Bundesministerium
für Bildung
und Forschung

Leitfaden für die Antragstellung im Rahmen der Fördermaßnahme „Studien in der Versorgungsforschung II“

Im Rahmen der Fördermaßnahme “Studien in der Versorgungsforschung II“ stellt das BMBF Fördermittel zur Verfügung, die für qualitative und/oder quantitative Untersuchungen von versorgungsrelevanten Fragen beantragt werden können. Jeder Antrag muss einem der drei nachfolgend genannten Module zugeordnet werden:

Modul 1: Qualitative Analysen
Modul 2: Nicht-interventionelle quantitative Studien
Modul 3: Interventionelle Studien zum Versorgungsgeschehen

Der vorliegende Leitfaden stellt die Anforderungen für die Antragstellung in der ersten Verfahrensstufe (Vorlage einer strukturierten Vorhabenbeschreibung; vgl. Punkt 7.2.1 der Bekanntmachung des Bundesministeriums für Bildung und Forschung der Richtlinien zur Förderung von Studien in der Versorgungsforschung II) detailliert dar und ergänzt die Förderrichtlinien www.gesundheitsforschung-bmbf.de/de/4441.php des BMBF.

Jeder Antrag besteht aus zwei Teilen:

a. der Vorhabenübersicht (Kontaktdaten, Kurzbeschreibung), die über ein Internetformular vorgelegt werden
b. der Vorhabenbeschreibung als PDF-Dokument inkl. Finanzierungsplan.

Beide Teile sind durch die Projektleiterin oder den Projektleiter elektronisch über ein Internet-Portal einzureichen. Sollte der Antrag von mehreren Partnern gemeinsam gestellt werden, ist ein verantwortlicher Projektleiter oder eine verantwortliche Projektleiterin als Ansprechpartner bzw. Ansprechpartnerin zu benennen, der bzw. die die Antragstellung koordiniert (Koordinator bzw. Koordinatorin).

Beachten Sie bei der Einreichung Ihres Antrags folgende Hinweise:

1. Es wird dringend empfohlen, den Antrag in englischer Sprache einzureichen, da die Begutachtung durch ein international besetztes Gremium erfolgt.
2. Die Koordinatorin/der Koordinator stellt zur Antragstellung zunächst folgende Unterlagen als **EIN** PDF-Dokument zusammen:

- die Vorhabenbeschreibung nach den Vorgaben dieses Leitfadens (Umfang: max. 20 Seiten, einseitig, Format: DIN A4, 11 Punkt Arial, 1,5-zeilig, Randbreite 2 cm)
- Sämtliche Anlagen (gemäß Vorgaben des Leitfadens)

3. Das Einreichen des Antrags erfolgt über das Internet-Portal https://www.pt-it.de/ptoutline/application/versstud10 durch die Koordinatorin/den Koordinator.
4. Zunächst werden die erbetenen Übersichtsangaben zum Vorhaben in das Internetformular eingetragen. Dabei sollen in der Kurzzusammenfassung die wichtigsten Ziele des Forschungsprojekts zusammengestellt werden und dem multidisziplinären Gutachterkreis einen ersten Überblick über die wesentlichen Inhalte des Antrags ermöglichen. Die Zusammenfassung darf nicht länger als 1600 Zeichen sein und sollte keine oder nur wenige Abkürzungen enthalten.
5. Nachdem alle Daten in die vorgegebenen Felder eingetragen sind, können diese über die Vorschaufunktion unter dem Menüpunkt „Kontrolle und Abgabe“ überprüft werden.
6. Anschließend kann unter dem Menüpunkt „Kontrolle und Abgabe“ die Vorhabenbeschreibung (s. Punkt 1) als PDF-Dokument hochgeladen werden. **HINWEIS:** Es kann nur ein einziges PDF-Dokument hochgeladen werden. Mit dem Hochladen weiterer Dokumente werden automatisch alle früheren PDF-Dokumente überschrieben.
7. Ebenfalls unter dem Menüpunkt „Kontrolle und Abgabe“ werden abschließend beide Antragsteile verbindlich eingereicht („Button: Antrag jetzt verbindlich einreichen“). Diese elektronische Version ist die Grundlage der Begutachtung.
8. Nach dem verbindlichen Einreichen des Antrags sind die im Internet verfügbaren Versionen der Vorhabenübersicht und der Vorhabenbeschreibung auszudrucken. Die Vorhabenübersicht darf nicht mehr den Aufdruck „Entwurf“ tragen.

Ihren Antrag (Vorhabenübersicht und Vorhabenbeschreibung) können Sie bis zum **22.11.2012** elektronisch einreichen. Verspätet eingehende Anträge können möglicherweise aus Verfahrensgründen nicht mehr berücksichtigt werden. Damit die Online-Version Bestandskraft erlangt, muss der Antrag in Papierform (s. Punkt 7) ungebunden mit der Unterschrift der Koordinatorin/des Koordinators sowie den in Tab. 9.1 aufgeführten Kooperationspartnern an den Projektträger im DLR für das BMBF, Gesundheitsforschung, Kennwort „Versorgungsforschungsstudien“, Heinrich-Konen-Str. 1, 53227 Bonn, http://www.pt-dlr.de/ innerhalb von zwei Wochen nach der o.g. Vorlagefrist (bis zum 06.12.2012) gesendet werden.

Anträge, die den Vorgaben dieses Leitfadens nicht entsprechen (z.B. keine verbindliche elektronische Einreichung), können ggf. nicht berücksichtigt werden. Das kann auch bedeuten, dass der Antrag nicht in das wissenschaftliche Begutachtungsverfahren aufgenommen wird.

Allgemeine Hinweise

- **Untersuchungen am Menschen**

Im Falle einer positiven Begutachtung muss dem Förderer vor Beginn von Untersuchungen am Menschen für die aktuelle Version des Studienprotokolls das uneingeschränkt positive Ethikvotum der zuständigen Ethikkommission vorgelegt werden. Falls diese ein Votum nicht für erforderlich hält, ist eine entsprechende Erklärung der Ethikkommission vorzulegen.

