Bundesministerium
für Bildung
und Forschung

Leitfaden für die Antragstellung im Rahmen der Förderinitiative: Innovative Therapieverfahren auf molekularer und zellulärer Basis

Im Rahmen der Fördermaßnahme 'Innovative Therapieverfahren auf molekularer und zellulärer Basis' stellt das BMBF Fördermittel zur Verfügung, die - abhängig vom Entwicklungsstand des Therapieansatzes - für Untersuchungen im Bereich der präklinischen Forschung ab dem „proof of principle“ (Modul 1: präklinische Forschung) oder für klinische Studien der Phase I oder II (Modul II: klinische Studie) beantragt werden können.

Der nachfolgende Leitfaden dient als Leitlinie zur Antragstellung. Die Randbedingungen der Förderung sind in der Förderrichtlinie des BMBF **(http://www.gesundheitsforschung-bmbf.de/de/1450.php)** dargestellt. Gleichzeitig mit der **formlosen Vorhabenbeschreibung** sind **elektronische Datenblätter** (Application Data Sheets) sowohl für das Konsortium (http://www.gesundheitsforschung-bmbf.de/de/1486.php) als auch für die Teilprojekte (http://www.gesundheitsforschung-bmbf.de/de/1488.php) auszufüllen. Die Datenblätter dienen der Erfassung aller eingegangenen Anträge und der Zuordnung zu den Fachdisziplinen.

Bis zum **30.03.2007** (Eingangsdatum) können Vorhabenbeschreibungen **in englischer Sprache** (Format: DIN A4, 11 Punkt Arial, 1,5-zeilig, doppelseitig bedruckt) beim Projektträger im DLR für das BMBF, Gesundheitsforschung, Heinrich-Konen-Str. 1, 53227 Bonn, (http://www.pt-dlr.de/) eingereicht werden.
Vorhabenbeschreibungen sind entsprechend den Vorgaben dieses Leitfadens zu gliedern und an den Projektträger in **20-facher Ausfertigung plus einer ungebundenen Kopiervorlage sowie auf CD-ROM im PDF Format** vorzulegen.

Anträge, die den Vorgaben dieses Leitfadens nicht entsprechen (z.B. bei denen keine elektronischen Daten (Application Data Sheets) vorliegen), können nicht berücksichtigt werden. Bitte überprüfen Sie anhand der „Übersicht zur Antragseinreichung“ (S. 3) die Vollständigkeit Ihrer Unterlagen.

Neben diesem Leitfaden gelten weiterhin die entsprechenden Merkblätter und Richtlinien des BMBF, soweit in diesem Leitfaden nicht ausdrücklich andere Regelungen getroffen sind.
Weiterführende Links für die Antragstellung finden Sie auf den Internetseiten des BMBF[1]. Die dort veröffentlichten Anforderungen/Informationen werden regelmäßig aktualisiert. Eine Durchsicht vor dem Einreichen eines förmlichen Antrages (zweite Verfahrensstufe) wird dringend empfohlen.

