Expert Conference on the Revision of the Declaration of Helsinki

28 February – 1 March 2013,Tokyo

Protective Provisions for Research Participants

- Council of Europe -

Prof. Elmar Doppelfeld, MD

Chair of the Working Group “Biomedical Research”
Committee on Bioethics (DH-BIO)
Chair (2005-2007) of the “Steering Committee on Bioethics (CDBI)”
Council of Europe
Chair (1994 – 2012) of the Permanent Working Party of
Research Ethics Committees
in Germany

Council of Europe

- Established in 1949 - “Intergovernmental body”
- 47 Member States (Population: ± 800 Mio)
- 5 Observer States (Canada, Holy See, Japan, Mexiko, USA)
- „Human Rights, Democracy“
- Harmonization of European legislation
- Conventions and additional Protocols: treaties!
  - Signature and ratification: decision of the Member States

❖ Convention for the Protection of Human Rights and Fundamental Freedoms of 4 November 1950

Common Basis of all Provisions

Goods of protection

Human dignity
Autonomy
Beneficence
Justice

Classification of Provisions

Legal Instruments

- Treaties
  - Oviedo Convention and additional Protocols, Council of Europe,1997
  - Directive 2001/20/EC,* European Union, 2001
- National Law

* Applicable only for drug trials

Other Provisions* („soft law“)

- Declaration of Helsinki, WMA 1964 - 2008
- International Guidelines, CIOMS 2002
- Universal Declaration on Bioethics and Human Rights, UNESCO 2005
- National Codes of Deontology
- Professional Codes

* The number of „other provisions“ is not known

N.B. „soft law“ may enter into legal force by implementation into national law on decision of a State

Reasons for legal Instruments

- Adoption of ethical principles into law of States
  - e.g. free and informed consent to protect autonomy required by German law for medical interventions since 1887,for research since 1900
- Main responsibilty of States to protect human rights and fundamental freedoms
- Obligation to regulate fields in direct relation to these rights
- Law as instrument for harmonization of the interests of different groups in a society
  - Legal instruments are binding for all groups concerned
  - Framework for the application of „soft law“

Legal Instruments and other Texts

- Council of Europe -

- Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine,
  Oviedo, 4.IV.1997, European Treaty Series - No. 164, ratified by 29 States
- Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research,
  Strasbourg, 25.I.2005, Council of Europe Treaty Series – No. 195

➢ Both are treaties and binding for States only by ratification

✧ Other provisions

– Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
(Adopted by the Committee of Ministers on 15 March 2006)

– Guide for Members of Research Ethics Committees (Adopted by the Steering Committee on Bioethics on 3 December 2010)

Primacy of the Human Being

„The interests and welfare of the human being shall prevail over the sole interest of society or science.“

(Article 2, Oviedo Convention)

Freedom of Research

"Scientific research in the field of biology and medicine shall be carried out freely, subject to the provisions of this Convention and the other legal provisions ensuring the protection of the human being." (Article 15, Oviedo Convention)

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." (Article 8, Research Protocol)

Risks and Benefits

„No risks and and burdens to the participant disproportionate to its potential benefits“

- Research without a potential direct benefit for the participant
  - no more than acceptable risk and acceptable burden
- Research with a potential direct benefit for the participant
  - Risk not disproportionate to the expected benefit
- Research on persons not able to consent
  - with a potential direct benefit: proportion risk/benefit
  - without a potential direct benefit: only minimal risk and minimal burden*

* These conditions have been introduced by the Oviedo Convention 1997 and have been adopted by national law or „soft law“

Sources: Articles 16,17, Oviedo Convention, Article 6, Research Protocol

Free and Informed Consent

Key condition for participation in research

- Full information in understandable language
- Consent or refusal without any undue influence
- No discrimination in case of refusal
- Specific attention for vulnerable persons

❖ Responsibility of ethics committees!

Protection of Persons undergoing Research

- No alternative of comparable effectiveness to research on humans
- Acceptable risk/benefit proportion
- Approval by the competent body after independent examination of the scientific merit, including assessment of the importance of the aim of the research, and multidisciplinary review of the ethical acceptability
- Information of the participants of research of their rights and the safeguards prescribed by law for their protection
- Consent or, in case of research on persons not able to consent, authorization by the legal representative expressly, specifically and documented. Free withdrawal of consent or authorization at any time.

