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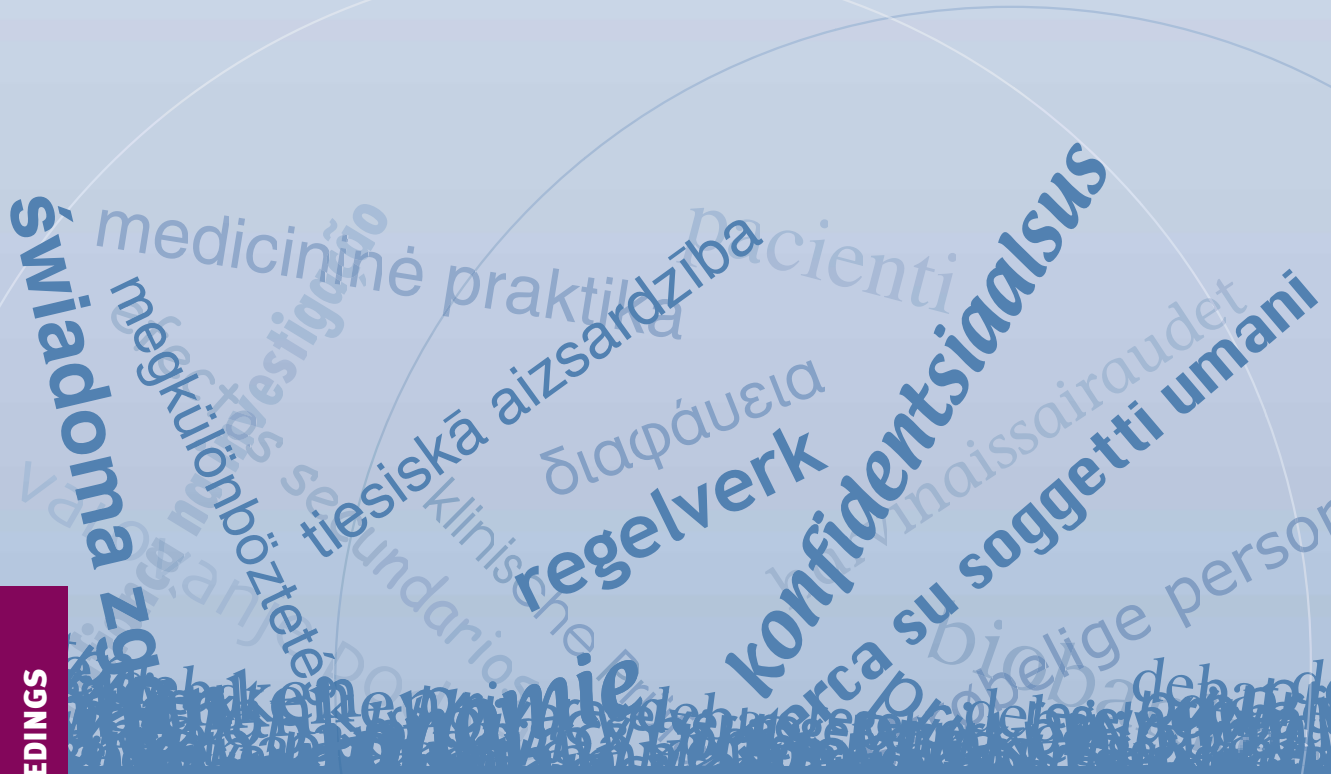

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"I see a new role for Europe's influence on global codes and models for independent control measures with strong lay representation. This has been extremely positive because lay people are as much ethical experts as researchers. … I would like us to project some of the European immaterial values that we use in our work also when we deal with research in developing countries."

– Povl Riis, past Chairman, Central Research Ethics Committee of Denmark

FOREWORD

The European Union is characterised by the ethical pluralism of its Member States. However, a common set of basic shared values does exist at European Union level. It is embodied in the European Charter of Fundamental Rights, which is an integral component of the Constitutional project of the Union.

The Charter of Fundamental Rights is a point of reference for all Community policy-making. The final aim is the development of a true "culture" of protection and promotion of human rights and fundamental freedoms in the Commission and throughout the European Union.

Several Articles in the Charter have an important role for research. Respect for human dignity, the banning of human reproductive cloning, the non-commercialisation of biological components derived from the human body, the prohibition of eugenic practices, the protection of privacy, the freedom of science – these are all examples of values enshrined in the Charter.

Ethics has become an integral component of governance, particularly for scientific research in Europe, within the European Union's research framework and also more generally. Ethics improves science and ensures that it is carried out in a responsible way and thus in line with the expectations of society.

This is being reflected in the evolution of the European Commission's regulatory framework from clinical trials to patenting, which increasingly requires Member States to pay due attention to ethics. Examples of how the Commission seeks to strengthen and raise awareness of the role of ethics in research can also be found in the ethical review process in the Sixth Framework Programme and calls for projects for research on ethics and science.

Ethical review does not only aim to ensure that research funded by the European Union is carried out in accordance with fundamental ethical principles. It also recognises how important it is that research protocols are approved by local Research Ethics Committees. Thus it respects both the principle of subsidiarity and the European Commission's own mandate with regard to ethics.

The purpose of the conference *Research Ethics Committees in Europe: Facing the Future Together*, the first of its kind, was to give the floor to a wide range of representatives of Research Ethics Committees from as many different countries as possible. The idea was for them to express themselves clearly and openly on the work developed locally or regionally and to identify needs and solutions to be faced at European level and across countries or group of countries.