[1] http://www.foerderportal.bund.de/

Allgemeine Hinweise

- **Bonität:**
  - Unternehmen der gewerblichen Wirtschaft können nur dann gefördert werden, wenn die Bonität des Unternehmens für die beantragte Laufzeit der Fördermaßnahme gesichert ist. Der Förderer behält sich daher vor, geeignete Unterlagen (z.B. testierte Jahresabschlüsse, Lageberichte, Betriebswirtschaftliche Auswertung) in der zweiten Verfahrenstufe bei Vorlage des förmlichen Förderantrages anzufordern, durch die nachzuweisen ist, dass die in den Vorhaben aufgeführten Ressourcen der Antragsteller für die gesamte Laufzeit der Förderung aufgebracht werden können.
- **Förderquoten:**
  - **Unternehmen der gewerblichen Wirtschaft können i.d.R.**
    - bei präklinischen Forschungsarbeiten bis zu **50%** ihrer projektbezogenen Kosten,
    - bei klinischen Studien der Phase I bis zu **50%** ihrer projektbezogenen Kosten,
    - bei klinischen Studien der Phase II bis zu **25%** ihrer projektbezogenen Kosten beantragen.
    - Die verbleibenden Kosten für die klinische Studie trägt der Konsortialpartner, der überwiegend die Ergebnisse wirtschaftlich verwerten wird (d.h. die Verwertungsrechte liegen laut „Business Development Concept" und Kooperationsvereinbarung bei diesem Partner; darzustellen unter Punkt 1.4.3 in der Beschreibung des Konsortiums).
    - Bei KMU[2] und Unternehmen aus den neuen Bundesländern (NBL, mit Ausnahme der Arbeitsmarktregion Berlin), kann über die oben genannten Förderquoten hinaus noch eine Erhöhung der Förderquote um 10% (jeweils für jede erfüllte Rahmenbedingung) gewährt werden.
  - **Universitäre und außeruniversitäre Forschungseinrichtungen können i.d.R.**
    - bei präklinischen Forschungsarbeiten, bei klinischen Studien der Phase I und II bis zu **100%** ihrer projektbezogenen Ausgaben beantragen.
- **Klinische Studien:**
  - Falls eine klinische Studie beantragt wird, sind neben der formlosen Beschreibung des Konsortiums (siehe Punkt 1 - Description of Consortium) die Synopse des Studien-protokolls im Umfang von 7 Seiten nach den Vorgaben dieses Leitfadens sowie **ein** Exemplar des vollständigen Studienprotokolls einzureichen (siehe Punkt 3.). Synopsen von Studienprotokollen, die den Vorgaben dieses Leitfadens nicht entsprechen, können nicht berücksichtigt werden. **Insbesondere führen fehlende Unterschriften zu einem Ausschluss aus dem weiteren Antragsverfahren.**
  - Im Falle einer positiven Begutachtung muss dem Förderer vor Beginn der Patientenrekrutierung das uneingeschränkt positive Ethikvotum (für die vorliegende Version des Studienprotokolls), eine Bestätigung über die erfolgte Registrierung in einem öffentlich zugänglichem Register (wie z.B. clinicaltrials.gov oder controlled-trials.com/ sowie die Sponsorenerklärung zur Verpflichtung auf die Leitlinien zur guten klinischen Praxis vorgelegt werden.

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[2]Kleine und mittlere Unternehmen im Sinne der Definition der Europäischen Kommission (http://ec.europa.eu/enterprise/enterprise_policy/sme_definition/index_de.htm). Das bedeutet, dass die Unternehmen weniger als 250 Beschäftigte, einen Jahresumsatz von höchstens 50 Mio. EUR oder eine Jahresbilanzsumme von höchstens 43 Mio. EUR haben und nicht zu 25% oder mehr des Kapitals oder der Stimmanteile im Besitz von Unternehmen sind, welche die KMU-Kriterien nicht erfüllen.

Übersicht zur Antragseinreichung

Inhaltliche Vorgaben:	**OK**
• Innovativer Therapieansatz für die klinische Anwendung, der aus der zell- und molekularbiologischen Grundlagenforschung erwachsen ist	
• ‚proof of principle' in einem krankheitsrelevanten Tiermodell (relevante Publikation bzw. Patentschrift beifügen)	
• Keine Grundlagenforschung, keine Entwicklung von Tiermodellen, keine klinische Studie der Phase III, keine Evaluation von innovativen off-label Anwendungen von zugelassenen Arzneimitteln, keine strahlentherapeutischen oder chirurgischen Methoden, keine individuellen Heilversuche	
• Medizinischer Nutzen (inkl. therapeutischem Nutzen im Vergleich zu existierenden Therapien)	
• Wirtschaftliche Verwertungsstrategie entsprechend des „Business Development Concept" o Produkt/Dienstleistung (Alleinstellungsmerkmale, Rechtsschutz, Stand der Technik, Entwicklungsrisiken etc.) o Markt & Marktsituation (Marktpotential, Marktsegment, Wettbewerber etc.) o Unternehmen (Finanzierung, Investoren, Expertise des Managementteams)	

