



The Organisation and Performance of regional Medical Ethics Committees in Germany

*International Conference on China's Ethics
Committee Development*

Shanghai, 8th December 2019

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Col – Statement and Caveat

- **There are no conflict of interests to declare.**
- **The views expressed here do not necessarily represent exactly those of the Association of Medical Ethics Committees in Germany.**

Content

- **Background and history**
- **Organisation of Medical Ethics Committees (MECs) in Germany**
- **Ethical and legal guidances for MECs in Germany**
- **Performance**
- **Conclusions**

Why are Medical Ethics Committees essential ?

1st Key Ethical Conflict in Medical Care and Research:

- It is unethical to administer a therapy whose safety and efficacy has not yet been properly proven.
- It is, however, unethical too to evaluate the benefit of a new therapy in humans as the risk of a negative harm / benefit balance cannot be excluded.

Why are Medical Ethics Committees essential?

2nd Key Ethical Conflict in Medical Care and Research:

- A patient rightly expects that his/her physician acts in his/her best interests. **Thus in routine health care the physician acts as a therapist only.**
- In research, however, the physician-investigator has to comply with the directions of the trial protocol, too.

 **Role conflict:**
therapist vs physician-investigator

Methods for the Resolution / Moderation of these ethical Conflicts

- Extensive preclinical testing
- Requirement of a detailed trial protocol
- Authorization by competent drug authority
- **Review of the research project by an Independent Medical Ethics Committee**

Methods for the Resolution / Moderation of these ethical Conflicts

- Safety monitoring, interim analyses and data monitoring committees
- **Voluntary Informed Consent**
- **Unalienable right to withdraw Informed Consent at any time**
- Compensation in case of harm
- Good Clinical Practice - conformity

Conflict – Resolution / Moderation

- Since 1975 the Declaration of Helsinki has been requesting that these ethical issues are mitigated and moderated by Independent Ethics Committees.
- Many international conventions like the ICH-GCP, the Additional Protocol of the Council of Europe and WHO/CIOMS have adopted this successful and by now very well-tried solution.

History of the ethical Assessment of Medical Research with Humans in Germany

History

- 1966 publication by H. Beecher*, stating that 22/100 published research projects were problematic from an ethical point of view.
- 1973 The first Medical Ethics Committees were founded in Germany (Ulm and Göttingen).
- 1975 Tokio: Revision of the Declaration of Helsinki, asking for an independent committee to review medical research projects.
- 1985 The Professional Code of Conduct of the German Medical Association requires physicians to consult a Medical Ethics Committee under public law prior to the start a research project with humans.
- 1995- Review by Medical Ethics Committees became an obligation in
2004 the German Medicines and the Medical Device Laws.

*Ethics and clinical research. N Engl J Med 1966; 274:1354–1360 9

Organisation of the Ethical Assessment of Biomedical Research in Germany - Background

Basic Law for the Federal Republic of Germany

- ✓ Human dignity shall be inviolable (Art.1)
- ✓ Every person shall have the right to life and physical integrity. Freedom of the person shall be inviolable. These rights may be interfered with only pursuant to a law. (Art.2)
- ✓ Arts and sciences, research and teaching shall be free. (Art.5)

These rights have to be protected by the state.

As the integrity and the autonomy of medical research participants is at risk there are special provisions by federal laws however for

- Studies with medicinal products (i.e. medicines)
- Studies with medical devices, incl. radiation exposure
- All biomedical and epidemiological research has to be approved by a MEC according to the Declaration of Helsinki and the German Physicians' Code of Conduct.

Structure of the Ethical Assessment of Biomedical Research in Germany

Medical Ethics Committees (MECs)

- 54 MECs under public law, organized by universities (34), Medical Associations of the federal states (17) and departments of health of federal states (3).
- Act in absolute independence, but in compliance with German and European Union laws and regulations. (→ accreditation)
- MECs are multidisciplinary: physicians(majority), pharmacologists, ethicists, lawyer/judges, biostatisticians, lay persons/patient representatives. Members have to declare competing interests.

Structure of the Ethical Assessment of Biomedical Research in Germany

- In Germany, universities with Medical Schools and Medical Associations are public law institutions and enjoy considerable autonomy.
- MECs are mainly governed by state law, not federal law.
- The members of MECs are elected by bodies authorised by public law or approved bylaws.
- The chairperson of the MEC is typically elected by the members of the MEC by secret ballot.
- Members work mainly in an honorary function.
- Business office with competent academic staff needed.

