



CHECKLIST FOR RESEARCHERS AND MEMBERS OF ETHICS COMMITTEES

1 THE RESEARCH PROTOCOL

1.1 Purpose and methods of research

Research that is deficient in framing of questions, its purpose or its methods is not only unscientific but also unethical. Therefore an ethics committee should also assess the points concerning its purpose and methods in a research protocol. The ethics committee should then pay particular attention to the following:

1.1.1 Planning of research

- justified need for the proposed research,
- framing of questions: has the research been planned so that it can respond to the problem?
- primary and secondary endpoint variables,
- time schedule for the research: is it realistic?
- size of the sample groups and methods of assessment,
- subject selection and exclusion criteria,
- description of measures to be conducted and monitoring of research subjects,
- research arrangements with justifications (reference group, use of placebos, randomisation, blinding).

1.1.2 Weighing of benefits and burdens

- expected health benefit for research subjects and its estimated probability,
- expected burdens and risks for research subjects and their estimated probability,
- options of treatment and estimation of their benefits and burdens compared with the treatment of the research subject,
- if no health benefit is expected for research subjects, comparison between the risks and the scientific benefit of the research.

1.1.3 Course of research, quality assurance and publishing

- course of research and description of measures,
- monitoring and reporting of adverse reactions,
- possible interim analyses,
- handling of results and statistical methods
- publication plan

1.2 Safety of research

The prerequisite for any medical research is that there is enough information on the safety of the research measures, and of the method, medicinal substance or other preparation to be studied before the research can be started. The circumstances during the measures and after them are also part of the safety of the research subjects. Ethics committees should pay particular attention to the following matters:

1.2.1 The product, method or measure studied

- the origin of the products or devices studied (manufacturer of products and composition of medicines);
- earlier findings and their evaluation from the point of view of the present research (laboratory examinations, animal experiments, possible earlier clinical trials);
- risks to the research subject (direct effects and adverse effects on the research subject, foetal effects and possible effects on future generations);
- psychological disadvantages and inconveniences for the research subject (concern, fear, insecurity);
- practical inconveniences to the research subject (special diet, mobility, sexual intercourse, other impacts on every-day life);
- monitoring and reporting of adverse effects during the research ;
- post-trial safety of the research subject (travel, harmful effects emerging afterwards).

1.2.2 The sponsor and the research staff

- the party sponsoring the research and its representative and possible co-operative partners;
- the party carrying out the research;
- the person in charge of research (education, specialities, experience of research),
- principal investigators of the research centres (education, specialities, experience of research),
- other research staff.

1.2.3 Equipment and research circumstances

- appropriateness of the equipment and devices used,
- readiness for dealing with complications and emergency,
- storage and handling of dangerous substances.

1.3 Vulnerable groups

Research protocol and the request for statement must include a statement whether research is going to be conducted with healthy subjects or patients, and whether there are vulnerable groups among the subjects to whom the additional requirements listed in sections 7 to 10 of the Medical Research Act (488/1999) apply. As a separate group can also be mentioned persons whose incapacity for taking part in the decision-making concerning themselves is temporary, but the research cannot wait for their capacity to restore (e.g. first aid situations). Vulnerable groups may also refer to other groups whose participation in research can be ethically precarious, although they are not separately mentioned in the law. Regarding these groups, the ethics committee shall take account, above all, of the following:

- if the research subjects include minors, pregnant women or nursing mothers, prisoners or persons, whose capacity because of mental health disorder, mental retardation or for comparable reason of giving his/her consent is limited;
- if there are other groups among the research subjects whose voluntariness can be questioned and how the voluntariness of their consent has been ensured (conscripts, employees or students of the investigators);
- could the research be carried out with research subjects other than these groups or with less invasive measures
- is the risk or stress for a minor or a incapacitated person entailed in research slight or greater than that (the Medical Research Act only allows a minor risk or stress);
- is the research expected to bring immediate benefit to the research subject's own health or special benefit to the health of persons belonging to the same group in regard to their age or state of health;
- how has the investigation of a minor's or a incapacitated person's own will been taken into account in the research protocol;
- see also special requirements for the information given to research subjects and their representatives (Information to the research subject, chapter 3) and for the consent form (Consent form, chapter 4).