Bei der Durchführung von Untersuchungen am Menschen und/oder der Gewinnung bzw. Verwendung von menschlichem Probenmaterial sind die Empfehlungen der Deklaration von Helsinki sowie die Richtlinien des CIOMS (Council for International Organization of Medical Sciences) und der WHO (World Health Organization): "Proposed International Guidelines For Biomedical Research Involving Human Subjects" in den jeweils geltenden Fassungen einzuhalten.

Die Registrierung der Studie im nationalen oder in einem internationalen Studienregister ist vorzusehen und bei Beginn der Studie nachzuweisen.

- **Gute wissenschaftliche Praxis**

Im Hinblick auf die Konzeption der Projekte werden die durch nationale und internationale Standards gegebenen Maßstäbe zugrunde gelegt. In diesem Zusammenhang wird u.a. auf folgende Dokumente hingewiesen (die Aufzählung ist nicht abschließend):

- Memorandum III „Methoden für die Versorgungsforschung“ des Deutschen Netzwerkes Versorgungsforschung e.V. (DNVF e.V., 2009 und 2010)
- Leitlinien für Gute Klinische Praxis (GCP), für Deutschland verbindlich umgesetzt durch die GCP-Verordnung, 2004
- Leitlinien und Empfehlungen zur Sicherung von Guter Epidemiologischer Praxis (GEP), 2008
- Gute Praxis Sekundärdatenanalyse (GPS), 2008
- Grundsätze zur Sicherung der guten wissenschaftlichen Praxis (DFG, 1998)

Module 1: Qualitative Empirical Analyses

Within module 1 funding will be granted for qualitative empirical analyses in health care research.

Please prepare your application **not exceeding 20 pages for the headings 1. to 10.** (DIN A4, one-sided, 11 point Arial, 1.5-lined, references in numerical order), plus a maximum of 1 page of references. Structure your application using the headings listed below. Make an entry under every heading/subheading (fill in n.a. if not applicable). Handwritten signatures of coordinating investigator and all major participants are mandatory on the confirmation of the electronic submission of the application (see table 9.1).

Note: Applications that fail to comply with these requirements will be considered incomplete and will constitute grounds to be rejected without peer review.

1. STUDY SYNOPSIS[1]

APPLICANT / COORDINATING INVESTIGATOR	*Name, employment status, institution and department (complete name)* *In case of multiple applicants the coordinating investigator should be listed first.*
TITLE	*The title of the study (not exceeding 140 characters) should be as precise as possible.*
ACRONYM	*Please give an acronym for the title of your study as well.*
TOPIC(S)	*The main research field being studied (e.g. outcome research, implementation research). If applicable the medical condition being studied is to be addressed as well (e.g. diabetes, depression, asthma).*
OBJECTIVE(S)	*Which principal research questions are to be addressed? Specify clearly the primary research question of the study that determine the research method, size and study population.*
TARGET POPULATION	*Describe the population which will be in the focus of the study.*
SAMPLE SIZE	*What is the proposed sample size?*
DATA COLLECTION	*Describe the methodical approach used for data collection.*
DATA ANALYSIS	*Describe the methodical approach used for data analysis.*
STUDY DURATION	*indicated in months (only whole numbers)*

[1] Only for this table „1. Study Synopsis“ 9 point Arial, single-line may be used.

2. RESEARCH QUESTION AND EVIDENCE FROM INTERNATIONAL RESEARCH

2.1 Health Care Issues

Which problem in German health care is to be addressed? Describe shortly the existing situation in health care.

2.2 Aim of the study

Which principal research questions are to be addressed? Bring them into order indicating major and minor motivations/starting hypotheses of the investigation planned. What is the novel aspect of the proposed study? Discuss your choice of the target population.

2.3 Evidence / Current State of Research

Set your study into perspective. Which studies have been conducted either by you or by others? What is the relevance of their results? Give references to any relevant systematic review(s)[2] and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, 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 major research question and the feasibility of the study.

2.4 Theoretical framework

Indicate the theoretical framework/the sensitising concept the study is built on.

2.5 Generalisation

Indicate the possibilities and the goals of generalisation of your planned study.

2.6 Gender aspects

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

3. EPIDEMIOLOGICAL AND ECONOMICAL RELEVANCE OF THE STUDY AND IMPACT ON HEALTH CARE

What impact will the results have on health care? Why is the study needed now? How often does the problem which is addressed by the study occur? How will the individual patient as well as the health care system benefit from the study?

4. DESIGN AND RESEARCH METHODS

4.1 Reasons for the chosen study design

Give an overview of the design you want to apply to answer the research questions above. Present the theoretical background of the chosen method and explain why you have chosen this study design.

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

4.2 Target/study population, Sampling

Justify the population to be studied. What is the proposed sample size and what is the justification for this assumption? Describe and explain your selection decisions and the sampling strategy. What are the decisive factors/criteria defining the sampling?

4.3 Field access and feasibility justification

Describe and justify your field access. Please give details how to overcome access barriers. What is the evidence that the intended recruitment is achievable? Demonstrate conclusively the potential for recruiting the required number of study subjects (the best piece of evidence being pilot studies and preceding studies in a similar population/same institutions). In case of a multicentre study, 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.

4.4 Data collection

Describe in detail your methods of data collection. Give the theoretical background and explanations for the data collection chosen. What is the impact of the method chosen for your data? How do you document the data?

