ARBEITSKREIS MEDIZINISCHER ETHIK-KOMMISSIONEN IN DER BUNDESREPUBLIK DEUTSCHLAND e.V.

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„Gemeinsamkeiten und Unterschiede bei der ethischen Bewertung von klinischer Forschung in den Ländern der EU“

Ethikkommissionen für Forschungsvorhaben am Menschen

Im Zuge der Entwicklung der medizinischen Forschung wurden Ethikkommissionen zunehmend als wichtig und schließlich als wichtigstes Instrument angesehen, um Personen zu schützen, die bei dieser Forschung als Probanden mitwirken. Alle Länder Europas und die meisten anderen forschenden Nationen haben in den vergangenen Jahrzehnten Kommissionen etabliert, die diese Funktion wahrnehmen sollen.

Was den Begriff “Forschung am Menschen” angeht, kann sowohl diskutiert werden, was “Forschung” ist, als auch, was “am Menschen” besagen soll.

“Forschung” muss sowohl gegenüber Diagnostik und Therapie als auch gegenüber Entwicklung abgegrenzt werden.

International wird der Terminus “human being” unterschiedlich ausgelegt. Einige Länder unterwerfen die Forschung an humanem biologischen Material (Norwegen) oder Forschung an humanen embryonalen Zellen einer Überprüfung durch lokale Ethikkommissionen. Andere haben für letzteres nationale Gremien geschaffen (UK, Frankreich, Deutschland).

Ethikkommissionen für Forschungsvorhaben am Menschen

Ein angemessenes Urteil über die Risiken und die Belastungen medizinischer Forschung für die Probanden sowie den erwarteten Nutzen für den Einzelnen, die Gruppe der Patienten oder die Gesellschaft als Ganzes fordert die Expertise aus vielen wissenschaftlichen und medizinischen Disziplinen. Zudem ist die Kompetenz in moralischen Beurteilungsfragen wie auch Kenntnis des Rechts und der Ethik wichtig. Diese Erfordernisse spiegeln sich auch in der Zusammensetzung der Kommissionen wider.

Mitglieder von Ethikkommissionen:

- In allen Europäischen RECs sollen Krankenhausärzte tätig sein. Vielfach stellen sie die Mehrheit (zusammen mit med. Forschern) (manchmal werden spez. Disziplinen gefordert: Pädiater, Biostatistiker, Pharmakologen etc.) . Unabhängig von formalen Erfordernissen sind diese Disziplinen faktisch sehr häufig repräsentiert.
- Juristen und Krankenschwestern und –pfleger sind als zweit- und drittwichtigste Gruppe gefordert.
- In vielen Ländern sind Vertreter der –Glaubensgemeinschaften, Theologen, Philosophen oder Ethikexperten Mitglieder von RECs (Zahl schwankt).
- In den Skandinavischen Ländern stellen Laien eine große Gruppe.
- Die Forderung, die Mitglieder zu schulen, wird immer wirksamer.

Mitglieder von Ethikkommissionen:

In den meisten Ländern werden Repräsentanten der Religion, Theologen, Philosophen oder ethische Experten als Mitglieder in die Komitees berufen. Somit ist der entscheidende Unterschied zwischen den Ländern Europas darin zu sehen, dass der Anteil dieser Repräsentanten sehr unterschiedlich sein kann. Das gleiche gilt für die Mitwirkung von Laien.

Mitglieder von Ethikkommissionen:

In Skandinavien stellen Laien eine erhebliche Gruppe dar und in Dänemark bilden sie sogar die Mehrheit aller Komitee-Mitglieder. Sie werden durch die Provinzräte gewählt. In anderen Ländern ist die Vertretung der Laien im Sinne einer Vertretung von Patienten oder Patientengruppen und nicht so sehr als ein demokratisches Erfordernis ausgestaltet.

In vielen Ländern entstanden RECs aufgrund staatlicher Initiativen mit unterschiedlichen Motiven (Aufnahme in die Europäische Union [Baltische Staaten, Spanien], Forderung nach rechtlicher Konsistenz [Frankreich], Debatte der Zivilgesellschaft [Brasilien], administrative Bemühungen [Mexiko, Argentinien], Druck der Pharmaindustrie [Chile, Argentinien], Initiativen von Bioethikinstituten [Argentinien]).

In Deutschland waren es der ärztliche Berufsstand und die Ärztekammern sowie die Medizinischen Fakultäten und Universitäten, die ein bundesweites System von Ethikkommissionen errichtet haben, das unter dem Rahmen des öffentlichen Rechts arbeitet.