Nachweise und formelle Vorgaben	**OK**
• Vorhaben in Englisch, DIN A4, 11 point Arial, 1,5-zeilig, doppelseitig bedruckt	
• 20 Kopien, 1 ungebundene Kopie, CD-ROM im PDF-Format, ggf. 1 vollständiges Studienprotokoll	
• Beschreibung des Konsortiums mit max. 9 Seiten	
• Zusammenfassung der wichtigsten Ziele des Projekts (max. 1200 Zeichen)	
• Übersicht über Finanzierungspläne für alle Teilprojekte	

Organisations- und Vorhabensabhängige Vorgaben:		**OK**
• Präklinische Projekte	Beschreibung des präklinischen Teilprojekts, max. 7 Seiten	
	Zusammenfassung des Teilprojektes (max. 1200 Zeichen)	
	Beachtung der GLP Richtlinien	
	bei Industriebeteiligung tragen die Unternehmen mind. 50% der eigenen projektbezogenen Kosten	
• Klinische Studien	Genehmigung der klinischen Studie durch die zuständige Oberbehörde (BfArM oder PEI)	
	GMP-Herstellungserlaubnis	
	Synopse des Studienprotokolls (max. 7 Seiten mit erforderlichen Unterschriften)	
	1 Exemplar des vollständigen Studienprotokolls	
	Beachtung der GMP- und GCP-Richtlinien	
	Ethische Bedenken nicht vorhanden, d.h. Risiko für Studienteilnehmer, Studienmanagement und - expertise etc. akzeptabel	
	Sponsorenerklärung (bei Durchführung einer klinischen Studie)	
• Klinische Studien Phase I	Bei Industriebeteiligung - Industrieunternehmen trägt mind. 50% der Kosten der klinischen Studie, wenn es die Ergebnisse überwiegend wirtschaftlich verwertet	
• Klinische Studien Phase II	Bei Industriebeteiligung - Industrieunternehmen trägt mind. 75% der Kosten der klinischen Studie, wenn es die Ergebnisse überwiegend wirtschaftlich verwertet	

Beantragbare Mittel und Förderquoten		**OK**
• Förderquoten	Hochschulen, Forschungs- und Wissenschaftseinrichtungen und vergleichbare Institutionen mit bis zu 100% der projektbezogenen Ausgaben	
	Helmholtz-Zentren und die Fraunhofer-Gesellschaft mit bis zu 100% der projektbezogenen Kosten	
	Unternehmen der gewerblichen Wirtschaft mit max. 50% der projektbezogenen Kosten der präklinischen Phase und klinische Studien der Phase I und max. 25% der projektbezogenen Kosten der klinischen Studien der Phase II	
• Bonus	Für KMU und Unternehmen aus den neuen Bundesländern kann ein Bonus von je 10% auf die Förderquote gegeben werden	
• Fördermittel	Vorhabenbezogene Verbrauchsmaterialien	
	i.d.R. Reisen bis zu einer Höhe von max. 1000 EUR/Wissenschaftler/p.a. Kurzaufenthalte für Doktoranden und Post-Docs im Labor des Partners, Personalaustausch zwischen Akademia und Wirtschaft	
	Projektbezogene Investitionen, d.h. Geräte, die nicht der Grundausstattung zuzurechnen sind oder wenn es für Antragsteller unmöglich ist, die vorhandene Grundausstattung wirtschaftlich zu nutzen, dazu gehört u.a. auch die nicht vorhandene Kapazität der vorhandenen Geräte oder die räumliche Entfernung des Standortes dieser Geräte (detaillierte Begründung bei Einreichung des förmlichen Förderantrages notwendig)	
	Produktion von Therapeutika nach GMP Standards	
	Fallpauschalen für die Prüfzentren (Personal- und Sachmittel)	
	Gebühren zur Registrierung der klinischen Studie	
	Kosten/Ausgaben für die Anmeldung eines Patents, die während der Laufzeit initiiert wurden i.d.R. bis zu 10.000 EUR, bei Vorlage eines ausgereiften Geschäftskonzeptes können auch internationale Anmeldungen finanziert werden, wenn diese durch die wirtschaftlichen Perspektiven gerechtfertigt werden können	
	Tierhaltungskosten	
	Overheadkosten von institutionell geförderten Einrichtungen (z.B. Helmholtzzentren) nach den vereinbarten Sätzen	
	Personal mit Qualifikation und Ausgaben- bzw. Kostenansätzen	
	Bei Dienstleistungen/Aufträgen ist entsprechend der Regelung der zuständigen Finanzbehörde die Mehrwertssteuer einzuberechnen	

