The Regulation and Organization of Research Ethics Review

Report of a Comparative International Workshop held at the Faculty of Law, University of Toronto, June 16-18, 2005

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### Table of Contents

Table of Contents .......................................................................................................................... 1
Acknowledgments........................................................................................................................ 3
A. Introduction............................................................................................................................. 4
B. Participants............................................................................................................................... 8
C. Workshop Proceedings ........................................................................................................1 1

Session 1: Research Ethics Review Structures: International Comparisons ........ 11
  Brazil......................................................................................................................... ........ 11
  Tanzania....................................................................................................................... .... 13
  Southeast Asia................................................................................................................. 15
  Russia................................................................................................................................ 16
  India.......................................................................................................................... ........ 17
  South Africa................................................................................................................... .. 18
  Turkey .............................................................................................................................. 19
  Discussion..................................................................................................................... ... 20

Session 2: Research Ethics Committee Oversight ......................................................... 21
  United Kingdom: Central Accreditation ............................................................................ 22
  Lithuania: Establishment of RECs and Setting Standards for their Activity ........ 23
  Canada: The NCEHR .................................................................................................... 25
  Discussion..................................................................................................................... ... 28

Session 3: Commercialization .......................................................................................... 29
  North America: Commercialization of Research and REC Review......................... 30
  India: Commercialization in India .............................................................................. 32
  Discussion..................................................................................................................... ... 34

Session 4: Specialized Review Bodies: Recent Initiatives, Future Possibilities........ 35
  Estonia: Review of Research involving a Genetic Databank................................... 35
  Canada: Review of Stem Cell Research ...................................................................... 36
  Canada: Public Consultation on Xenotransplantation ............................................. 38
  Discussion..................................................................................................................... ... 39

Session 5: Specialized Review for Public Health Research .......................................... 40
  Canada: Research Review during the SARS Crisis .................................................... 40
  Emergency Preparedness and Human Subjects Research ........................................ 42
  Discussion..................................................................................................................... ... 44

Session 6: The Role of International Bodies ................................................................. 44
  Role of the World Health Organization........................................................................ 44
  The Council for International Organizations of Medical Sciences (CIOMS)........ 47
  Discussion..................................................................................................................... ... 49

Session 7: The Role of International Instruments in Research Ethics Review............ 50
  Europe: The Oviedo Convention ................................................................................. 50
  Europe: The European Directive on Clinical Trials ................................................. 52
  Latin America: A Need for International Instruments? .......................................... 53
Alternatives to International Law: Promotion of Equivalent Standards .............. 55
Discussion ..................................................................................................................... 56
Session 8: Promotion of Equitable Research Practices .............................................. 56
South Africa: The Concept of an International Duty of Care .................................. 57
Cameroon: Promotion of Equitable Research Practices ......................................... 59
Canada: CIHR Guidelines for Health Research Involving Aboriginal Peoples .... 61
Discussion ..................................................................................................................... 62
Session 9: Liability in the Context of Research Review .......................................... 64
Nigeria: Litigating The “Trovan” Tragedy ............................................................... 64
Australia: Common Law Liability .......................................................................... 66
Hungary: Civil Law Liability ..................................................................................... 69
Discussion ..................................................................................................................... 70
D. Synthesis of International Surveys ..................................................................... 72
Introduction ............................................................................................................... 72
I. Research Review Structures .................................................................................. 73
II. RECs: Oversight and Governance ....................................................................... 76
III. Specialized Review Bodies and Guidelines ......................................................... 79
IV. RECs: Conflicts of Interest and Commercialization of Research ..................... 81
V. Citizen Participation in Research Review ............................................................ 82
VI. Transparency of Research Review ...................................................................... 83
VII. Liability & Health Care Coverage .................................................................... 84
VIII. International Research ....................................................................................... 87
IX. Benefit-Sharing ..................................................................................................... 88
X. Current Challenges ................................................................................................ 89
Conclusion ................................................................................................................... 90
E. Participant Biographies ......................................................................................... 91
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This workshop report was collaboratively written under the supervision of Tom Archibald and Trudo Lemmens. The results reflect the diligence and skill of our assistants. Angela Long and Sasha Kontic prepared the Session Synopses in Section C, Elizabeth Cuéllar Barroso prepared the synthesis of our international survey responses in Section D, and Daniel Brinza summarized the survey results in chart format for the enclosed wall chart. Writing and editing assistance was provided by John Chenery early in the project, and Linda Hutjens later on.