4.5 Method of data analysis

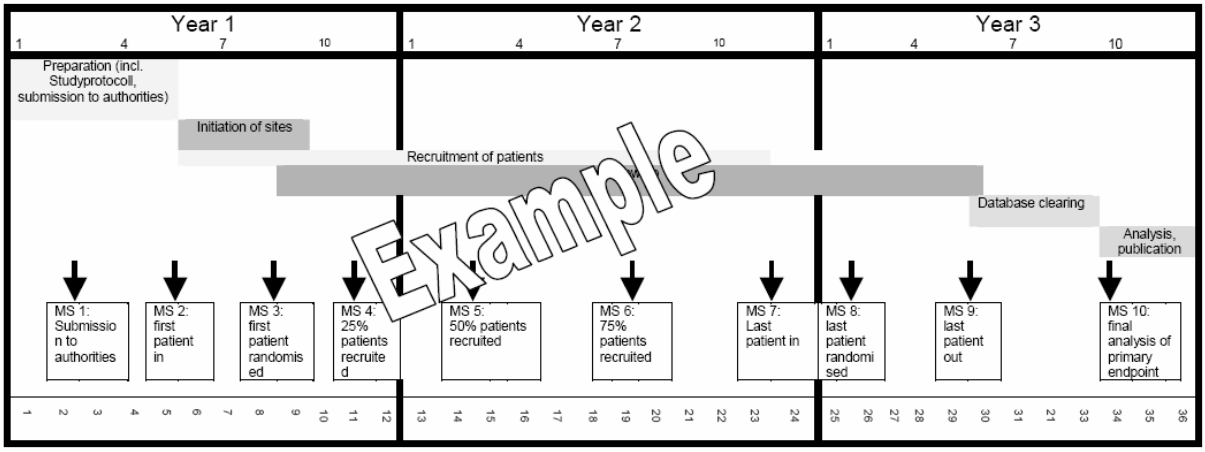
Illustrate your method of data analysis and data interpretation and provide the methodical background. Explain why this method is chosen and describe the planned steps of data analysis.

4.6 Expected results

Give a brief overview of the expected results and their scope and significance. What gain of knowledge can be expected?

5. WORK PLAN

How is the study put into practice? Illustrate the necessary steps and responsibilities. As funding by BMBF will critically depend on the progression of the study according to milestones, please provide a proposal of milestones reflecting planning, recruitment status and data clearing/analysis progress. Make sure that stages and milestones of the study are shown in the diagram. An example of such a diagram is given below.



6. QUALITY ASSURANCE AND SAFTETY

What are the proposed measures for quality assurance during the research process? Please specify how you will ensure that results are verifiable intersubjectively. Comment on the necessity of an external quality assurance/monitoring.

7. ETHICAL AND LEGAL CONSIDERATIONS

Give a description of ethical considerations relating to the study (assessment of risks and benefits, care and protection for research participants, protection of research participants' confidentiality, informed consent process, and crisis intervention) and how to address them adequately. A final version of the study protocol has to be submitted to the funding organisation together with the statement by the ethics committee before possible funding.

8. USE AND IMPLEMENTATION OF RESEARCH RESULTS

Beyond regular scientific publication please outline intended measures to disseminate and implement the results within the health care system. Describe what the results are used for (e.g. patient information, teaching purposes, information for health care providers, changing of health care practise) and the actors involved (e.g. sickness funds, professional societies, general practitioners etc.).

9. STUDY MANAGEMENT

9.1 Major participants

Please indicate roles of major participants, including persons responsible for design, management and analysis of the study. The role of the coordinating investigator has to be defined as specific as possible. It is important that his/her role can be distinguished clearly from the roles/functions of co-investigators in the study.

#	Name	Affiliation	Responsibility / Role	Signature
			Principal/Coordinating Investigator	
			…	
			….	
			Responsible for Special Methodo-logical Aspects/Statistics	
			Recruiting centres (e.g. hospitals, nursing homes, network of health care providers)	
			Study supporting facilities/ institutions (e.g. sickness funds)	
			Responsible for Quality Assurance/Data Management	
			Self-help, support and advocacy organizations of patients (if applicable)	

Please indicate the expertise of all above-mentioned participants by citing own relevant publications and/or specifying their major role in ongoing comparable studies (list only publications of the last 5 years, about 5 publications per person, and/or a maximum of 5 relevant third party funded projects conducted in the area during the five past years). Give

the professional background of all participants. Ensure that the team of investigators has the necessary ranges of disciplines and expertise to carry out the study.

Include tabular scientific Curricula vitae (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, methodological expert) under 12.

Note: Any potential conflicts of interest must be disclosed in the appendix. The rules set forth in the “Uniform Requirements for Manuscripts Submitted to Biomedical Journals” have to be observed by analogy (www.thelancet.com).

9.2 Study-supporting facilities

If data of a sickness fund is used for the study, the access to data must be assured. Sickness funds need to declare that the necessary data is available and will be provided (cf. appendix no. 2). Issues of data protection need to be addressed. If an umbrella organisation or a network of several centres is involved, it is sufficient that the authorised representative of the organisation or the network enters the commitment.

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

9.3 International collaborations

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

10. FINANCIAL DETAILS OF THE STUDY

10.1 Financial Summary

Indicate total duration of the study, the period of time for which funding is requested, and when funding should begin. The funding is usually granted for up to three years.

Funds can only be granted for research activities. Do not include patient care costs.

	PM	Justification of funding requested	Year 1	Year 2	Year 3	(EUR)
Personnel	x					
Scientific						
Non-scientific						
Other						
Consumables	x					
Subcontracts	x					
Case Payment	x					
Travel	x					
Equipment	x					
Overhead/lump sum*	x					
Total amount	x					

PM: Persons Months
*****Academic institutions (Hochschulen und Fachhochschulen) can apply for a lump sum up to 20% of total for indirect costs

10.2 Co-Financing by industry and/or other third parties

Co-financing by industry, sickness funds 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, e.g. travelling costs).
- 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 after the review process is finished.

After notion of award has been made appropriate agreements on intellectual property rights, confidentiality and publication of results are to be concluded between all those playing a leading part in the conduct of the study.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.[3]

10.3 Other funding

In case you have already submitted the same request for financial support or parts hereof to the BMBF or other institutions, please mention this here. Indicate those third parties which will provide funds, free services, or consumables such as trial medication or medical products.