Source: Article 16, Oviedo Convention

Research on Persons unable to consent

- All conditions to meet scientific quality
- Justification for research on persons unable to consent
- Risks and benefits:
  - Potential direct benefit for the research participant:
    risks in relation to the expected benefit
  - No potential direct benefit for the research participant:
    protective provisions prescribed by law,only minimal risk and minimal burden!
- Authorization by the legal representative according to national law
  - Full information on the research project for the legal representative
  - Best interest of the represented person
  - Refusal or withdrawal of the authorisation at any time without any form of discrimination against the represented person
  - ✧ No financial or other interest of the legal representative

Sources: Article 17, Oviedo Convention, Chapter V, Research Protocol

Specific Situations

Research during pregnancy or breastfeeding

Research without a potential direct benefit for the pregnant woman, or for her embryo, foetus or child after birth, only

- contribution to the benefit of that group
- no comparable research on women who are not pregnant
- only minimal risk and only minimal burden

Research on persons deprived of liberty

Permission of research on this persons by law!

Research without a potential direct benefit only

- no comparable research on persons not deprived of liberty
- contribution to the benefit of that group
- only minimal risk and only minimal burden

Sources: Articles 18 and 20, Research Protocol

Research in Emergency clinical Situations

Permission and determination of protective additional conditions for research in emergency situations by law when:

- a person is not in a state to give consent, and
- because of the urgency of the situation, it is impossible to obtain in a sufficiently timely manner, authorisation from the legal representative or an authority or a person or a body to be called upon to give authorization
- research of comparable effectiveness cannot be carried out on persons in non-emergency situations;

Specific provisions

- approval for research in emergency situations by the competent body
- respect of expressed objections if known
- research project without a potential direct benefit for the participant: only minimal risk and only minimal burden
- Information as soon as possible of the participant or of the legal representative to ask for consent or authorization for continued participation
- Postponed consent/authorization, no waver of consent/authorization!

Source: Article 19, Research Protocol

Responsibility of Ethics Committee

Independent examination of research projects (REC)

- Submission of every research project for independent examination of its ethical acceptability to a REC; transnational project: submission in each State in which the project or parts of it are performed
  - In some States are RECs entitled to examine in addition the scientific quality and legal aspects
- Purpose of the examination: protection of the dignity, rights, safety and well-being of research participants.
- Appropriate range of expertise and experience adequately reflecting professional and lay views.
- The independence of the REC must be guaranteed
- Harmonization of information for the REC: List of items in the Appendix to the Research Protocol

❖ Approval of a research project by an authority, if required by national law only after the examination by a REC!

Sources: Article 16,Oviedo Convention, Chapter III,Research Protocol

Safety and Supervision

- Minimisation of risk and burden, supervision by a qualified clinical professional
- Assessment of health status prior to inclusion in research, particular considerations on participants in the reproductive stage of life
- Non-interference with necessary clinical interventions
  - no delay nor deprivation of medically necessary preventive, diagnostic or therapeutic procedures.
  - control groups shall be assured of proven methods of prevention, diagnosis or treatment.
  - use of placebo: no methods of proven effectiveness or withdrawal or withholding of such methods does not present an unacceptable risk or burden
- New developments
  - re-examination of a project if justified in the light of scientific developments or events arising in the course of the research.
  - need to discontinue or to change the research project
  - need to inform research participants, or their representatives of the developments or events;
  - additional consent or authorisation for participation?
- Information of the competent body of the reasons for any premature termination of a research project.

Source: Chapter VII, Research Protocol

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 27, Research Protocol)

Confidentiality and Right to Information

Confidentiality

Protection of personal data collected during biomedical research

Legal provisions to prohibit inappropriate disclosure of information submitted to an ethics committee

Right to information

- Right to know any information on health collected in the research project, right not to know (Article 10 of the Oviedo Convention)
- Accessibility to other personal information in conformity with the law on data protection

Availability of results

- Submission of a report or summary to the ethics committee or the competent body after termination of the project
- Availability of the conclusions of the research to participants in reasonable time, on request
- Appropriate measures of the researcher to make public the results of research in reasonable time

Source: Chapter VIII ,Research Protocol