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## Leitfaden für die Antragstellung „Zweite Förderphase des Krankheitsbezogenen Kompetenznetzes Diabetes mellitus“

vom 13. August 2010

### INHALTSVERZEICHNIS:

Einleitung	2
1. Description of network management ( <i>only applicable for existing network</i> )	4
2. Description of Consortium	5
3. Description of Subprojects	8
A. Research Projects	8
B. Clinical Trial	13
C. Register / Cohort Study	23
D. Biomaterial Bank	30

# Einleitung

Im Rahmen der Fördermaßnahme „Krankheitsbezogene Kompetenznetze“ stellt das BMBF Fördermittel für die Weiterentwicklung und den Ausbau der krankheitsbezogenen vernetzten Forschung in Deutschland zur Verfügung.

**Anträge sind entsprechend den Vorgaben dieses Leitfadens zu gliedern. Anträge, die den Vorgaben des Leitfadens nicht entsprechen, können ohne weitere Prüfung abgelehnt werden.**

Die Rahmenbedingungen der Förderung für ein krankheitsbezogenes Kompetenznetz zum Thema Diabetes mellitus sind in der Förderrichtlinie [www.gesundheitsforschung-bmbf.de/de/2366.php](http://www.gesundheitsforschung-bmbf.de/de/2366.php) des BMBF niedergelegt.

Die Forschungsanträge **in englischer Sprache** (Format: DIN A4, einseitig, 11 Punkt Arial, doppelseitig bedruckt) können ab sofort **bis spätestens zum 11. November 2010** beim

Projekträger im DLR  
Gesundheitsforschung  
Heinrich-Konen-Str. 1  
53227 Bonn

eingereicht werden.

Der nachfolgende Leitfaden beinhaltet ein Gliederungsschema für die Einreichung des Forschungsantrags:

1. Strukturantrag des KKN Diabetes mellitus (Description of network management)
2. Verbundantrag (Description of Consortium)
3. Teilprojektantrag (Description of Subprojects)

Der Strukturantrag soll nur vom bereits geförderten Kompetenznetz Diabetes mellitus ausgefüllt werden. In diesem sollen die bisherigen Infrastrukturkomponenten des Netzes wie die Netzsteuerung, Kommunikation, IT-Management, Qualitätssicherung, Dienstleistung, Service, Öffentlichkeitsarbeit und Nachwuchsförderung für das bisherige Kompetenznetz Diabetes mellitus dargestellt und Vorstellungen zur Weiterentwicklung der Struktur dargelegt werden. Dieser soll max. 15 Seiten betragen.

Bei den Verbundanträgen darf die Vorhabenbeschreibung 5 Seiten für das übergeordnete Konzept und 10 Seiten pro geplantes Teilprojekt nicht überschritten werden. Für die Beantragung der Teilprojekte sind die entsprechenden Gliederungen (A – D) zu verwenden.

Eine Teilnahme am Auswahlverfahren ist nur durch Einreichung eines Antrags möglich. Der Antrag besteht aus einer **Vorhabenbeschreibung** entsprechend dem Leitfaden und einer projektbezogenen **Vorhabenübersicht** (Excel-Tabelle, Anträge\_KKN\_Diabetes.xls).

Die Vorhabenbeschreibungen sind entsprechend den Vorgaben dieses Leitfadens zu gliedern und dem Projekträger in zehnfacher Ausfertigung plus einer ungebundenen Kopiervorlage sowie im PDF Format auf CD-ROM vorzulegen.

In der beizufügenden Vorhabenübersicht ([http://www.gesundheitsforschung-bmbf.de/\\_media/Anträge\\_KKN\\_Diabetes.xls](http://www.gesundheitsforschung-bmbf.de/_media/Anträge_KKN_Diabetes.xls)) sind die allgemeinen Projektangaben, der Finanzplan und spezielle Angaben zur Projektausrichtung in die vorgegebenen Formularfelder einzutragen. Diese Tabelle ist neben den Vorhabenbeschreibungen im xls-Format auf CD-ROM vorzulegen.

Falls die Vorhaben eine klinische Studie beinhalten, sind zusätzlich die Unterschriften des Studienleiters und des Biometrikers erforderlich.

Die Begutachtung von eingereichten Forschungsanträgen zu themenoffenen Querschnittsprojekten zu den beiden Kompetenznetzen Adipositas und Diabetes Mellitus erfolgt im Nachgang zu den Begutachtungsverfahren der beiden Kompetenznetze. Forschungsanträge zu Querschnittsprojekten sind demzufolge entsprechend zu markieren.

Im Rahmen der Gutachtersitzung sind Informationsgespräche des Gutachterkreises mit den Antragstellern vorgesehen. Auf Verbundebene ist eine Präsentation mit Übersichtsvorträgen und / oder Übersichtspostern geplant.

# 1. Description of network management

*This part is only applicable for the already funded competence network diabetes mellitus. According to the following points the existing and future network management/structure should be described **not exceeding 15 pages**.*

1. Existing network structure
2. Main aims for the future network structure
3. Requested funding (*please summarize in appropriate table*)

## 2. Description of Consortium

Please prepare your application in English **not exceeding 5 pages for the consortium and 10 pages for each subproject proposal.**

Signatures of principal / coordinating investigator are mandatory.

### 1. GENERAL INFORMATION ON THE CONSORTIUM

<b>APPLICANT / COORDINATING INVESTIGATOR</b>	<p><i>In case of multiple applicants the principal investigator / coordinating investigator of the project who will take responsibility for conducting the entire project should be listed first.</i></p> <ul style="list-style-type: none"> <li>• First name, last name, academic title</li> <li>• Institution and department (complete name)</li> <li>• Postal address</li> <li>• Telephone</li> <li>• Fax</li> <li>• E-mail address</li> </ul>																							
<b>TITLE</b>	<p><i>The title of the project (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 organisation. Acronym is optional.</i></p>																							
<b>CONDITION/TOPIC</b>	<p><i>The exact medical condition being addressed.</i></p>																							
<b>OBJECTIVE(S)</b>	<p><i>Which principal research questions are to be addressed? Specify clearly the primary goal of the project. Which results are expected?</i></p>																							
<b>KEY WORDS</b>	<p><i>Maximum 6</i></p>																							
<b>PROJECT DURATION</b>	<p><i>In months</i></p>																							
<b>SUMMARY</b>	<p><i>Please give a summary of the main goals and methodological approach of the project (max. 1600 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.</i></p>																							
<b>PARTICIPATING PARTNERS</b>	<p><i>Example:</i></p> <table border="1"> <thead> <tr> <th>Subproject No.</th> <th>Partner</th> <th>Titel of Sub-project</th> <th>Function in the consortium</th> <th>Contribution</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>University of X....</td> <td>Identification of pharmacogenetic polymorphisms by high-throughput screening</td> <td>Coordination</td> <td>Monitoring, evaluation and processing of results</td> </tr> <tr> <td>2</td> <td>University of Y....</td> <td>Significance of CYP2C9 polymorphism for oral anti-diabetica</td> <td>Preclinical partner</td> <td>Establishing pharmacogenetic assays</td> </tr> <tr> <td>..</td> <td>...</td> <td>...</td> <td>...</td> <td>...</td> </tr> </tbody> </table>				Subproject No.	Partner	Titel of Sub-project	Function in the consortium	Contribution	1	University of X....	Identification of pharmacogenetic polymorphisms by high-throughput screening	Coordination	Monitoring, evaluation and processing of results	2	University of Y....	Significance of CYP2C9 polymorphism for oral anti-diabetica	Preclinical partner	Establishing pharmacogenetic assays	..	...	...	...	...
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..	...	...	...	...																				
<b>CONSORTIUM FROM THE FIRST PHASE</b>	<input type="checkbox"/> yes <input type="checkbox"/> no																							