1. Description of Consortium

1.1. GENERAL INFORMATION ON THE CONSORTIUM

The description of the consortium (No. 1.1. - 1.3.) should not exceed **5 pages.**

The description of the business development concept (No.1.4.) should not exceed **4 pages.**

1.1.1 Title of the consortium

The title of the consortium (max. 140 characters) should be as precise as possible. In case of funding, this title will be quoted in the annual reports of the funding organisation. Please indicate an acronym (max. 40 characters) derived from the title of the proposal.

1.1.2 Coordinator of the consortium

Name, address, telephone, fax, e-mail.

1.1.3 Scheduled duration

Please indicate the time period, for which funding is requested (up to 3 years), and the date, when funding should begin.

1.1.4 Project summary of consortium

Please give a summary of the main goals of the project (max. 1200 characters). The project summary serves two main purposes:
i) It will inform the multidisciplinary review committee of the principal aims of the project.
ii) If your project is funded the summary will be published on the internet through an electronic information system. (It should therefore be concise as well as comprehensible to a lay public).
Please avoid abbreviations and include suitable key words to ease electronic search.

1.2. MEDICAL ASPECTS OF INNOVATION AND RELEVANCE OF THE PROJECT

1.2.1 Medical problem

What is the medical problem? What is the medical need to be addressed? (e.g. burden of the disease, prevalence, incidence, reasons for the project)?

1.2.2 Objectives/Research goal

What is the objective? Which results are expected?

1.2.3 Novel aspect and future impact

What is the novel aspect of the proposed therapy? Specify the impact.

1.2.4 Evidence

How has the evidence been assessed? (e.g. recent research, pilot studies, review of publications, ongoing related studies). Which were the major findings?

1.3. DESCRIPTION OF THE CONSORTIUM ORGANIZATION

1.3.1 Summary of consortium structure

Example:

Subproject No.	Partner	Title of Subproject	Function in the consortium	Contribution
1	*xyz GmbH*	*Preclinical evaluation of novel XY for the treatment of breast cancer*	*Coordination*	*Monitoring, evaluation and processing of results*
	abc GmbH	*GMP-Production*	*Subcontractor of xyz GmbH*	*GMP-production of XY*
2	*University of…*	*Targeting of XY in mice*	*Preclinical partner*	*Validation of animal models*

1.3.2 Cooperation

What structure is available, respectively will be implemented for an efficient cooperation within the consortium. How will the consortium be managed? What are the contributions of the individual partners? Enterprises need to list major subcontractors within their subproject.

1.3.3 Work packages/timeframe/ milestones

In which time-frame major work-packages will be achieved; what milestones are planned?

1.3.4 Summary of financial plan for all subprojects

Example:

Subproject No.	Partner	Total costs of project	Applied BMBF Funds	Co-financed by industry or other sources
1	*xyz GmbH*	*500.000 €*	*250.000 €*	*250.000 €*
	Abc GmbH	*inc. subcontracts of 100.000 €*		
2	*University of…*	*300.000 €*	*300.000 €*	*0*

1.4 BUSINESS DEVELOPMENT CONCEPT

- Since funding is provided in order to accelerate the development of new therapeutic processes and products which are of high medical relevance and economically viable your business development concept will be an essential basis for the funding decision. In case you are not able to provide solid data, please provide estimates and comments.
- As a starting basis for documenting your business development concept you may use a statement by a technology transfer institution (http://www.technologieallianz.de), your business plan for investors or similar documents provided by an industrial partner of your consortium.
- The following list will point out essential features which need to be adjusted according to the development status of your project and the structure of your consortium.
- If necessary (i.e. in case of various indications resulting in different business development concepts) differentiate your documentation accordingly.

