Standards for responsible conduct of research at Health

Fundamental guidelines designed to assist the individual researcher and research group at Health in the transparent and trustworthy planning, execution and conclusion of a research project. Each point states when a requirement is mandatory. To help researchers, each point also states how additional information may be collected. Some of the standards are specific to the health scientific research area, while other standards are joint standards covering several professional areas.

Guidelines for responsible conduct of research at Health.

Anyone involved in research activities at Health shall observe Aarhus University's joint policies and guidelines on research integrity and responsible conduct of research. Furthermore, anyone involved in research at Health Aarhus University (AU) shall be aware of and observe a range of specific requirements for research studies performed in the field of health science. Below we account for these requirements.

1. From project initiation to project conclusion - ensuring responsible conduct of research

This section presents a range of fundamental guidelines designed to aid the transparent and trustworthy planning, execution and conclusion of a research project. Each point is accompanied by a note stating if the text presents a *requirement* that must be observed. Each point also states where further information is available.

1.1 *Preparing a research project*

The project description, or protocol, contains a description of the research project. This section and Section 2 on Data present some of the points that need to go into the project description.

Before initiating a research project, it is essential that clear agreements between all participants are discussed and presented in the project description.

This includes agreeing on the following:

- Who participates in the project and which functions and responsibilities have been conferred on the various participating persons/parties.
- Who manages the project and the project manager's function and mandate.
- Which functions and responsibilities are delegated to any external project participants.
- Who will hold potential patent rights derived from the project, the Technology Transfer Office at Aarhus University should be contacted to clarify this aspect.
- Preparation of publications and distribution of authorship in accordance with international provisions, as described in the ICMJE guidelines, also known as the Vancouver guidelines (also see Section 3).
- Who is responsible for the funding of the project, and who will be applying for funding.
- How disputes will be settled, including who holds decision power if consensus is lacking.

As a rule, a cooperation agreement covering the parties involved in the project should always be prepared. The legal aspects of any cooperation agreement or contract with external partners allocating rights to the project results shall be approved by the Technology Transfer Office (TTO) and by the head(s) of the department(s) to which the project will be affiliated.

Guidelines on how to prepare agreements when initiating a research project are detailed in the Danish Ministry of Higher Education and Science's publication from 2009; Guidelines for Good Scientific Practice (in Danish).

All research projects that rely on external funding in the Central Denmark Region shall follow *Provisions on Externally Funded Projects etc., in the Central Denmark Region* (In Danish abbreviated to FAS-regulativet) on administrative handing of the project, including provisions on accounting and staff.

1.2. *Experimental studies*

- The project description shall be completed before experiments are initiated, unless the experiments form part of a pilot study. A pilot study is a pre-study used to specify any guidelines for the final project description. It must be clear when pilot studies conclude and when the final project description, which will form the basis for the subsequent collection of any publication data, will be available.
- The project description shall be drafted in a manner allowing the tests to be repeated, even years later. This means that complete traceability is required with regard to the origin and creation of data.
- During the project, any errors or deviations from the initially planned course of action are stated in the project description/protocol. Any amendments to the project description shall be clear and the reason and date they were made shall be stated. Furthermore, it shall be stated who introduced each amendment.
- If any of the collected data are excluded from the final publication, this shall be stated clearly and the reasons why data were excluded shall also be provided.
- Anyone conducting research in animals shall observe the provisions of the Danish Animal Testing Act, and no such testing may be initiated without previous approval from the Danish Animal Experiments Inspectorate.
- Anyone involved with studies in animals shall have completed an animal study training course.
- Projects which may potentially lead to the development of biological weapons are subject to the approval of Centre for Biosecurity and Biopreparedness.

General guidelines on how to prepare a project description for experimental studies are detailed in the Danish Ministry of Higher Education and Science's publication from 2009; Guidelines for Good Scientific Practice (in Danish).

1.3. *Clinical studies*

- All research projects involving humans or biological material from humans shall be conducted in pursuance of the Helsinki Declaration. If the project is covered by the Danish Act on the Committee on Research Ethics, it shall be notified with the Committee on Research Ethics in the Region where the person responsible for the study is employed.
- Furthermore, research projects initiated and performed at Aarhus University Hospital or any other hospital in the Central Denmark Region shall be reported to the Danish Data Protection Agency through the Joint Regional Notification Service (Regionens Fællesanmeldelse). Research projects initiated and performed at Aarhus University shall be reported directly to the Danish Data Protection Agency.
- Research projects involving pharmaceuticals also require the approval of the Danish Health and Medicines Authority.
- Research projects involving pharmaceuticals and/or utensils shall be performed in accordance with the GCP Executive Order (Good Clinical Practice for Clinical Studies in Pharmaceuticals in Humans). Researchers at Aarhus University may contact the GCP Unit for advice on the guidelines on good clinical practice and monitoring of the project to ensure that provisions are observed.
- In research projects which do not require notification to the Danish research ethics committee system, but to which information from medical records is submitted, such submission of information from medical records shall be approved by the Danish Health and Medicines Authority.
- The Danish research ethics committee system and the Danish Health and Medicines Authority both

have guidelines on the drafting of project descriptions for clinical studies. A joint project description covering all of these points in detail may be prepared.