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We thank the authors for their hard work and dedication.
SECTION A. Introduction

“The Regulation of Research Ethics Review: A Comparative International Workshop” took place at the Faculty of Law at the University of Toronto June 16 to 18, 2005. The workshop was part of the “International and Comparative Perspectives on Regulation of Genomic Research” project funded by Genome Canada.

This workshop brought together experts on legal and regulatory issues in biomedical research from selected representative countries in the Northern and Southern hemispheres, and representatives from international organizations such as the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS). Participants came to share experiences, problems and ideas on the regulation of research involving human subjects. It is an issue that raises many complex concerns that vary from country to country, depending on factors such as infrastructure, scientific advancement, disease burden and economic development. Wealthier countries may be dealing with issues such as regulating research and use of controversial procedures, as laid out in Professor Thérèse Leroux’s presentation on xenotransplantation, and implementing strong regional norms, as detailed in Professor Elmar Doppelfeld’s presentation on Europe’s Oviedo Convention. Meanwhile, poorer countries are struggling to protect their citizens from unethical research practices while trying to encourage research that will help to relieve their immense disease burden. Presentations by Professor Trudo Lemmens, Dr. Anant Bhan, Professor Alexander Capron and Dr. Godwin Ndossi highlighted this dichotomy.

The goals of the workshop were to discuss legal, ethical and regulatory challenges in the context of international biomedical research and to explore the issue of research ethics review in a larger context, as distinguished from the legal and/or regulatory regimes that govern it. In addition, the workshop allowed participants to learn about biomedical research issues in other countries that could be relevant to their own work and to meet others working in this field so that such exchanges can continue. Finally, the workshop presented an opportunity to critically analyze some of the emerging themes that challenge participants, such as the increasing commercialization of biomedical research, the rise of accreditation of Research Ethics Committees (RECs) and the role of international organizations and specialized review bodies.

The workshop sessions covered four broad themes:

(1) Research Ethics Review Structures
(2) The Role of International Bodies and Instruments in Research Regulation
(3) The Promotion of Equitable Research Practices
(4) Other Legal Mechanisms in the Research Context
Biomedical research involving humans is typically governed by research ethics review systems revolving around RECs. Determining whether human subject research is ethically sound means scrutiny to ensure that it complies with standard ethical principles that include autonomy, beneficence, non-maleficence and justice.

Under the first workshop theme, a comparison of research ethics review structures throughout the world was conducted by examining the regulatory structures in seven countries and regions – Brazil, Tanzania, Southeast Asia, Russia, India, South Africa and Turkey. The main goal was to compare local ethics review models, based on institutional RECs, with more centralized approaches involving regional or national review and compliance measures and to highlight important variations between countries regarding the structure and functions of RECs.

After examining the operations of specific research ethics systems, the workshop looked at several emerging trends. The first was the need to oversee research ethics review. A central problem noted in the literature surrounding research ethics review is the lack of oversight of RECs. These committees are required to evaluate research protocols, but how can we be sure that the committees themselves are adhering to proper ethical standards? An accreditation system for RECs has been proposed as one way of ensuring that they are following basic procedures and minimum ethical standards. Presentations by Professor Terry Stacey, Dr. Gytis Andrulionis and Dr. Richard Carpentier addressed the issue of oversight.

The workshop then considered commercialization of research and the growing worldwide trend for scientific research to be led by the private sector, particularly the pharmaceutical and biotechnology industries. Without oversight of research ethics approval, how can conflicts of interest in the ethical review process be avoided? Presentations by Professor Trudo Lemmens and Dr. Anant Bhan explained how this problem is being addressed in North America and India respectively.