1.4.1 Executive summary (max. 1200 characters)

- Describe the key elements of your business development concept.
- Include description of business model (how the therapeutic approach will be marketed and generate revenue).

1.4.2 Assessment of Innovation

- Description of innovative approach, development stage of therapeutic concept, prior art/comparison with existing therapies, innovative character, unique selling proposition
- Assessment of regulatory aspects of your scientific, clinical and economic activities.

1.4.3 Intellectual Property Rights

- Freedom to operate - analysis in respect to patent and exploitation strategy (technical and commercial).

1.4.4 Patients and Pricing

- Description of patient group targeted and addressed therapeutic benefit, including improvement of health, life quality and/or life span of individual patient groups.
- Potential cost reduction for health care costs including assessment of health care providers or patient to pay for planned therapeutic concept.
- Prospective pricing (if not available, provide bench-marking data).

1.4.5 Market and Competitors

- Size and value of the target market(s) (annual sales in €).
- Marketing strategy and description of the competitive environment (niche market, orphan drug status vs. blockbuster application, existing and/or potential competitors etc., pilot/lead customer, sales channels).
- Include financial information regarding sales, cost and profit forecast for the 3 years following market entry (if applying for a clinical study phase II).

1.4.6 Funding and Financials

- Present financial concept (equity, credits, public funding), future demand for capital/funding until company is cash positive or the therapeutic approach will be sold/out-licensed.
- Describe exit possibilities for (potential) investor(s).

1.4.7 Time plan & Risk assessment

- Major planned milestones until market entry
- Assessment of scientific and economic risks as well as a risk mitigation plan and possible exit points.
- Possible restrictions/limitations in the application of therapeutic approach.

1.4.8 Company/Academic Facility

- How many years are you operating in this therapeutic field?
- Organization (one or multiple investors, owners, % of the shares, longstanding commitment of investors, if applicable) and structure.
- Type of production facilities or other facilities available/needed to develop therapeutic approach (make or buy concept)

1.4.9 Human Resources & Management Team

- Skills and expertise of the members of the management team to promote therapeutic approach and drive into medical practice/therapeutic market.
- Description of previous and relevant business experience from the same business sector and technology field of the management team.
- Structure and expertise of preclinical research teams (e.g. knowledge transfer with employee turnover, commitment of entire teams to one project etc.) as well as clinical teams (e.g. coordination of previous clinical studies in the same field).

2. Description of Individual Subprojects

2.1 PRECLINICAL RESEARCH PROJECT

The following outline is relevant for *preclinical research projects* only.
In case you want to apply for funding of a *clinical study*, please proceed to outline 3.

The description of each preclinical research project should not exceed **7 pages max**.

2.1.1 Title of the subproject

The title of the subproject (max. 140 characters) should be precise. In case of funding this title will be quoted in the annual reports of the funding organisation. Please indicate an acronym (max. 40 characters) derived from the title of the subproject.

2.1.2 Principal investigator of the subproject

Name, address, telephone, fax, e-mail.

2.1.3 Scientific discipline and previous work

Please name your discipline and your special field of work. Describe the major findings of your previous work. Give 5 of your most relevant publications of the past 3 years.

2.1.4 Scheduled duration

Please quote

- the time period for which funding is requested (max. 3 years).
- the date when funding should begin.

2.1.5 Summary

Please give a summary of the main goals of the subproject (max. 1200 characters). The summary serves two main purposes:
i) It will inform the multidisciplinary review committee of the principal aims of the subproject.
ii) If your subproject is funded the summary will be published on the internet through an electronic information system. (It should therefore be concise as well as comprehensible to a lay public). Please avoid abbreviations and include suitable key words to ease electronic search.

2.2. INNOVATION AND RELEVANCE OF THE SUBPROJECT

2.2.1 Objectives / Research Goal

What is the objective? What is the aim of the study? What results are expected?

2.2.2 Novel aspect and future impact

What is the novel aspect of the proposed therapy? What is the relevance of the subproject in the context of the consortium? Specify the impact of the results on clinical practice, understanding of the disease or disease intervention.