This conference, designed to focus on the practical aspects of Research Ethics Committees' daily endeavour, has resulted in very fruitful and vivid discussions on what can be done at a European level to help the work of Research Ethics Committees at local or regional level.

I know that very practical initiatives have already emerged from those discussions, as this report shows, and I will ensure that they are properly followed up by the Commission services.

Janez Potočnik

"It is particularly appropriate that we do this today, the sixtieth anniversary of the liberation of Auschwitz... I am arguing that we need to re-examine the moral legitimacy of what we do, and not be concerned solely with the nice little refinements to the rules and regulations, the processes and the consent forms."

– Alexander Capron, Director of the Ethics, Trade, Human Rights and Health Law, World Health Organisation

INTRODUCTION

Science is advancing rapidly and will change society profoundly. Scientific research and the development of new products and services continually bear on ethical values, and its procedures and results must respect the integrity, the dignity and the privacy of everyone concerned. Ethical issues are therefore integral components of responsible research practices, especially in the field of medicine.

The Commission's Science and Society Action Plan[1] of December 2001, and the EU's Sixth Research Framework Programme[2] argue the need to establish public dialogue on new technologies at the European level and to integrate ethics into research practices. Some tools to achieve this goal are networking, a dialogue platform and the promotion of research on ethics. In particular, Action 32 of the Science and Society Action Plan provides for the establishment of networks between local ethics committees.

Various national systems of research ethics committees (RECs) operating at different levels have been established in the 25 EU Member States and in other countries within the European Research Area (ERA)[3]. As committees are working independently, their methods of operation vary widely within each country and from country to country.

Within this framework, the conference *Research Ethics Committees in Europe: Facing the Future Together*, held in Brussels on 27 and 28 January 2005, focused on RECs which evaluate, at **local** or **regional** level, all types of research protocols involving human beings. More than 300 partici-pants, most of them representatives from RECs in 32 of the 34 ERA countries[4], attended this event.

The first of its kind, this conference intended to open a debate with REC members in order for them to identify the state of the art, consider the good practices, obstacles and pitfalls participants had encountered, and thus to identify future initiatives, actions and activities.

To allow as lively and open discussion among participants as possible, a large part of the conference was structured around **four workshops**, approaching the work carried out by RECs along four axes[5], which were identified as the main issues facing REC members, even though some may obviously include overlapping items.

This report therefore focuses on the workshop discussions, conclusions and recommendations. The interested reader will find the various, rich and diverse presentations made by more than 30 speakers on the conference website at the following address:

http://europa.eu.int/comm/research/conferences/2005/recs/index_en.htm

1 http://europa.eu.int/comm/research/science-society/action-plan/action-plan_en.html
2 http://europa.eu.int/comm/research/fp6/index_en.html
3 ERA countries are the 25 Member States, the four candidate countries (Bulgaria, Croatia, Romania and Turkey) and the other countries associated with the Sixth Framework Programme (Iceland, Israel, Liechtenstein, Norway and Switzerland).
4 Only Croatia and Liechtenstein were not represented.
5 Workshop 1 - Organisation, infrastructure and the role of RECs at country level
Workshop 2 - Standard operating procedures and quality assurance
Workshop 3 - Interaction with relevant parties
Workshop 4 - Training and dissemination of good practices

1 WORKSHOP 1
ORGANISATION, INFRASTRUCTURE AND THE ROLE OF RECS AT COUNTRY LEVEL

"The diversity of methods to respond to new circumstances is a challenge to harmonisation." – **Caroline Trouet, Belgium**

"The function of RECs is not to help researchers seeking funding for research projects." – **Dominique Sprumont, Switzerland**

"Ethics review should be a matter of adventure rather than of bureaucracy." – **Jiri Simek, Czech Republic**

"Moving from secrecy to a sort of 'peer review' system." – **Cristina Avendaño-Solà, Spain**

"You don't pay the judge to get justice." – **Bert Vanderhaegen, Belgium**

More questions than answers

Even after more than 20 years of ethical review of clinical trials, many of the fundamental questions about the role, scope and structure of ethics committees remain a matter of debate rather than of consensus. This workshop revealed different nuances on everything from assuring independence to expertise of members, and from mechanisms of funding to levels of transparency.

If research ethics committees (RECs) are to play their role as guardians of the dignity of research subjects, insisted Dr Jiri Simek of the Institute of Medical Ethics at Charles University in Prague, they must keep their independence from sponsors, researchers, institutes, regulatory authorities, and even from central ethics committees. Methods of nomination, qualifications for membership and training are crucial influences on independence, he argued. He felt that training should include at least the basics of hermeneutic or discursive ethics.

Caroline Trouet, of the Belgian pharmaceutical industry association pharma.be, noted the increasing complexity of the tasks facing RECs, their gradual assumption of legal status – and their subjection to national and European Union legal controls and even legal liability. But she also highlighted the diversity of responses countries had adopted to meet these new circumstances, and the consequent challenges posed by any attempt at harmonisation or standardisation.

Professor Dominique Sprumont of the Institute of Health Law at the University of Neuchâtel in Switzerland emphasised the emergence of



a formal legal view of the role of RECs. This is exemplified by a landmark Swiss court ruling that their function is not to help researchers seeking funding for research projects, but to carry out what is a state duty to review clinical trials in respect of the public interest.

