langfristige Sicherung des Studienprotokolls und der Forschungsdaten und -ergebnisse

Um Transparenz über die durchgeführte Forschung zu erreichen, wird empfohlen bei Förderung das Studienprotokoll in einem öffentlich zugänglichen Register zu hinterlegen.

Die Veröffentlichung der aus dem Forschungsvorhaben resultierenden Ergebnisse 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, die im jeweiligen Fach anerkannten strengen Qualitätssicherungsverfahren anwenden. Es wird empfohlen solche Zeitschriften auszuwählen, die unmittelbar nach Erscheinen über das Internet für Nutzer entgeltfrei zugänglich sind. Publikationsgebühren für Open Access Publikationen sind zuwendungsfähig.

Weitere nützliche Arbeitshilfen sind zu finden in der QUEST-Toolbox[8] des Berliner Instituts für Gesundheitsforschung sowie in der Toolbox des Open Science Center der LMU München[9].

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[1] ARRIVE (Animal Research: Reporting of In Vivo Experiments)-Guidelines: https://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/NC3Rs%20ARRIVE%20Guidelines%202013.pdf

[2] Leitlinien zur Guten Zellkulturpraxis: https://www.nature.com/articles/bjc2014166

[3] Deklaration von Helsinki: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

[4] ICH-GCP: https://ichgcp.net/de/

[5] EU-Richtlinie 2005/28/EG: https://eur-lex.europa.eu/legal-content/DE/TXT/?uri=CELEX%3A32005L0028 , EU-Verordnung Nr. 536/2014: https://eur-lex.europa.eu/legal-content/de/TXT/?uri=CELEX%3A32014R0536

[6] CONSORT- und STARD-Statements: http://www.consort-statement.org, http://www.equator-network.org/reporting-guidelines/stard/

[7] Z.B. https://www.preclinicaltrials.eu/ ; 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.

Partizipation

Die Beteiligung und der Einbezug relevanter Akteure – allen voran von Vertreterinnen und Vertretern aus Patienten- und Bürgerschaft – erhöhen Qualität und Nutzen der Gesundheitsforschung. Deshalb sind partizipative Ansätze in der Planung, Durchführung und an der Verwertung der Ergebnisse des Vorhabens vorzunehmen bzw. einzuplanen. Ist eine Einbindung nicht oder nicht in allen o. g. Projektschritten möglich, sind die Gründe hierfür zu benennen. Wir verweisen in diesem Zusammenhang auf Hinweise von INVOLVE, einer Organisation, die sich im Auftrag des National Institute for Health Research im Vereinigten Königreich intensiv mit der Einbindung von Öffentlichkeit und Patientinnen bzw. Patienten in die Forschung befasst („Briefing Notes for Researchers“; http://www.invo.org.uk/resource-centre/resource-for-researchers/).

[8] https://www.bihealth.org/en/quest-center/mission-approaches/englische-uebersetzung/the-quest-toolbox/

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

Guideline for Project Application

Applications that fail to comply with the requirements of this guideline will be considered as not eligible and will be rejected without further review.

1. DESCRIPTION OF CONSORTIUM

The overall description of the consortium should not exceed 10 pages *(DIN A4, at least 11 point Arial, single space). Structure your application using the headings listed below and make an entry under every heading/subheading.*

1.1 PROJECT SUMMARY

SYNOPSIS	
Coordinator	*Title, first and last name* *Institution* *Address* *Telephone and Fax* *Email address*
Acronym	
Full title	
Cooperation Partners *(max. 9)*	*Partner 1 – Title, first and last name* *Institution* *Address* *Telephone and Fax* *Email address*
	Partner 2 – Title, first and last name *Institution* *Address* *Telephone and Fax* *Email address*
	Please add more partners as required
Summary of the Proposal	*max. 500 words*
Requested Total Funding for the Consortium	
Requested Funding Peri-od	*max. 3 years*

„Acronym of the Consortium“

1.2 RESEARCH QUESTION(S)

1.2.1 Aims and objectives

What are the aims and objectives of the project?? Which overarching aspect/s of musculosceletal diseases will be addressed by the consortium? Which diseases do these aspects concern? Why is this clinically relevant?

