Clinical trial regulation and ethical committees

EAHP statements 6.4. 6.5.

JG|U UNIVERSITÄTSmedizin. MAINZ

Pharmacy, Prof. Dr. Irene Krämer

Disclosure

- Conflict of interest:
  Dr Irene Krämer received speakers' fee and/or honoraria from Amgen, Boehringer Ingelheim, Abbvie, MSD

Self assessment questions

- Ethics committees only approve Phase 1-3 clinical trials of medicinal products
  Yes or No

- Recommendations for research ethics committees are based on the Declaration of Helsinki (latest version)
  Yes or No

- Ethical aspects do not play a role in daily pharmacy practice
  Yes or No

Ethics committee of the state of Rhineland Palatinate

Chair person
Co-chairs
Members
Medical professionals
Non-medical professionals
e.g. other health care professionals
legal professionals
patient advocates
CEO

Approach
interdisciplinary
independent
transparant

Glück

hatte ein Bote, dem ein mit sehr wirksamen Schlaftabletten gefüllter Karton abhanden kam: da es sich um das ungiftige Contergan handelte, brauchte er weder Polizei noch Rundfunk zu alarmieren,

mehr Glück

aber noch der Finder: wie er sich auch entscheidet, ihm wird nichts passieren, er wird Ruhe haben und nachts gut schlafen. Sollte ihn jedoch das schlechte Gewissen zu einer Verzweiflungstat treiben, so wird er nach dem Erwachen merken, daß man mit

Contergan

nur schläft und nicht verzweifelt.

Special Communication

World Medical Association Declaration of Helsinki
Ethical Principles for Medical Research Involving Human Subjects

World Medical Association

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington, DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

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 be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects

best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research

Recommendations of the Ethics committee based on

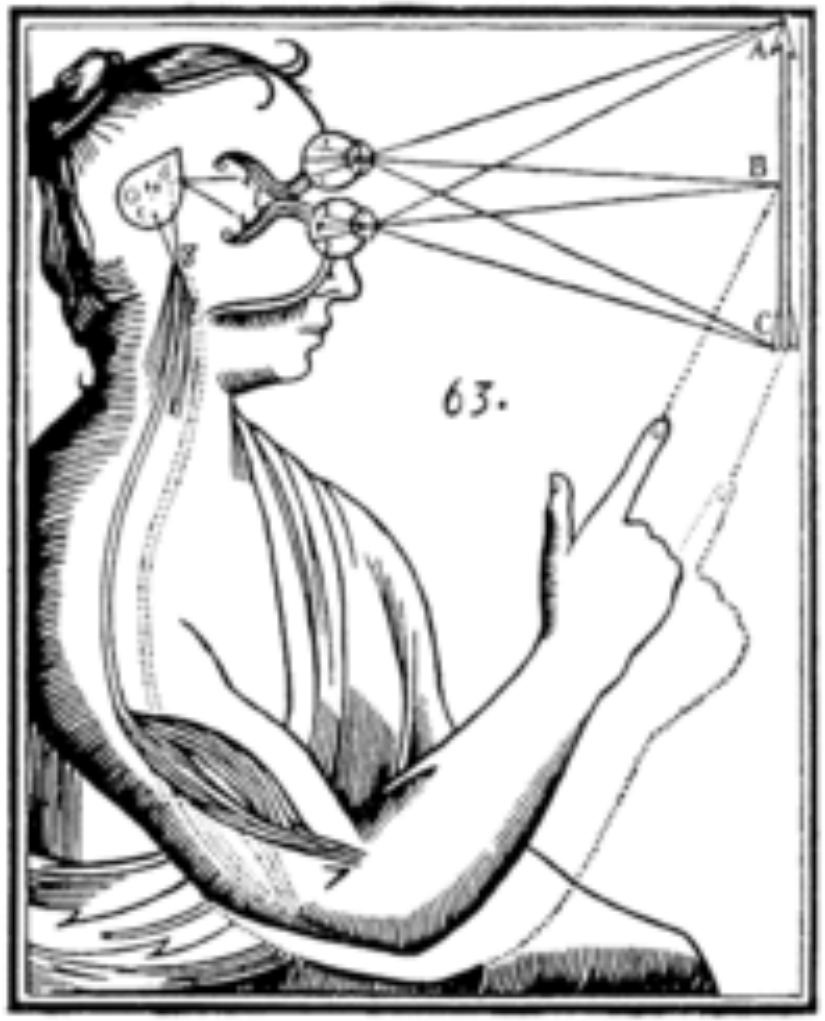
- Ethical principles
- Scientific quality
- Lawfulness

Protection of research subjects AND of responsible medical professionals

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must 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

Ethik-Kommission bei der Landesärztekammer Rheinland-Pfalz



Mandatory Consultation by the Ethics committee before starting a Clinical Research project

Types of Research Projects

Clinical trials with medicinal products (AMG)
Clinical trials with medical devices (MPG)
Interventional clinical studies
Non-interventional clinical studies
Epidemiological studies
Studies on Bio-material