2.2.3 Methods

Please describe briefly the methods you intend to apply.

2.2.4 Working packages/timeframe/milestones

Please describe the work-packages, the milestones you plan to achieve and the time-frame which is necessary.

2.2.5 Compliance with GLP

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

2.2.6 Financial Plan

Please structure the financial plan by completing the table financial plan for subproject No... as outlined on the next page (2.3).

2.2.7 Co-financing

Please indicate any co-financing of the studies by industry or other sources.

2.2.8 Other funding

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

If this is not the case please declare:
"A request for funding 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.

2.2.9 Plan for exploitation of the results derived from the subproject

Please indicate how the expected results of the studies will be used. Describe the proposed arrangements for disseminating the results of the research to potential users for aspects not covered by the business development concept.

2.3. FINANCIAL PLAN FOR SUBPROJECT NO. …

Type of expenditure	**1st year** (months)	**2nd year** (months)	**3rd year** (months)	**1st year** (EUR)	**2nd year** (EUR)	**3rd year** (EUR)	**Total of BMBF funds applied (EUR)**	**Co-financed by industry or others (EUR)**
PERSONNEL								
Scientist*	*6*	*12*	*12*	*22.698*	*45.398*	*45.398*	*113.494*	*0*
Graduate student*	*12*	*12*	*12*	*22.698*	*22.698*	*22.698*	*68.094*	*0*
Technician*		*12*	*12*		*33.564*	*33.564*	*67.128*	*0*
Engineer*	*12*	*12*		*39.336*	*39.336*		*78.672*	*0*
Others*								
CONSUMABLES	**---**	**---**	**---**					
EQUIPMENT (to specify**)**	**---**	**---**	**---**					
COMMISSIONS/ F&E subcontractors (to specify)	**---**	**---**	**---**					
TRAVEL	**---**	**---**	**---**					
OTHER (to specify)	**---**	**---**	**---**					
TOTAL of BMBF funds applied								
TOTAL of co-financed by other sources								

(Insert lines according to space required)

3. Description of Clinical Study

3.1 STUDY SYNOPSIS

The following outline is relevant for projects with focus on *clinical studies* only.

The description of the clinical research project (study synopsis as required by the respective registration authority) **should not exceed 7 pages max.** (DIN A4, at least 10 point Arial, single space). Make an entry under every heading/subheading.

Note that in addition to the study synopsis **one** complete study protocol has to be submitted.

Signatures of principal/coordinating investigator and responsible biostatistician are mandatory, as well as of collaborators who contribute substantially, e.g. as investigator of a substudy. It is acceptable to submit separate signature pages of collaborators.

3.1.1 STUDY SUMMARY

APPLICANT / COORDINATING INVESTIGATOR	Name, address, telephone, fax, e-mail *In case of multiple applicants the principal investigator / coordinating investigator[3] of the study who will assume responsibility for conducting the clinical study, should be listed first.*
TITLE OF STUDY	*The title of the study (not exceeding 140 characters) should be as precise as possible. In case of funding this title shall be quoted in the annual reports of the funding organisations. Acronym is optional.*
CONDITION/TOPIC	*The medical condition being studied (e.g. Parkinson, depression, asthma)*
OBJECTIVE(S)	*Which principal research questions are to be addressed? Specify clearly the primary hypotheses of the study that determine sample size calculation (not exceeding 140 characters).*
INTERVENTION(S)	*Description of the experimental and the control treatments or interventions as well as dose and mode of application. For diagnostic tests or procedures the experimental test and the gold-standard or reference procedure should be described.* Experimental intervention: Control intervention / Reference therapy if applicable: Duration of intervention per patient/subject: Accompanying measures: (e.g pharmacokinetic analyses, biomarkers):
KEY INCLUSION AND EXCLUSION CRITERIA	Key inclusion criteria: Key exclusion criteria: Special Populations (elderly, children, gender, impaired organ function):
OUTCOME(S)	Primary endpoint(s) (e.g. for dose-finding in Phase I, e.g. for assessment of activity in Phase II) Key secondary endpoint(s): Assessment of safety:

[3] "Investigator" as defined in the harmonised "Guideline for Good Clinical Practice" of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH GCP) (http://www.emea.eu.int). This definition should be used accordingly for non-drug studies / studies: *(1.34 Investigator) "A person responsible for the conduct of a clinical study at a study site. If a study is conducted by a team of individuals at a study 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 study.*"

DURATION OF TREATMENT AND FOLLOW-UP	Duration of treatment per patient: Follow-up per patient:
STUDY DESIGN	*Study type (e.g. single agent or combination, parallel group, cross-over)* *Type of controls e.g.(active / placebo)* *Measures taken against bias e.g. randomized / non-randomized, type of masking (single, double, observer blind),*
STATISTICAL ANALYSIS	Efficacy: Description of the primary efficacy analysis and population: Safety: Secondary endpoints:
SAMPLE SIZE	To be assessed for eligibility (n = …) To be allocated to study (n = …) To be analysed (n = …) (reasons for and handling of drop outs)
STUDY DURATION	First patient / subject in / last patient / subject out: Duration of the entire study:
PARTICIPATING CENTERS	*How many centres will be involved?*

3.2. THE MEDICAL PROBLEM

Which medical problem is to be addressed? What is the novel aspect of the proposed study? 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 EVIDENCE

Set your study into perspective. Which studies have been conducted either by you or by others? What is the relevance of their results and what are the key differences compared with your study? Give references to any relevant systematic review(s) and/or (own) pilot studies, feasibility studies, relevant previous/ongoing studies, case reports/ series. If you believe that no relevant previous studies have been done, give details of your search strategy for existing information. This should both detail the background of the starting hypotheses and the feasibility of the study.

3.2.2. THE NEED FOR A CLINICAL STUDY

What impact will the results have on clinical practice or understanding of the proposed intervention or underlying disease? Discuss possible a positive as well as negative study outcome. What is the risk of inconclusive results?

3.3 JUSTIFICATION OF DESIGN ASPECTS

3.3.1 CONTROL(S) / COMPARATOR(S)

Justify the choice of control(s)/comparison(s) or justify the conduct of a single agent study.

Are placebo controls acceptable/feasible? Which previous studies established efficacy and safety of the chosen control regimen?

3.3.2 INCLUSION/EXCLUSION CRITERIA

Justify the population to be studied, include reflections on generalizability and representative-ness.

3.3.3 OUTCOME MEASURES

Justify the endpoints chosen. Are there other studies 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? If you have chosen surrogate endpoints (e.g. biomarkers) justify. How accurate can the outcome be measured in relation to clinical practice (e.g. when patient's visits are restricted to a periodical or irregular schedule, interval censored data).

3.3.4 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 study groups? Can/should the study population be subdivided into strata?
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).

3.3.5 PROPOSED SAMPLE SIZE / POWER CALCULATIONS

What is the proposed sample size and what is the justification for the assumptions underlying the sample size determinations (statistical hypotheses, statistical error probabilities and power calculations). If the sample size is not based on statistical hypotheses justify why another approach has been chosen and why that enables to answer the medical question of the study. In particular, in Phase I studies: describe the dose escalation scheme and the stopping rule, and in Phase II studies, distinguish between single stage and two/multistage designs, give the samples sizes at each stage and the stopping rules. In comparative studies, 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. Justify the size of difference that the study is powered to detect, or in case of a non-inferiority or equivalence study, the size of difference that the study 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. Give event rates, means and medians of quantitative outcomes, etc., as appropriate.

3.3.6 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. With regard to the planned study estimate the drop-out rate.

3.4 STATISTICAL ANALYSES

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? Discuss the robustness of your results e.g. with respect to unavoidable incomplete or missing data. If high-throughput data are generated (e.g. when using micro-arrays) which methods are used to adjust for multiplicity and an inflated error of false positive results?

3.5 ETHICAL CONSIDERATIONS

Discuss briefly the acceptability of the risk incurred by the individual participant versus the potential benefit for the participant / population concerned. In particular in Phase I studies: What measures have been taken to detect serious adverse events immediately such that the study can be terminated or taken on hold? What are the most important issues about which the patients have to be informed?