1.2.2 Scientific background and preliminary data

Give sufficient details of past and current research to show that the project aims are scientifically justified, and that the work will add distinct value to what is already known, or in progress.

1.2.3 Existing infrastructure and previous achievements

Describe the quality and scope of existing infrastructure and previous achievements relevant for the application, e.g. methods developed, biobanks, well-characterized patient cohorts, databases. To which extent is the new consortium based on already running cooperation(s)? Please describe how established structures and methods, data or results from the earlier projects funded within the "Forschungsnetz Muskuloskelettale Erkrankungen" are taken into account, if applicable.

1.2.4 Added value of the interdisciplinary collaboration

Please explain the interdisciplinary approach of your research. What is the expected added value of the interdisciplinary approach? What is the novel aspect of the proposed interdisciplinary investigation?

1.2.5 Patient participation

How were the patients' needs, goals, and preferences considered in developing the research concept and in defining endpoints[10]? How are patient representatives / patient advocacy groups involved in the research project?

1.2.6 Gender specific aspects

Please describe how you consider gender aspects in your research plan.

1.3 STRUCTURE AND WORK PROGRAMME OF THE CONSORTIUM

1.3.1 Description of consortium organization

Please explain the structure of your consortium in detail including a list of all Principal Investigators. How will the consortium be managed? Which partners will cooperate directly and how will this contribute to the interdisciplinary approach? If two or more Principal Investigators participate from the same partner institution, please list them separately and indicate their role in the consortium.

[10] s. auch eine *Einführung von INVOLVE zugehörig zum Britischen National Institute for Health Research, NHS „Briefing note for Researchers“:* http://www.invo.org.uk/resource-centre/resource-for-researchers/

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Sub-project No.	Principal Investigator & Institution	Title of subproject	Function in the consortium
1	*Prof. XY University of..*	*Preclinical evaluation of novel XY for the treatment of breast cancer*	*Consortium coordination and PI of the subproject; Monitoring, evaluation and processing of results*
	Dr. YZ abc GmbH		*Industry partner for GMP-production of XY*
2	*Prof. ABC University of..*	*Collection of blood samples*	*Clinical partner for validation of biomarker*

1.3.2 Work programme

Please explain your work programme in detail. How will the aims be reached? Which tasks will be done? It is not necessary to describe each experiment, but enough detail must be given to show why the research is likely to be competitive in its field. In case of multiple investigators: indicate which tasks will be taken over by whom in the different subprojects.

1.3.3 Milestone plan

Please schedule meaningful and measurable/observable markers and events that indicate the progress of the project.

Example:

WP no.	*Milestone (▼)*	*year 1*	*year 2*	*year 3*	*year 4*
1	*Animal experiments approval granted*	▼			
2	*Experimental setup and system modification completed*	▼			
3	*Data acquisition started*	▼			
4	*Data acquisition completed*				▼
5	*Data analysis completed*				▼

1.3.4 Data handling

Please explain how research data or information generated in this project will be made available in your consortium and for future reuse.

1.3.5 Contingency plan

Please explain measures and mechanisms to develop adequate contingency plans in case a scientific subproject or clinical trial fails.

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1.4 IMPACT, DISSEMINATION AND EXPLOITATION

1.4.1 Expected impact for patients and health care system

How will the proposed research contribute to an improvement of the current situation of patients and/or to reducing the burden and costs of diseases in Germany?

1.4.2 Dissemination and exploitation strategy

What are the strategies for the dissemination and exploitation of results especially beyond journal publications? Indicate what measures will be used by the consortium to disseminate and communicate the expected project results to appropriate stakeholders. Please describe your exploitation strategy with regard to possible product development, patents or intellectual property rights (IPR), if applicable.

1.5 FINANCIAL SUMMARY

Please provide a financial summary of the consortium, divided by subprojects. Please make sure that all overhead costs (e.g., "Projektpauschale" for universities and university clinics) are properly considered.

	Subproject 1	***Subproject 2***	***Subproject 3***	
Name of the PI				
Institution				
Other involved Partners				
Budget				***Total for the Consortium***
Personnel				
Consumables				
Equipment				
Travel				
Other Costs				
Overhead				
Total Budget				
Requested Budget				

1.6 REFERENCES

Please list key references here (max. 20 references, font size not less than 6 pt).

