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**Forschungsethik. Eine Einführung**

**Stuttgart: Verlag J.B. Metzler 2010**

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## **Dokumentation**

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- 1. World Medical Association (2008): Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects**  
<http://www.wma.net/en/30publications/10policies/b3/17c.pdf> (25.4.2010)
- 2. Council of Europe (2005): Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research**  
<http://conventions.coe.int/treaty/en/Treaties/Html/195.htm> (25.4.2010)
- 3. Council for International Organizations of Medical Sciences (CIOMS) (2002): International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 5**  
[http://www.cioms.ch/frame\\_guidelines\\_nov\\_2002.htm](http://www.cioms.ch/frame_guidelines_nov_2002.htm) (25.4.2010)

# **1. World Medical Association (2008): Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects**

<http://www.wma.net/en/30publications/10policies/b3/17c.pdf> (25.4.2010)

## **A. INTRODUCTION**

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.
2. Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.
3. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.
4. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."
5. Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.
6. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.
7. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.
8. In medical practice and in medical research, most interventions involve risks and burdens.
9. Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.
10. Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and

standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

## **B. PRINCIPLES FOR ALL MEDICAL RESEARCH**

11. It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.
12. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.
13. Appropriate caution must be exercised in the conduct of medical research that may harm the environment.
14. The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.
15. The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.
16. Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. The responsibility for the protection of research subjects must always rest

with the physician or other health care professional and never the research subjects, even though they have given consent.

17. Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.
18. Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.
19. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.
20. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.
21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.
22. Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees.
23. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.
24. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.
25. For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where

consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.

26. When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.
27. For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden.
28. When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.
29. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.
30. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

### **C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE**

31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.
32. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:
  - The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
  - Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.
33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.
34. The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.
35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.

## **2. Council of Europe (2005): Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research**

<http://conventions.coe.int/treaty/en/Treaties/Html/195.htm> (25.4.2010)

### **CHAPTER I – Object and scope**

#### **Article 1 – Object and purpose**

Parties to this Protocol shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to any research involving interventions on human beings in the field of biomedicine.

#### **Article 2 – Scope**

1. This Protocol covers the full range of research activities in the health field involving interventions on human beings.
2. This Protocol does not apply to research on embryos in vitro. It does apply to research on foetuses and embryos in vivo.
3. For the purposes of this Protocol, the term “intervention” includes:
  - i. a physical intervention, and
  - ii. any other intervention in so far as it involves a risk to the psychological health of the person concerned.

### **CHAPTER II – General provisions**

#### **Article 3 – Primacy of the human being**

The interests and welfare of the human being participating in research shall prevail over the sole interest of society or science.

#### **Article 4 – General rule**

Research shall be carried out freely, subject to the provisions of this Protocol and the other legal provisions ensuring the protection of the human being.

#### **Article 5 – Absence of alternatives**

Research on human beings may only be undertaken if there is no alternative of comparable effectiveness.

#### **Article 6 – Risks and benefits**

1. Research shall not involve risks and burdens to the human being disproportionate to its potential benefits.
2. In addition, where the research does not have the potential to produce results of direct benefit to the health of the research participant, such research may only be undertaken if the research entails no more than acceptable risk and acceptable burden for the research participant. This

shall be without prejudice to the provision contained in Article 15 paragraph 2, sub-paragraph ii for the protection of persons not able to consent to research.

#### **Article 7 – Approval**

Research may only be undertaken if the research project has been approved by the competent body after independent examination of its scientific merit, including assessment of the importance of the aim of research, and multidisciplinary review of its ethical acceptability.

#### **Article 8 – Scientific quality**

Any research must be scientifically justified, meet generally accepted criteria of scientific quality and be carried out in accordance with relevant professional obligations and standards under the supervision of an appropriately qualified researcher.

### **CHAPTER III – Ethics committee**

#### **Article 9 – Independent examination by an ethics committee**

1. Every research project shall be submitted for independent examination of its ethical acceptability to an ethics committee. Such projects shall be submitted to independent examination in each State in which any research activity is to take place.
2. The purpose of the multidisciplinary examination of the ethical acceptability of the research project shall be to protect the dignity, rights, safety and well-being of research participants. The assessment of the ethical acceptability shall draw on an appropriate range of expertise and experience adequately reflecting professional and lay views.
3. The ethics committee shall produce an opinion containing reasons for its conclusion.