## **2. ACHIEVEMENTS OF THE FIRST FUNDING PERIOD**

*Only fill out if applicable*

**2.1. Describe achievements in infrastructure, organisational support and implementation of instruments.**

**2.2. Describe the contribution of the consortium to the development of the entire competence network in the first funding phase. What were the most important achievements of networking e.g. methods developed, biobanks, well-characterized patient cohorts, databases, service components?**

## **3. FUTURE OBJECTIVES AND INNOVATION OF THE CONSORTIUM**

### **3.1. RESEARCH OBJECTIVES OF THE CONSORTIUM**

Describe planned research priorities with respect to the current state of the art. Give a clearly defined thematic focus. Which medical problem is to be addressed? Which results are expected?

### **3.2. NOVEL ASPECT AND FUTURE IMPACT**

What is the novel aspect of the proposed investigations? Which impact will the results have on clinical practice (e.g. prevention, diagnosis, therapy) or understanding of the addressed disease?

### **3.3. CONTRIBUTION OF THE CONSORTIUM TO THE COMPETENCE NETWORK ON DIABETES MELLITUS**

Describe planned activities and their impact to strengthen interaction and cooperation in the network.

## **4. STRUCTURE OF THE PLANNED CONSORTIUM**

### **4.1. INTERNAL MANAGEMENT AND OVERALL CONCEPT OF THE CONSORTIUM**

Which 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? Which structure is available, respectively will be implemented for an efficient cooperation within the entire competence network?

### **4.2. NETWORKING**

Give an assessment of how the future project is contributing to the goals of the competence network. Describe how an added value is reached and synergy is realized.

### 4.3. TIMEFRAME/MILESTONES

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

### 5. FINANCIAL SUMMARY

**Example:**

Subproject No.	Partner	Total costs of project	Applied BMBF Funds	Obtained re-search grants, relating to network infrastructure	Co-financed by industry or other sources
1	xyz GmbH	500.000 €	250.000 €	250.000 € (DFG)	250.000 €
2	University of...	300.000 €	300.000 €	150.000 € (BMBF)	0

### 3. Description of subprojects (N XY, refer to main list)

The following outline is generally relevant for research projects. In case you want to apply for funding of a **clinical trial** (including a diagnostic study), a **register/cohort study**, or a **biobank**, please proceed to the respective outlines in part B to D of this guideline.

#### A. Research Project (subproject)

The description of each research project should not exceed 10 pages maximum.

##### 1. GENERAL INFORMATION ON THE SUBPROJECT

<b>PRINCIPLE INVESTIGATOR AND CO-INVESTIGATORS OF THE SUBPROJECT</b>	Name, address, telephone, fax, e-mail <ul style="list-style-type: none"> <li>• First name, last name, academic title</li> <li>• Institution and department (complete name)</li> <li>• Postal address</li> <li>• Telephone</li> <li>• Fax</li> <li>• E-mail address</li> </ul>
<b>TITLE</b>	<i>The title of the project (not exceeding 140 characters) should be precise. In case of funding this title shall be quoted in the annual reports of the funding organisation. Acronym (max 40. characters) is optional.</i>
<b>OBJECTIVE(S)</b>	<i>Which principal research questions are to be addressed? Specify clearly the primary goal of the project. Which results are expected?</i>
<b>KEY WORDS</b>	<i>Maximum 6</i>
<b>SCHEDULED DURATION WITHIN ENTIRE PROJECT</b>	<i>In months. Please quote i) the time period for which funding is requested (max. 3 years) and ii), the date when funding should begin.</i>
<b>SUMMARY</b>	<i>Please give a summary of the main goals and the methodological approach 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 subproject. 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.</i>
<b>PROJECT FROM THE FIRST PHASE</b>	<input type="checkbox"/> yes <input type="checkbox"/> no

##### 2. RESULTS OF THE FIRST FUNDING PERIOD

Only fill out if applicable

###### 2.1. SUMMARY

Provide a summary of your project. If your project is a **clinical trial**, fill out the “protocol summary” for clinical trials.

## **2.2. ORIGINAL AIMS OF THE PROJECT**

Describe the original aims at the starting point of your project.

## **2.3. SCIENTIFIC RESULTS**

Describe (no more than 3 pages) the scientific highlights so far of your project. Compare the obtained results with the schedule and milestones envisaged in the initial proposal.

## **2.4. RELEVANT PUBLICATIONS AND PATENTS**

List all publications directly resulting from the activities of the funded project (here, only those publications are to be cited in which sponsoring through the BMBF in the context of the competence network has been mentioned univocally). Attach an abstract of these publications, where available, in an annex list also any patents or patent applications. Indicate if a publication represents the joint activities of two or more network groups.

## **2.5. NETWORKING**

Provide a summary (max 1 page) how you have contributed to networking. Focus (i) on the use of the consortium/network structure by the project and (ii) on the special contributions of the project to the overall aims of the consortium and the entire network.

# **3. DESCRIPTION OF THE SUBPROJECT/FOLLOW-UP PROPOSAL**

## **3.1. STATE-OF-THE-ART AND OWN PREVIOUS WORK**

Describe the international state-of-the-art and your own previous work in the field. Give 5 of your most relevant publications of the past 3 years and the relevant patents over the last 5 years.

## **3.2. AIMS**

What is the hypothesis to be tested? What is the aim/purpose of the subproject? What results are expected? Which are the novel aspects of the subproject?

## **3.3. METHODOLOGY**

Please describe briefly the key methods used in the proposed project. Indicate which methods are established in your group and which methods will be established through collaborations. For subtasks entirely delegated to other groups please provide a letter of collaboration.

## **3.4. RESOURCES**

Does the project involve utilization of (characterized) biomaterial banks or collections, patient registers or cohorts? If yes, please specify the nature of the respective infrastructure and how access is granted and organised. Are potential co-founders informed? If yes, how? How is the co-authorship regulated?