If this is not the case please declare:
"A request for funding this study has not been submitted to any other address. In case I submit such a request I will inform the Federal Ministry of Education and Research immediately".

11. REFERENCES

Please list publications you have quoted within your application. References should be listed according to numerical appearance in the text.

12. APPENDICES

In addition to the supplements listed below, further supplements may be attached, if necessary.

1. Declarations of commitment of participating centres
Participating/recruiting centres must declare their commitment on a separate sheet including their signatures (if an umbrella organisation or a network of several recruiting centres is involved, it is sufficient that the authorised representative of the organisation or the network, signs the sheet) and giving the following details, if applicable:

a) Name of investigator
b) Institution
c) Trial name
d) Trial duration
e) Inclusion/exclusion criteria
f) Strategy for the determination of recruitment figures at the recruiting centre
g) Number of patients expected to be recruited for the trial under the above mentioned criteria
h) Detailed description of the working package conducted by each/the participating centre(s)
i) Conflict of interest
j) Signature

2. Declarations of commitment of sickness funds or other institutions providing data (e.g. German Pension Fund)
If data from sickness funds or other institutions is used for the study, the access to data needs to be clarified and documented.

a) Contact person

[3] 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)

b) Institution
c) Study name
d) Data provided (inclusion/ exclusion criteria, number of patients)
e) Data protection
f) Conflict of interest
g) Signature

3. CVs of academic staff members of participating institutions

Include tabular scientific CVs (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, study statistician, not all collaborating partners at all study sites).

4. Declaration of conflicts of interest

Any potential conflicts of interest must be disclosed. The rules set forth in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" have to be observed by analogy (www.thelancet.com).

Module 2: Quantitative Studies without Intervention

In module 2 quantitative studies will be funded which analyse the German health care system without intervening in the events of care.

Please prepare your application **not exceeding 20 pages for the headings 1. to 10.** (DIN A4, one-sided, 11 point Arial, 1.5-lined, references in numerical order), plus a maximum of 1 page of references. Structure your application using the headings/subheadings listed below. Make an entry under every heading/subheading (fill in n.a. if not applicable). Handwritten signatures of coordinating investigator and all major participants are mandatory on the confirmation of the electronic submission of the application (see table 9.1).

Note: Applications that fail to comply with these requirements will be considered incomplete and will constitute grounds to be rejected without peer review.

1. STUDY SYNOPSIS[4]

APPLICANT / COORDINATING INVESTIGATOR	*Name, employment status, institution and department (complete name)* *In case of multiple applicants the coordinating investigator should be listed first.*
TITLE	*The title of the study (not exceeding 140 characters) should be as precise as possible.*
ACRONYM	*Please give an acronym for the title of your study as well.*
TOPIC(S)	*The main research field being studied (e.g. outcome research, implementation research). If applicable the medical condition being studied is to be addressed as well (e.g. diabetes, depression, asthma).*
OBJECTIVE(S)	*Which principal research questions are to be addressed? Specify clearly the primary research question of the study that determine the research method, size and study population.*
STUDY TYPE	*e.g. analysis of secondary data, prospective cohort study*
TARGET POPULATION	*Describe the population which will be in the focus of the study.*
SAMPLE SIZE	*What is the proposed sample size?* To be assessed for eligibility (n = …) To be allocated to study (n = …) Expected to be analysed (n = ….)
DATA COLLECTION	*Comment shortly on the feasibility of recruitment and main methods against bias which will be used within this study.*
DATA / STATISTICAL ANALYSIS	*Short description of statistical methods to be used.*
STUDY DURATION	First study subject (e.g. patient) in to last study subject out: Duration of the entire study: *indicated in months (only whole numbers)*
PARTICIPATING CENTERS	How many recruiting/participating centers will be involved? (n)

[4] Only for this table „1. Study Synopsis“ 9 point Arial, single-line may be used.

1. RESEARCH QUESTION AND EVIDENCE FROM INTERNATIONAL RESEARCH

2.1 Health Care Issues

Which problem in German health care is to be addressed? Describe shortly the existing situation in health care.

2.2 Aim of the study

Which principal research questions are to be addressed? Bring them into order indicating major and minor starting hypotheses of the investigation planned. What is the novel aspect of the proposed study? Discuss your choice of the target population.

2.3 Evidence / Current State of Research

Set your study into perspective. Explicitly outline the scientific innovation of the proposed project. Which studies have been conducted either by you or by others? What is the relevance of their results? Give references to any relevant systematic review(s)[5] and/or (own) pilot studies, feasibility studies, relevant previous/ongoing trials, case reports/ series. If there are existing international studies on the topic to be investigated, discuss the applicability of the international study results for the German health system, and outline the necessity to conduct the study in Germany. 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 major research question and the feasibility of the study.

2.4 Gender aspects

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

3. EPIDEMIOLOGICAL AND ECONOMICAL RELEVANCE OF THE STUDY AND IMPACT ON HEALTH CARE

What impact will the results have on health care? Why is the study needed now? How often does the problem which is addressed by the study occur? How will the individual patient as well as the health care system benefit from the study?

4. DESIGN AND RESEARCH METHODS

If you find that one of the proposed methodical approaches is not appropriate to answer your research question, please give clear and comprehensible reasons and justify the alternative approach, e.g. study design, you have chosen.

4.1 Reasons for the study design

Give an overview of the design of the prospective study and explain why you have chosen this design. Describe the scheme and give a schematic diagram (flow chart) of design, procedures, and stages. Outline the reasons for choosing a non-interventional approach over an interventional study, if not obvious.

[5] for definition of a systematic review, see Oxman, AD (1994). Checklists for review articles, BMJ; 309; 648-51.

4.2 Target/Study population, Sampling

Describe the target population and justify the population to be studied (inclusion and exclusion criteria). What is the proposed sample size and what is the justification for that calculation? Include reflections on possibilities of generalisation. Make sure that inclusion and exclusion criteria are comparable to usual care situation (external validity).