#### **Article 10 – Independence of the ethics committee**

1. Parties to this Protocol shall take measures to assure the independence of the ethics committee. That body shall not be subject to undue external influences.
2. Members of the ethics committee shall declare all circumstances that might lead to a conflict of interest. Should such conflicts arise, those involved shall not participate in that review.

#### **Article 11 – Information for the ethics committee**

1. All information which is necessary for the ethical assessment of the research project shall be given in written form to the ethics committee.
2. In particular, information on items contained in the appendix to this Protocol shall be provided, in so far as it is relevant for the research project. The appendix may be amended by the Committee set up by Article 32 of the Convention by a two-thirds majority of the votes cast.

#### **Article 12 – Undue influence**

The ethics committee must be satisfied that no undue influence, including that of a financial nature, will be exerted on persons to participate in research. In this respect, particular attention must be given to vulnerable or dependent persons.

## **CHAPTER IV – Information and consent**

### **Article 13 – Information for research participants**

1. The persons being asked to participate in a research project shall be given adequate information in a comprehensible form. This information shall be documented.
2. The information shall cover the purpose, the overall plan and the possible risks and benefits of the research project, and include the opinion of the ethics committee. Before being asked to consent to participate in a research project, the persons concerned shall be specifically informed, according to the nature and purpose of the research:
  - i. of the nature, extent and duration of the procedures involved, in particular, details of any burden imposed by the research project;
  - ii. of available preventive, diagnostic and therapeutic procedures;
  - iii. of the arrangements for responding to adverse events or the concerns of research participants;
  - iv. of arrangements to ensure respect for private life and ensure the confidentiality of personal data;
  - v. of arrangements for access to information relevant to the participant arising from the research and to its overall results;
  - vi. of the arrangements for fair compensation in the case of damage;
  - vii. of any foreseen potential further uses, including commercial uses, of the research results, data or biological materials;
  - viii. of the source of funding of the research project.
3. In addition, the persons being asked to participate in a research project shall be informed of the rights and safeguards prescribed by law for their protection, and specifically of their right to refuse consent or to withdraw consent at any time without being subject to any form of discrimination, in particular regarding the right to medical care.

### **Article 14 – Consent**

1. No research on a person may be carried out, subject to the provisions of both Chapter V and Article 19, without the informed, free, express, specific and documented consent of the person. Such consent may be freely withdrawn by the person at any phase of the research.
2. Refusal to give consent or the withdrawal of consent to participation in research shall not lead to any form of discrimination against the person concerned, in particular regarding the right to medical care.
3. Where the capacity of the person to give informed consent is in doubt, arrangements shall be in place to verify whether or not the person has such capacity.

## **CHAPTER V – Protection of persons not able to consent to research**

### **Article 15 – Protection of persons not able to consent to research**

1. Research on a person without the capacity to consent to research may be undertaken only if all the following specific conditions are met:
  - i. the results of the research have the potential to produce real and direct benefit to his or her health;
  - ii. research of comparable effectiveness cannot be carried out on individuals capable of giving consent;
  - iii. the person undergoing research has been informed of his or her rights and the safeguards prescribed by law for his or her protection, unless this person is not in a state to receive the information;
  - iv. the necessary authorisation has been given specifically and in writing by the legal representative or an authority, person or body provided for by law, and after having received the information required by Article 16, taking into account the person's previously expressed wishes or objections. An adult not able to consent shall as far as possible take part in the authorisation procedure. The opinion of a minor shall be taken into consideration as an increasingly determining factor in proportion to age and degree of maturity;
  - v. the person concerned does not object.
2. Exceptionally and under the protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorised subject to the conditions laid down in paragraph 1, sub-paragraphs ii, iii, iv, and v above, and to the following additional conditions:
  - i. the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition;
  - ii. the research entails only minimal risk and minimal burden for the individual concerned; and any consideration of additional potential benefits of the research shall not be used to justify an increased level of risk or burden.
3. Objection to participation, refusal to give authorisation or the withdrawal of authorisation to participate in research shall not lead to any form of discrimination against the person concerned, in particular regarding the right to medical care.