Clinical trials with medicinal products

- Phase 1 to 3, safety, efficacy
- randomized, (placebo)controlled, blinded studies
- sponsors (Pharmaceutical industry)
- Clinical research organizations (CRO)

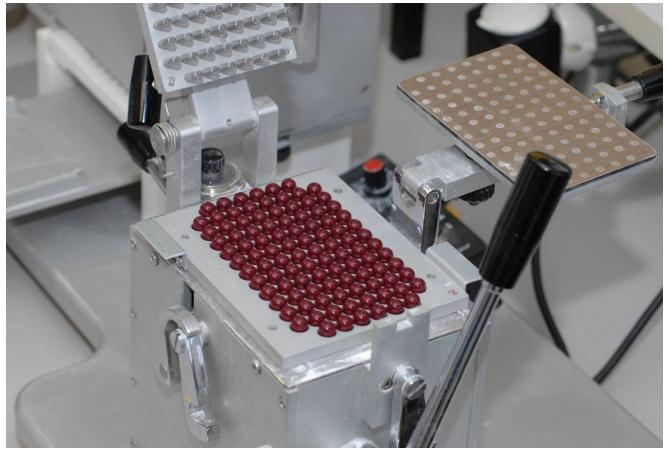
Clinical trials with medical devices

- new applications
- safety
- assessment of performance

Evaluation and approval according to the Medicinal Products Act and Medical Devices Act, Regulation EU Nr. 536/2014

Clinical research

- Investigator initiated
- Interventional, non-interventional
- Clinical trial material prepared by hospital pharmacy

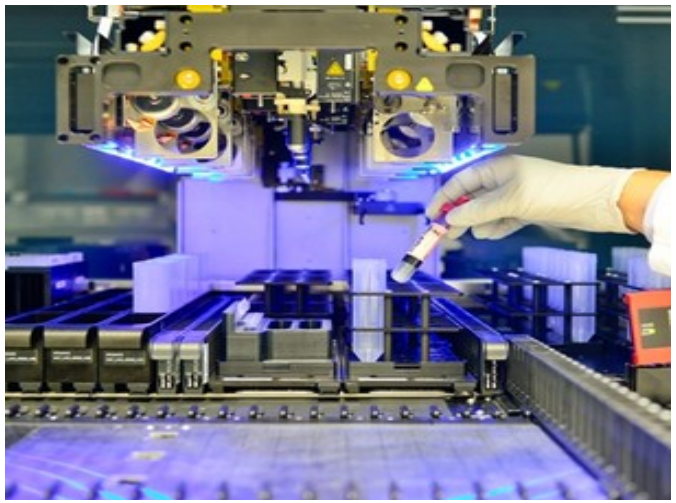


Clinical research with particulars

- questionnaires
- interviews
- registries
- Phase 4 studies

Clinical research with bio-material

- liquid bio-banks
- cell and tissue banks
- gene analysis



Consultation according to professional regulations

Declaration of Helsinki 2013, § 23

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 amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

Evaluation of
Periodic safety update reports
Serious adverse events

Meetings of the Research Ethics Committee

- Monthly or twice monthly
- About 40 topics
  applications, ammendments, safety reports
- Pre-reading of the documents by the members
- Application assigned to an expert member
  pre-assessment and report by the expert
- Questions and answers round
- Decision making

- Chairperson
  signature of the protocol
  signature of the notification for the applicant

Points to consider

- Patient information
  too long (20-30 pages), bad translations, not understandable
  too short, not complete, meaningless
  not appropriate for paediatric patients of different age groups
- Informed consent document
  not corresponding to the regulations
  data protection
- Gene analyses
  Incidental findings with genomic sequencing
  Implications for genetic counseling practice
  medically actionable findings, right to know and to opt out
- Investigation of bio-material (WMA declaration of Taipei)
  purpose limitation principle

Protection of vulnerable groups and individuals

-

minimal burden
minimal harm

Annual Workload

500 New applications

800 Amendments

Good reasons for participation as pharmacist in the Research Ethics Committee

- Placement of pharmaceutical aspects
- Placement of real-life aspects

- Thinking out of the box
- Personality development
- Volunteer spirit activity for patients

- Development of better understanding for the needs of clinical reseachers
- Reputation for pharmacy profession
- Keeping pharmaceutical knowledge up-to-date

Procedures of a Research Ethics Committee in Germany

Time for questions and comments

Clinical Ethics Committee

Ethikkomitee der Universitätsmedizin Mainz

Willkommen auf den Seiten des Ethikkomitees der Universitätsmedizin Mainz !

Das Ethikkomitee der Universitätsmedizin Mainz hat seine Arbeit am 3.5.2005 aufgenommen.
Es hat sich zur Aufgabe gestellt, Mitarbeiter/innen, Patienten und Angehörige sowie den Vorstand zu beraten, die Mitarbeiter der Universitätsmedizin in klinischer Ethik fortzubilden sowie ethische Leitlinien für die Universitätsmedizin Mainz zu entwickeln (siehe auch Aufgaben und Satzung des Ethikkomitees).