Cristina Avendaño-Solà, a member of the REC at the Puerta de Hierro University Hospital in Spain, offered an overview of the development of the Spanish RECs system in the wake of the EU Directive[6]. This has brought a new level of coherence and transparency to the review process, through establishing a 'lead' REC to give an opinion on a multicentre trial, with obligatory consultation among all other RECs involved, and with an on-line register of multicentre trials.

Sigrid Skavlid of the central secretariat for RECs in Norway also provoked widespread interest with her account of the new electronically-based application system in operation there since the start of 2005, aimed at bringing greater transparency into clinical trials review procedures.

Defending independence

There were strong defenders of the voluntary approach to REC membership as a guarantee of independence, and with ethics review seen as a matter of adventure rather than of bureaucracy, it was recognised that some controls were required. Some participants saw the evolution towards greater professionalism as a guarantee of independence, while others viewed it as a threat to independent thinking.

Differing views were expressed on how to cope with the risk that independence might be compromised by close relationships between local committees and local investigators and sponsors, or by payment of REC members. Institutional RECs were depicted as being closer to – and more confident in – investigators, entailing the need for independence to be guaranteed by supervision. By contrast, regional committees may enjoy a greater detachment

6 Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (Official Journal L 121, 1/5/2001 pp. 34-44) - http://pharmacos.eudra.org/F2/eudralex/vol-1/home.htm

"It is unfortunate that this meeting is taking place only now, and that those who are making the decisions, who were in charge of producing the Directive on clinical trials, at both European and Member State levels, have not sought greater contact with those who have been very active for quite some time trying to work towards this Directive."
– Senator Claude Huriet, Member of the Unesco International Bioethics Committee

from investigators, but may be subject to influence from their appointing authority.

Overall, although some participants considered the composition of RECs to be insufficiently precisely laid down in the EU Directive, some consensus emerged on the merits of wide membership of RECs – both to boost independence, and also to provide the widest possible range of expertise to cope with ever more sophisticated demands.

Transparency is important not only as a matter of public interest – subject to due reserve over confidential information – but also as a guarantee of quality. Easier communication between RECs was described as part of a move away from a system of secrecy and lack of mutual confidence to a sort of 'peer review' system, in which RECs routinely justify their opinions. A general raising of standards was also desirable to prevent REC-shopping by sponsors looking for a lax assessment.

Scarce resources

Much of the discussion focused on how to fund RECs adequately – and from what sources.

Examples provided of RECs' fees ranged from zero up to €2 500 per assessment, with numerous concessions made to academic research. Many participants saw a risk to impartiality if there are direct payments from clients to RECs for services provided: "You don't pay the judge to get justice" it was observed.

But payment from the state was merited, it was argued – since the state was demanding the service. The Directive has not only required a central opinion on a multicentre trial, but has required a fast turnround time, which is often difficult to meet. RECs need administrative support to be able to meet their new obligations.

And even where new systems have been set up by the state, there are often serious resource problems in making the system function. In Spain, the authority that inspects and demands performance from RECs is not the same one that provides the resources; there is thus a resource gap because of an institutional gap.

Increased responsibilities, increased liability?

There was vigorous debate over how the imposition of new responsibilities on RECs was also creating increased liability for them. It was suggested that the state – and even researchers themselves – might be delegating more responsibility than they should onto shoulders that were ill-equipped to carry such a burden. And it was pointed out that risks of liability were a strong disincentive to potential recruits to RECs.

The questions extended to the scope of ethics review (and even the scope of the meeting itself) – should it cover only interventive trials with medicines, all trials with medicines, or go even wider, and at what cost? It was pointed



out that clinical trials with medicines no longer hold a monopoly on discussions of ethics – even engineers nowadays conduct high-quality ethics assessments of new projects. Rainer Gerold, Director for Science and Society at the European Commission, noted the wider need for discussions beyond bioethics – in non-medical research in primates, in nanotechnology, and in the full range of EU-funded research projects.

2 WORKSHOP 2 STANDARD OPERATING PROCEDURES AND QUALITY ASSURANCE

"We cannot tell if the decision was right unless we have the reasons for it."
– **Elisabeth Rynning, Sweden**

"The central allocation system has dramatically improved the timelines for researchers in terms of how soon they can get to an ethics committee. … The main benefit of the UK system is that we have delivered."
– **Janet Wisely, United Kingdom**

How standardised should RECs be?

Workshop 2 asked whether RECs already follow standardised procedures, and whether and how the competent authority is involved. The chief tool discussed for quality assurance was certification.

To fuel debate, the workshop first examined two national cases. Dorottya Mogyorósi of Hungary's Medical Research Council explained how Hungary's ethics review as regards human reproduction operates at three levels: the national (the Ministry of Health), the regional (medical universities and central hospitals) and the local (healthcare institutions). At national level, the minister appoints REC members and standard operating procedures (SOPs) are laid down by decree. They cover the committees' composition, meeting frequency, the officer's duties, appointment of substitute members, access to documents, decision-making, statistics, and so on. The RECs fulfil the following roles: they give preliminary opinions on embryo storage, they grant permits for research, they evaluate policies at home and abroad, and they supervise healthcare providers.

The system faces the problem that as there are so few healthcare providers, it is hard to find independent expert members – everyone relies on the same experts. It is also hard to guarantee confidentiality, and sanctions are needed to discourage this being breached.