### **Article 16 – Information prior to authorisation**

1. Those being asked to authorise participation of a person in a research project shall be given adequate information in a comprehensible form. This information shall be documented.
2. The information shall cover the purpose, the overall plan and the possible risks and benefits of the research project, and include the opinion of the ethics committee. They shall further be

informed of the rights and safeguards prescribed by law for the protection of those not able to consent to research and specifically of the right to refuse or to withdraw authorisation at any time, without the person concerned being subject to any form of discrimination, in particular regarding the right to medical care. They shall be specifically informed according to the nature and purpose of the research of the items of information listed in Article 13.

3. The information shall also be provided to the individual concerned, unless this person is not in a state to receive the information.

#### **Article 17 – Research with minimal risk and minimal burden**

1. For the purposes of this Protocol it is deemed that the research bears a minimal risk if, having regard to the nature and scale of the intervention, it is to be expected that it will result, at the most, in a very slight and temporary negative impact on the health of the person concerned.
2. It is deemed that it bears a minimal burden if it is to be expected that the discomfort will be, at the most, temporary and very slight for the person concerned. In assessing the burden for an individual, a person enjoying the special confidence of the person concerned shall assess the burden where appropriate.

### **CHAPTER VI – Specific situations**

#### **Article 18 – Research during pregnancy or breastfeeding**

1. Research on a pregnant woman which does not have the potential to produce results of direct benefit to her health, or to that of her embryo, foetus or child after birth, may only be undertaken if the following additional conditions are met:
  - i. the research has the aim of contributing to the ultimate attainment of results capable of conferring benefit to other women in relation to reproduction or to other embryos, foetuses or children;
  - ii. research of comparable effectiveness cannot be carried out on women who are not pregnant;
  - iii. the research entails only minimal risk and minimal burden.
2. Where research is undertaken on a breastfeeding woman, particular care shall be taken to avoid any adverse impact on the health of the child.

#### **Article 19 – Research on persons in emergency clinical situations**

1. The law shall determine whether, and under which protective additional conditions, research in emergency situations may take place when:
  - i. a person is not in a state to give consent, and
  - ii. because of the urgency of the situation, it is impossible to obtain in a sufficiently timely manner, authorisation from his or her representative or an authority or a person or body which would in the absence of an emergency situation be called upon to give authorisation.
2. The law shall include the following specific conditions:

- i. research of comparable effectiveness cannot be carried out on persons in non-emergency situations;
  - ii. the research project may only be undertaken if it has been approved specifically for emergency situations by the competent body;
  - iii. any relevant previously expressed objections of the person known to the researcher shall be respected;
  - iv. where the research has not the potential to produce results of direct benefit to the health of the person concerned, it has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same category or afflicted with the same disease or disorder or having the same condition, and entails only minimal risk and minimal burden.
3. Persons participating in the emergency research project or, if applicable, their representatives shall be provided with all the relevant information concerning their participation in the research project as soon as possible. Consent or authorisation for continued participation shall be requested as soon as reasonably possible.

#### **Article 20 – Research on persons deprived of liberty**

Where the law allows research on persons deprived of liberty, such persons may participate in a research project in which the results do not have the potential to produce direct benefit to their health only if the following additional conditions are met:

- i. research of comparable effectiveness cannot be carried out without the participation of persons deprived of liberty;
- ii. the research has the aim of contributing to the ultimate attainment of results capable of conferring benefit to persons deprived of liberty;
- iii. the research entails only minimal risk and minimal burden.

### **CHAPTER VII – Safety and supervision**

#### **Article 21 – Minimisation of risk and burden**

1. All reasonable measures shall be taken to ensure safety and to minimise risk and burden for the research participants.
2. Research may only be carried out under the supervision of a clinical professional who possesses the necessary qualifications and experience.