4.3 Feasibility

Describe and justify your approach to get access to the necessary study objects or data. Please give details how to overcome access barriers. Demonstrate conclusively the potential for recruiting the required number of study subjects/objects (the best piece of evidence being pilot data collections and studies in a similar population/institution) or data(bases). Justify that the analysed situation is comparable to the situation in usual health care.

4.4 Data collection

Describe in detail your methods of data collection. Give a short explanation for the method chosen. What is the impact of the method chosen for your data? Which instruments will be used to record the data? Are the instruments validated and reliable?

Or do you plan to use existing data? Give detailed information on the dataset to be used: Specify the type of dataset, e.g. routine data from sickness funds, or scientific use files. Describe the quality of the existing data. Which characteristics/items that are enclosed in the existing data will be used for this study? How generalizable are the expected results derived from this dataset?

4.5 Methods against bias

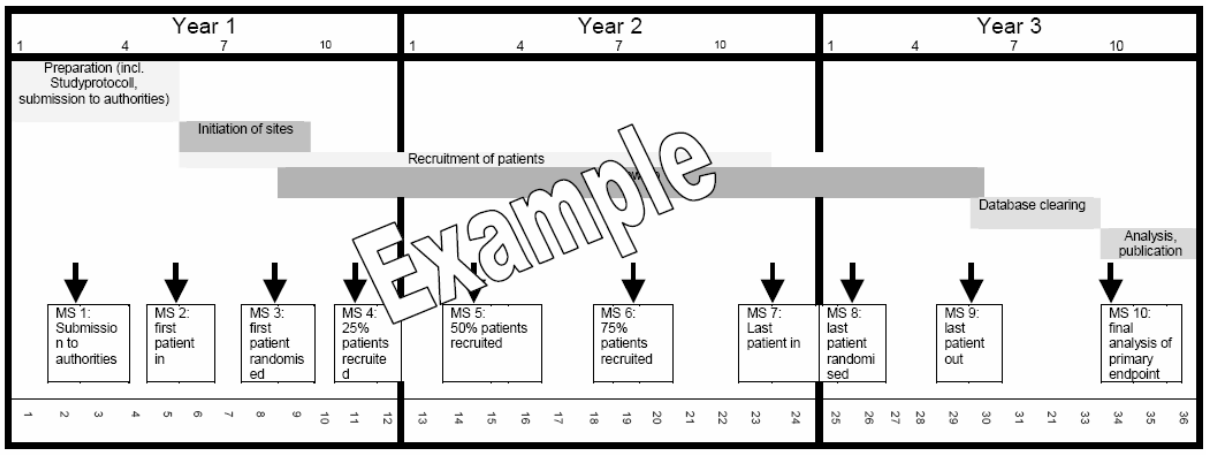
What methods against bias will be implemented? Please comment on anticipated non-response and missing data.

4.6 Biostatistical concept / statistical analysis

Illustrate your method of data analysis. Explain why this method is chosen and describe the planned steps of data analysis. What is the proposed strategy of statistical analysis? Which data items and variables will be included in the analysis? Which are the independent and dependent variables? Which additional information will be documented to adjust for confounding? Please provide examples of the statistical models and assumptions that will be used. Justify clearly the size of the sample and/or the number of study subjects/objects necessary for this analysis.

5. WORK PLAN

How is the study put into practice? Illustrate the necessary steps and responsibilities. As funding by BMBF will critically depend on the study progression according to milestones, please provide a diagram reflecting preparation, data acquisition and/or recruitment, follow-up and data clearing/analysis. Make sure that study stages and milestones are shown in the diagram. An example of such a diagram is given below.



6. QUALITY ASSURANCE AND SAFETY

What are the proposed measures for quality assurance during the research process? How will the data integrity and plausibility be controlled? If applicable, describe the actual organisational and technical measures for quality assurance and quality control. Depending on the type of study, is anonymisation or pseudonymisation of data planned?

7. ETHICAL AND LEGAL CONSIDERATIONS

Give a description of ethical considerations relating to the study (assessment of risks and benefits, care and protection for research participants, protection of research participants' confidentiality, informed consent process) and who to address them adequately. A final version of the study protocol has to be submitted to the funding organisation together with the statement by the ethics committee before possible funding.
Please give an explanation on the legal situation concerning the data set (e.g. owner of data). How will the existing legal requirements for data safety be met? If using secondary data describe the legal path of data access. In this case an agreement of the owner of the data is essential.

8. USE AND IMPLEMENTATION OF RESEARCH RESULTS

Beyond regular research publication please outline intended measures to disseminate and implement the results within the health care system. Describe what the results are used for (e. g. patient information, information for health care providers, changing of health care practise) and the actors involved (e.g. sickness funds, professional societies, general practitioners).

9. STUDY MANAGEMENT

9.1 Major participants

Please indicate roles of major participants, including persons responsible for design, management and analysis of the study. The role of the coordinating investigator has to be defined as specific as possible. It is important that his/her role can be distinguished clearly from the roles/functions of co-investigators in the study.

#	**Name**	**Affiliation** *(only institution and city, no complete address)*	**Responsibility / Role**	**Signature**
			Principal/Coordinating Investigator	
			…	
			Responsible for Special Methodo-logical Aspects/Statistics	
			Recruiting centres (e.g. hospitals, nursing homes, network of health care providers)	
			Study supporting facilities/ institutions *(e.g. sickness funds, central laboratories)*	
			Responsible for Quality Assurance/Data Management	
			Self-help, support and advocacy organizations of patients (if applicable)	

Please indicate the expertise of all above-mentioned participants by citing own relevant publications and/or specifying their major role in ongoing comparable studies (list only publications of the last 5 years, about 5 publications per person, and/or a maximum of 5 relevant third party funded projects conducted in the area during the five past years). Give the professional background of all participants. Ensure that the team of investigators has the necessary ranges of disciplines and expertise to carry out the study.

Include tabular scientific CVs (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, study statistician, not all collaborating partners at all study centres) under 12.