## **3.5. WORKING PLAN INCLUDING MILESTONES**

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

## **3.6. NETWORKING**

What is the special contribution of the subproject to the goals of the consortium and the entire network? How does the project benefit from the consortium and the entire network?

## **3.7. REFERENCES**

Publication list according to numerical appearance in the text.

### **3. 8. FINANCIAL PLAN**

Please structure the financial plan by completing the table “financial plan for subproject No...” as outlined in the table below.

### **3.9. CO-FINANCING**

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

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

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

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

### **3.10. DISSEMINATION AND EXPLOITATION STRATEGIES**

Please indicate how the expected results of the subproject will be used. Describe the proposed arrangements for disseminating the results of the research to potential users.

Appendix: Financial Plan for Subproject No. ...

Type of expenditure	1 <sup>st</sup> year (months)	2 <sup>nd</sup> year (months)	3 <sup>rd</sup> year (months)	1 <sup>st</sup> year (EUR)	2 <sup>nd</sup> year (EUR)	3 <sup>rd</sup> year (EUR)	Total of BMBF funds applied (EUR)	Co-financed by industry or others (EUR)
<b>PERSONNEL</b>								
Scientist*(TV-L 13)	6	12	12	28.182,78	56.365,56	56.365,56	140.913,90	0
Graduate student*(TV-L13/2)	12	12	12	28.182,78	28.182,78	28.182,78	84.548,34	0
Technician*								
Engineer*								
Others*								
<b>CONSUMABLES</b>								
<b>EQUIPMENT</b> (to specify)								
<b>COMMISSIONS</b> (to specify)								
<b>TRAVEL</b>								
<b>OTHER</b> (to specify)								
<b>TOTAL of BMBF funds applied</b>								
<b>TOTAL of co-financed by other sources</b>								

\* Please use global employment rates of the BMBF for calculating the salaries

(Insert lines according to space required)

**Appendix: Financial Plan for first funding period (if applicable)**

Type of expenditure	1 <sup>st</sup> year (months)	2 <sup>nd</sup> year (months)	3 <sup>rd</sup> year (months)	1 <sup>st</sup> year (EUR)	2 <sup>nd</sup> year (EUR)	3 <sup>rd</sup> year (EUR)	Total of BMBF funds applied (EUR)	Co-financed by industry or others (EUR)
<b>PERSONNEL</b>								
Scientist*								
Graduate student*								
Technician*								
Engineer*								
Others*								
<b>CONSUMABLES</b>								
<b>EQUIPMENT</b> (to specify)								
<b>COMMISSIONS</b> (to specify)								
<b>TRAVEL</b>								
<b>OTHER</b> (to specify)								
<b>TOTAL of BMBF funds applied</b>								
<b>TOTAL of co-financed by other sources</b>								
funds spent till end of 1 <sup>nd</sup> funing period								

## B. Clinical Trial

The application for a clinical trial should **not exceed 10 pages for the headings 1. to 11.**, including a maximum of 1 page of references (DIN A4, 11 point Arial). Structure your application using the headings listed below. Make an entry under every heading. For the information of the reviewers, refer to the respective chapter in the trial protocol for further details if necessary. **Signatures of principal / coordinating investigator and responsible biostatistician are mandatory. Submit application, appendix, and the trial protocol according to GCP.**

### 1. STUDY SYNOPSIS

<b>APPLICANT / COORDINATING INVESTIGATOR</b>	Name, address, telephone, fax, e-mail  <i>In case of multiple applicants the principal investigator / coordinating investigator<sup>1</sup> of the trial who will assume responsibility for conducting the clinical trial, should be listed first.</i> <ul style="list-style-type: none"> <li>• First name, last name, academic title</li> <li>• Employment status</li> <li>• Institution and department (complete name)</li> <li>• Postal address</li> <li>• Telephone</li> <li>• Fax</li> <li>• E-mail address</li> </ul>
<b>TITLE OF STUDY</b>	<i>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.</i>
<b>CONDITION/TOPIC</b>	<i>The medical condition being studied.</i>
<b>OBJECTIVE(S)</b>	<i>Which principal research questions are to be addressed? Specify clearly the primary hypotheses of the trial that determine sample size calculation.</i>
<b>INTERVENTION (S)</b>	<i>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.</i>  <u>Experimental intervention:</u>  <u>Control intervention:</u>  <u>Duration of intervention per patient/subject:</u>
<b>KEY INCLUSION AND EXCLUSION CRITERIA</b>	<u>Key inclusion criteria:</u> <u>Key exclusion criteria:</u>
<b>OUTCOME(S)</b>	<u>Primary efficacy endpoint:</u> <u>Key secondary endpoint(s):</u> <u>Assessment of safety:</u>
<b>STUDY TYPE</b>	<i>e.g. randomized / non-randomized, type of masking (single, double, observer blind), type of controls (active / placebo), parallel group / cross-over</i>
<b>STATISTICAL ANALYSIS</b>	<u>Efficacy:</u> <u>Description of the primary analysis and population</u> <u>Safety:</u>

<sup>1</sup> "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) This definition should be used accordingly for non-drug trials/ studies: (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."

	<u>Secondary endpoints:</u>
<b>SAMPLE SIZE</b>	<u>To be assessed for eligibility (n = ...)</u> <u>To be allocated to trial (n = ...)</u> <u>To be analysed (n = ...)</u>
<b>TRIAL DURATION</b>	<u>First patient/subject in to last patient/subject out:</u> <u>Duration of the entire trial:</u>
<b>SUMMARY</b>	Please give a summary of the main aspects of the project (max. 1600 characters). The project summary serves two main purposes: i) It will inform the multidisciplinary review committee of the principal aspects e.g. goals, design, subjects, expected outcome of your 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.
<b>PARTICIPATING CENTERS</b>	<i>How many centres will be involved?</i> <i>How many centres have signed an agreement to participate? To be detailed in the trial protocol</i>
<b>PROJECT FROM THE FIRST PHASE</b>	<input type="checkbox"/> <i>yes, please fill out chapter 2.</i> <input type="checkbox"/> <i>no, please proceed to chapter 3.</i>

## 2. CLINICAL TRIAL OF THE FIRST FUNDING PERIOD

*Only fill out if applicable*

### 2.1 General Information

#### 2.1.1. Title / Acronym

#### 2.1.2. Principal / Coordinating Investigator

Name, address, Tel, Fax, E-mail

#### 2.1.3. Persons responsible for design, management, and analysis of the trial

Name, address, Tel, Fax, E-mail

#### 2.1.4. Medical problem

Description of the medical problem

#### 2.1.5. Hypothesis

What was the hypothesis to be tested?