3.6 STUDY MANAGEMENT

3.6.1 CLINICAL STUDY EXPERTISE

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

#	Name	Affiliation	Responsibility / Role	Signature
			Sponsor of the study	
			Principal/Coordinating Investigator	
			Study Statistician [4]	

Please indicate studies expertise of all above-mentioned participants by citing relevant previous work, publications and/or specifying major role in ongoing study(s) (to be identified; max. 5 publications of the last 5 years). Ensure that the team of investigators has the necessary range of disciplines and expertise to carry out the study.

3.6.2 STUDY-SUPPORTING FACILITIES

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

3.7 STUDY TIMELINE FLOW

As funding by BMBF will critically depend on the study progression according to the milestones, please provide a proposal of milestones reflecting planning, recruitment status and data clearing/analysis progress. Include a diagram showing trial stages and milestones.

3.8 FINANCIAL SUMMARY

Please give a rough estimation of the costs expected for the clinical study and the total duration of the study.

Item	Year 1-3	Total
Clinical Project Management		
Project Management: Study Design and Preparation (e.g. Statistical Planning, Protocol, Case Report Form (paper-CRF, e-CRF), Informed Consent	€	€
Case Payment	€	€
Data management, IT (e.g. Database Set-up and Validation Data Entry, Coding, Query Management)	€	€
Biometry	€	€
Quality Assurance (e.g. on-site Monitoring, Data Monitoring and Safety Committee	€	€
Travel (e.g. Study Committees, Meetings)	€	€
Reference Centres	€	€
Materials	€	€
Study Drug	€	€
Fees, Insurance	€	€
Equipment	€	€
Others	€	€
TOTAL	**€**	**€**

[4] Assure that the biostatistician has the expertise to carry out clinical studies, e.g.: GMDS certificate, http://www.gmds.de/texte/zertifikate-weiteres.html; ICH guidance E9 *"Statistical Principles of Clinical Trials"*

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

3.9.1 Co-financing by industry and/or other third parties

In case of industry participation: Co-financing by industry or other third parties is at least

- 50% of the costs for a phase I study.
- 75% of the costs for a phase II study.

The application should briefly describe the type and volume of the co-financing, indicating the respective company or other third party. Details are to be specified in the study protocol:

- 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 funding organization after the review process is finished.
- Declare conflicts of interest

Please don't make any agreements before notion of award has been made; please contact the funding organisation first! Appropriate agreements on intellectual property, confidentiality, publication of results, property rights should be concluded between all those playing a leading part in the conduct of the study. Make sure that the agreements cover ALL relevant points in detail, especially in respect to the exploitation of the results, e.g. proportion of contribution of partners reflected in patents and first as well as last authorship in publications.

3.9.2 OTHER FUNDING

In case you have already submitted the same request for financial support or parts hereof to other institutions, 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".

3.10 DECLARATIONS

3.10.1 Sponsors declaration

The awarding of funds is linked to the condition that the institution employing the principal / coordinating investigator assumes full responsibility and all functions and obligations of the sponsor as listed in chapter 5 of the harmonised Guideline for Good Clinical Practice of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH GCP), notwithstanding the fact that the funding organisation provides additional external funds. In particular, appropriate agreements should be

concluded with the parties conducting the study in order to ensure that the responsibility referred to above can be exercised. A corresponding declaration has to be submitted comprising the assurance that

1. the study will be conducted in accordance with the principles of ICH GCP and
2. the institution will assume the sponsor's responsibilities in accordance with chapter 5 of ICH GCP.

The text of the sponsor's declaration is available on the funding organisation's web sites (http://www.gesundheitsforschung-bmbf.de/_media/_Sponsorerklaerung_07-07-05.pdf). Please use this text for your declaration, which must be duly signed by a representative of the employing institution and the principal / coordinating investigator. The sponsor's declaration should be joined to the application.

3.11 STUDY PROTOCOLL

Please provide one complete study protocol.