#### **Article 22 – Assessment of health status**

1. The researcher shall take all necessary steps to assess the state of health of human beings prior to their inclusion in research, to ensure that those at increased risk in relation to participation in a specific project be excluded.

2. Where research is undertaken on persons in the reproductive stage of their lives, particular consideration shall be given to the possible adverse impact on a current or future pregnancy and the health of an embryo, foetus or child.

#### **Article 23 – Non-interference with necessary clinical interventions**

1. Research shall not delay nor deprive participants of medically necessary preventive, diagnostic or therapeutic procedures.
2. In research associated with prevention, diagnosis or treatment, participants assigned to control groups shall be assured of proven methods of prevention, diagnosis or treatment.
3. The use of placebo is permissible where there are no methods of proven effectiveness, or where withdrawal or withholding of such methods does not present an unacceptable risk or burden.

#### **Article 24 – New developments**

1. Parties to this Protocol shall take measures to ensure that the research project is re-examined if this is justified in the light of scientific developments or events arising in the course of the research.
2. The purpose of the re-examination is to establish whether:
  - i. the research needs to be discontinued or if changes to the research project are necessary for the research to continue;
  - ii. research participants, or if applicable their representatives, need to be informed of the developments or events;
  - iii. additional consent or authorisation for participation is required.
3. Any new information relevant to their participation shall be conveyed to the research participants, or, if applicable, to their representatives, in a timely manner.
4. The competent body shall be informed of the reasons for any premature termination of a research project.

### **CHAPTER VIII – Confidentiality and right to information**

#### **Article 25 – Confidentiality**

1. Any information of a personal nature collected during biomedical research shall be considered as confidential and treated according to the rules relating to the protection of private life.
2. The law shall protect against inappropriate disclosure of any other information related to a research project that has been submitted to an ethics committee in compliance with this Protocol.

#### **Article 26 – Right to information**

1. Research participants shall be entitled to know any information collected on their health in conformity with the provisions of Article 10 of the Convention.

2. Other personal information collected for a research project will be accessible to them in conformity with the law on the protection of individuals with regard to processing of personal data.

#### **Article 27 – Duty of care**

If research gives rise to information of relevance to the current or future health or quality of life of research participants, this information must be offered to them. That shall be done within a framework of health care or counselling. In communication of such information, due care must be taken in order to protect confidentiality and to respect any wish of a participant not to receive such information.

#### **Article 28 – Availability of results**

1. On completion of the research, a report or summary shall be submitted to the ethics committee or the competent body.
2. The conclusions of the research shall be made available to participants in reasonable time, on request.
3. The researcher shall take appropriate measures to make public the results of research in reasonable time.

### **CHAPTER IX – Research in States not parties to this Protocol**

#### **Article 29 – Research in States not parties to this Protocol**

Sponsors or researchers within the jurisdiction of a Party to this Protocol that plan to undertake or direct a research project in a State not party to this Protocol shall ensure that, without prejudice to the provisions applicable in that State, the research project complies with the principles on which the provisions of this Protocol are based. Where necessary, the Party shall take appropriate measures to that end.

### **CHAPTER X – Infringement of the provisions of the Protocol**

#### **Article 30 – Infringement of the rights or principles**

The Parties shall provide appropriate judicial protection to prevent or to put a stop to an unlawful infringement of the rights or principles set forth in this Protocol at short notice.

#### **Article 31 – Compensation for damage**

The person who has suffered damage as a result of participation in research shall be entitled to fair compensation according to the conditions and procedures prescribed by law.

#### **Article 32 – Sanctions**

Parties shall provide for appropriate sanctions to be applied in the event of infringement of the provisions contained in this Protocol.

## **CHAPTER XI – Relation between this Protocol and other provisions and re-examination of the Protocol**

### **Article 33 – Relation between this Protocol and the Convention**

As between the Parties, the provisions of Articles 1 to 32 of this Protocol shall be regarded as additional articles to the Convention, and all the provisions of the Convention shall apply accordingly.

### **Article 34 – Wider protection**

None of the provisions of this Protocol shall be interpreted as limiting or otherwise affecting the possibility for a Party to grant research participants a wider measure of protection than is stipulated in this Protocol.