RECs reviewing clinical trials of medicinal products in the UK are regulated by UKECA, the UK Ethics Committee Authority, Janet Wisely of the Central Office for RECs (COREC) said. The country's National Health Service accounts for 198 RECs and COREC co-ordinates those in England. The Governance Arrangements for NHS Research Ethics Committees (GAfREC)[7] lay down RECs' scope, role, size, composition and standards – but not detailed operating proced-

7 *http://www.corec.org.uk/applicants/help/guidance.htm#gafrec*



ures. COREC has developed standard operating procedures along with a sophisticated REC Administrators' Database (RED) to back them up.

The procedure comprises submission using a common online application form, central processing for clinical trials of medicinal products and multi-site trials (smaller studies can still be submitted locally), a check for conflict of interest then simple allocation to the earliest available slot nationwide. This has the benefits of speed – the average processing time is down to around 50 days – efficiency (REC agendas are kept full), the provision of tracking and management information and the automatic generation of standard letters. The system copes with 8 500 applications a year at a cost of €16 million.

Accreditation

Several countries, among them Italy, the Netherlands, Spain and the UK, already accredit or inspect RECs and there is general support for the idea. As RECs rely on volunteer effort, any system adopted should be sympathetic. A possible model, which is easy to implement, would be to start with self-assessment and follow this with peer review, as is done in the UK. RECs are provided with standard self-assessment forms and reference standards, and once they complete them they are given a preliminary quality status. Following the peer review visit, they are accredited either definitively or provisionally. Areas for improvement are addressed via an agreed work plan. Initial training of assessors can be done by a professional audit company and afterwards this task can be handed over to peers.

A number of issues came up during the discussion. Procedures should be transparent and publishing them on the web is a good way to achieve this. Care needs to be taken to manage the balance between national and local powers and to clarify the role of RECs in relation to other authorities, for instance those responsible for data protection, tissue use and reproduction.

More specific decisions need to be taken on who should carry out site-specific assessments (which are not based on ethical issues), and what limits there are to REC requests for further information from applicants (this is a matter to which judgement has to be applied within the remit of the EU Directive). General problems of approach arise when dealing with industrial research, as the REC system grew up with an academic culture. In particular, ways are needed to prevent conflicts of interest at local level among small pools of experts, investigators and local institutions.

Quality issues

Elisabeth Rynning of Uppsala University in Sweden set out some of the issues surrounding quality assurance. Some international documents in the area have the force of law, whereas others are used for guidance (the situation differs from country to country). There is a question as to how far ethics should be regulated – does law displace ethics? Of whom do RECs

"The European Union and the Council of Europe share the same principles and concerns – and we share the same experts. ... We have to present a united front. If we work together we will be more effective and we will have a greater impact in the field. A possibility would be to work together for the preparation of guidelines on ethics and research applications."
– Carlos de Sola, Head of the Bioethics Department, Secretary of the Steering Committee on Bioethics (CDBI), Council of Europe



need to be independent? How can conflicts of interest be avoided? What expertise is needed? How can the public be represented and what does 'lay' actually mean?

It is clear that even in a voluntary system, expertise is a major factor in quality. Apart from scientific and legal specialists, various other disciplines such as ethics, sociology, psychology and economics, have a place. Ethicists have the role not of saying what is right, but of clarifying the process of deciding what is right. Of course some skills, notably those concerning particular medical specialities, can be brought in, when needed, if they do not exist in the permanent membership.

RECs should give their reasons for refusing an application and an appeals procedure is recommended. Where RECs' decisions are binding, it is probably best to refer appeals to a central committee. But where RECs' opinions are only advisory, a refusal by the competent authority, following such an opinion, should probably be tried in court. Minorities on the committee should also have the right of appeal.

The workshop examined the quality assurance systems in place in Sweden and in the Czech Republic. Sweden has six regional RECs plus a central appeals committee, which are government bodies and therefore not accredited. There are a common website and application form. The system is fee-based and REC members, who are appointed by the government, are paid a small fee for their services. The Czech Republic has had a state accreditation system since 2004, which encourages standardisation and thus facilitates RECs' co-operation with each other and with researchers.

The scope of regulation

As RECs exercise delegated public authority, they should be regulated by law, and this law must strike the balance between flexibility and predictability.

A growing burden for RECs is the ongoing monitoring of trials, which can generate an immense amount of work – as many as 400 notifications per trial. One way to cope with this workload may be to delegate it to a subcommittee. Monitoring should be based on the annual report and has to extend into hard-to-police areas such as internet recruitment, where different countries may require different changes to be made. In the rare event that a REC does have doubts, it should call on the competent authority to stop the trial.

Other difficult areas are how to review trials in countries where the Helsinki Declaration has not been adopted, whether one REC refusal invalidates all parts of a multinational trial, and whether scientific quality is part of the ethical opinion. Bad science is unethical, but this may be an aspect that can be screened out by a scientific

review board, before applications reach the REC, as is done in Slovenia. One deceptively simple issue that was raised is: can an ethical opinion be wrong? It seems that it certainly can be wrong on grounds of form – a REC may fail to follow the proper procedure – but it is not clear what criteria exist for querying a decision on grounds of content.

Finally, the thorny issue of independence was examined: can RECs be too close to one institution? Is appointment by the profession, as is done in Germany, more independent than appointment by government?