### 2.2. TRIAL DESIGN

#### 2.2.1. Trial design

#### 2.2.2. Amendments

#### 2.2.3 Trial interventions/Follow-ups

#### 2.2.4. Inclusion/Exclusion criteria

#### 2.2.5. Duration of the trial

#### 2.2.6. Originally planned time schedule

### **2.2.7. Current time schedule**

Recruitment, treatment, follow-up, and analysis periods

### **2.2.8. Outcome measures**

Primary and secondary outcome measures

### **2.2.9. Methods against bias**

What are the used methods against bias? (e. g. randomization method, blinding)

### **2.2.10 Power calculations**

#### **2.2.11. Patient Recruitment**

2.2.11a Originally planned number of patients

2.2.11b Current number of patients

#### **2.2.12. Trial sites**

2.2.12a Originally planned number of recruiting centres

2.2.12b Current number of recruiting centres

## **2.3. TRIAL-SUPPORTING FACILITIES**

What trial-specific facilities and other resources are being used for conducting the trial?

What are the used measures for quality assurance? Please comment on the supervision of the trial.

## **2.4 CO-FINANCING**

Please indicate any co-financing of the trial by industry.

## **2.5. Results**

How will the results of the trial be used (impact on clinical practice or understanding of intervention/disease)? Will the results be generalizable beyond the immediate research setting?

## **2.6. RELEVANT PUBLICATIONS AND PATENTS**

List all publications directly resulting from the activities of the funded project (here, only those publications are to be cited in which sponsoring through the BMBF in the context of the competence network has been mentioned univocally). Attach an abstract of these publications, where available, in an annex list also any patents or patent applications. Indicate if a publication represents the joint activities of two or more network groups.

## **AIM OF THE PROPOSED TRIAL**

### **3.1. MEDICAL PROBLEM**

Which medical problem is to be addressed? What is the novel aspect of the proposed trial? 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. EVIDENCE**

Set your trial into perspective. 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)<sup>2</sup> and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/ series. If you believe that no relevant previous trials 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 trial.

### **3.3. THE NEED FOR A TRIAL**

What impact will the results have on clinical practice or understanding of the proposed intervention or underlying disease? Why is a trial needed now? How will a) the individual patient and b) society/science benefit from the trial?

### **3.4. STRATEGIES FOR THE EXPLOITATION OF RESULTS**

What will be your strategies for the dissemination of results? Indicate how the expected results of the trial will be used; discuss dissemination of results, especially beyond regular journal publication, describe intended measures, detail potential economic impact.

### **3.5. ADDED VALUE**

Comment on the interaction within the consortium and other potential roles within the network.

## **4. JUSTIFICATION OF DESIGN ASPECTS**

### **4.1. FREQUENCY AND SCOPE OF STUDY VISITS**

What is the proposed frequency and scope of study visits and, if applicable, the duration of post-trial follow-up? Give a schematic diagram (flow chart) of design, procedures and stages.

### **4.2. CONTROL(S)/COMPARATOR(S)**

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

### **4.3. INCLUSION/EXCLUSION CRITERIA**

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

### **4.4. OUTCOME MEASURES**

Justify the endpoints chosen: 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? Justify appropriateness and limitations of composite endpoints, if applicable.

#### **Determination of primary and secondary measures**

How will primary and secondary endpoints be derived from actual measurements, e.g. how is the figure used in the statistical test calculated from the variables initially measured in the subjects?

### **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?

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).

<sup>2</sup> For definition of a systematic review, see Oxman, AD (1994). Checklists for review articles, BMJ; 309; 648-51.

#### 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, 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.

#### Compliance / Rate of loss to follow up

Provide details for assumptions on compliance issues. On what evidence are the compliance figures based?

What is the assumed rate of loss to follow up? On what evidence is the loss to follow up rate based? How will losses to follow up or non-compliance be handled in the statistical analysis?

#### 4.7. FEASIBILITY OF RECRUITMENT

What is the evidence that the intended recruitment rate is achievable (e.g. pilot study)?

##### a) Pilot study

Has any pilot study been carried out using this design?

##### b) Achievability of recruitment rate

What is the evidence that the intended recruitment rate is achievable? Demonstrate conclusively the potential for recruiting the required number of suitable subjects (the best piece of evidence being pilot studies and preceding studies in a similar population/same institutions). How did you assess that you can recruit the necessary number of patients in each participating centre? Show justification of numbers of eligible patients per trial site in a table. The recruitment plan should show the projected recruitment including the criteria for the selection of trial sites.

#### International collaborations

If the proposed trial includes non-German centres or collaboration with organisations in other countries please give full details of funding arrangements agreed or under consideration in the trial protocol. Please detail the power of the German component of the trial, as well on its own as part of the international study.

### 5. 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?

### 6. ETHICAL CONSIDERATIONS

Give a description of ethical considerations relating to the trial (assessment of risks and benefits, care and protection for research participants, protection of research participants' confidentiality, informed consent process).

### 7. TRIAL MANAGEMENT

#### 7.1 MAJOR PARTICIPANTS *(please indicate roles of major participants)*

#	Name	Affiliation	Responsibility / Role	Signature
			Principal/Coordinating Investigator	

Please indicate trial expertise of all above-mentioned participants by citing relevant publications and/or specifying major role in ongoing trials (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 trial.

Professional backgrounds/expertise should be detailed in an appendix to the trial protocol (refer to the respective chapter in the trial protocol).

Who is responsible for statistics? Professional background/expertise<sup>3</sup> should be given. Though not mandatory, certification is highly desirable.

#	Name	Affiliation	Responsibility/Role	Signature
			Trial Statistician/ Responsible for Statistics	

## 7.2 TRIAL-SUPPORTING FACILITIES

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

## 7.3 QUALITY ASSURANCE/MONITORING

What are the proposed measures for quality assurance? Describe and justify the monitoring strategy (percentage of source data verification, number of items to be monitored, number of monitor visits per trial site).

## 7.4 SAFETY

Please comment on the planned supervision of the trial (DMSC); give name and affiliation of independent DMSC members.

*Arrangements for the management of the trials will vary according to the nature of the trial proposed. However, all should include an element of expert advice and monitoring, that is entirely independent of the principal/coordinating investigator and the medical institution involved. This will normally take the form of a scientific advisory board/trial steering committee (TSC) and/or an independent data monitoring and safety committee (DMSC).*

*It is recognised that these arrangements may not always be appropriate and the committees needed may vary according to the nature of the trial. Thus, the arrangements for supervision should be detailed and justified. The role of these committees can comprise to monitor and supervise the progress of the trial (including the safety data and the critical efficacy endpoints at intervals), to review relevant information from other sources, to ensure adherence to protocol, to consider interim analyses, to advise whether to continue, modify, or stop a trial, and provide the funding organisations with information and advice.*

*Applicants should submit their proposed arrangements for overseeing of the trial and a suggested **membership and affiliations** for the committee(s) (name, title, address and telephone number should be given in the trial protocol). A minimum of 3 members should be named.*

## 8. REFERENCES

Publication list according to numerical appearance in the text.