### **Article 35 – Re-examination of the Protocol**

In order to monitor scientific developments, the present Protocol shall be examined within the Committee referred to in Article 32 of the Convention no later than five years from the entry into force of this Protocol and thereafter at such intervals as the Committee may determine.

## **CHAPTER XII – Final clauses**

### **Article 36 – Signature and ratification**

This Protocol shall be open for signature by Signatories to the Convention. It is subject to ratification, acceptance or approval. A Signatory may not ratify, accept or approve this Protocol unless it has previously or simultaneously ratified, accepted or approved the Convention.

Instruments of ratification, acceptance or approval shall be deposited with the Secretary General of the Council of Europe.

### **Article 37 – Entry into force**

1. This Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date on which five States, including at least four member States of the Council of Europe, have expressed their consent to be bound by the Protocol in accordance with the provisions of Article 36.
2. In respect of any State which subsequently expresses its consent to be bound by it, the Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date of the deposit of the instrument of ratification, acceptance or approval.

### **Article 38 – Accession**

1. After the entry into force of this Protocol, any State which has acceded to the Convention may also accede to this Protocol.
2. Accession shall be effected by the deposit with the Secretary General of the Council of Europe of an instrument of accession which shall take effect on the first day of the month following the expiration of a period of three months after the date of its deposit.

### **Article 39 – Denunciation**

1. Any Party may at any time denounce this Protocol by means of a notification addressed to the Secretary General of the Council of Europe.
2. Such denunciation shall become effective on the first day of the month following the expiration of a period of three months after the date of receipt of such notification by the Secretary General.

#### **Article 40 – Notifications**

The Secretary General of the Council of Europe shall notify the member States of the Council of Europe, the European Community, any Signatory, any Party and any other State which has been invited to accede to the Protocol of:

- a. any signature;
- b. the deposit of any instrument of ratification, acceptance, approval or accession;
- c. any date of entry into force of this Protocol in accordance with Articles 37 and 38;
- d. any other act, notification or communication relating to this Protocol.

In witness whereof the undersigned, being duly authorised thereto, have signed this Protocol.  
Done at Strasbourg, this 25th day of January 2005, in English and in French, both texts being equally authentic, in a single copy which shall be deposited in the archives of the Council of Europe. The Secretary General of the Council of Europe shall transmit certified copies to each member State of the Council of Europe, to the non-member States which have participated in the elaboration of this Protocol, to any State invited to accede to the Convention and to the European Community.

#### **Appendix**

Information to be given to the ethics committee

Information on the following items shall be provided to the ethics committee, in so far as it is relevant for the research project:

##### **Description of the project**

- i. the name of the principal researcher, qualifications and experience of researchers and, where appropriate, the clinically responsible person, and funding arrangements;
- ii. the aim and justification for the research based on the latest state of scientific knowledge;
- iii. methods and procedures envisaged, including statistical and other analytical techniques;
- iv. a comprehensive summary of the research project in lay language;
- v. a statement of previous and concurrent submissions of the research project for assessment or approval and the outcome of those submissions;

##### **Participants, consent and information**

- vi. justification for involving human beings in the research project;
- vii. the criteria for inclusion or exclusion of the categories of persons for participation in the research project and how those persons are to be selected and recruited;

- viii. reasons for the use or the absence of control groups;
- ix. a description of the nature and degree of foreseeable risks that may be incurred through participating in research;
- x. the nature, extent and duration of the interventions to be carried out on the research participants, and details of any burden imposed by the research project;
- xi. arrangements to monitor, evaluate and react to contingencies that may have consequences for the present or future health of research participants;
- xii. the timing and details of information for those persons who would participate in the research project and the means proposed for provision of this information;
- xiii. documentation intended to be used to seek consent or, in the case of persons not able to consent, authorisation for participation in the research project;
- xiv. arrangements to ensure respect for the private life of those persons who would participate in research and ensure the confidentiality of personal data;
- xv. arrangements foreseen for information which may be generated and be relevant to the present or future health of those persons who would participate in research and their family members;

**Other information**

- xvi. details of all payments and rewards to be made in the context of the research project;
- xvii. details of all circumstances that might lead to conflicts of interest that may affect the independent judgement of the researchers;
- xviii. details of any foreseen potential further uses, including commercial uses, of the research results, data or biological materials;
- xix. details of all other ethical issues, as perceived by the researcher;
- xx. details of any insurance or indemnity to cover damage arising in the context of the research project.