2. DESCRIPTION OF A SUBPROJECT

The description of each subproject should not exceed 5 pages *(DIN A4, at least 11 point Arial, single space). The financial summary may be added on a 6th page. Structure your application using the headings listed below and make an entry under every heading/subheading. Please continue with further subprojects numbered consecutively.*

In case you want to apply for funding of a clinical trial or an animal study please also fill out the additional templates No. 3 and/or 4.

2.1 PROJECT SUMMARY

Project No.	
Title	
Principal Investigator	*Name, Institution* *Postal address* *Telephone, Fax* *E-mail address*
Additional Partners (if applicable)	*Name, Institution* *Postal address* *Telephone, Fax* *E-mail address*
Abstract	*max. 300 words*

2.2 GENERAL INFORMATION ON THE SUBPROJECT

2.2.1 Aim of the subproject and research question(s) addressed

Please describe the aims of the subproject and the research question(s) addressed. What results are expected?

2.2.2 Own previous work, resources and expertise

Which own previous work is directly relevant for the hypothesis and the research question(s)? Describe the necessary resources in place for the accomplishment of the project: infrastructure, capacities, specific expertises and previous achievements (e.g. methodologies, cells/tissues, animal models, patient cohorts etc.)

2.2.3 Research approach

Describe the methodologies and technical approaches used in the subproject. How are the required resources integrated in the project? Indicate the added value of the interdisciplinary approach.

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2.2.4 Work plan

Please describe your work plan in detail (work packages, time frame, milestones). Which tasks will be done? How will the aims of the subproject be reached? How will gender aspects be addressed?

2.2.5 Added value for the consortium

Describe the cooperation with other consortium partners. What is the added value of this cooperation? What is the relevance of the subproject in the context of the consortium and the overall research question?

2.2.6 Key references

Please list key references here (max. 10 references, font size not less than 6 pt).

2.2.7 Financial summary

	Partner 1 (PI)		***Partner 2***		**Total Budget for Subpro-ject**
	Budget (in €)	**Justification/ Specification**	**Budget** (in €)	**Justification/ Specification**	
Personnel					
Consumables					
Equipment					
Travel					
Other Costs					
Overhead					
Total Budget					
Requested Budget					

3. DESCRIPTION OF CLINICAL STUDY

The following outline is only relevant for subprojects with clinical studies.

*The description of the clinical research project **should not exceed 7 pages** (DIN A4, at least 11 point Arial, single space). Structure your application using the headings listed below and make an entry under every heading/subheading.*

*Additionally two appendices are to be included in the proposal (one page each). **Do not** submit any other appendices (e.g. letter of intent, letter of support).*

3.1 STUDY SYNOPSIS

APPLICANT/COORDINATING INVESTIGATOR	Name, address, telephone, fax, e-mail *In case of multiple applicants the principal investigator / coordinating investigator[11] of the trial who will assume responsibility for conducting the clinical trial, should be listed first.*
TITLE OF STUDY	*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. Acronym is optional.*
CONDITION	*The medical condition being studied (e.g. asthma, myocardial infarction, depression)*
OBJECTIVE(S)	*Which principal research questions are to be addressed? Specify clearly the primary hypotheses of the trial that determines sample size calculation.*
INTERVENTION(S)	*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:
KEY INCLUSION AND EXCLUSION CRITERIA	Key inclusion criteria: Key exclusion criteria:
OUTCOME(S)	Primary efficacy endpoint: 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*

[11] 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).
1.34 Investigator: “A person responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.” 1.19 Coordinating investigator: “An investigator assigned the responsibility for the coordination of investigators at different centres participating in a multicenter trial.” Diese Definition sollte auch für nicht-pharmakologische Studien verwendet werden.

STATISTICAL ANALYSIS	Efficacy: Description of the primary efficacy analysis and population: Safety: *Please describe the strategy for assessment of safety issues in the study. Which are relevant safety variables?* 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): *if applicable* *How many centers will be involved? Please also list the cities.*
OTHER SUBMISSION OF PROPOSAL ELSEWHERE	*Please state, if the same or a similar version of this proposal has been submitted in another funding programme, e.g. DFG clinical trials programme.*

3.2 RELEVANCE

Which medical problem is to be addressed? Which principal research questions are to be addressed? Bring them into order indicating major and minor motivations / starting hypotheses of the investigation planned.