## 9. TRIAL TIMELINE FLOW / MILESTONES

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

<sup>3</sup> e.g. GMDS certificate, <http://www.gmds.de/texte/zertifikate-weiteres.html>; see also: ICH guidance E9 "Statistical Principles of Clinical Trials"

## **10. FINANCIAL DETAILS OF THE STUDY**

### **10.1 FINANCIAL SUMMARY**

Indicate total duration of the trial, the period of time for which funding is requested, and when funding should begin.

The overall expenditure should be summarized in the table below. Please, provide both man months and € for employment costs and state the requested funds separately for each year of the trial. Funds can only be granted for research activities. Do not include patient care costs.

	Organizational Segment	Institution/ Participant/ Trial Site	No of items/ Kind of equipment/ Explanation	Qualification of staff	TVöD/ BAT	Total months	Total years	Total (€)	y1 (m/€)	y2 (m/€)	y3 (m/€)	y... (m/€)
1	Clinical project management											
2	Project management											
3	Data Management											
4	Biometry											
5	Monitoring		number of visits per site number of days per visit monitoring costs per day total no of visits (€/ visit)									
6	Trial committees	no of DMSC members	no of meetings (€/ person)									
7	Meetings/ Travel	no of attendees	no of meetings (€/ person)									
8	Case payment		examinations per subject/patient hours of staff per subject/patient €/ patient x no of patients									
9	Reference centers		no of samples (€/ sample)									
10	Materials		consumables trial manuals, files, forms									
11	Trial drug		€/ patient									
12	Insurance		€/ patient									
13	Fees											
14	Equipment											
15	Other											
<b>TOTAL</b>								€	€	€	€	€

m = staff indicated in months; € = other expenditures indicated in Euro

## 10.2 EQUIPMENT

Please list larger instruments available to you for the trial. In case you apply for instruments which are available where you work, but which are not at the project's disposal, please give detailed information.

### Application of instrumentation

Please list all requested instrumentation with price information.

## 10.3 CO-FINANCING BY INDUSTRY AND/OR OTHER THIRD PARTIES

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

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

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

Details are to be specified in the trial protocol:

- Describe the type and volume of support (including any services or consumables provided free of charge, e.g. drugs for the trial).
- 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 trial and the publication of its results. A statement giving such assurances will be demanded by the funding organizations after the review process is finished.

**Please don't make any agreements before notion of award has been made; please contact the funding organisations 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 trial.

### Agreement with manufacturer on variation of authorisation:

If the trial is aimed at extending the indication of a drug, modifying its mode of administration/preparation or dosage, or target population, the manufacturer of the drug must assure in writing that he will undertake to apply for a variation of the authorisation at the Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices) if the trial result is favourable. A corresponding statement should be joined to the protocol.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.<sup>4</sup>

## 10.4 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 trial 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".

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<sup>4</sup> Detailed information can be found in particular in the "Gemeinsamer Standpunkt zur strafrechtlichen Bewertung der Zusammenarbeit zwischen Industrie, medizinischen Einrichtungen und deren Mitarbeitern" (Common position concerning the consideration of cooperation between industry, medical institutions and their staff from the aspect of criminal law) published by the Verband forschender Arzneimittelhersteller (Association of Research-Based Pharmaceutical Companies) (<http://www.vfa.de/de/vfa/gemeinsamerstandpunkt.html>)

## 11. STUDY PROTOCOL IN ACCORDANCE WITH ICH GCP

Append the trial protocol in English in accordance with ICH GCP (cf. chapter 6 of ICH GCP, "Clinical Trial Protocol and Protocol Amendment(s)"). The topics laid down there may be adjusted slightly to reflect the needs of non-drug studies.

Should you consider any requirement not applicable, relevant or appropriate, a clear statement justifying the omission of the information specified shall be provided on each occasion.

The final version of the protocol has to be submitted to the funding organization together with the statement by the ethics committee after the review process, but prior to any notion of award.

**Note:** Any potential conflicts of must be disclosed in the study protocol. The rules set forth in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" have to be observed by analogy ([www.thelancet.com](http://www.thelancet.com)).

## C. Register / Cohort Study

Please prepare your application in English **not exceeding 10 pages for the headings 1. to 9.**, including a maximum of 1 page of references (DIN A4, 11 point Arial). **Signatures of principal / coordinating investigator and responsible biostatistician/data manager are mandatory.**

### 1. SYNOPSIS

<b>APPLICANT / COORDINATING INVESTIGATOR</b>	Name, address, telephone, fax, e-mail  In case of multiple applicants the principal investigator / coordinating investigator should be listed first. <ul style="list-style-type: none"> <li>• First name, last name, academic title</li> <li>• Employment status</li> <li>• Institution and department (complete name)</li> <li>• Postal address</li> <li>• Telephone</li> <li>• Fax</li> <li>• E-mail address</li> </ul>
<b>TITLE</b>	<i>The title of the project (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.</i>
<b>CONDITION/TOPIC</b>	<i>The medical condition being studied.</i>
<b>OBJECTIVE(S)</b>	<i>Which principal research questions are to be addressed? Specify clearly the primary goal of the project. Which results are expected?</i>
<b>KEY WORDS</b>	<i>Maximum 6</i>
<b>TYPE OF PROJECT</b>	
<b>PROBANDES (KEY INCLUSION AND EXCLUSION CRITERIA)</b>	
<b>MAIN OUTCOMES TO BE ANALYSED</b>	
<b>STATISTICAL ANALYSIS</b>	<i>Strategy:</i> <i>Anonymisation or Pseudonymisation of data:</i>
<b>SIZE AND DURATION OF REGISTER/STUDY</b>	
<b>SUMMARY</b>	<i>Please give a summary of the main goals of the project (max. 1600 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.</i>
<b>PARTICIPATING CENTERS</b>	
<b>PROJECT FROM THE FIRST PHASE</b>	<input type="checkbox"/> yes <input type="checkbox"/> no

### 2. RESULTS OF THE FIRST FUNDING PERIOD

*Only fill out if applicable*

#### 2.1. SUMMARY

Provide a summary of your project. Please, also fill out the “protocol summary for clinical trials” (see below).

## **2.2. ORIGINAL AIMS OF THE PROJECT**

Provide a summary of your project.

## **2.3. SCIENTIFIC RESULTS**

Describe (no more than 3 pages) the scientific highlights so far of your project. Compare the obtained results with the schedule and milestones envisaged in the initial proposal.

## **2.4. RELEVANT PUBLICATIONS AND PATENTS**

List all publications directly resulting from the activities of the funded project. Here, only those publications are to be cited in which sponsoring through the BMBF in the context of the competence network has been mentioned univocally.

Attach an abstract of these publications, where available, in an annex list also any patents or patent applications. Indicate if a publication represents the joint activities of two or more network groups.