The ethics committee may request additional information necessary for evaluation of the research project.

### **3. Council for International Organizations of Medical Sciences (CIOMS) (2002): International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 5**

[http://www.cioms.ch/frame\\_guidelines\\_nov\\_2002.htm](http://www.cioms.ch/frame_guidelines_nov_2002.htm) (25.4.2010)

#### **THE GUIDELINES**

##### **Guideline 1: Ethical justification and scientific validity of biomedical research involving human beings**

The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people's health. Such research can be ethically justifiable only if it is carried out in ways that respect and protect, and are fair to, the subjects of that research and are morally acceptable within the communities in which the research is carried out. Moreover, because scientifically invalid research is unethical in that it exposes research subjects to risks without possible benefit, investigators and sponsors must ensure that proposed studies involving human subjects conform to generally accepted scientific principles and are based on adequate knowledge of the pertinent scientific literature.

##### **Guideline 2: Ethical review committees**

All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees. The review committees must be independent of the research team, and any direct financial or other material benefit they may derive from the research should not be contingent on the outcome of their review. The investigator must obtain their approval or clearance before undertaking the research. The ethical review committee should conduct further reviews as necessary in the course of the research, including monitoring of the progress of the study.

##### **Guideline 3: Ethical review of externally sponsored research**

An external sponsoring organization and individual investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organization, and the ethical standards applied should be no less stringent than they would be for research carried out in that country. The health authorities of the host country, as well as a national or local ethical review committee, should ensure that the proposed research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards.

**Guideline 4: Individual informed consent**

For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee.

**Guideline 5: Obtaining informed consent: Essential information for prospective research subjects**

Before requesting an individual's consent to participate in research, the investigator must provide the following information, in language or another form of communication that the individual can understand:

- that the individual is invited to participate in research, the reasons for considering the individual suitable for the research, and that participation is voluntary;
- that the individual is free to refuse to participate and will be free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled;
- the purpose of the research, the procedures to be carried out by the investigator and the subject, and an explanation of how the research differs from routine medical care;
- for controlled trials, an explanation of features of the research design (e.g., randomization, double-blinding), and that the subject will not be told of the assigned treatment until the study has been completed and the blind has been broken;
- the expected duration of the individual's participation (including number and duration of visits to the research centre and the total time involved) and the possibility of early termination of the trial or of the individual's participation in it;
- whether money or other forms of material goods will be provided in return for the individual's participation and, if so, the kind and amount;
- that, after the completion of the study, subjects will be informed of the findings of the research in general, and individual subjects will be informed of any finding that relates to their particular health status;
- that subjects have the right of access to their data on demand, even if these data lack immediate clinical utility (unless the ethical review committee has approved temporary or permanent non-disclosure of data, in which case the subject should be informed of, and given, the reasons for such non-disclosure);
- any foreseeable risks, pain or discomfort, or inconvenience to the individual (or others) associated with participation in the research, including risks to the health or well-being of a subject's spouse or partner;
- the direct benefits, if any, expected to result to subjects from participating in the research