- Clinical studies, both interventional and observational studies, shall be registered in a public international database, e.g. ClinicalTrials.gov. Assistance for such registration is provided by Èn Indgang.
- If the project includes laboratory analyses performed in a research laboratory, the laboratory should - to the extent possible - follow the guidelines on Good Laboratory Practice (GLP), published by the OECD. If the laboratory analyses are performed at a hospital-based laboratory, the same minimum requirements apply, but such laboratories are often accredited and thus implicitly comply with the GLP.

General guidelines on how to prepare a project description for clinical studies are detailed in the Danish Ministry of Higher Education and Science's publication from 2009; Guidelines for Good Scientific Practice (in Danish).

1.4. *Clinical studies on medical devices*

Medical devices are used to test, monitor, manage or relieve disease in humans. The following are examples of medical devices: syringes, surgical equipment, hospital beds, pacemakers, hip implants and crutches. Clinical testing of medical devices in humans includes any testing involving humans that aims to establish or validate the safety or performance of medical devices. The devices tested may be novel or well-known devices already marketed in Denmark.

All clinical testing of medical devices shall be reported to the Danish research ethics committee system, as projects involving clinical testing are considered health science research projects.
Studies should be reported to the Committee on Research Ethics in the Region where the person responsible for the study is employed. Central Denmark Region, Region of Southern Denmark, North Denmark Region, Region Zealand, Capital Region of Denmark, the Faroese Committee on Biomedical Research Ethics. The Committee will then assess if the proposed testing is in accordance with the Danish Act on Research Ethics Committees. The duty to notify the Committee on Research Ethics covers all clinical tests, regardless of any CE marking.

Furthermore, testing of medical devices shall be reported to the Danish Health and Medicines Authority, which is responsible for the technical/professional assessment of the clinical testing of the devices. At the Danish Health and Medicines Authority's website on medical devices, an introduction to clinical testing of medical devices is available along with instructions on how to lodge an application for testing of medical devices.

For an overall presentation of the preparation and approval of clinical studies, please see Appendix 1, p. 10

1.5 *Register-based research*

In register-based research, the primary research material is electronic data.

Traditional register-based research projects, interview and questionnaire surveys and other projects not involving biological material shall be reported to and approved by the Danish Data Protection Agency if the project comprises sensitive person-attributable data . Reporting is done through the Joint Regional Notification Service (Regionens Fællesanmeldelse) to the Danish Data Protection Agency or directly to the Danish Data Protection Agency, if the research is rooted at Aarhus University.

According to Sections 7 and 8 of the Personal Data Processing Act, sensitive information includes:

- Race or ethnic background
- Political, religious or philosophical conviction
- Affiliation to unions
- Information on health and sexual matters
- Information on criminal matters, substantial social problems and
- other purely private matters.

In pursuance of Section 7, subsection 1 of the Danish Personal Data Processing Act, the concept of *health matters* includes:

- A physical person's previous, current and future physical or mental condition and information about
- Use of medicine and abuse of alcohol, drugs and similar euphoriants.

Projects that only involve non-personal information about its participants are not notifiable with the Danish Data Protection Agency and do not require approval. The statutory provisions, however, shall be observed, but the Data Protection Agency does not enforce any specific requirements related to the project.

Additionally, exemptions from the duty of notification to the Data Protection Agency may be granted in special cases, in pursuance of the Executive Order on Exemptions from the Duty of Notification.

With a view to coordinating and creating coherence in register- and data-based research activities in Denmark, the Coordinating Body for Register-based Research was established to monitor cooperation between researchers and stakeholders responsible for the registers.

The Danish Health and Medicines Authority shall approve any submission of patient record information to e.g. a register-based research project or made to identify patients who are to participate in a questionnaire survey.

The passing on of information from an approved database shall be approved by the database administrator.