3.2.1 PREVALENCE, INCIDENCE, MORTALITY

Please state the prevalence, e.g. per 100.000 residents, incidence, e. g. per 100.000 residents per year and mortality (case fatality rate) of the disease, according to most reliable data.

3.2.2 BURDEN OF DISEASE

Please provide suitable indicators to describe the burden of disease, e. g. DALYs (disability-adjusted life years). Please provide information on the socio-economic burden of disease.

3.2.3 IMPROVEMENT OF THERAPY / IMPACT OF THE TRIAL

Novelty: *Which therapy options are available for treatment of the disease? What is the novel aspect of the proposed trial? Does the trial challenge existing paradigms?*

Clinical impact*: Provide information on the possible impact on the delivery of health care and on clinical practice. Which evidence gap is to be closed?*

Patient benefit*: Describe the possible clinical / real life benefit(s) for the patients. Detail the potential impact on relieving the burden of disease and / or treatment (e.g. dose reduction, avoiding adverse effects, shortening futile treatment times).*

Socioeconomic impact*: Reflect on the socioeconomic impact of the trial.*

3.2.4 PATIENT INVOLVEMENT

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Please describe how patient involvement is implemented in the planning, conduct and exploitation of results of the trial[12]. Please note: Patient involvement is mandatory wherever feasible and constructive.

Who?: Which patients, patient representative(s), patients' self-help group(s) or patient advocacy group(s) was / were involved in the planning of the trial? Who is planned to be involved during the conduct of the ongoing trial? Who is planned to be engaged in dissemination of the results?

How? How have patient representative(s), patients' self-help group(s) or patient advocacy group(s) been involved in the planning of the trial? How were the patients' needs, goals, concerns and preferences considered? How will patient representative(s), patients' self-help group(s) or patient advocacy groups be engaged during the conduct of the trial and dissemination of results?

When? When were / are patients, patient representative(s), patients' self-help group(s) or patient advocacy group(s) involved in e. g. developing the main question, developing the trial design, defining endpoints, accompanying the ongoing trial, communicating trial results? Is engagement at specific time points or continuous engagement (including feedback loops) planned?

Patient involvement can be implemented in different stages of the trial and to a different extent. Please justify why your concept is adequate for the planned trial.

3.3 EVIDENCE

Set your trial into perspective. This section should detail the background of the starting hypotheses of the trial and the need for the trial (e.g. operationalisation of a patient-relevant endpoint, feasibility of a patient-relevant therapy regimen).

How novel is the addressed question? A description of how you searched for the evidence (databases, search terms, limits) is mandatory: Please indicate the electronic databases searched. MEDLINE, Cochrane Central, the Cochrane library, clinicaltrials.gov, Deutsches Register Klinischer Studien (DRKS) and International Clinical Trials Search Portal (ICTRP) are recommended as a minimum, but other databases may be relevant in special occasions. Include search terms, limits, date of search and time period covered. Provide a narrative summary: Which trials have been conducted either by you or by others? What is the relevance of their results? Give references to any relevant systematic review(s)[13] and / or pilot studies, feasibility studies, relevant previous / ongoing trials, case reports / series. State what your study adds to the existing body of evidence.

A full electronic search strategy for one database, including any limits used, has to be presented in appendix 2 (max. one page). Guidance concerning search techniques can be found in the following document:

http://www.cochrane.de/sites/cochrane.de/files/uploads/20130523_Manual_Literaturrecherche_Final.pdf

[12] s. auch eine Einführung von INVOLVE zugehörig zum Britischen National Institute for Health Research, NHS „Briefing note for Researchers“: http://www.invo.org.uk/resource-centre/resource-for-researchers/

[13] Eine Definition für einen systematischen Review finden Sie unter Cook DJ, Mulrow CD, Haynes RB. Systematic Reviews: Synthesis of Best Evidence for Clinical Decisions. Ann Intern Med 1997; 126 (5): 376-380

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Please note that insufficient clinical evidence precludes funding.[14]

3.4 JUSTIFICATION OF DESIGN ASPECTS

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

3.4.1 CONTROL(S) / COMPARATOR(S)

Justify the choice of control(s) / comparison(s): Is placebo acceptable? Which trials establish efficacy and safety of the chosen control regimen?