Forschungsethikkommissionen können die wachsene Arbeitslast nur mit qualifizierzten Mitarbeitern einer Geschäftsstelle bewältigen.

Wegen der erhobenen Gebühren in der Arzneimittelforschung können auch ärmeren Länder und Hochschulen eine solche Geschäftsstelle einrichten, wenn die Mittel adäquat verteilt werden.

Gemeinsamkeiten und Unterschiede

- Forderung nach Zentralisierung
- Forderung nach Harmonisierung
- Forderung nach der Beibehaltung des lokalen Prinzips mit jeweils eigenem Beurteilungsspielraum

Vier Kennzeichen der Moral

1. Im Mittelpunkt der Moral stehen Urteile, durch die ein menschliches Handeln positiv oder negativ bewertet, gebilligt oder missbilligt wird.

2. Moralische Urteile sind kategorisch. Sie bewerten Handlungen unabhängig davon, wieweit diese den Zwecken oder Interessen des Akteurs entsprechen.

3. Moralische Urteile beanspruchen intersubjektive Verbindlichkeit.

4. Moralische Urteile bewerten Handlungen ausschließlich aufgrund von Faktoren, die durch Ausdrücke von logisch allgemeiner Form ausgedrückt werden können.

Dieter Birnbacher, Analytische Einführung in die Ethik, 3. Aufl. 2013, Schema S. 13

„Wollte man versuchen, die eigene Auffassung dessen, was die Tugend verlangt, auf eine Menge von Regeln zu reduzieren, so würden – einerlei wie scharfsinnig und besonnen man bei der Zusammenstellung dieses Regelwerks verführe – unweigerlich Fälle auftauchen, bei denen uns eine mechanische Anwendung der Regeln verfehlt vorkäme, und zwar nicht unbedingt deshalb, weil man seine Gesinnung geändert hätte, sondern weil die eigenen Anschauungen über derlei Dinge es gar nicht zulassen, von irgendeiner allgemeinen Formel erfaßt zu werden.“

(McDowell, Wert und Wirklichkeit, Frankfurt a.M. 1998, 84)

„Von Gelegenheit zu Gelegenheit weiß man, was man tun soll, sofern man es überhaupt weiß, aber man weiß es nicht dadurch, daß man allgemeine Prinzipien anwendet, sondern dadurch, daß man eine bestimmte Art von Person ist: jemand, der Situationen in einer bestimmten, für ihn bezeichnenden Weise sieht.“ (ebd., 105)

- The results from a survey we prepared in 2003 for the EC showed that research ethics committees and their members felt committed to the same principles: Helsinki-Declaration, Oviedo-Convention
- Nobody indicated that a special philosophical or ethical tradition of a country or a region would be important or even binding for the work of the REC.

- In those countries where no legal regulation for the work of RECs existed before Directive 2001/20/EC committee members expressed the need of a clear and binding system.
- In those countries where the vote of the REC already represented a binding decision for the researchers experts discussed the change in the role of RECs (judgement vs. advice) critically.

The European Directive (Directive 2001/20/EC, Art. 6, (5)) made obvious that it is an obligation of the state to ensure the functioning of a system of ethical evaluation and regulation:

„Article 6: Ethics Committee

For the purposes of implementation of the clinical trials, Member States shall take the measures necessary for establishment and operation of Ethics Committees.

The Ethics Committee shall give its opinion, before a clinical trial commences, on any issue requested.“

The Directive and its implementation did not change the status quo as far as membership of RECs is concerned.

Different structures may be in accordance with the Directive:

- A committee system with only one level has to be distinguished from a two level system.
- A single level system can be central (Slovenia) or local (Belgium) or regional (France).
- In a two level system the national or central level may take very different shapes:

  - function of a consultant (Committee at the German Federal Chamber of Physicians)
  - instance of appeal (Poland, Netherlands)
  - coordinating authority (Netherlands)

Nevertheless the obligation to translate the Directive into national law was a starting point for legislation and policy making in the member states that sometimes was not explicitely required and in some respects even took opposite directions:

Centralization

Greece: The directive has been incorporated into Greek Law through Ministerial Decision DYC3/89292 and State Journal B‘ 1973/31.12.2003. This implementation created a National Committee which takes the final decision regarding research projects.

Portugal: Law 46/2004 (19th August) implements the Directive. It has introduced several changes in the system of ethical review. An opinion is now required from the newly created central ethics committee; the central committee is allowed to ask a local committee to fulfil this task.

Decentralization

Slovenia: The Slovenian Directive on Clinical Drug Testing is based on the European Directive.

There is a certain move towards decentralisation, local RECs are empowered to take up part of the responsibilities of the National Medical Ethics Committee.