- the expected benefits of the research to the community or to society at large, or contributions to scientific knowledge;
- whether, when and how any products or interventions proven by the research to be safe and effective will be made available to subjects after they have completed their participation in the research, and whether they will be expected to pay for them;
- any currently available alternative interventions or courses of treatment;
- the provisions that will be made to ensure respect for the privacy of subjects and for the confidentiality of records in which subjects are identified;
- the limits, legal or other, to the investigators' ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality;
- policy with regard to the use of results of genetic tests and familial genetic information, and the precautions in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives or to others (e.g., insurance companies or employers) without the consent of the subject;
- the sponsors of the research, the institutional affiliation of the investigators, and the nature and sources of funding for the research;
- the possible research uses, direct or secondary, of the subject's medical records and of biological specimens taken in the course of clinical care (See also Guidelines 4 and 18 Commentaries);
- whether it is planned that biological specimens collected in the research will be destroyed at its conclusion, and, if not, details about their storage (where, how, for how long, and final disposition) and possible future use, and that subjects have the right to decide about such future use, to refuse storage, and to have the material destroyed (See Guideline 4 Commentary);
- whether commercial products may be developed from biological specimens, and whether the participant will receive monetary or other benefits from the development of such products;
- whether the investigator is serving only as an investigator or as both investigator and the subject's physician;
- the extent of the investigator's responsibility to provide medical services to the participant;
- that treatment will be provided free of charge for specified types of research-related injury or for complications associated with the research, the nature and duration of such care, the name of the organization or individual that will provide the treatment, and whether there is any uncertainty regarding funding of such treatment;
- in what way, and by what organization, the subject or the subject's family or dependants will be compensated for disability or death resulting from such injury (or, when indicated, that there are no plans to provide such compensation);
- whether or not, in the country in which the prospective subject is invited to participate in research, the right to compensation is legally guaranteed;
- that an ethical review committee has approved or cleared the research protocol.

**Guideline 6: Obtaining informed consent: Obligations of sponsors and investigators**

Sponsors and investigators have a duty to:

- refrain from unjustified deception, undue influence, or intimidation;
- seek consent only after ascertaining that the prospective subject has adequate understanding of the relevant facts and of the consequences of participation and has had sufficient opportunity to consider whether to participate;
- as a general rule, obtain from each prospective subject a signed form as evidence of informed consent – investigators should justify any exceptions to this general rule and obtain the approval of the ethical review committee (See Guideline 4 Commentary, Documentation of consent);
- renew the informed consent of each subject if there are significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of subjects to continue to participate; and,
- renew the informed consent of each subject in long-term studies at pre-determined intervals, even if there are no changes in the design or objectives of the research.

**Guideline 7: Inducement to participate**

Subjects may be reimbursed for lost earnings, travel costs and other expenses incurred in taking part in a study; they may also receive free medical services. Subjects, particularly those who receive no direct benefit from research, may also be paid or otherwise compensated for inconvenience and time spent. The payments should not be so large, however, or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment ("undue inducement"). All payments, reimbursements and medical services provided to research subjects must have been approved by an ethical review committee.

**Guideline 8: Benefits and risks of study participation**

For all biomedical research involving human subjects, the investigator must ensure that potential benefits and risks are reasonably balanced and risks are minimized.

- Interventions or procedures that hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual subject must be justified by the expectation that they will be at least as advantageous to the individual subject, in the light of foreseeable risks and benefits, as any available alternative. Risks of such 'beneficial' interventions or procedures must be justified in relation to expected benefits to the individual subject.
- Risks of interventions that do not hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual must be justified in relation to the expected benefits to society (generalizable knowledge). The risks presented by such interventions must be reasonable in relation to the importance of the knowledge to be gained.

**Guideline 9: Special limitations on risk when research involves individuals who are not capable of giving informed consent**

When there is ethical and scientific justification to conduct research with individuals incapable of giving informed consent, the risk from research interventions that do not hold out the prospect of direct benefit for the individual subject should be no more likely and not greater than the risk attached to routine medical or psychological examination of such persons. Slight or minor increases above such risk may be permitted when there is an overriding scientific or medical rationale for such increases and when an ethical review committee has approved them.

**Guideline 10: Research in populations and communities with limited resources**

Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:

- the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

**Guideline 11: Choice of control in clinical trials**

As a general rule, research subjects in the control group of a trial of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention. In some circumstances it may be ethically acceptable to use an alternative comparator, such as placebo or "no treatment".

Placebo may be used:

- when there is no established effective intervention;
- when withholding an established effective intervention would expose subjects to, at most, temporary discomfort or delay in relief of symptoms;
- when use of an established effective intervention as comparator would not yield scientifically reliable results and use of placebo would not add any risk of serious or irreversible harm to the subjects.