Organisation of MECs in Germany

In 1983 the MECs founded the Association of MECs in Germany (AKEK), which

- Organizes continued education for MECs' members,
- Harmonises the procedures of MECs in Germany,
- Represents the MECs in the public,
- Represents the interests and positions of MECs in the political debate and policy making in Germany and in the European Union.

The Association organises two annual meetings (each 2 ½ days). The homepage will be provided in English soon: www.akek.de .

Cross-Sector Roundtable of Stakeholders

- **Drug Authorities**
- **Commercial Sponsors**
- **Academic Sponsors**
- **Contract Research Organisations**
- **Association of MECs**

meet twice a year (about 15 persons) to solve problems effectively and to inform each other about recent developments. AMECs serves as host.

Inspection Order of Ethics Committees

- **The scientific quality of the planned investigation**
- **The lawfulness**
- **The ethical acceptability**
- **The medical acceptability**

Ethical Guidances for MECs in Germany

Deontological (study of duties) Ethics:
(since Hippocrates, referring to physicians)

Stresses:

- data privacy and confidentiality
 - **care for the beneficence of the patient only**
 - **to do the sick no harm (non-maleficence)**
 - gratefulness to teachers and willingness to share knowledge and experience
- **attitude and action orientated**

Ethical Guidances for MECs in Germany

Principle-based Ethics*:

- four prima facie principles:
 - **Autonomy** and respect for the dignity of the patient or healthy volunteer, e.g. Informed Consent, 'man must not be a means to an end'
 - **Beneficence**
 - **Non-maleficence**
 - **Justice** → to act in a fair and equitable manner as far as the distribution of research risks or burdens and benefits are concerned.

There is no hierarchical order → The MECs have to balance these principles.

Ethical Guidances for MECs in Germany

- ✓ **The Declaration of Helsinki, current version**

Legal Guidances for MECs

- ✓ **The Basic Law of Germany**
- ✓ **The German Medicines Law***
- ✓ **The German Medical Devices Act***
- ✓ **The German Radiation Protection Law***

***These German laws specify in detail the compulsory requirements for the permission of research with humans.**

The German Medicines Law, Art. 40

- „The foreseeable risks and disadvantages of the study are acceptable from a medical point of view in consideration of the potential benefit for the research subject, *and* the expected relevance of the test drug for medicine.“

 **Two separate risk/benefit analyses have to be done**

The Scope of the Ethical Assessment of Clinical Trial Applications

Clinical trials with medicines are regulated by the EU-CTD and corresponding national laws; the Clinical Trial Directive 2001/20/EU asks MECs to review;

- the relevance of the clinical trial and the trial design;
- whether the evaluation of the anticipated benefits and risks is satisfactory and whether the conclusions are justified;

The Scope of the Ethical Assessment of Clinical Trial Applications*

- the protocol;
- the suitability of the investigator and supporting staff;
- the investigator's brochure;
- the quality of the research facilities;
- the adequacy and completeness of the written information to be given, and the procedure to be followed for the purpose of obtaining informed consent;

The Scope of the Ethical Assessment of Clinical Trial Applications*

- provision for indemnity or compensation in the event of injury or death attributable to a clinical trial;
- any insurance or indemnity to cover the liability of the investigator and sponsor;
- the amounts and, where appropriate, the arrangements for rewarding or compensating investigators and trial subjects and the relevant aspects of any agreement between the sponsor and the site;
- the arrangements for the recruitment of subjects.

The Role of MECs in Germany – Drug Trials

- About 1000 applications/yr for drug trials
- About 3 % of all submissions get rejected
- About 3% of all submissions pass without any modification
- **More than 90% of all submissions pass only with modifications, protecting patients' rights , well-being and safety.**

There are about 400 applications/yr for medical device trials and about 8500 applications/yr for research with humans(non-drug, non-device), identifiable biosamples or data to be reviewed.

Conclusions

- The system of MECs is well developed in Germany.
- The level of protection of research participants is very high. No serious damage has happened in the last 25 years.
- The MECs deliberate and decide completely autonomous, but in compliance with the laws.
- The regional organisation of MECs in Germany is due to historical and federalistic circumstances.
- The Association of MECs in Germany is unique in the EU and is very important for the independent representation of the interests of research participants and MECs.

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