If no consent can be obtained because of the urgency of the matter or the patient's state of health, the following must appear from the research protocol

- is it possible to anticipate the situation so that the patient's or his/her representative's consent can be asked for in advance;
- is it possible to obtain a written informed consent from the patient's representative;
- is the measure so urgent that consent by the research subject or his/her representative cannot be waited for;
- expected immediate benefit of the research measure to the patient's health;
- consent from the research subject or his/her representative (if the research subject is still incapacitated) has to be obtained as soon as possible.

1.4 Data protection

In addition to the Medical Research Ethics Act and the international obligations concerning the status of research patients, ethics committees shall take into account the provisions on the privacy of research subjects, which is regulated at the national level primarily by the Personal Data File Act (523/1999) and the Act on the Openness of Government Activities (621/1999). The Personal Data File Act implements the requirements of the Directive 95/46/EC/24.10.95 by the European Community. The Office of the Ombudsman for Data Protection provides steering and guidance regarding the handling of personal data and supervises the handling of personal data with a view to implementing the objectives of the Personal Data File Act.

In medical research that is not exclusively based on registered data, the registration of personal, health and research data of research subjects presupposes almost without exception an express consent by the research subject. Data protection considerations are of particular interest in research based on DNA samples when the link exist between a sample and the personal data of the person concerned or his/her family. What is said about personal data, can also be taken into account in research based on DNA samples, even when there is no link between the sample and personal data (e.g. storing of samples after the research has been completed, cf. also TUKIJA's guidelines for

pharmaceutical research based on DNA samples). Thus the ethics committees have to pay particular attention on the following:

1.4.1 Purpose, responsibilities and information sources used

- purpose and necessity of the handling of personal data (individualised research object);
- the person or institution in charge of keeping the register and persons involved (research registers must be kept separate from patient data: the identity of the keeper of the register and if the responsibilities for it have been shared);
- information sources used in research (where is the information intended to be acquired from and on which grounds);
- extent of the information to be compiled: what information is necessary for the research.

1.4.2 Handling and protection of information

- confidentiality of information;
- use and handling of information;
- protection of information in various phases of research (e.g. coding, anonymising);
- consideration and implementation of the right of access to information of the registered persons;
- handling of information during the analysis;
- access to code key;
- how long will the information be stored;
- description of the register and its availability to research subjects.

1.4.3 Delivery and disposal of information

- delivery of information (e.g. to sponsors: what information, to whom, for what purpose, on what grounds, is the data identifiable);
- persons and authorities that have access to patient documents, research findings, and access to code keys (to whom, on what grounds);
- post-trial handling of data (filing or disposal).

1.5 Economic considerations

The ethical assessment of medical research is also affected by economic considerations. An ethics committee should try to assess at a more general level if research has enough funding to be feasible and that the research subjects can be taken care of properly. Economic considerations may likewise affect the recruitment of research subjects either through remuneration payable to research subjects or fees payable to investigators (cf. Decree 600/2000 of the Ministry of Social Affairs and Health). The ethics committee should also make sure that the voluntariness of the research subjects is not endangered. The ethics committee must pay particular attention to the following:

- source of funding,
- financial resources for the research: specified cost estimate,
- possible conflicting interests (e.g. employment vis-à-vis the sponsor),
- insuring research subjects: medicines-related injuries insurance and/or patient insurance are the minimum requirements,
- remuneration of research subjects

2 SUMMARY OF THE RESEARCH PROTOCOL

- in Finnish or Swedish,
- clear, avoiding abbreviations and foreign expressions (understandable also to lay people),
- maximum five pages,
- title of research, names of the sponsor and the person in charge of the research,
- other known research centres and their main investigators,
- purpose, goal and justifications for research (motive, primary and secondary endpoint variables,
- study design and methodology,
- in the case of clinical trial on pharmaceuticals, basic information on the pharmacology of the medicinal substance (e.g. what group does the substance belong to),
- safety of the medicinal substance/method studied on the basis of previously obtained information (findings and side effects of animal experiments and earlier phases),
- size of sample groups, main criteria for inclusion and exclusion,
- possible vulnerable groups involved
- measures conducted on research subjects and their predicted risks, benefits and burdens,
- treatment choices,
- justification for the use of placebos,
- handling of personal data and data protection arrangements (sources, recording and storing, transfer and disposal).