## **2.5. NETWORKING**

Provide a summary (max 1 page) how you have contributed to networking. Focus (i) on the use of the network structure by the project and (ii) on the special contributions of the project to the overall aims of the network.

# **3. AIM OF THE PROJECT**

## **3.1 MEDICAL PROBLEM**

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

## **3.2 EVIDENCE**

Set your project into perspective. Give references to relevant publications and running comparable projects. What is the novel aspect that will be studied by the proposed project?

## **3.3 THE NEED FOR THE PROJECT**

What impact will the results have on clinical practice or understanding of the disease? Why is the project needed now? How will a) the individual patient and b) society/science benefit from the register/study?

## **3.4 STRATEGIES FOR THE EXPLOITATION/DISSEMINATION OF RESULTS**

Indicate how the expected results of the project will be used; discuss dissemination of results, especially beyond regular journal publication, describe intended measures, detail potential economic impact. If applicable, how is the scientific community informed of the availability of data?

## **3.5 ADDED VALUE**

Comment on the interaction within the consortium and other potential roles within the network.

# **4. JUSTIFICATION OF DESIGN ASPECTS**

## **4.1. TYPE OF PROJECT**

Is it a clinical/epidemiological register or cohort study?

In case of an epidemiological register/cohort study: Is the project population-based? Which degree of completeness will be achieved? Which region will be covered?

In case of a clinical register/ cohort study: Which institutions of the health care system will contribute to the project (number of private practices, regional and university hospitals, regions covered, completeness of patients recorded by the institutions)?

Describe and justify the population to be studied (inclusion/exclusion criteria). Include reflections on generalisability and representativeness.

What is the planned duration for the project?

#### **4.2. DATA ITEMS TO BE ANALYSED**

Justify the data items chosen: Are there other projects that have utilized them before or guidelines proposing these data items? What is the planned follow-up for a single patient? Discuss the relevance of the data items for the target population. Are gender specific aspects adequately addressed?

#### **4.3. METHODS AGAINST BIAS**

What measures against bias due to selection or confounding will be implemented? Which additional information will be documented to for confounding? Please comment on anticipated non-response and missing data.

#### **4.4. DATA ACQUISITION AND STORAGE**

How will the patients be elected and recruited for the project? How will the participating institutions be motivated for a timely and accurate data acquisition? Which instruments will be used to record the data? Are the instruments validated and reliable? Which standards will be used to classify diagnoses and stages of the diseases?

Describe the concept of data acquisition and storage. How will the personal responsible for data acquisition be trained?

Comment on the accessibility of data origins and on the possibilities to use or integrate already existing sources of data.

#### **4.5. BIOMETRIC CONCEPT / STATISTICAL ANALYSES**

What is the proposed strategy of statistical analysis? Which data items and variables will be included in the analyses? What are the intended recruitment rate and total number of patients necessary for these analyses? Which concrete statistical evaluations are planned at what time and which methods will be used? What is the assumed rate of loss due to follow up or missing/incomplete data? On what evidence are these assumptions based?

#### **4.6. FEASIBILITY OF RECRUITMENT**

What is the evidence that the intended recruitment rate and total number of patients for the project is achievable? Demonstrate conclusively the potential for recruiting the required number of suitable subjects (the best piece of evidence being pilot data collections and projects in a similar population/institution).

#### **4.7. International collaborations**

If the proposed project includes non-German centres or collaboration with organisations in other countries please give full details of funding arrangements agreed or under consideration.

### **5. ETHICAL CONSIDERATIONS**

Comment on ethical considerations relating to the project (confidentiality, informed patient consent).

### **6. PROJECT MANAGEMENT**

**6.1. MAJOR PARTICIPANTS** *(please indicate roles of major participants)*

#	Name	Affiliation	Responsibility / Role	Signature
			Principal/Coordinating Investigator	
			Responsible for Statistics	
			Responsible for Quality Assurance/Data Management	

Please indicate the expertise of all above-mentioned participants by citing own relevant publications and/or specifying major role in ongoing comparable research projects (list max. 5 publications of the last 5 years per person). Give the professional background of all participants.

## 6.2. PROJECT-SUPPORTING FACILITIES

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

## 6.3. QUALITY ASSURANCE

Describe and justify the concept for quality assurance. How is the data integrity and plausibility be controlled? Describe the actual organisational and technical measures for quality assurance and quality control (e.g. second control of data which cannot be controlled by plausibility tests, coding of data, second control of coding, documentation of data corrections). How and when will they be implemented? Are these e.g. outlined in a special quality manual (“Operationshandbuch”)? Comment on the usefulness of feedback strategies concerning data quality.

Which indicators are used to measure and quantify the quality of the register concerning e.g:

- structures (e.g. indicators measuring data plausibility)
- processes (e.g. indicators measuring the organisation of data acquisition)
- results (e.g. indicators measuring correctness, completeness, representativeness and accuracy).

Comment on the necessity of an external quality assurance/monitoring.

## 6.4. DATA SAFETY CONCEPT

How will the existing legal requirements for data safety be met? Describe the data safety concept applied and the planned data flow (diagram). If applicable, provide positive vote of the data security organisation in charge. Depending on the type of project, is anonymisation or pseudonymisation of data planned? Comment on the following aspects of the data safety concept, if applicable:

- Technical and organisational instruments
- Central patients list (localisation)
- Identification data
- Pseudonymisation and depseudonymisation (localisation)
- Informed patient consent
- Patient right of access to personal data
- Storage time of data
- Workflow for quality assurance
- Safety of data transmission and documentation
- Policy document including all legal regulations and agreements

## 7. REFERENCES

Publication list according to numerical appearance in the text.

## **8. TIMELINE FLOW / MILESTONES**

As funding by BMBF will critically depend on the progress according to milestones, please provide a proposal of milestones reflecting planning, recruitment status and data clearing/analysis progress. Include a diagram showing stages and milestones. Comment on the possibility of sustainable establishment of the project after BMBF funding, if applicable.

## **9. FINANCIAL DETAILS OF THE STUDY**

### **9.1. FINANCIAL SUMMARY**

Indicate total duration of the project, the period of time for which funding is requested, and when funding should begin.

The overall expenditure should be summarized in the table below. Please, provide both person-months and € for employment costs and state the requested funds separately for each year of the project.

	Organizational Segment	Institution/ Participant/ Trial Site	No of items/ Kind of equipment/ Explanation	Qualification of staff	TVöD/ BAT	Total months	Total years	Total (€)	y1 (m/€)	y2 (m/€)	y3 (m/€)	y... (m/€)
1	Scientific Management											
2	Organisational Management											
3	Data (Security) Management											
4	Statistical data analysis											
5	Quality assurance											
7	Meetings/ Travel	no of attendees	no of meetings (€/ person)									
8	Documentation payment		documentation per subject/patient hours of staff per subject/patient €/ patient x no of patients									
10	Materials		Consumables									
			trial manuals, files, forms									
14	Equipment											
15	Other											
<b>TOTAL</b>								€	€	€	€	€

m = staff indicated in months; € = other expenditures indicated in Euro

## 9.2. EQUIPMENT

In case you apply for instruments which are available where you work, but which are not at the project's disposal, please give detailed information.