Note: Any potential conflicts of interest must be disclosed in the appendix. The rules set forth in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" have to be observed in analogy (www.thelancet.com).

9.2 Recruiting centres/Study-supporting facilities and institutions

Recruiting centres must detail their commitment on a separate sheet (cf. appendix no. 1) as detailed under 11. If an umbrella organisation or a network of several recruiting centres is involved, it is sufficient that the authorised representative of the organisation or the network enters the commitment. If secondary data of a sickness fund to be used for the study, the access to data must be assured. Sickness funds need to declare that the necessary data is available and will be provided (cf. appendix no. 2). Issues of data protection need to be addressed.

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

9.3 International collaborations

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

10. FINANCIAL DETAILS OF THE STUDY

10.1 Financial Summary

Indicate total duration of the study, the period of time for which funding is requested, and when funding should begin. Funding is usually granted for up to 3 years.

	PM	Justification of funding requested	Year 1	Year 2	Year 3	(EUR)
Personnel	x					
Scientific						
Non-scientific						
Other						
Consumables	x					
Subcontracts	x					
Case Payment	x					
Travel	x					
Equipment	x					
Overhead/lump sum*	x					
Total amount	x					

PM: Persons Months
*****Academic institutions (Hochschulen und Fachhochschulen) can apply for a lump sum up to 20% of total for indirect costs

Funds can only be granted for research activities. Do not include patient care costs.

10.2 Co-Financing by industry and/or other third parties

Co-financing by industry, sickness funds 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, e.g. drugs or medical products 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 after the review process is finished.

After notion of award has been made appropriate agreements on intellectual property rights, confidentiality and publication of results are to be concluded between all those playing a leading part in the conduct of the study.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.[6]

10.3 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 drugs or medical products.

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

11. REFERENCES

Please list publications you have quoted within your application. References should be listed according to numerical appearance in the text.

12. APPENDICES

In addition to the supplements listed below, further supplements may be attached, if necessary.

1. Declarations of commitment of participating centres
Participating/recruiting centres must declare their commitment on a separate sheet including their signatures (if an umbrella organisation or a network of several recruiting centres is involved, it is sufficient that the authorised representative of the organisation or the network, signs the sheet) and giving the following details, if applicable:

a) Name of investigator
b) Institution
c) Trial name
d) Trial duration
e) Inclusion/exclusion criteria
f) Strategy for the determination of recruitment figures at the recruiting centre
g) Number of patients expected to be recruited for the trial under the above mentioned criteria
h) Detailed description of the working package conducted by each/the participating centre(s)
i) Conflict of interest
j) Signature

2. Declarations of commitment of sickness funds or other institutions providing data (e.g. German Pension Fund)
If data from sickness funds or other institutions is used for the study, the access to data needs to be clarified and documented.

a) Contact person
b) Institution

[6] 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)

c) Study name
d) Data provided (inclusion/ exclusion criteria, number of patients)
e) Data protection
f) Conflict of interest
g) Signature

3. CVs of academic staff members of participating institutions

Include tabular scientific CVs (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, study statistician, not all collaborating partners at all trial sites).

4. Declaration of conflict of interest

Any potential conflict of interest must be disclosed. The rules set forth in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" have to be observed by analogy (www.thelancet.com).

Module 3: Interventional Trials in Health Care Research

Within module 3 funding will be granted for trials assessing the effectiveness of therapeutic regimens in routine clinical practise.
Please prepare your application **not exceeding 20 pages for the headings 1. to 10.** (DIN A4, one-sided, 11 point Arial, 1.5-lined, references in numerical order), plus a maximum of 1 page of references. Structure your application using the headings/subheadings listed below. Make an entry under every heading/subheading (fill in n.a if not applicable). Handwritten signatures of coordinating investigator and all major participants are mandatory on the confirmation of the electronic submission of the application (see table 9.1).
Note: Applications that fail to comply with these requirements will be considered incomplete and will constitute grounds to be rejected without peer review.

1. TRIAL SYNOPSIS[7]

APPLICANT / COORDINATING INVESTIGATOR	*Name, employment status, institution and department (complete name)* *In case of multiple applicants the coordinating investigator of the trial should be listed first.*
TITLE OF TRIAL	*The title of the trial (not exceeding 140 characters) should be as precise as possible.*
ACRONYM	*Please give an acronym for the title of your study as well.*
TOPIC(S)	*The main research field being studied (e.g. outcome research, implementation research). If applicable the medical condition being studied is to be addressed as well (e.g. diabetes, depression, asthma).*
OBJECTIVE(S)	*Which principal research questions are to be addressed? Specify clearly the primary research question/hypothesis of the trial that determines sample size calculation.*
STUDY TYPE	*e.g. randomized/non-randomized, type of controls (active, placebo), parallel group/cross-over*
INTERVENTION	*Describe the experimental as well as the control intervention.*
TARGET POPULATION/ SAMPLE SIZE	*Describe the population which will be in the focus of the trial.* *What is the proposed sample size?* To be assessed for eligibility (n = …) To be allocated to trial (n = …) To be analysed (n = ….)
OUTCOME(S)	Primary Patient-Relevant Endpoint of the Trial: Key Secondary Endpoint(s):
DATA COLLECTION	*Comment shortly on the feasibility of recruitment and main methods against bias which will be used within this trial.*
STATISTICAL ANALYSIS	*Short description of methods used for answering the research question, e.g. study design.*
TRIAL DURATION	First study subject (e.g. patient) in to last study subject out: Duration of the entire trial: *indicated in months (only whole numbers)*
PARTICIPATING CENTERS	How many recruiting centers will be involved? (n)

[7] Only for this table „1. Trial Synopsis“ 9 point Arial, single-line may be used.

2. RESEARCH QUESTION AND EVIDENCE FROM INTERNATIONAL RESEARCH

2.1 Health Care Issues

Which problem in German health care is to be addressed? Describe shortly the existing situation in health care.