3.4.2 INCLUSION / EXCLUSION CRITERIA

Justify the population to be studied, include reflections on generalisability and representativeness.

3.4.3 INTERVENTION(S)

Justify the choice of your planned intervention(s). Illustrate your intervention scheme graphically in the appendix. Please consider following the TIDieR checklist and guide for describing the intervention.[15]

3.4.4 OUTCOME MEASURES

Justify the endpoints chosen: Are the chosen endpoints relevant for the patients? Are there other trials that have utilized this endpoint? Are there any guidelines proposing this endpoint / these endpoints? Discuss the clinical relevance of the outcome measures for the target population. Have the measures been validated?

3.4.5 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 randomization?

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).

3.4.6 PROPOSED SAMPLE SIZE / POWER CALCULATIONS

What is the proposed sample size and what is the justification for the assumptions underlying the power calculations? Include a comprehensible, checkable description of the power calculations and sample sizes detailing the outcome measures on which these have been based for both control and experimental groups; give event rates, means and medians, the software used for sample size calculation etc., as appropriate. Justify the size of difference that the trial is powered to detect, or in case of a non-inferiority or equivalence study, the size of difference that the trial is powered to exclude. It is important that the sample size calculations take into account anticipated rates of non-compliance and losses to follow up.

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.

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[14] vgl. hierzu Clark S and Horton R (2010). Putting research into context – revisited; The Lancet; 376(9734); 10-11

[15] Hoffmann T, Glasziou P, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687

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3.4.7 FEASIBILITY OF RECRUITMENT

What is the evidence that the intended recruitment rate is achievable (e.g. pilot study)? Describe from what data you assessed the potential for recruiting the required number of suitable subjects.

3.5 STATISTICAL ANALYSIS

What is the proposed strategy of statistical analysis? What is the strategy for analysing the primary outcome? If interim analyses are planned, please specify. Are there any subgroup analyses?

3.6 ETHICAL CONSIDERATIONS

Discuss briefly the acceptability of the risk incurred by the individual participant versus the potential benefit for the participant / population concerned.

3.7 STRATEGIES FOR DATA HANDLING

Describe what measures will be implemented 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). Also mention at which stage data sharing will be ensured. Please use existing standards and data repositories where appropriate.

3.8 TRIAL MANAGEMENT

3.8.1 MAJOR PARTICIPANTS

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

#	Name	Affiliation	Responsibility/Role
			Principal/Coordinating Investigator
			Trial Statistician [16]
			….

3.8.2 TRIAL EXPERTISE

Please indicate trial expertise of all above-mentioned participants by citing relevant publications and / or specifying major role in ongoing trial(s) (to be identified; 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.

3.8.3 TRIAL-SUPPORTING FACILITIES

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

3.9 REFERENCES

[16] Assure that the biostatistician has the expertise to carry out clinical trials, e.g.: GMDS certificate (http://www.gmds.de/organisation/zertifikate/zertifikate.php), ICH guidance E9 *"Statistical Principles of Clinical Trials".*

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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).

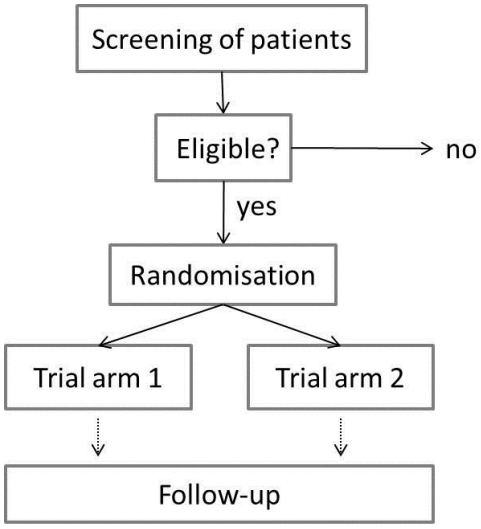
APPENDICES

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

1. INTERVENTION SCHEME / TRIAL FLOW

Provide a schematic diagram of the trial design illustrating the trial flow including interventions and procedures. DO NOT provide a visit schedule, procedure table, time table etc. or any other further explanations. Only abbreviations can be listed in a legend.