2. Data

Scientific data are to be collected and stored in accordance with current statutory rules and other provisions. Data are any material collected systematically for research purposes including electronic data from, e.g. registers but also interviews, images, human material such as blood or tissue or material from

animals, including biobanks. When person-attributable human material is used, permission is needed from both the Danish research ethics committee system and the Data Protection Agency. Furthermore, it should be checked that the persons involved have not lodged a non-usage statement with the Tissue Use Register (Vævsanvendelsesregistret).

The Danish Act on Processing of Personal Data outlines the basic principles to be observed whenever personal data are processed. The Danish Data Protection Agency is the central independent authority, which supervises adherence to the provisions of the Danish Act on Processing of Personal Data.

Below, we outline the general guidelines for responsible conduct of research with regard to data handling:

- The project description shall present how data are collected and recorded.
- Project descriptions shall be stored for a 5-year-period after the project concludes, i.e. in accordance with AU´s Policy on Responsible Research Practice.
- Any corrections made to data during data collection and data recording shall be clear, and the reasons for any changes made shall be stated in order to ensure complete transparency for all changes and additions and thereby ensure data traceability.
- Further instructions on the storage and safekeeping of data are available from The Data Protection Agency's Standard Terms for Research Projects and Executive Order on Safety Precautions (in Danish).
- Data can only be passed on from a previous project to a current project following approval from the Danish Data Protection Agency.
- If data are collected or analysed abroad, an agreement should be made with the project partner in the country in question before data collection is initiated. The researcher based in the country where the data are collected is responsible for obtaining the necessary approvals and permissions and for ensuring that the country's statutory and other provisions are observed. As data will subsequently reach Denmark, the provisions of the Danish Act on Processing of Personal Data shall be observed with regard to the handling and storage of data. For further information, please contact the Technology Transfer Office at Aarhus University.
- In pursuance of the Danish Act on Processing of Personal Data, any data - including biological material - shall be anonymised no later than at the end of the project, unless continued storage is required according to other statutory provisions. Subsequently, it must not be possible to identify any of the individuals who participated in the research project. Anonymisation is achieved when no data can be related to any person, i.e. when no research subjects can be identified from the data. Research projects conclude on the date stated when the project is registered. Data shall not be deleted when the project concludes, but shall be anonymised and stored for a period of 5 years in pursuance of the AU's Policy on Responsible Research Practice, and the Danish Code of Conduct for Research Integrity. Storage also serves to ensure the traceability of data after publication of the research results.
- If the project is a medical trial performed in pursuance of the *Guidelines for Good Clinical Practice*, data shall, in accordance with the Executive Order on Good Clinical Practice, be stored for a minimum period of 5 years as from the conclusion of the trial.

- Data are to be stored at the institution where the research was conducted. However, any conditions made by the project's funding provider should be taken into account. Data that can be related to any person may not be stored on a personal computer, and paper print-outs of such data shall be locked away securely. With regard to storage of data, the provisions outlined in Danish Act on Processing of Personal Data and in the Executive Order on Good Clinical Practice apply. The services of the Danish Data Archive (Dansk Data Arkiv)are available for data storage.

The Personal Data Processing Act's requirements for clinical trials involving medicines and clinical tests of medical devices are described in detail at the Danish Data Protection Agency's website.

3. Publication and authorship

In connection with publication of results once a research project has concluded, the following apply:

- All results from concluded studies should be published – including any negative or inconclusive results.
- Results are to be published as early as possible. It is acceptable that patent applications may give rise to some delay.
- All authors, including supervisors, shall meet all of the following authorship criteria, developed by the ICMJE group (ICMJE), also known as the Vancouver Guidelines:

  - Substantial contribution to idea or design, data collection, analysis or interpretation of the data

    and
  - draft of manuscript or critical revision of the manuscript's content

    and
  - approval of the final manuscript.

    and
  - consent to being responsible for all aspects of the manuscript by making sure that any issues concerning precision and merit of all parts of the work have been sufficiently investigated and solved.

Authorship is based on a requirement that all authors meet all four authorship criteria, cf. ICMJE. Anyone who is attributed authorship shall fulfil the authorship criteria, and everyone fulfilling the authorship criteria shall be attributed authorship.

Rejection of authorship, ghost authorship, gift authorship, guest authorship and planted authorship constitute a breach of responsible conduct of research. For further information, please see Guidelines on Good Scientific Practice (2009, in Danish).

- The criteria used to establish the author sequence should be agreed upon by all project partners at the beginning of the project and may subsequently be revised by joint agreement.
- Contributions from project partners and intellectual contributions from others should be

recognised and cited in the text or under "Acknowledgements" with a wording, which was previously accepted by the persons being acknowledged. Financial or other substantial material aid received for the project should also be stated. Specific guidelines apply to public acknowledgement of private funding of research at state-owned research institutions - see private funding of research (in Danish).