Creation of an instance of appeal

Ireland: An appeal can be made to the Ethics Committees Supervisory Body for a second REC opinion or against the original REC decision.

The 1987 &1990 Acts stipulate that no legal action can be taken against an REC. There is provision for clinical indemnity for all members of ethics committees in the Department of Health guidance.

Creation of a state agency for drugs

Lithuania: This was implemented through a Ministry of Health Decree of 11 May 2004.
The most significant change in the system was that approval from the State Drug Control Agency is required for clinical trials on medicinal products in addition to a positive opinion from an REC.

Legal strengthening of the REC opinions

Italy: The directive has been implemented through Legislative Decree no. 211 of 24 June 2003. The RECs have now the power to give a legally binding opinion to a research protocol.

Spain: The directive was implemented by Royal Decree 223/2004, Article 60, 62 and 65 of Law 25/1990. It will affect protocols of tests involving minors or incapacitated adults, where expert advice will be required by RECs. It will also require follow-up procedures for protocols receiving a positive opinion.

Belgium: The law implementing the Directive came into force on 7 May 2004. RECs now have a legal status and evaluate protocols according to defined criteria.

Only slight changes

The Netherlands: There have been slight changes regarding the criteria and organisation of the review with the new law which came into force on 1 March 2006.

Sweden: Modifications concerning clinical trials where minors and incapacitated adults are involved; single opinion for multi-centres trials; time frame for ethics review; particular expertise in the RECs.

Poland: The directive was implemented in the legislation of 2002. Ministry of Health Act Nr.221 poz.1864.

Latvia: Addition to the Pharmacy law: 20.08.02 and amendment (30.04.04) to the Cabinet Regulations no.312.

One has to mention committees that evaluate specific kinds of research in the biomedical sphere:

In Germany, the Central Ethics Committee for Stem Cell Research (Zentrale Ethik-Kommission für Stammzellenforschung, ZES) was established in 2002 with the enactment of the Stem Cell Act. The 18 members and deputy-members of the ZES are appointed by the German Federal for three-year periods. The ZES is charged wit the task of reviewing and evaluating applications for import and use of human ES cells according to the Stem Cell Act and has to submit a written opinion on each application to the licensing authority, the RKI.

In the Netherlands, the Centrale Commissie Mensgebonden Onderzoek (CCMO) is directly responsible for evaluating research on children and for research proposals in gene therapy.

Institutional Review Boards (IRBs) :

In some cases there may be a need for ethical evaluation of research on human beings where the law does not require that evaluation (requirements of sponsors or of scientific journals etc.).
If the ethics committees that are competent according to drug law do not evaluate this kind of research (e.g. surveys, interviews …) the work is sometimes done by institutional review boards.

Le comité d'éthique pour la recherche médicale et en santé de l'Inserm (Ermes) a été mis en place en 2000 avec pour vocation d'être un acteur à part entière dans le dialogue entre la communauté scientifique et médicale de l'Inserm et la société dans son ensemble.

Continuing problems

- Despite the legal and institutional requirements it is not always easy to find experts willing to do the work.
- In different European regions there are difficulties to find trained lawyers.
- In some Central and Eastern European countries there are not enough philosophers familiar with the field of biomedicine.
- The absence of members is still a problem (cf. Huriet 2001, national report France for EULABOR 2006).
- The Directive does not provide a legal framework to conduct research in situations of emergency (c. CoE, Protocol on Biomedical Research, Art. 19)

Conclusions

A review of the process of implementation reveals several aspects that are somewhat problematic.

To successfully accomplish the task of reviewing all research projects necessitates a working and well funded committee.

Especially in some eastern European countries a lack of funding for those committees may endanger the functionality of the committees and make compliance with the 60 day limit (Directive 2001/20/EC, Art. 6, (5)) a difficult task to say the least.

Where a central committee combines several functions this can mean an accumulation of power.

Ethikkommissionen für die Forschung am Menschen:	RECs
Nationale Beratungsgremien („Ethikräte“):	NECs
Klinische Ethikkommissionen („Ethikkomitees“):	CECs
Kommissionen für gute wissenschaftliche Praxis:	CRIs

Mandat	Berater	Entscheider	Moderator
NEC	✓		✓
REC	✓	✓	
CEC	✓		✓
CRI	✓	✓	✓

PRIVIREAL

2001-2005

Implementation of the data protection directive in relation to medical research and the role of ethics committees

PRIVIREAL

PRIVILEGED

EULABOR

EUREC

European Network of Research Ethics Committees - EUREC

EUREC is a network of national networks and associations of Research Ethics Committees (RECs) in Europe. The network aims at the development of high quality standards in clinical trials in order to protect human subjects. Therefore the members of EUREC commit themselves to create this network in order to

- facilitate exchanges of knowledge, know-how and information
- disseminate training materials among members of RECs, and
- conduct research on characteristics of biomedical research conducted on human beings.