Basic example for a schematic diagram of the trial design:



2. SEARCH STRATEGY

To substantiate the evidence presented in section 3.3, please present the full search strategy for one electronic database (e.g. MEDLINE, the Cochrane library or clinicaltrials.gov) 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 3.3. For guidance refer to section 3.2.5 in the document that can be accessed at https://www.cochrane.de/sites/cochrane.de/files/public/uploads/20130517_Manual_Literaturrecherche_Final-1.pdf.

Example for a full search strategy in MEDLINE (conducted to identify randomized controlled, blinded trials of antipsychotic drugs in treatment resistant patients with schizophrenia):

Search strategy for Medline (30th June 2013)

1 exp Schizophrenia/ (86112)
2 exp Psychotic Disorders/ (38267)
3 schizo$.mp. (127884)
4 or/1-3 (153641)
5 ("treatment resist$" or "therapy resist$" or "drug resist$" or "chemical resist" or "treatment refract$" or "treatment fail$" or nonrespon$ or non-respon$ or "non respon$" or "not respon$" or "no respon$" or "partial respon$" or "partially respon$" or "incomplete respon$" or "incompletely respon$" or unrespon$ or "failed to respond" or "failed to improve" or "failure to respon$" or "failure to improve" or "failed medication$" or refractory or resistant or (inadequate$ adj3 respon$)).mp. (621509)

6 exp Drug Resistance/ (253660)
7 5 or 6 (667475)
8 exp Antipsychotic Agents/ (122182)
9 antipsychoti$.mp. (50055)
10 neurolept$.mp. (20926)
11 benperidol/ or chlorpromazine/ or chlorprothixene/ or clopenthixol/ or Clopenthixol/ or clozapine/ or droperidol/ or flupenthixol/ or fluphenazine/ or fluspirilene/ or haloperidol/ or iloperidone/ or loxapine/ or mesoridazine/ or Methotrimeprazine/ or molindone/ or olanzapine/ or Penfluridol/ or Perazine/ or perphenazine/ or pimozide/ or prochlorperazine/ or promazine/ or promethazine/ or quetiapine/ or Reserpine/ or risperidone/ or sulpiride/ or thioridazine/ or thiothixene/ or trifluoperazine/ or Trifluperidol/ or triflupromazine/ or Veralipide/ or Tiapride Hydrochloride/ (69795)
12 (acetophenazine or amisulpride or aripiprazole or asenapine or benperidol or bromperidol or butaperazine or carpipramine or chlorproethazine or chlorpromazine or chlorprothixene or clocapramine or clopenthixol or clozapine or cyamemazine or dixyrazine or droperidol or fluanisone or flupehenazine or flupenthixol or fluphenazine or fluspirilene or haloperidol or iloperidone or levomepromazine or levosulpiride or loxapine or lurasidone or melperone or mesoridazine or molindone or moperone or mosapramine or olanzapine or oxypertine or paliperidone or penfluridol or perazine or pericyazine or perphenazine or pimozide or pipamperone or pipothiazine or prochlorperazine or promazine or promethazine or prothipendyl or quetiapine or remoxipiride or reserpine or risperidone or sertindole or stelazine or sulpiride or sultopride or thiopropazate or thioproperazine or thioridazine or thiothixene or tiapride or trifluoperazine or trifluperidol or triflupromazine or veralipide or ziprasidone or zotepine or zuclopenthixol).mp. (93792)
13 or/8-12 (149852)
14 4 and 7 and 13 (3026)
15 exp clinical trial/ (785982)
16 exp randomized controlled trials/ (102420)
17 exp cross-over studies/ (35635)
18 randomized controlled trial.pt. (384946)
19 clinical trial.pt. (501097)
20 controlled clinical trial.pt. (89142)
21 (clinic$ adj2 trial).mp. (597724)
22 (random$ adj5 control$ adj5 trial$).mp. (507275)
23 (crossover or cross-over).mp. (66025)
24 ((singl$ or double$ or trebl$ or tripl$) adj (blind$ or mask$)).mp. (179088)
25 randomi$.mp. (582908)
26 (random$ adj5 (assign$ or allocat$ or assort$ or reciev$)).mp. (165555)
27 or/15-26 (1088679)
28 14 and 27 (1048)

4. DESCRIPTION OF AN ANIMAL STUDY

The following outline is only relevant for subprojects with animal studies.