- Before submission of a manuscript, a joint authorship statement, detailing the type and extent of every author's contribution, should be signed. As a minimum, the statement should be kept by the primary author.
- It is recommended that unless statements to the contrary are made, the corresponding author is responsible for ensuring that the article is based on trustworthy research. Some journals demand that one or several authors guarantee that the entire work was made in a trustworthy manner, and that such guarantee forms part of the publication.
- Hidden double publication, i.e. identical or nearly identical publications, sometimes translated into other languages are not acceptable. Conversely, secondary publication (e.g. an English language article subsequently published in Danish in the Journal of the Danish Medical Association) is allowed when this is done openly. Use of the same data or subsets hereof in various presentations does not constitute double publication, provided any data-overlap between the previous and current work is clearly stated to ensure that assessors and readers gain full insight.
- It is important that the contents of the article is in accordance with the information provided in the resume/abstract.
- When authoring and publishing through other channels than journals, the provisions described above should still be followed.

Special authorship rules are in place for large multi-author groups, previously coined multicentre studies. When a large multi-author group conducts studies, the group should identify the persons who will be directly responsible for the manuscript from the onset. These persons should meet the authorship criteria as defined above, and these authors will be the main responsible authors. Journals frequently mention the remaining members of such groups under Acknowledgements. (For more details, please see ICMJE. Multi-author groups, p. 3)

3.1. *Guidelines for reporting*

To increase the homogeneity and strengthen the quality of the reporting of various types of studies, it is recommendable to consult the international guidelines in the field, these are available from the Equator-network.

3.2. *Conflicts of Interest*

All authors shall state any conflict of interest. We recommend using the "ICMJE Uniform Disclosure Form for Potential Conflicts of Interest". Interest conflicts arise when authors or their institutions, assessors or editors are affected by financial or personal interests, which may influence their

judgement, i.e. cause bias. Potential conflicts of interest may be present even when a person believes that an issue does not influence his or her handling of a manuscript.

Editors and proof-readers should not handle their own Manuscripts, nor manuscripts from their own organisation, nor should they in any way depend (economically, advisory board or similar) on private corporations who have an interest in the field. This rule serves to ensure that no changes are introduced in the final revision of the manuscript without the approval of the authors.

4. Cooperation agreements with industry and other institutions

As a researcher you may cooperate with others in various ways. Based on the contents and conditions, it is possible to distinguish between three types of cooperation:

1: Unrestricted grant. In this type of cooperation, a field or topic is typically specified that the grantor wants to support, but it is clearly stated that the only condition made by the grantor is to be informed of the project's results.

2: Commissioned research/funded activities. In this type of cooperation, a consultancy service is provided. All rights therefore belong to the external party and special provisions apply (concerning funded activities) to the calculation of the remuneration as all costs, direct as well as indirect ones, shall be covered.