EUREC provides information on activities of the different RECs in European countries, the implementation of European directives in national law and concrete trial proposals, the legislation concerning medical trials, the organisation of national networks of RECs, and national debates concerning research ethics. EUREC assists to learn how European cross-national trials can be realized without striking national law nor European directives.

Consent und Assent in der Forschung an nicht volljährigen Probanden

Informed consent for paediatric clinical trials in Europe

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“ Paediatric clinical trials are often conducted as multinational trials. Informed consent or assent is part of the ethics committee approval for clinical trials. The consent requirements vary between countries due to national laws and regulations, which are not harmonised in Europe. These discrepancies can present challenges for paediatric clinical trials. The aim of this study was to assemble these consent and assent requirements across the European Economic Area. The collated national requirements have not been publicly available before, despite a real need for this data.”

“Assent and consent: differences in use and definitions

Both the term ‘consent’ and ‘assent’ are interpreted differently in legal texts between EEA countries. Generally, each country's national legislation includes legal age ranges and requirements for either consent or assent from a child, in addition to any legal (parental or guardian) signatures. The definition of these two terms rests on the need of these signatures: either given by the trial subject alone, or in conjunction with the parents/guardians. Usually, consent is defined according to the legal age limit of majority, which differs between countries. This is not the case in all countries, like the Netherlands where infant informed consent is needed, in addition to parental consent in children between 12 and 17 years of age. Assent is a non-legal agreement, and an additional parental/guardian signature (consent) is always required before the participation of the child in a trial is legally accepted.”

“Differences in consent and assent age limits and legal signatures

In most of the EEA countries, 18 years is the legal age for independent consent, but the following exceptions should be noted: 14 years in Austria, 15 years in Finland and Denmark and 16 years in the UK. These exceptions come with certain limitations and with the obligation to notify parents/legal guardians. However, across all the EEA countries, 32 different age groupings to the legal age exist for recommended additional assent or consent needed from the child participating in the CT. These groupings include, for example, 4–11 years, 12–14 years and 14–17 years. Only three countries (Croatia, Lithuania and Slovakia) have not specified age groups for assent or consent.”

Table 1

The Informed Consent and Assent Tool Kit—informed consent requirements for paediatric clinical trials in Europe

Country	Legal age of consent†	Mandatory/suggested age ranges defined for assent (or consent if assent not used)‡	Number of required signatories	Official language requirements	Consent template(s)/guidelines/information sources
Austria	Not specified Practice—14 years	8–13 years EC may require younger assents	Both parents	German	http://www.medunigraz.at/ethikkommission/Forum/index.htm http://www.ethikkommissionen.at/ http://www.uibk.ac.at/strafrecht/scheil/scheil-einfuehrung-in-die-arzneimittelpruefung-bei-kindern-und-jugendlichen---kks--kids-ip.pdf
Belgium	18 years	4–11 years (some sites do not use under 12 years) 12–14 years 14–17 years	One parent at recruitment, but both parents at some point for signatures	Dutch, French; German at site request	http://www.fagg-afmps.be/en/human_use/medicines/medicines/research_development/ethic_committee/templates_informed_consent/ Do not have paediatric templates
Bulgaria	18 years	6–11 years 12–14 years 14–17 years—use own consent+parental signature also required	Both parents	Bulgarian	No national EC websites available in English Bulgarian Drug Agency -> clinical trials http://en.bda.bg/index.php?option=com_conte

Die Erweiterung der Landschaft von Forschungsethikkommissionen

Case Study Non-Mandatory Ethics Bodies at Austrian Universities

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“Why are non-mandatory ethics bodies established? All in all, the non-mandatory ethics bodies analysed for this case study are rather new institutions. The first was established in 2005. Other units were founded in the years 2006, 2008, 2009 and 2010 respectively. In 2011, three new organizations were set up. One ethics body of this sample was only installed in 2012. Interviewees mentioned several reasons for this trend of establishing non-mandatory ethics bodies at Austrian universities. One explanation provided by many interviewees is pressure from national and international funding bodies and/or journals, which increasingly require ethical clearance for funding and publication. This obligation is particularly strong in research that involves human subjects and animals, although this is covered by national legislation anyway. “