Please list all requested instrumentation with price information.

## 9.3. CO-FINANCING BY INDUSTRY AND/OR OTHER THIRD PARTIES

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

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

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

Details are to be specified:

- Describe the type and volume of support (including any services or consumables provided free of charge).
- 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 project and the publication of its results. A statement giving such assurances will be demanded by the funding organizations after the review process is finished.

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 project.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.<sup>5</sup>

## 9.4. 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 for the project.

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".

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<sup>5</sup> Detailed information can be found in particular in the "Gemeinsamer Standpunkt zur strafrechtlichen Bewertung der Zusammenarbeit zwischen Industrie, medizinischen Einrichtungen und deren Mitarbeitern" (Common position concerning the consideration of cooperation between industry, medical institutions and their staff from the aspect of criminal law) published by the Verband forschender Arzneimittelhersteller (Association of Research-Based Pharmaceutical Companies) (<http://www.vfa.de/de/vfa/gemeinsamerstandpunkt.html>)

## D. Biomaterial Bank

Please prepare your application in English **not exceeding 10 pages for the headings 1. to 9.**, including a maximum of 1 page of references (DIN A4, 11 point Arial). **Signatures of principal / coordinating investigator and responsible biostatistician/data manager are mandatory.**

### 1. SYNOPSIS

<b>APPLICANT / COORDINATING INVESTIGATOR</b>	<p><i>Name, address, telephone, fax, e-mail</i></p> <p><i>In case of multiple applicants the principal investigator / coordinating investigator of the project who will take responsibility for conducting the entire project should be listed first.</i></p> <ul style="list-style-type: none"> <li>• <i>First name, last name, academic title</i></li> <li>• <i>Institution and department (complete name)</i></li> <li>• <i>Postal address</i></li> <li>• <i>Telephone</i></li> <li>• <i>Fax</i></li> <li>• <i>E-mail address</i></li> </ul>
<b>TITLE</b>	<i>The title of the project (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 organisation. Acronym is optional.</i>
<b>CONDITION/TOPIC</b>	<i>The medical area being addressed.</i>
<b>OBJECTIVE(S)</b>	<i>Please specify the relation of the project within the network or to single subprojects. Comment on the correlation/connection to the entire consortial research.</i>
<b>KEY WORDS</b>	<i>Maximum 6</i>
<b>PROJECT DURATION</b>	<i>In month</i>
<b>SUMMARY</b>	<i>Please give a summary of the main goals of the project (max. 1600 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.</i>
<b>PARTICIPATING CENTERS</b>	
<b>PROJECT FROM THE FIRST PHASE</b>	<input type="checkbox"/> <i>yes</i> <input type="checkbox"/> <i>no</i>

### 2. RESULTS OF THE FIRST FUNDING PERIOD

*Only fill out if applicable*

#### 2.1. SUMMARY

Provide a summary of your project.

#### 2.2. ORIGINAL AIMS OF THE PROJECT

Describe the original aims at the starting point of your project

#### 2.3. SCIENTIFIC RESULTS

Describe (no more than 3 pages) the scientific highlights so far of your project. Compare the obtained results with the schedule and milestones envisaged in the initial proposal.

#### **2.4. RELEVANT PUBLICATIONS AND PATENTS**

List all publications directly resulting from the activities of the funded project. Here, only those publications are to be cited in which sponsoring through the BMBF in the context of the competence network has been mentioned univocally. Attach an abstract of these publications, where available, in an annex. List also any patents or patent applications. Indicate if a publication represents the joint activities of two or more network groups.

#### **2.5. NETWORKING**

Provide a summary (max 1 page) how you have contributed to networking. Focus (i) on the use of the network structure by the project and (ii) on the special contributions of the project to the overall aims of the network.

### **3. AIM OF THE PROJECT**

Which medical area/disease entity is to be addressed? Does the biomaterial bank relate to a specific disease(s)? What are the novel aspects that will be studied by the proposed biomaterial bank itself or within the network and/or subprojects? Which principal research questions/hypotheses to be addressed, if applicable in cooperation with subprojects? Bring them into order indicating major and minor motivations / starting hypotheses of the investigation(s) planned.

#### **3.1. EVIDENCE**

Set your BMB into perspective. Do related (systematic) collections exist? In which context were these collections sampled (basic and/or clinical research, treatment context)? Have relevant results been drawn? Give references to any relevant (systematic) BMB(s) and/or (own) publications, if applicable. What are the novel aspects of the planned BMB?

#### **3.2. THE NEED FOR A BMB**

What impact will potential results provide for the clinical practice or understanding the disease? Why is a (systematic) collection necessary? How will the society/science benefit from the BMB?

#### **3.3. RATEGIES FOR THE EXPLOITATION/DISSEMINATION OF RESULTS AND MATERIALS**

What will be your strategies for the dissemination of results? Indicate how the expected results of the BMB will be used; discuss dissemination of results, especially beyond regular journal publication, describe potential sustainability measures (i.e. open to scientific community or non-academic research). If applicable, how is the scientific community in general informed of the availability of samples?

#### **3.4. ADDED VALUE**

Comment on the interaction within the consortium and other potential roles within the network.

### **4. ORGANISATION AND BREADTH OF INTENDED BMB**

#### **4.1. TYPE OF BMB**

What organisational model does apply to your intended BMB? Is the BMB itself performing research? Is the purpose of the BMB exclusively the collection and distribution of biomaterials and data without own research projects? Will the BMB project provide services (RNA/DNA extraction, immunohistology/TMA, PCR, Affymetrix Chips, etc) on assignment of other projects in the consortium?

- Centralised collection (multiple providers, primary storage in one place and limited access for third parties) or
- decentralized collection (multiple providers, primary storage in one place, broad access for and investigations by third parties different from the holder) or
- decentralized collection of cooperative nature (storage and/or investigation of collected materials primarily decentral)

What biological material is intended to be sampled (nature [tissue or sample type] and numbers)?

Comment on the primary goal of the material collection:

- Is the material primarily stored for routine diagnostic or therapeutic purposes and can additionally be used for research questions? If applicable, in which amount yet? Is the treatment context embedded in a clinical study (purpose commitment)? If applicable, in which amount yet?
- Is the material only sampled and stored for research question(s)?

What is the planned duration for the BMB?

#### **4.2. POPULATION TO BE STUDIED**

Describe and justify the (patient) population to be studied (inclusion/exclusion criteria). Include reflections on generalisability.

#### **4.3. DATA AND MATERIAL ACQUISITION AND STORAGE**

Describe the concept of data and material acquisition and storage.