Einmal im Jahr bietet das Ethikkomitee der Universitätsmedizin Mainz Interessierten, Medizinern, Pflegenden und Bürgern zu unterschiedlichsten Themen einen großen

Ethiktag der Universitätsmedizin Mainz

an, siehe Termine.

Der 10. Ethiktag der Universitätsmedizin Mainz wird am
23. November 2018, ab 13.00 Uhr,
im großen Hörsaal der Frauenklinik,
Geb.102, EG, in der Universitätsmedizin Mainz

Kliniken & Einrichtungen
Über die Universitätsmedizin

Ansprechpartner

Vorsitzender:
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Direktor des Institutes für Geschichte, Theorie und Ethik der Medizin der Universitätsmedizin Mainz
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Duties of the Clinical Ethics Committee

- Education and continuing education of the hospital staff regarding clinical ethics
- Development of local guidelines for patient-oriented procedures based on ethical principles
- Consultation of the board of directors and medical directors of the clinics regarding ethical issues in medical treatment and nursing care
- Ethics consultation in individual patients requested by physicians, nurses, patients or there families/caregivers

Procedures of the Clinical Ethics Committee

- Monthly meetings
- Members: medical professionals, nurse professionals, catholic and protestant pastoral caregivers, hospital social workers, legal professional, pharmacist
- Reflection on recent patient-individual consultations
  exchange of views (e.g. religious, cultural aspects)
  conflicts with the advance directive
- Discussion of new regulations and court judgements regarding treatment of patients

Distribution of Cannabis herb/raisin by pharmacy

Cannabis als Medizin

Mit dem am 10. März 2017 in Kraft getretenen Gesetz zur Änderung betäubungsmittelrechtlicher und anderer Vorschriften hat der Gesetzgeber die Möglichkeiten zur Verschreibung von Cannabisarzneimitteln erweitert. Ärztinnen und Ärzte können künftig auch Medizinal-Cannabisblüten oder Cannabisextrakt in pharmazeutischer Qualität auf einem Betäubungsmittelrezept verschreiben. Dabei müssen sie arznei- und betäubungsmittelrechtliche Vorgaben einhalten. Neben den neuen Regelungen bleiben die bisherigen Therapie- und Verschreibungsmöglichkeiten für die Fertigarzneimittel Sativex® und Canemes® sowie das Rezepturarzneimittel Dronabinol bestehen.

Mit Inkrafttreten des Gesetzes hat das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) eine Cannabisagentur eingerichtet. Die Cannabisagentur wird den Anbau von Cannabis zu medizinischen Zwecken in Deutschland steuern und kontrollieren. Die Cannabisagentur wurde als neues Fachgebiet in der Abteilung „Besondere Therapierichtungen“ im BfArM eingerichtet.

Die Bundesopiumstelle im BfArM führt eine Begleiterhebung zur Anwendung von Cannabisarzneimitteln durch, um weitere Erkenntnisse über die Wirkung von Cannabis als Medizin zu gewinnen.

Weitere Inhalte

- Cannabisagentur
- Hinweise für Ärzte
- Hinweise für Apotheker
- Hinweise für Patienten
- Begleiterhebung

Ausschreibung

- Supplement zum Amtsblatt der Europäischen Union

Pressemitteilung

- Cannabis als Medizin

Distribution of cannabis herb/raisin for inpatients

- Approved medicinal products: Sativex®, Canemes®, Marinol®
- Cannabis herb/raisin for pharmacy preparations
  Identity testing in the pharmacy

- Added value of pharmacy preparations (herb, capsules, oral liquid)?
- Evidence of cannabis herb compared to standardized approved medicinal products or pharmacy preparations?
- Dosage form of herbs – vaporisation in the hospital?

- Switch to oral liquid forms during hospital stay?
  Congruent to professional ethics?

Switch of cannabis herb/raisin to oral liquid form or approved medicinal products during hospital stay?

Time for comments and discussion

Distribution of pentobarbital for assisted suicide

- Organized (medically) assisted suicide forbidden by law in Germany
- March 2017 court judgement, that terminally ill patients under certain conditions have the right to obtain pentobarbital
- Meanwhile 80 applications submitted to BfArM/narcotic drug agency
  No decisions made yet (moral conflict)
- March 2018 Di Fabio (lecturer in constitutional law):
  „The right of the individual patient to do suicide, does not induce the obligation of the government to assist suicide“

  „Pharmacists can not be forced to distribute the lethal dosage of pentobarbital“
  Not congruent to professional ethics, freedom of conscience

Distribution of pentobarbital for assisted suicide by pharmacy?

Time for comments and discussion

Take home messages

- Pharmacists should participate in research ethics committees and clinical ethics committees
- Pharmacists should place pharmaceutical aspects and the professional ethics in the committees
- Professional ethics are to be regarded in daily pharmacy practice

Self assessment questions (with answers)

- Ethics committees only approve Phase 1-3 clinical trials of medicinal products
  No

- Recommendations for research ethics committees are based on the Declaration of Helsinki (latest version)
  Yes

- Ethical aspects do not play a role in daily pharmacy practice
  No