3 ETHICAL EVALUATION BY THE PERSON IN CHARGE OF THE RESEARCH

The person in charge of research must be professionally and scientifically competent and acquainted with the research concerned, he/she must observe and assess the ethical considerations related to the research (also when they do not give cause for immediate measures, e.g. owing to considerable usefulness of the research) and be willing to assume responsibility for the research to the extent required in section 5 of the Medical Research Act. Based on this criteria, he/she shall give an evaluation of the ethical considerations that the research may entail or that it may give rise to.

4 INFORMATION TO THE RESEARCH SUBJECT

The information to research subjects should include all the essential information on the research that the subjects need to be able to give their informed consent. It should be written using easily understandable language, and research subjects should be provided sufficient time to familiarise themselves with its contents. Unless the research subjects are clearly confined to Finnish or Swedish speaking persons, the information must be available in both languages. If there are persons in the sample who do not understand either of the domestic languages, the information sheet must be available in the language that the research subjects well understand. The standard of language should correspond to the language used by the subject group. For example, there may be a specific information sheet for children or persons suffering from dementia besides the possible information to their representatives. A good information sheet is short, matter-of-fact and understandable. The information should be given personally to each research subject both orally and in writing. All research subjects must be provided an opportunity for asking questions. The written information should include, above all, the following:

4.1 Facts about the research

- it should be made clear that it is question of a research,

- title of the research (short and clear, a longer sub-title if that is needed),
- addressing the subject (usually formal: modified according to the group of subjects)
- names of the organisation carrying out the research, of the sponsor and of the persons in charge of the research and of the keeper of the register,
- research funding and possible conflicting interests (e.g. if the investigator is employed by the sponsor),
- purpose and nature of the research,
- estimated number of persons taking part in the research,
- main inclusion and exclusion criteria,
- contact persons for additional information and for adverse events (name, telephone number even outside office hours).

4.2 Voluntariness of participation and withdrawal of consent

- voluntariness of participation in the research,
- right to withdraw consent at any time and without giving a reason for it,
- a mention that withdrawal does not affect the care of the research subject or the patient-doctor relationship,
- a mention that research may also be interrupted from the part of the party performing it and anticipated reasons for that.

4.3 Impacts of participation to research

- course of research and description of the measures involved (also the number of visits and duration of research);
- methods used and study arrangement (reference group, use of placebos, randomising, blinding. In randomised placebo controlled studies information on the possibility of being left without effective treatment and its probability);
- anticipated benefits of the study and their estimated probability to the subject him/herself, or to the embryo, foetus or suckling involved. If there will be no benefit, or there is so far no evidence of it, this must be clearly mentioned;
- anticipated adverse effects, risks and inconveniences of the measures or the substance studied and their probability to the subject him/herself, or to the embryo, foetus or suckling involved;
- if the research subject is a patient, choices of treatment and their benefits, disadvantages, risks and inconveniences and their probability to the subject him/herself, or to the embryo, foetus or suckling involved;
- additional measures caused by research compared with ordinary treatment (extra visits etc.);
- impact of research on every-day life (special diet, mobility, sexual intercourse, other effects);
- information the research subject will receive during and after the research (e.g. treatment with placebos, genetic information).

4.4 Data protection

- right to verify personal data and right to correction of that data, unless research register is used solely for scientific research or statistics;
- confidentiality of personal and health data and research findings and of the samples collected (sources of information, recording and storing of data, transfer and disposal of data, persons and authorities that have access to patient and research documents, deliveries under the responsibility or supervision of the keeper of the register and the researching physician);
- if the data or samples collected are intended to be used for a purpose other than the original one, an individualised definition of that purpose.