The description of the animal research project (study synopsis as required by the respective registration authority) ***should not exceed 7 pages*** *(DIN A4, at least 11 point Arial, single space). Please make an entry under every heading/subheading.*

4.1 STUDY SYNOPSIS

Coordinating Investigator/ additional applicants	*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.* *Title, first and last name* *Institution* *Address* *Telephone and Fax* *E-Mail address*
Title of Project	
Topic	
Aim(s)	
Keywords	

4.2 RESEARCH DESIGN & WORKPLAN

4.2.1 RIGOROUS EXPERIMENTAL DESIGN

Explain the experimental approach how the animal model being used can address the scientific objectives. Explain the study's relevance to human biology.

Please use the subsections below to further describe the experimental approaches, study designs and techniques of your research project. Indicate and justify if any of the subsections does not apply.

4.2.1.1 Experimental procedures

Describe the experiments, study design and techniques that will be used. Please justify, e.g. drug formulation and dose, anaesthetic and surgical procedures, equipment (how, when, where, why?). Justify the number of experimental and control groups. Which steps will be taken to minimize the effects of subjective bias? How is an experimental unit defined?

4.2.1.2 Experimental animals

Please comment on the experimental animals: species, strain, sex, developmental stage, age, weight, source of the animals, genetic modification status, etc.

4.2.1.3 Housing and husbandry

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Please comment on housing and husbandry: type of facility e.g. specific pathogen free [SPF]; type of cage or housing; bedding material; number of cage companions, type of food, access to food and water, environmental enrichment etc.

4.2.1.4 Sample size

Specify and justify the total number of animals used in the experiment (or each experiment), and the number of animals in each experimental group. Explain how the number of animals was arrived at. Provide details of any sample size calculation used (expected effect size, the software used for sample size calculation etc.). Give evidence / references for the estimated effect size. Indicate the number of independent replications of each experiment, if relevant.

4.2.1.5 Allocating procedures & methods against bias

Describe how animals are allocated to the experimental groups. Is randomization and / or matching feasible? Describe steps to minimize the effects of subjective bias.

4.2.1.6 Experimental outcomes

Define and justify the primary and secondary experimental outcomes assessed (e.g. cell death, molecular markers, behavioral changes).

4.2.1.7 Gender aspects

Indicate how gender specific aspects are addressed regarding the research questions, the analyses, and the relevance of the results. If you find that gender aspects do not apply to your research questions, please give a comprehensive justification.

4.2.1.8 Statistical analysis

What is the proposed strategy of statistical analysis? Provide details of the statistical methods used for each analysis. Justify any methods used to assess whether the data meet the assumptions of the statistical approach. Specify the unit of analysis for each dataset (e.g. single animal, group of animals)? How will missing data and subjects withdrawn from the trial be handled statistically? Please include a biostatistician for data analysis in your financial planning.

4.2.2 WORK PACKAGES

Explain your work plan in detail. Define and describe work packages. Which tasks will be done? How will the aims be reached?

4.2.3 MILESTONE PLAN

Indicate work packages (WP) into which the project is divided and schedule events that indicate the completion of major deliverables. Milestones are measurable / observable events and serve as progress markers.

No. of WP	Milestone (▼)	year 1				year 2				year 3			
					▼						▼		
								▼					
										▼			

4.3 TEAM AND EXPERTISE

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Please indicate the major participants of this project, i.e. persons responsible for design, conduct and analysis of the project.

#	Name	Affiliation	Role
			Principal investigator
			Methodological expertise
			Biostatistician (required for animal studies)
			….

Ensure that the team of participating investigators has the necessary range of disciplines and expertise to carry out the proposed project.

4.4 STRATEGIES FOR DATA HANDLING

Describe what measures will be implemented to ensure data management, maintenance and long-term accessibility for future reuse of your results (also by third parties). Please use existing standards and data repositories where appropriate.

4.5 REFERENCES

Please list key references here (max. 20 references, font size not less than 6 pt).