Next, the workshop turned to specialized review procedures. Biomedical research encompasses a multitude of research activities, from classic drug research to xenotransplantation and stem cell research. These new kinds of research raise different ethical concerns, as well as a question: do we need specialized bodies, central review processes and/or standards for specific kinds of research? Some types of research might require faster, more centralized review by a transparent and perhaps more democratically accountable regulatory body. The workshop looked at how research ethics review was applied to several kinds of biomedical research. Professor Ants Nömper presented on the Estonian experience with genetic databanking, Dr. Michael Enzle discussed the Canadian experience with stem cell research and Professor Thérèse Leroux’s presentation covered xenotransplantation in Canada.
Two subsequent presentations dealt with specialized research conducted within the public health context, especially in emergencies such as Toronto’s SARS crisis in the summer of 2003. Should RECs even be involved in emergency situations or should research conducted in crisis conditions be exempt from normal ethical review because of public health concerns? Robert Williams, Bioethicist at Scarborough Hospital, described the problems his REC encountered during the SARS crisis. Dr. Bernard Dickens explored the broader subject of how human subject research can be dealt with in emergency situations.

The next theme for the workshop was the role of both international bodies and instruments in research ethics review. Research on human subjects is often conducted on populations outside the “home state” of researchers, funding agencies or commercial sponsors. This raises important questions about what established international bodies are doing in this area and how international guidelines and regulations apply to research review in host countries where domestic laws are either nonexistent or fall below international standards. The workshop examined issues such as equivalent standards; the extraterritorial application of national norms; conflicts among national norms; conflicts between national norms and international guidelines; and the impact of religious norms in specific legal systems.

In the next session, the focus shifted to initiatives by international organizations to develop and implement international standards of research review, and standards for RECs themselves. Professor Alexander Capron, of the World Health Organization, and Dr. Juhana Idänpään-Heikkilä, of the Council for International Organizations of Medical Sciences, spoke about the role of their organizations in research ethics review. In the second part of the session, speakers focused on how international standards, guidelines or other documents can penetrate the national legal systems that regulate research review. Dr. Elmar Doppelfeld described the functioning of both the Oviedo Convention and the European Directive on Clinical Trials, and Dr. Andrés Peralta discussed the role of the Latin American Forum for Ethics Review Boards (FLACEIS). Finally, Dr. James Lavery and Dr. Michael McDonald described how countries that sponsor international research can protect research subjects in host countries by adopting the “Equivalent Protection” doctrine.

Promotion of equitable research practices was the next workshop theme. One of the constant criticisms of biomedical research, especially in the context of externally sponsored research, is that human research subjects in host countries are often denied treatment after the end of the protocol. Workshop participants canvassed several proposals for eliminating these inequities. In the first session, Dr. Solomon Benatar discussed benefit sharing between all research participants, including human subjects, Dr. Godfrey Tangwa conveyed the African experience using the principle of distributive justice, and Dr. Geneviève Dubois-Flynn focused on the particular research ethics guidelines applicable to Canada’s aboriginal peoples.
Finally, the workshop turned to an examination of the potential for domestic private law (negligence, contract law and other doctrines) to regulate research and promote the integrity of research review. Can a fault-based compensation system properly regulate these matters? Are special legislative measures in place to modify private law in this area? Speakers concentrated on sources of liability found in these systems, and on questions of remedy and allocation of fault, as well as the use of legislation to limit or increase liability on researchers and RECs. Professor Colin Thomson outlined Australia’s common law liability system while Dr. Dorottya Mogyorósi discussed the civil law liability system in Hungary. The question of how standards of research and research review can be drawn from the sponsoring country or international organization was also considered. Can liability be attached to international researchers, institutions or RECs, either in the sponsoring country or international organization or the host country, on the basis of the host country’s standards? To the extent that such standards are “portable” between the sponsoring country or international organization and the host country, liability can increase in both jurisdictions. The *Abdullahi v. Pfizer* case (the “Trovan” study lawsuit) in the U.S., discussed in depth by Professor Remigius Nwabueze, illustrated the difficulties that litigants face in bringing civil suits against researchers from different countries.