**Guideline 12: Equitable distribution of burdens and benefits in the selection of groups of subjects in research**

Groups or communities to be invited to be subjects of research should be selected in such a way that the burdens and benefits of the research will be equitably distributed. The exclusion of groups or communities that might benefit from study participation must be justified.

**Guideline 13: Research involving vulnerable persons**

Special justification is required for inviting vulnerable individuals to serve as research subjects and, if they are selected, the means of protecting their rights and welfare must be strictly applied.

**Guideline 14: Research involving children**

Before undertaking research involving children, the investigator must ensure that:

- the research might not equally well be carried out with adults;
- the purpose of the research is to obtain knowledge relevant to the health needs of children;
- a parent or legal representative of each child has given permission;
- the agreement (assent) of each child has been obtained to the extent of the child's capabilities; and,
- a child's refusal to participate or continue in the research will be respected.

**Guideline 15: Research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent**

Before undertaking research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent, the investigator must ensure that:

- such persons will not be subjects of research that might equally well be carried out on persons whose capacity to give adequately informed consent is not impaired;
- the purpose of the research is to obtain knowledge relevant to the particular health needs of persons with mental or behavioural disorders;
- the consent of each subject has been obtained to the extent of that person's capabilities, and a prospective subject's refusal to participate in research is always respected, unless, in exceptional circumstances, there is no reasonable medical alternative and local law permits overriding the objection; and,
- in cases where prospective subjects lack capacity to consent, permission is obtained from a responsible family member or a legally authorized representative in accordance with applicable law.

**Guideline 16: Women as research subjects**

Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation. However, a thorough discussion of risks to the pregnant woman and to her fetus is a prerequisite for the woman's ability to make a rational decision to enrol in a clinical study. In this discussion, if participation in the research might be hazardous to a fetus or a woman if she becomes pregnant, the sponsors/ investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive

methods before the research commences. Where such access is not possible, for legal or religious reasons, investigators should not recruit for such possibly hazardous research women who might become pregnant.

**Guideline 17: Pregnant women as research participants.**

Pregnant women should be presumed to be eligible for participation in biomedical research. Investigators and ethical review committees should ensure that prospective subjects who are pregnant are adequately informed about the risks and benefits to themselves, their pregnancies, the fetus and their subsequent offspring, and to their fertility. Research in this population should be performed only if it is relevant to the particular health needs of a pregnant woman or her fetus, or to the health needs of pregnant women in general, and, when appropriate, if it is supported by reliable evidence from animal experiments, particularly as to risks of teratogenicity and mutagenicity .

**Guideline 18: Safeguarding confidentiality**

The investigator must establish secure safeguards of the confidentiality of subjects' research data. Subjects should be told the limits, legal or other, to the investigators' ability to safeguard confidentiality and the possible consequences of breaches of confidentiality.

**Guideline 19: Right of injured subjects to treatment and compensation**

Investigators should ensure that research subjects who suffer injury as a result of their participation are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability or handicap. In the case of death as a result of their participation, their dependants are entitled to compensation. Subjects must not be asked to waive the right to compensation.

**Guideline 20: Strengthening capacity for ethical and scientific review and biomedical research**

Many countries lack the capacity to assess or ensure the scientific quality or ethical acceptability of biomedical research proposed or carried out in their jurisdictions. In externally sponsored collaborative research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible in such countries contribute effectively to national or local capacity to design and conduct biomedical research, and to provide scientific and ethical review and monitoring of such research.

Capacity-building may include, but is not limited to, the following activities:

- establishing and strengthening independent and competent ethical review processes/ committees
- strengthening research capacity

- developing technologies appropriate to health-care and biomedical research
- training of research and health-care staff
- educating the community from which research subjects will be drawn

**Guideline 21: Ethical obligation of external sponsors to provide health-care services**

External sponsors are ethically obliged to ensure the availability of:

- health-care services that are essential to the safe conduct of the research;
- treatment for subjects who suffer injury as a consequence of research interventions; and,
- services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.