3 WORKSHOP 3 INTERACTION WITH RELEVANT PARTIES

"Interaction between researchers and research ethics committees is not a guillotine solution, it happens over a long time."
– **Elmar Doppelfeld, Germany**

"It would be foolish to develop any significant relationship with the pharmaceutical industry, because it is bound to come up with all sorts of conflicts, and the RECs just haven't the powers to come out well from such a relationship."
– **Richard Nicholson, United Kingdom**

"We might do better to define the limits of biomedical research to include not only drugs, but also psychological research and research in social sciences." – **Renzo Pegoraro, Italy**

Action for more interaction

A REC interacts – or rather could interact – with an increasing number of parties. If its members are sufficiently skilled and the committees well organised and properly funded, the interaction with all the different parties could proceed smoothly. But interaction is often faulty and there are plenty of possibilities for improvement. The workshop therefore provided a mix of an action plan and wishful thinking for interaction with relevant parties, particularly the pharmaceutical industry and society in general.

Professor Elmar Doppelfeld of the University of Bonn defined three fields of interaction:

> Interaction as co-operation
External expertise from patient organisations, philosophers, lawyers, medical doctors, etc. might be needed to assess a research protocol. If, for instance there is a paediatrician in the REC, there will be no need to invite another paediatrician to discuss a protocol about paediatrics, but if no paediatrician is available in the REC, it would be appropriate to consult one. Sometimes the law requires RECs to seek external ethical guidance: in Germany they must consult an external expert in the field of gene therapy. Interaction as co-operation could have a bad side effect in relation to confidentiality and security of data, and it is a problem no country has solved.

> Interaction with authorities
RECs interact with regional as well as national and international authorities. For instance the Directive lays down that a file for a research project must go to both an REC and the national competent authority, and each assessment is made independently of the other. Discrepancies between the REC and the national authority could create confusion among the researchers and sponsors, increasing the risk of lawsuits against the RECs or the national





authorities. The Directive has blurred the tasks of each body. In France, for instance, the national agency has also begun to look at the ethical aspects of trials.

> Alternative interaction

There could be fields of research, for instance databases containing personal data (identifiable or not), which are going to be assessed by either a REC or a competent authority.

The parties to interact with are numerous, but commonly include other RECs, researchers, sponsors (the pharmaceutical industry, scientific societies, public agencies), various experts (philosophers, lawyers, medical doctors, etc.), the competent authorities, patient organisations and the public in general.

The power of the pharmaceutical companies

The pharmaceutical industry is, for obvious reasons a key party to interact with because if the process of approval of a protocol goes smoothly and efficiently, patients can, in an ideal world, have better medicines quicker. Apart from anything else, better dialogue with the industry can minimise the non-publication of negative results and help define legal and insurance aspects. But caution is called for. Professor Renzo Pegoraro of the University of Padua pointed out that RECs must always ensure the safety of the patients, critically analyse the scientific and ethical content of clinical trials, and avoid any gifts, grants or other funding from the industry. Most trials are commercially sponsored and this financial interest is often bound to influence the design and planning of clinical trials. The safest path is to remember that transparency is the best guarantee of quality: different interests should be recognised and managed constructively.

Ways need to be found to move ethics upstream in the process of developing new treatments. The drugs companies would appreciate having a clear point of contact with each REC, whom they can ask for information and clarification. Conversely, some RECs feel comfortable addressing queries to the medical doctor who is responsible for the research project within the pharmaceutical company. However Richard Nicholson, Editor of the Bulletin of Medical Ethics, warned RECs to be careful in their flirtation with the industry. A proposal was made to organise communication with the industry on a national level and, again on a national level, to arrange training meetings for researchers and sponsors alike.

A surprising amount of pharmaceutical-sponsored clinical research is taking place in the Central and Eastern European countries, which benefit from early access to new treatments. However, concerns were expressed that patients might be harmed if high standards are not enforced.

The overall view was that most pharmaceutical companies seek a good ethical image, are ready to comply, and are slowly but surely improving their ethical standards. The expectation is that European countries are raising the level of quality concerning ethics in clinical trials – not least because of the stronger role of the RECs.

The perfect website

Marie Moores of Theradex (Europe) asked for more communication between sponsors and researchers on one hand and RECs on the other. This would reduce costs, so maintaining the attractiveness of Europe for conducting clinical trials, and also avoid unnecessary delays in obtaining approval.

The latter goal evoked several comments on the role of RECs in educating researchers in ethics. The general assumption is that RECs do not interact enough with researchers to promote good quality research. Ms Moores recommended that RECs establish websites along the lines of the excellent Swiss one[8], containing information on:

> the legal basis of research in the respective country
> the national procedure for making an REC submission
> contact details of all RECs by region
> required documents
> provision of information in a second official EU language
> serious adverse events reporting requirements
> guidance on common errors made by applicants.

Resources are an important issue here : communication takes time and RECs should be equipped with secretariats that can carry out the necessary work. Efficiency would also be improved through the better use of websites and public registers of ethical reviews.

8 *http://www.swissethics.ch*

Human rights concerns

Interaction with society covers both dialoguing with the general public to extend knowledge of clinical trials and promote the importance of research on human beings and, more specifically having lay members of RECs.

Professor Pegoraro mentioned an interesting Italian project involving 64 RECs. The REM (Rights and Ethics in Medicine) project, initiated by the Istituto Mario Negri del Sud in Chieti (Italy), arranges meetings and seminars for REC members, the general public, health workers, authorities, and various groups of citizen organisations. Besides the interaction with society, the RECs have the opportunity to interact with each other and share knowledge and experience. The project has also created a discussion forum on the web.

The issue of lay members is anything but clear-cut. One participant warned against using members of patient organisations as lay members of RECs: they know almost everything about their own disease, but not necessarily anything about other diseases. And lay people's levels of education can be a problem.