2.2 Aim of the trial

Which principal research questions are to be addressed? Bring them into order indicating major and minor motivations/starting hypotheses of the investigation planned. What is the novel aspect that will be studied by the proposed trial?

2.3 Evidence / Current State of Research

Set your trial into perspective. What is the rationale for the intervention? Be aware that the efficacy of the intervention has to be substantiated. Which trials have been conducted either by you or by others in order to demonstrate the efficacy of the intervention? What is the relevance of their results? Give references to any relevant systematic review(s)[8] and/or (own) pilot studies, feasibility studies, or relevant previous/ongoing trials. Please present your project in the context of the national and international state of research.

2.4 Gender aspects

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

3. EPIDEMIOLOGICAL AND ECONOMICAL RELEVANCE OF THE TRIAL AND IMPACT ON HEALTH CARE

What impact will the results have on health care? How significant is the trial in terms of its potential impact on improving human health? Why is the trial needed now? How often does the problem which is addressed by the trial occur? How will the individual patient as well as the health care system benefit from the trial?

How does the intervention investigated compare to other interventions for the same condition? Describe any commercial/economical interest of a company/health care provider/sickness or pension fund in the results of the trial or explain why no such interest exists.

4. DESIGN AND RESEARCH METHODS

4.1 Reasons for the study design

Give an overview of the study design of the trial. Please justify your choice shortly. Describe the intervention and give a schematic diagram (flow chart) of design, procedures, and stages.

[8] for definition of a systematic review, see Oxman, AD (1994). Checklists for review articles, BMJ; 309; 648-51.

4.2 Target/Study population

Justify the population which will be in the focus of the trial. Define inclusion and exclusion criteria for the trial objects; include reflections on generalisability. Make sure that inclusion and exclusion criteria are representative for the population that receives/is going to receive the intervention within the regular health care setting (external validity). Justify the choice of control(s)/comparison(s): Is there a gold standard?

4.3 Feasibility of recruitment

What is the evidence that the intended recruitment rate is achievable (e.g. pilot study)? Demonstrate conclusively the potential for recruiting the required number of suitable subjects (the best piece of evidence being pilot studies and preceding trials in a similar population/in the same institutions). The recruitment plan should show the projected recruitment including the criteria for the selection of trial sites. Make sure that the recruiting institutions are representative for the institutions where the intervention is carried out / is going to be carried out within the regular health care setting.

4.4 Outcome measures

Justify the endpoints chosen. Discuss the clinical relevance of the outcome measures for the target population. If you use outcome parameters other than mortality, morbidity (complaints and complications), or health-related quality of life as primary endpoints, please explain why you consider them to be appropriate and valid for measuring patient-relevant outcome. Justify appropriateness and limitations of composite endpoints, if applicable.

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 study subjects to trial groups? If you find that randomisation is not possible, please justify in detail and explain which other methods are used to guarantee consistency of the control(s) and comparable(s).

What measures against bias due to selection or confounding will be implemented? Which additional information will be documented to uncover or avoid confounding? Please comment on anticipated non-response or missing data. Give details on methods to avoid biased assessment of results (e.g. blinded assessment of outcome)?

4.6 Proposed sample size/power calculations

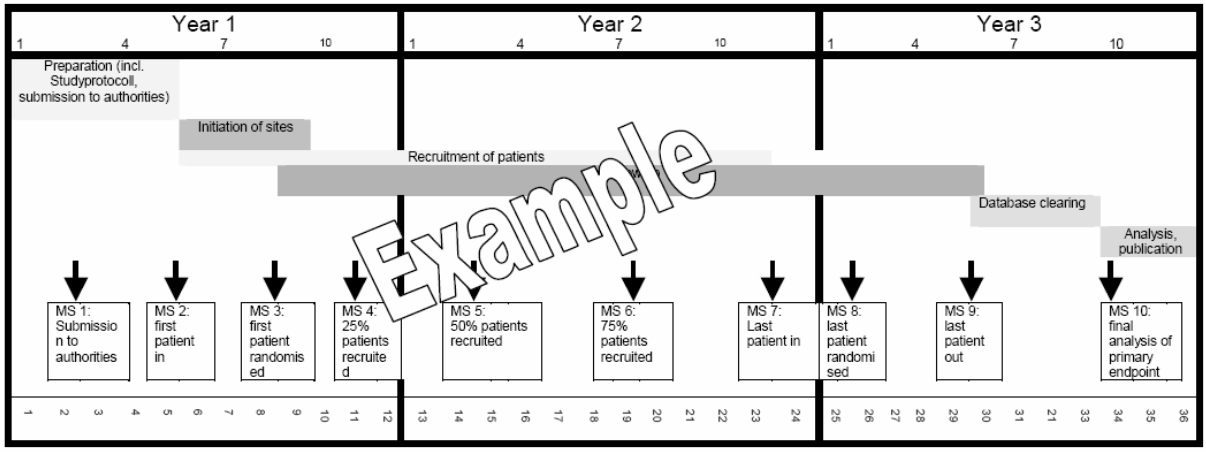
What is the proposed sample size and what is the justification for the assumptions underlying the power calculations? Include a comprehensible, checkable description of the power calculations and sample sizes detailing the outcome measures on which these have been based for both control and experimental 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.

4.7 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? How will missing data and study objects withdrawn from the trial be handled statistically?

5. WORK PLAN

How is the trial put into practice? Illustrate the necessary steps and responsibilities. As funding by BMBF will critically depend on the progression of the trial according to milestones, please provide a diagram reflecting preparation, initiation of centres, recruitment, follow-up, and data clearing/analysis. Make sure that trial stages and milestones are shown in the diagram. An example of such a diagram is given below.



6. QUALITY ASSURANCE AND SAFTETY

What are the proposed measures for quality assurance? Describe the actual organisational and technical measures for quality assurance and quality control. How and when will they be implemented? Are these e.g. outlined in a special quality manual or Standard Operating Protocol? Comment on the necessity of an external quality assurance/monitoring.