- Which data are intended to be sampled and stored (data of patient, data of the sample(s), data of sample analysis)?
- Describe, if applicable, yet obtained numbers and comment on data protection.
- Does the database, or is intended to contain clinical, genetic or pathological information?
- Who does or will provide that input and where?
- Who is responsible for update and maintenance of the data base?
- Which instruments will be used to record the data? Are the instruments validated and reliable?
- How will the personal responsible for data acquisition be trained?
- How will the patients be selected and recruited for the BMB?
- Which standards will be used to classify diagnoses and stages of the disease(s)?
- Comment on the potential accessibility of related resources (if applicable, cf. 2.1) and on the possibilities to use or integrate already existing sources or data.

#### **4.4. FEASIBILITY OF COMPREHENSIVE SAMPLING**

What is the evidence that the intended recruitment rate and total number of samples/patients for the BMB is achievable? In case of existing (systematic) collections, which publications of the last 2 years are based on this material bank?

#### **4.5. INTERNATIONAL COLLABORATIONS**

If the proposed BMB includes non-German centres or collaboration with organisations in other countries please give full details of funding arrangements agreed or under consideration.

### **5. ETHICAL CONSIDERATIONS**

Specify the ethical considerations relating to the BMB (informed patient consent, purpose commitment declaration, interest in property, personal rights). Do you/did you ask for permission to use the clinical/genetic/pathological data for research purposes? At best, a 'Letter of Intent' (LOI) from respective partners/institutions is provided.

## 6. BMB OPERATORSHIP AND MANAGEMENT

### 6.1. OWNERSHIP

Who will be the operator of the BMB? What will be the legal form of the BMB? Where is the ownership defined?

- Is the acquisition of ownership intended or the concession of life estate (w/o acquisition of ownership) on the samples? If any of these, by what means can the different regulations be met?

According to your organisational model, what measures are intended to support potential long-term usage?

- How is access to the BMB organised? Are potential co-founders informed? If yes, how?

- How is the co-authorship regulated?

- How are formal aspects, e.g. ethical review and/or rationing with scarce material taken into account? If applicable, how many material/data applications did you receive in the last 2 years? If applicable, how were/are material/data applications reviewed (e.g. independent board?)

- Do scientists pay for samples? (how much)? Is there a fee difference between internal and external usage?

### 6.2. MAJOR PARTICIPANTS *(please indicate roles of major participants according to your organisational model)*

#	Name	Affiliation	Responsibility / Role	Signature
			Principal/Coordinating Investigator	

Who is responsible for statistics? Professional background/expertise should be given.

#	Name	Affiliation	Responsibility/Role	Signature
			Responsible for Statistics	

Who is responsible for quality assurance and the data documentation?

#	Name	Affiliation	Responsibility/Role	Signature
			Responsible for Data Assurance	

Please indicate the expertise of all above-mentioned participants by citing own relevant publications and/or specifying major role in ongoing comparable research projects (list max. 5 publications of the last 5 years per person).

### 6.3. BMB-SUPPORTING FACILITIES

Which BMB-specific facilities and other resources are available for conducting the systematic collection?

### 6.4. QUALITY ASSURANCE

Describe and justify the concept for quality assurance. Describe the actual organisational and technical measures for quality assurance and quality control (coding of data, second control of coding, documentation of data corrections). Are GLP guidelines implemented? Have quality procedures been developed? Are they formulated in specific manuals (Standard operation procedures, SOPs)?

### 6.5. DATA PROTECTION CONCEPT

How will the existing legal requirements for data protection be met? Describe the data protection concept applied and the planned data and work flow (diagrams). If applicable, provide positive votes of the data protection organisation in charge. Depending on organisational model and purpose of the BMB, is anonymisation of data applicable? Comment on the following aspects of the data protection concept:

- Technical and organisational instruments
- Central patients list (localisation)
- Patient identification data
- Pseudonymisation and depseudonymisation (localisation, where does this process take place)
- Informed patient consent
- right of withdrawal
- purpose commitment declaration
- Storage time of data
- Workflow for quality assurance
- Safety of data transmission and documentation
- Criteria of material dissemination
- Policy document including all legal regulations and agreements

## 7. REFERENCES

Publication list according to numerical appearance in the text.

## 8. TIMELINE FLOW/MILESTONES

As funding by BMBF will critically depend on the progress according to milestones, please provide a proposal of milestones reflecting planning, recruitment status and data clearing/analysis progress. Include a diagram showing stages and milestones. Comment on the possibility of sustainable establishment of the BMB after BMBF funding.

## 9. FINANCIAL DETAILS OF THE STUDY

### 9.1. FINANCIAL SUMMARY

Indicate total duration of the BMB project, the period of time for which funding is requested, and when funding should begin.

The overall expenditure should be summarized in the table below. Please, provide both man months and € for employment costs and state the requested funds separately for each year of the project.

### 9.2. EQUIPMENT

In case you apply for instruments which are available where you work, but which are not at the project's disposal, please give detailed information.

Please list all requested instrumentation with price information.

### 9.3. CO-FINANCING BY INDUSTRY AND/OR OTHER THIRD PARTIES

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

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

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

Details are to be specified:

- Describe the type and volume of support (including any services or consumables provided free of charge).
- 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 BMB and the publication of its results. A statement giving such

assurances will be demanded by the funding organizations after the review process is finished.

**Please don't make any agreements before a formal notion of award has been received; 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 BMB.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.<sup>6</sup>

#### **9.4. 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 for the BMB.

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".

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<sup>6</sup> Detailed information can be found in particular in the "Gemeinsamer Standpunkt zur strafrechtlichen Bewertung der Zusammenarbeit zwischen Industrie, medizinischen Einrichtungen und deren Mitarbeitern" (Common position concerning the consideration of cooperation between industry, medical institutions and their staff from the aspect of criminal law) published by the Verband forschender Arzneimittelhersteller (Association of Research-Based Pharmaceutical Companies) (<http://www.vfa.de/de/vfa/gemeinsamerstandpunkt.html>)

	Organizational Segment	Institution/ Participant/	No of items/ Kind of equipment/ Explanation	Qualification of staff	TVöD/ BAT	Total months	Total years	Total (€)	y1 (m/€)	y2 (m/€)	y3 (m/€)	y... (m/€)
1	Scientific BMB Management											
2	Organisational BMB Management											
3	Data (Security) Management											
4	Statistical data analysis											
5	Quality assurance											
6	Meetings/ Travel	no of attendees	no of meetings (€/ person)									
7	Documentation payment		documentation per sample/patient hours of staff per sample/patient									
8	Materials		€/ patient x no of patients									
9	Equipment		Consumables, laboratory expenses									
10	Other											
<b>TOTAL</b>								€	€	€	€	€

m = staff indicated in months; € = other expenditures indicated in Euro