In France, a law has recently been passed to include lay people in RECs, as patient organisations have long argued. The lack of patient representation has been a major cause of complaints from patients and relatives. As well as taking part in ethics discussions, patient groups can contribute to discussions about research in general and help identify areas for research.


Tomas Rosenbaum of Ealing Hospital (UK) emphasised that laypersons had to be real representatives of the local community: "It is important that the members of an REC reflect the local community as accurately as possible. This is my own experience working in an REC in a community with rather varied ethnic and cultural values. We have tried to engage the different ethnic groups, but not very successfully."

There was no agreement as to how many members of a REC should be lay people. In Denmark the majority of REC members are lay people, but Renzo Pegoraro felt that perhaps two or three lay members would be appropriate. Definitions of 'layperson' are also not crystal clear, and range from being a non-medical doctor to a man or woman picked at random from the local community.

Reviewing non-interventional research

Dr Joze Trontelj of Slovenia's National Medical Ethics Committee pointed out that there is a need for guidance and regulation of observational research (i.e. non-interventional research that does not involve invasive medical procedures) – a field that RECs normally do not cover. He said that observational studies do not require approval by the competent authority, and they are often not reviewed for ethical acceptability.

At present there is little regulation in place to support the ethical review of observational research. Dr Trontelj said that experience from Slovenia shows that ethical standards can be improved by such a review, and listed some problems that might arise if non-interventional research is not assessed by an REC:

> a hidden aim to increase the market share, although not based on real advantages
> patients may be recruited when that is not in their best interest
> the cost to public health care system may be increased without real benefit
> activities may run against the principles of business ethics.

"The Clinical Trials Directive could have been improved if the Commission and Council had accepted more of the amendments of the European Parliament... the time for the ethics committees should be longer and the time for the authorities should be shorter. It should also be made more flexible for non-commercial trials. We always know what industry wants in the European Parliament, but we do not always know what non-commercial actors in research want. We have to learn to co-operate better."

– Peter Liese MEP, Member of the Environment, Public Health and Food Safety Committee of the European Parliament

4 WORKSHOP 4 TRAINING AND DISSEMINATION OF GOOD PRACTICES

"Members of ethics committees tend to work on a pro bono basis. What I object to is being expected to pay for my own training to ensure that I remain abreast of recent developments."
– **Enrique Riera Castellano, Spain**

"With regard to cost, I cannot understand how regulations can be put in place giving such huge responsibility to ethics committees without assuring the budgets are there."
– **Christa Janko, Austria**

"We should protect knowledge but we should also protect human dignity and human rights. When we have a conflict of values, we learn how to deal with the conflict. What are the right ways to reach a consensus and what is the price? Sometimes we have to pay a very high moral price for consensus. But that's the way science and ethics develop."
– **Professor Zbigniew Szawarski, Poland**

REC training: one size does not fit all

In Workshop 4, participants made it clear that training members of and administrators for research ethics committees (RECs) is both desirable and desperately needed. But this training is made difficult due to several issues. Some can be resolved with time, money and hard work; others are not easily resolved because they stem from deeply ingrained ways of thinking.

The top issues impeding the training of REC members are interrelated: lack of time and lack of money for training. The expectations of society, study subjects and researchers put enormous pressure on RECs. Many felt the EU Directive has increased demands on RECs at a time when both science and ethics are becoming more complex, but without providing the means to meet them. Some worried that a training requirement would act as a deterrent to attracting new REC members.

Balancing professionalism with diversity

Participants reached a general consensus that one kind of training course will not meet the needs for all REC members and administrators. Different kinds of training courses are needed to match their different needs and their different levels of experience.

Participants voiced a concern that 'one-size-fits-all' training would produce 'professionalised' committee members. REC members already



worry that they get into the habit of dealing with questions in the same way. Participants wanted training that would promote a culture of ethical thinking within RECs while maintaining a diversity of informed opinion.

Participants want to know how to distinguish among existing training programmes, because they vary in quality. Many suggested that accreditation was the answer.

A lack of training has serious consequences: RECs and their members will be held in low esteem, perceived merely as obstacles to research, or just another piece of bureaucracy. In turn, REC membership feels more like a duty rather than a vital job.

Formal and informal solutions

Where fresh ways of thinking are the goal, internal training can be offered both cost-effectively and with minimal time demands. François Chapuis of Claude Bernard University in Lyons shared the French example, in which colleagues within an REC train each other – a lawyer trains non-lawyers in the legal perspective, a doctor gives the medical perspective, etc. This type of training fosters respect for and recognition of differences. It takes place for one hour before the official REC meeting, twice per month for six months. Topics range from the history of ideas and international guidelines to methodology and emerging issues.

Other RECs may need to give their members more basic training. Formal training course models were described by Professor Ruud ter Meulen of the University of Maastricht, Hermann Amstad of the Swiss Academy of Medical Sciences and participants from Austria and the UK. All the courses shared a common approach encompassing active learning, core concepts and individual modules.

Active learning is the cornerstone. In an active learning environment, participants build their knowledge structure by talking with each other. Understanding the regulations governing research should be a starting point. From there specific issues can be discussed. The learning environment needs to offer balance between self-exploration and systematic support. It should also offer multiple perspectives, strategies and concepts. It is also important that it match the real-life situation within which the knowledge learned will be applied. Course material should focus on the different perspectives embodied by REC members, and teachers should be leading experts who facilitate exchange.

Overall, participants thought that interactive, interdisciplinary exchange with an underpinning of relevant materials was the best way to train REC members. All training should be targeted at the individual's role and background in the REC. The exchange could take many forms:

> internal and formal training courses
> national and international conferences
> REC networks both national and international
> interactive website
> REC newsletter.