This report of “The Regulation of Research Ethics Review: A Comparative International Workshop” will summarize each presentation. Perhaps more importantly, it will also highlight some of the issues raised by participants in response to the presentations. It is hoped that the emphasis on these issues will lead to further thought, discussion and scholarship on the issue of research ethics review.
SECTION B. Participants

Australia

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Workshop Proceedings

Session 1: Research Ethics Review Structures: International Comparisons

The workshop’s opening session gave participants a representative sampling of regulatory models found internationally. Throughout the world, research ethics systems in the context of human subject research are structured very differently. Some countries have centralized research ethics review systems, in which RECs function at a national and/or regional level, while others have systems in which ethical review of research is primarily conducted through local RECs. Our selection of countries was designed to represent each major global region. Further details of the systems of these countries, as well as many others, can be found later in this report.

Brazil

Presentation by Dr. Corina Bontempo

Dr. Corina Bontempo de Freitas is the Executive Secretary of Brazil’s National Commission for Research Ethics (CONEP).

Human subject research is widespread in Brazil. Dr. Bontempo estimated that every year Brazilian authorities approve about 15,000 research protocols involving 600,000 human subjects. However, in 2002, it was also verified that 4% of protocols submitted to the National Commission had not received the requisite ethics approval (there would be 11,058 research subjects participating in these unethical protocols). Guidelines governing research ethics approval in Brazil were set up by the National Health Council - NHC, and although they are not legally binding, there are other legal documents that support the requisites.

The research ethics system in Brazil is centralized and regulated by the federal state under Res. NHC 196/96. The federal government, under the auspices of the Ministry of Health and of the National Health Council, has the authority to enact rules with respect to monitoring people’s health. The National Health Council created the National Commission for Research Ethics (CONEP), which enacted binding guidelines for the approval of research involving human beings, after careful review of international systems of research ethics review and consultation to the research community. The National Commission coordinates and stimulates establishment of Institutional Research Ethics Committees (RECs).
The approval process for research protocols varies depending on the type of research. Some kinds of research require approval from both the REC and CONEP; some require approval from the REC and ongoing monitoring by CONEP, and some require only institutional REC approval (about 90%). The special areas of research that require both levels of approval are set out in the guidelines. Examples are: genetics, human reproduction, new health equipment and devices, research with indigenous populations and research with international co-operation. Research that requires monitoring by CONEP includes some cases of genetics, human reproduction and new pharmaceutical products. All other research protocols require only REC approval.

CONEP is responsible for:

- Promoting specific ethical standards for research, including research in special areas, as well as recommendations for the application of said standards
- Establishing the path to research ethics approval
- Establishing guidelines for the risk/benefit analysis of the research
- Ensuring that the rights of the research participants are protected
- Instituting RECs
- Ensuring approval within 60 days where CONEP approval is required
- Monitoring research where CONEP monitoring is required
- Setting up an information system to monitor the ethical aspects of research (National Information System for Research Ethics – SISNEP)

While CONEP is responsible for proposing to the National Health Council the norms and guidelines by which research involving humans will be judged, the institutional RECs (of which there are currently 341 in Brazil) are responsible for evaluating research protocols and determining whether they are in accordance with these guidelines. In some cases, specified in the norms, REC sends the protocol to CONEP for final approval.

Generally, the RECs are responsible for:

- Reviewing research protocols for ethical approval in accordance with the NHC guidelines
- Consulting and providing education on research ethics
- Ongoing monitoring of research activities
- Receiving reports from research parties with respect to adverse events or abuse
- Compelling institutions to investigate ethical irregularities
- Keeping in contact with CONEP

One of the goals of Brazil’s centrally-coordinated research ethics system is nationwide application of research ethics review. One of the tools for achieving this is SISNEP, the online repository of information about research ethics approval. SISNEP provides all
forms and documents that researchers must submit to get ethical approval for their research protocols. The protocol must be registered online, which allows standardization of the process. The repository provides information to both CONEP and to the RECs about research protocols that have been, or that are in the process of being reviewed. Specific information is also available to the public and to researchers.