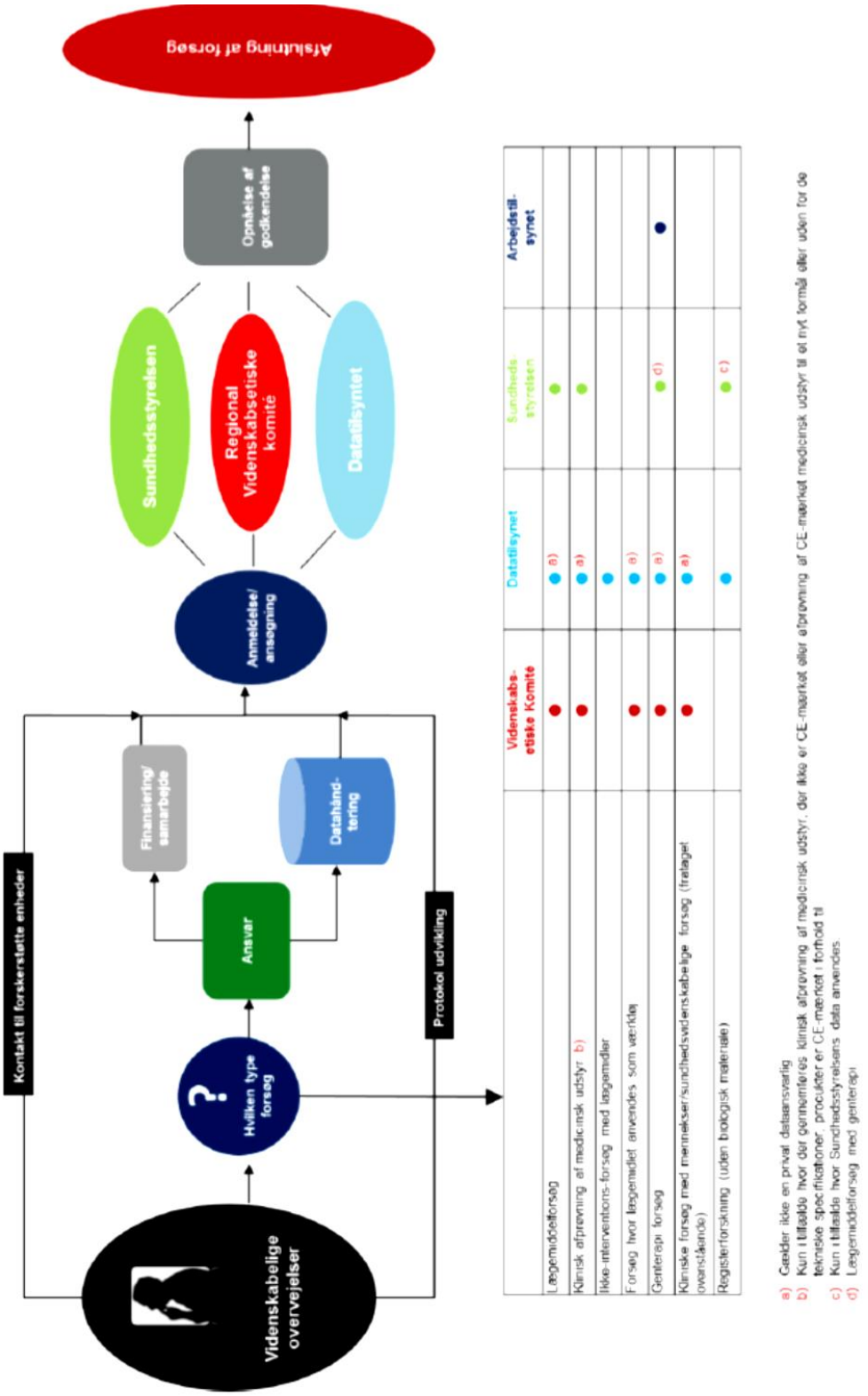
3: Subsidised research. In this type of cooperation, the university may co-finance projects provided that the researchers can document their research interest in the projects. According to Guideline External Funding 2013 (Danish: Instruks Eksterne Midler 2013), the Department Head is responsible for ensuring that a real research interest exists. In this type of cooperation, both parties provide various contributions, and agreements need to be made to establish the parties' rights in relation to the project's results.

It is important in all types of cooperation that the parties' rights and obligations are clear, and it is therefore necessary to enter into a written agreement in each individual case. The agreement should describe who holds project-related rights and how each party contributes.

When cooperating with industry in particular, it is necessary to prepare a written agreement that establishes the rights and obligations of the parties in relation to the project. The cooperation agreement will allow the parties to form realistic expectations and will typically reflect who has initiated the partnership, including who have prepared the protocol and how the project is funded; and it will include a schedule detailing how the results may be published.

For further information and advice and guidance, please contact the Technology Transfer Office. Aarhus University has prepared a set of General Guidelines for Cooperation Agreements (In Danish). Correspondingly, the university hospitals have adopted a set of Joint Guidelines concerning the adoption of cooperation agreements in the clinical field.

Appendix 1. Overview of approval of clinical studies. From *Getting Started with Clinical Research* (In Danish: *Kom godt i gang med klinisk forskning*).



	Videnskabsetiske Komité	Datatilsynet	Sundhedsstyrelsen	Arbejdstilsynet
Lægemiddelforsøg	●	● a)	●	
Klinisk afprøvning af medicinsk udstyr, b)	●	● a)	●	
Ikke-interventions-forsøg med lægemidler		●		
Forsøg hvor lægemidlet anvendes som vanlig	●	● a)		
Genterapi forsøg	●	● a)	● d)	●
Kliniske forsøg med mennesker/sundhedsvidenskabelige forsøg (trataget ovenstående)	●	● a)		
Registerforskning (uden biologisk materiale)		●	● c)	

a) Gælder ikke en privat dataansvarlig
b) Kun i tilfælde hvor der gennemføres klinisk afprøvning af medicinsk udstyr, der ikke er CE-mærket eller afprøvning af CE-mærket medicinsk udstyr til et nyt formål eller uden for de tekniske specifikationer, producenter er CE-mærket i forhold til
c) Kun i tilfælde hvor Sundhedsstyrelsens data anvendes
d) Lægemiddelforsøg med genterapi