Certain constants in the arena of ethical review should be noted, because it will be difficult to train REC members and administrators to address them in a standard way throughout the EU. First, there is a clash of interests among four groups dependent on RECs: potential human subjects, researchers, pharmaceutical companies and the institution within which the REC works. Secondly, it can be a difficult task to get people who hold senior positions in their field to take a training course. Because they are experts in their fields, they often feel that they are already knowledgeable about ethical issues and how to handle them

CONCLUSIONS AND RECOMMENDATIONS

Workshop 1 – Organisation, infrastructure and the role of RECs at country level

Still plenty to do

The growing scope of demands made on RECs in a rapidly changing environment requires a rapid and reasoned response if the many challenges they face – legal, scientific, and logistical – are to be met.

To boost independence, the multifaceted composition of RECs, including laypersons, is at least one way to deal with conflict of interest and the search for independence. So too are payment systems that de-link the REC from the client – such as payment into a central body that funds individual RECs.

To ensure adequate expertise in the assessment of protocols, RECs need to be organised so that they can access sufficient additional experts locally, or so that highly specialised protocols are referred to regional or central level where sufficient expertise is available.

To cope with the growing demand for high-quality and rapid assessment, some harmonisation and simplification of practice is needed to reduce confusion and delay, and even to circumvent the national barriers that some of the current diversity of approaches imposes.

For RECs themselves, there is a clear need for them to recognise the shift in their environment. Whether they like it or not, they are being obliged to move towards a more professional approach, from an advisory to a statutory role, from self control to inspection, to greater transparency, to more harmonisation – and to greater accountability. To fail to take account of those changes and to adapt accordingly is to court disaster.

For the authorities at all levels, there are challenges to be met in terms of resources. They must be ready to organise funding for services they are requiring RECs to perform. These include appropriate scientific and administrative support, information exchange, training and advice.

For national and European-level authorities, greater clarity is needed over the appropriate composition of RECs so they can perform satisfactorily: the EU has a role in promoting and sponsoring further in-depth reflection among all interested parties on the way ahead, while national authorities need to clarify RECs' legal responsibilities (and their limits to it).




National authorities also need to review the relationship between RECs to ensure consistent quality standards.

For sponsors (and particularly the pharmaceutical industry) there is a role in informing RECs of the broader context of clinical research and of what is at stake in overall research efforts.

Everyone needs to recognise the interdependence of all players in promoting high-quality trials with the highest respect for subjects, to develop what will ultimately be high-quality treatments.

Workshop 2 – Standard operating procedures and quality assurance

Taking quality seriously

As the participating countries and RECs are at very different levels of development, some have already accomplished most of the actions proposed at local (committee) and national level, while others are only just starting. Most participants see quality assurance as a necessary and important tool for achieving consistent decisions and ensuring public confidence in RECs.

At local level:
RECs are encouraged to map their activities, to decide whether standard operating procedures (SOPs) are necessary, and to develop, adopt and publish their SOPs. National and international experience can be useful in avoiding reinventing the wheel. International training courses will allow REC members to learn from the best practices.

Participation in peer evaluation and accreditation schemes can be a useful quality assurance tool once national standards are in place. In the long term, accreditation results should be used to further develop the procedures and to decide upon necessary training.

At national/regional level:
Legislation should be put in place to define RECs' authority, scope of responsibility, core requirements and funding. Currently, the ethical review of pharmaceutical research is legally well covered in many countries, but this is not the case for non-pharmaceutical medical research and non-medical human research (e.g. social sciences).

Regional and local RECs should be helped to network, for instance by organising conferences and workshops, and accreditation should be organised.

At EU level:
As a short-term goal, a dedicated website for RECs, providing details of events in the field of research ethics, as well as an overview of the relevant international and EU documents and links to the national RECs or associations, would be very useful in facilitating information exchange.

The European Commission should also support further practical and technical co-operation through workshops, conferences and possibly a regular REC forum.

Further events should be organised to discuss:
> the ethical review of non-medical human research (e.g. social sciences, psychology etc.)
> the ongoing monitoring of approved research projects (as currently done for pharmaceutical research)
> approaches to the accreditation and audit of RECs
> the specific questions of placebo-controlled clinical trials and volunteer studies.

Even if there is no demand for these areas to be regulated at EU-level, there certainly is a need for EU level discussions and guidance towards a consensus.

Workshop 3 – Interaction with relevant parties

Four key dialogue partners

The conclusions and recommendations of Workshop 3 were that RECs should improve interaction with the following parties:

Researchers:
Better interaction with researchers could result in better protocols. RECs ought to involve the researchers in the planning stage of setting up a clinical trial. RECs should try to educate researchers in ethics. That could lower some of the hurdles researchers face before they approach a REC with a research protocol.

The pharmaceutical industry:
Better communication with this important stakeholder could lead to better protocols, avoid unnecessary delays, improve the protection of patients, and minimise the publication of negative results. It could also maintain the attractiveness of Europe for conducting clinical trials. RECs ought to establish excellent websites and to involve the industry at an earlier stage of making a protocol. This would facilitate better protocols.

Other RECs:
Networks of RECs, nationally and internationally, could lead to harmonisation and best practice of the process of the ethical assessment of protocols. Served by a common secretariat, which could arrange internal meetings, develop a strategy for the improvement of RECs and administer an interactive website, the RECs could share knowledge and experience to the benefit of all parties, not least the patients.