Please comment on the planned supervision of the trial. Arrangements for the management of the trials will vary according to the nature of the study proposed. However, all should include an element of expert advice and monitoring, that is entirely independent of the coordinating investigator and the institution(s) involved. This will normally take the form of a scientific advisory board/trial steering committee. Applicants should submit their proposed arrangements for overseeing of the trial and, if applicable, a suggested membership for a committee (name and affiliation of independent members).

7. ETHICAL AND LEGAL CONSIDERATIONS

Give a description of ethical considerations relating to the study (assessment of risks and benefits, care and protection for research participants, protection of research participants' confidentiality, informed consent process, and crisis intervention) and how to address them adequately. A final version of the study protocol has to be submitted to the funding organisation together with the statement by the ethics committee before possible funding.

8. USE AND IMPLEMENTATION OF RESEARCH RESULTS

Beyond regular scientific publication please outline intended measures to disseminate and implement the results within the health care system. Describe what the results are used for (e.g. patient information, teaching purposes, information for health care providers, changing of health care practise) and the actors involved (e.g. sickness funds, professional societies, general practitioners etc.).

9. TRIAL MANAGEMENT

9.1 Major participants

Please indicate roles of major participants, including persons responsible for design, management and analysis of the trial. The role of the coordinating investigator has to be defined as specific as possible. It is important that his/her role can be distinguished clearly from the roles/functions of co-investigators in the trial.

#	**Name**	**Affiliation** *(only institution and city, no complete address)*	**Responsibility / Role**	**Signature**
			Principal/Coordinating Investigator	
			…	
			….	
			Responsible for Trial Statistics	
			Recruiting centres (e.g. hospitals, nursing homes, network of health care providers)	
			Trial-supporting facilities/ institutions (e.g. sickness funds)	
			Responsible for Quality Assurance/Data Management	
			Self-help, support and advocacy organizations of patients (if applicable)	

Please indicate the expertise of all above-mentioned participants by citing own relevant publications and/or specifying their major role in ongoing comparable trials (only list publications of the last 5 years, about 5 publications per person, and/or a maximum of 5 relevant third party funded projects conducted in the area during the five past years).). Give the professional background of all participants. Ensure that the team of investigators has the necessary ranges of disciplines and expertise to carry out the trial.

Include tabular scientific Curricula vitae (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, trial statistician, not all collaborating partners at all trial centres) under 12.

Note: Any potential conflicts of interest must be disclosed in the appendix. The rules set forth in the “Uniform Requirements for Manuscripts Submitted to Biomedical Journals” have to be observed by analogy (www.thelancet.com).

9.2 Recruiting centres/trial-supporting facilities

Recruiting centres must detail their commitment on a separate sheet (cf. appendix no. 1) as detailed under 11. If an umbrella organisation or a network of several recruiting centres is involved, it is sufficient that the authorised representative of the organisation or the network enters the commitment. If data of a sickness fund is used for the trial, the access to data must be assured. Sickness funds need to declare that the necessary data is available and will be provided (cf. appendix no. 2). Issues of data protection need to be addressed.

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

9.3 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 appendix. Please detail the power of the German component of the trial on its own as well as part of the international study.

10. FINANCIAL DETAILS OF THE TRIAL

10.1 Financial Summary

Indicate total duration of the trial, the period of time for which funding is requested, and when funding should begin. Funding is usually granted for up to 3 years.

Funds can only be granted for research activities. Do not include patient care costs.

	PM	Justification of funding requested	Year 1	Year 2	Year 3	(EUR)
Personnel	x					
Scientific						
Non-scientific						
Other						
Consumables	x					
Subcontracts	x					
Case Payment	x					
Travel	x					
Equipment	x					
Overhead/lump sum*	x					
Total amount	x					

PM: Persons Months
*****Academic institutions (Hochschulen und Fachhochschulen) can apply for a lump sum up to 20% of total for indirect costs

10.2 Co-Financing by industry and/or other third parties

Co-financing by industry, sickness funds 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, e.g. drugs or medical products 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 after the review process is finished.

After notion of award has been made appropriate agreements on intellectual property rights, confidentiality and publication of results are to be concluded between all those playing a leading part in the conduct of the trial.

Reference is made to the legal provisions relevant to cooperation between industry, medical institutions and their staff.[9]

10.3 Other funding

In case you have already submitted the same request for financial support or parts hereof to the BMBF or other institutions, please mention this here. Indicate those third parties which will provide funds, free services, or consumables such as trial medication or medical products.

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

11. REFERENCES

Please list publications you have quoted within your application. References should be listed according to their numerical appearance in the text.

12. APPENDICES

In addition to the supplements listed below, further supplements may be attached, if necessary.

1. Declarations of commitment of participating centres
Participating/recruiting centres must declare their commitment on a separate sheet including their signatures (if an umbrella organisation or a network of several recruiting centres is involved, it is sufficient that the authorised representative of the organisation or the network, signs the sheet) and giving the following details:

a) Name of investigator
b) Institution
c) Trial name
d) Trial duration
e) Inclusion/exclusion criteria
f) Strategy for the determination of recruitment figures at the recruiting centre
g) Number of patients expected to be recruited for the trial under the above mentioned criteria
h) Detailed description of the working package conducted by each/the participating centre(s)
i) Conflict of interest
j) Signature

[9] 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)

2. Declarations of commitment of sickness funds or other institutions providing data (e.g. German Pension Fund)

If data from sickness funds or other institutions is used for the trial, the access to data needs to be clarified and documented.

a) Contact person
b) Institution
c) Trial name
d) Data provided (inclusion/ exclusion criteria, number of patients)
e) Data protection
f) Conflict of interest
g) Signature

3. CVs of academic staff members of participating institutions

Include tabular scientific CVs (max. 1 page per person) for academic staff members playing a leading role (i.e. applicant and co-applicants, trial statistician, not all collaborating partners at all trial sites).

4. Declaration of conflict of interest

Any potential conflict of interest must be disclosed. The rules set forth in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" have to be observed by analogy (www.thelancet.com).