“Several respondents also mentioned public scandals that had endangered the image and credibility of their research institutions. These scandals had triggered the establishment of an ethics body. Instances for such scandals referred to in the interviews included the use of animals for research that was considered unnecessary and cruel, the improper use of human corpses for car crash tests, the removal of bone chippings from corpses without prior informed consent by relatives, cases of plagiarism as well as research that was considered mumbo jumbo. Another driving force for creating ethics bodies was the major reorganisation of Austrian universities in the 2002. In the context of this reorganisation medical schools became independent from comprehensive universities and took the already existing research ethics committees with them. Universities which by that had lost their ethics committees had to establish new ones. “

In most organisations the submission of a research project is based on the applicant's voluntary decision. Applicants are rarely obliged to submit a proposal. In the minority of universities such an obligation is laid down in the respective code of conduct. Most universities do not foresee any sanction if a researcher fails to provide a proposal for review. One university, however, requires researchers to submit all projects to the ethics commission in order to get an overview of all research done at the university. In addition, this measure should safeguard that only research projects, which have been quality checked, are submitted to the responsible Ministry for notification or approval of animal testing. If a research proposal was not provided despite the fact that this would have been mandatory, the researcher is admonished. If this happens once, it is excused.

If failure happens more often, it is reported to the ombudsperson for good scientific practice.

In general, it is up to the individual researcher to decide whether he/she submits a proposal to the ethics body or not. Most ethics committees thus only can become active after a researcher took the initiative. Only a few committees can take the initiative on their own.
Applications for ethical clearance originate mainly from disciplines that conduct research on humans and animals. Interviewees most often mentioned the following disciplines: medicine, sport science, life science, psychology and experimental economy. There were little or almost no applications from the humanities and social sciences.

Ethics bodies in Austria today are clearly “responsibilisation in the making”. Despite the achievements reported by their chairpersons, it is currently unclear whether they work well in terms of “managing contestation” and “responsibilisation”. In order to address these questions, research into the impact of ethics bodies is necessary. Elements of potential impact include: (1) increased awareness of researchers for ethical issues; (2) increased quality of proposals in terms of recognizing and addressing research ethics; (3) increased number of publications in journals that require ethical clearance; (4) ability to acquire contract money. A number of interesting further questions should be asked, such as: Does a focus on supporting rather than penalising help to institutionalize responsibilisation? Are there differences in effectiveness and efficiency between various types of ethics bodies in terms of impact– in particular between service bodies, control bodies and bodies promoting ethical reflection? Does the composition of the ethics body- e.g. involvement of employees - have an impact on researchers’ commitment to responsibility (i.e., responsibilitsation)? Is it possible and desirable to broaden ethics review and include questions of social impact?

Neuentwicklungen in Deutschland

Deutsche Sporthochschule Köln

FH Paderborn

Hochschule Fulda

Hochschule für Gesundheit (Bochum)

Fachhochschule Kiel

> “Die Bildung einer Ethikkommission wird derzeit vorangetrieben.”

Hochschule Coburg

Hochschule Osnabrück

Vielen Dank für Ihre Aufmerksamkeit !

KU Linz: Institut für Praktische Philosophie / Ethik

Fragen

Gewährleistet das Verfahren einen angemessenen Schutz oder behindert es nur die Forschung?

Wie ist mit dem Problem der „therapeutic misconception“ umzugehen?

Ist die Unterscheidung zwischen Kindern als Probanden und anderen Einwilligungsunfähigen gerechtfertigt?

Warum wählt man überhaupt, wenn man Rat von außen wünscht, nicht den Rat eines Einzelnen, sondern den einer Gruppe und riskiert damit die Mehrstimmigkeit?

Welche Art von Expertise wird von Ethikern erwartet?

Wie erfolgt die Abgrenzung zwischen Moral und Ethik sowie zwischen Ethik und Recht?

Wie sichert man die Unabhängigkeit der Ethikkommissionen und ihrer Mitglieder?

Weitere Fragen:

Ist die Trennung zwischen Forschung und Behandlung aufrecht zu erhalten?

Gibt es innovative Verfahren, die obschon mit hohem Risiko behaftet, durch die Möglichkeit eines Heilungserfolgs gerechtfertigt sein können?

Wie ist mit Daten aus Routinebehandlungen umzugehen?

Gibt es eine moralische Pflicht der Patientinnen und Patienten, ihre Daten für den Fortschritt der Medizin („anonym“) zur Verfügung zu stellen?

Haben Ärztinnen und Ärzte eine Pflicht, solche Daten zu sammeln und der Scientific community zugänglich zu machen?

Sollte es dafür incentives geben?

Gibt es Publikationspflichten in diesem Bereich?

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