Society:
The general public needs to be informed of the work of RECs, or may not appreciate them or understand the importance of their work. With a better-informed society there is a chance of promoting a general acceptance of clinical research. Good websites with open access to the public, and meetings with different groups of people from various parts of society could be a way forward.

RECs should have lay members because their composition should reflect the cultural and social diversity of the local community. It is especially recommended to recruit laypersons from patient organisations. This lay representation should improve the quality of the committees' ethical judgements. The European Commission should take the initiative to educate patient groups to be more qualified in participating in RECs.

Workshop 4 – Training and dissemination of good practices

A two-tier European training system

It was clear from Workshop 4 that REC training – from the basics to the specifics – is very badly needed and is welcomed by participants. Active learning and international, interdisciplinary exchange were mentioned as important

components of this training. Finally, participants felt that it was of great importance that training be targeted to the individual's background and role in the REC. With these three fundamental aspects in mind, the following recommendations were generally agreed upon. All initiatives should be acted upon as soon as is feasible. The European Commission should provide funding so that everyone who needs to may take advantage of the opportunities these recommendations represent.

The national authorities and the European Commission should establish formal training programmes, but with the input of REC members and administrators. Training should be two-tiered.

Basic training should cover such topics as:
> the mission of a research ethics committee
> general review criteria
> regulations governing research
> research design
> risk/benefit analysis.

More specific training should come in the form of modules on such topics as placebo-controlled trials, genetic research, conflicts of interest, and vulnerable populations.

The European Commission should conduct a detailed survey of REC training programmes and activities already in existence in order to identify successful training models and incorporate them into formal training programmes.

The European Commission should establish an annual summer school for members and administrators of RECs.

The European Commission should develop an interactive EU website for RECs that links to national committees or national associations (depending on the country and its laws) and to important supporting materials and learning materials to be shared on a local, national and EU level. This website should provide targeted distance learning to REC members and administrators.

National authorities should work together to create a network of national networks of RECs, called EUREC, open to national associations of RECs or to national RECs and possibly funded by the European Commission. This network should facilitate the exchange of knowledge and information, disseminate teaching material among members, and act as the interlocutor with the European Commission as regards the local implementation of directives.

The European Commission should favour national efforts to link quality control and accreditation of RECs.

To educate the public about what they do, local REC members and administrators should accept invitations to speak at schools and churches and other community groups. This will foster a

"Genomic databases constitute research tools, and it is crucial for research to advance that they remain open, public and international. … At the level of fundamental research [my committee] considered it essential that human genomic databases be considered global public goods, like the environment, and that knowledge useful to human health does not really belong to any private citizen, company or country. Thus human genomic databases are a public resource."
– Bartha Knoppers, Chairwoman of the International Ethics Committee of the Human Genome Organisation

"Limits to the freedom of science are being talked about as never before... but the incorrect use of inventions cannot be used to arouse public distrust of scientists. We must convey the view that science is impartial and disinterested, and must be allowed to be free and creative. It is difficult to be creative without being free, and I think the fundamental ethics of science lies in its methodological rigour and its freedom. There should be no limit to science."
– Pia Elda Locatelli MEP, Member of the Industry, Research and Energy Committee of the European Parliament

EUREC DECLARATION
Brussels, 27 January 2005

Creation of a European Network of Research Ethics Committees – EUREC

1. Representatives from national associations of RECs decided to work together in order to maintain and develop high quality standards in the protection of human subjects in Europe.

2. They committed themselves to create a network of national networks of RECs, called EUREC, open to national associations of RECs or to national RECs.

3. The purpose of the network is to facilitate exchanges of knowledge, know-how and information, to disseminate teaching material among members and to be the interlocutor of the European Commission for aspects regarding local implementation of directives.

4. Another purpose will be to conduct research on research (i.e. research on characteristics of biomedical research conducted on human beings), based on the activity of RECs, in order to facilitate understanding on what is ongoing and developed.

5. An interactive website (www.eurec.org) will be created to share information and materials.

6. To facilitate the achievement of the network's basic objectives, the founders will seek support via public funding from their individual national authorities as well as from the European Commission.

Under the auspices of: Povl Riis (Denmark), Carlos de Sola (Council of Europe) and Claude Huriet (France)

Signatories: François Chapuis (France), Elmar Doppelfeld and Michael Fuchs (Germany), Jozef Glasa (Slovak Republic), Ritva Halila (Finland), Finn Kamper-Jørgensen (Denmark), Dominique Sprumont and Hermann Amstad (Switzerland), Joze Trontelj (Slovenia), subsequently joined by Peter Rehak and Ernst Singer (Austria), Rena Vrahimi-Petridou (Cyprus) and Anneke Jensma (The Netherlands)

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Ethics has become an integral component of governance, particularly as regards scientific research in Europe, both within the European Union's research framework programme and also more generally. Ethics improves science and ensures that it is carried out in a responsible way and thus in line with the expectations of society. Research Ethics Committees bring together specialists and lay people to make sure that human rights and ethical standards are upheld whenever scientific research is conducted.

In January 2005, the European Commission held a conference entitled Research Ethics Committees in Europe: Facing the Future Together, which was attended by 300 representatives of Research Ethics Committees located in 32 different countries of the European Research Area. These people, whose responsibility is to evaluate, at local or regional level, all types of research protocols involving human beings, discussed the key issues that arise in managing and improving the ethical oversight of research. This brochure presents their key debates and conclusions.

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