4.5 Costs, remuneration, insurance, and treatment after the research

- costs entailed to the research subject (travel costs and loss of earnings);
- compensation for inconvenience payable to the research subject (only healthy volunteers);
- impact of refusal or interruption on the compensations payable;
- insurance taken for the benefit of the research subject and treatment in case of adverse events related to the research;
- possible treatment after the research has been completed

5 CONSENT FORM

The separate consent form should be, as a rule, only one page long, but it should cover all the essential information for which a written consent is needed. Since a description of the research has been given in the context of written information for the research subject, the details of the research need not be repeated, but it is enough to identify the research as the same which the information sheet concerns. The same requirements for the language and intelligibility apply to the consent form as to the written information. The consent form as such must include at least the following:

5.1 Title of the research and parties involved

- title of the research and name of the party carrying it out;
- name, social security number or date of birth and address of the research subject;
- name of the person who has given the research subject information about the research (if there is suspicion of interdependence between the patient and the investigator, the person giving information and the receiving his/her consent should be another person);
- name of the person receiving consent

5.2 Contents

- request to take part in the research concerned;
- a statement that the research subject has been given information about the research both in writing and orally and that the subject has been provided an opportunity for asking questions;
- free consent by the research subject and his/her representative to taking part in the research;
- if the research subject belongs to one of the vulnerable groups (children, incapacitated persons, pregnant or nursing mothers, prisoners), this must appear in the consent form. No separate mention of this is needed otherwise. (See below, paragraph 5.5 Minors and adult incompetents);
- free consent by the research subject and/or his/her representative to collecting and registering personal data;
- if personal data are also collected from other registers, an individualised consent by the research subject and/or his/her representative to searching data from those registers;
- if the data collected would be used for a purpose other than the original one, an individualised consent for that purpose and a mention that a new consent will be asked for separately, if the use cannot be defined yet;
- what information would be delivered further, to whom and to what extent, and an assurance that without an authorisation based on the law information can only be delivered to the persons or authorities referred to under the responsibility and supervision of the keeper of the register and the researching physician;
- protection of the confidentiality of data (anonymising or other protection measures).

5.3 Withdrawal of consent and compensation

- a mention of the right to withdraw his/her consent at any time without giving any reason and without any impact on his/her right to receive the needed treatment;
- a mention of the right to compensation for ? injury caused by a research measure;
- a mention of the right to compensation for participating in the research and the impact of withdrawal of consent on it.

5.4 Signatures and dates

- date and signature by the deliverer of information with clarification of signature;
- date and signature by the research subject or his/her representative with clarification of signature;
- date and signature by the receiver of consent with clarification of signature;
- a copy of the consent form to the research subject

5.5 Minors and adult incompetents

If a research subject is an incapacitated person or a minor, a consent by the guardian (minors) or a family member or other person close to the person or by the legal representative (adult incapacitated persons) is needed. If there are minors, pregnant women or nursing mothers or prisoners among the research subjects, it might be necessary to draw up a separate consent form for their use. If a minor has reached the age of 15 and, in view of his/her age, stage of development and type of his/her illness is capable of understanding the significance of the research, and the research is likely to be of direct benefit of his/her health, consent by the guardian is not needed. In such cases the guardian has to be informed (Medical Research Act, section 8 (3)) and the minor must be told about this obligation. If a minor is capable of understanding the significance of a research, also his/her written consent is required, even if the guardian's consent would be needed in addition. In case an incapacitated person objects, his/her opinion shall be complied with, taking account of his/her age and stage of development.

6 INFORMATION TO THE RESEARCH STAFF

- does the research plan (or its appendix) give sufficient instructions to the research staff for carrying out the research?

7 PATIENT DIARIES AND ADDITIONAL INFORMATION TO THE RESEARCH SUBJECT

8 OTHER APPENDICES

- statements by National Agency for Medicines, if applicable (stage of notification procedure)
- opinion or authorisation by another authority (Ministry of Social Affairs and Health, ethics committee on animal experimentation, Radiation and Nuclear Safety Authority etc.);
- previous ethical assessments