Tanzania

Presentation by Dr. Godwin Ndossi

Dr. Godwin Ndossi is Managing Director of the Tanzania Food and Nutrition Centre in Dar es Salaam, Tanzania.

Tanzania is an east African country with a high incidence of disease as well as high rates of poverty and illiteracy. Due to its disease burden, Tanzania urgently needs medical supplies, technology and treatment, resulting in an increase in the volume and scope of research conducted in the country.

Research review in Tanzania appears to be highly centralized. All biomedical research must receive ethical approval from the National Health Research Ethics Review Committee (NHRERC) in accordance with policies set out by the National Institute of Medical Research (NIMR) in consultation with the Ministry of Health. However, as Dr. Ndossi noted, while the research ethics review system is centralized, the research system is not. This results in an overlap of functions with many different organizations overseeing, funding and carrying out health research. For example, the Commission for Science and Technology (COSTECH) co-ordinates research and grants permits to foreign researchers. The NIMR also co-ordinates research, as well as conducting research and monitoring health research. The Medical Research Coordinating Committee (MRCC), a subcommittee of the NIMR, receives and reviews research protocols and approves scientific research.

Institutions are responsible for establishing their own RECs and doing ethical review of research protocols at their own institutions. As with Brazil, there are national guidelines, but they are not legally binding and are difficult to enforce. In the discussion period, Dr. Ndossi noted that even if a research project does not receive REC approval, it is difficult to stop it from happening. In many cases, with the exception of drug trials (where REC approval is mandatory), researchers simply opt to proceed with their protocol, without approval.

In addition to the external challenges of an overlapping research approval system, there are operational and technical challenges within the NHRERC. Operational challenges include lack of funding and lack of independent decision-making. The NHRERC has
high operational costs and relies solely on the government for funding, thus compromising its operational autonomy. Some of the technical challenges are lack of training in research ethics and general non-compliance with specified guidelines, whether local or international. In addition, there are conflicts of interest between researchers and those funding the research, and no clear guidelines dealing with important issues of community consent or cultural diversity.

There are also no guidelines regarding what happens once the research has been completed. In Tanzania, medical research, particularly clinical trials with new drugs, is one of the only ways for people to receive any medical attention. However, once the research is complete, the human subjects lose their access to the drugs as well as the medical care. The drugs must then be purchased or done without. In addition, the facilities and services of medical professionals leave as soon as the protocol is completed. The current research ethics system in Tanzania, concluded Dr. Ndossi, cannot cope with these issues.

In order to remedy some of these challenges, Dr. Ndossi suggested:

- More ethical training for those involved in making research ethics decisions
- Creating awareness about ethical issues in medical research
- Increasing the available funding, as well as the funding base, for research ethics committees
- Increasing the capacity of research ethics committees to monitor and evaluate research
- Enhancing compliance with ethical guidelines both at the local and international levels

In the ensuing discussion, one interesting feature of the Tanzanian research review process was highlighted. Participants noted that with the increasingly global nature of medical research, countries often have difficulty monitoring the activities of foreign researchers. In Canada, for example, there is no policy requiring foreign researchers (such as the “helicopter geneticists” who go to remote regions to study indigenous populations) to obtain prior ethics approval unless they receive funding from one of the major Canadian funding councils governed by the Tri-Council Policy Statement. In Tanzania, by contrast, the government registers all foreign researchers through a body called COSTECH. Researchers must obtain COSTECH permits before they are allowed to enter the country to conduct research. These permits are also tied to the ethics approval process, since REC approval must be obtained before a COSTECH permit will be granted. There are sanctions for those who are caught engaging in research without a permit and thus, presumably, without ethics approval. As a regulatory strategy for international researchers, this mechanism appears to have some promise.
Southeast Asia

Presentation by Dr. Cristina Torres

Dr. Cristina Torres, the Regional Coordinator of the Forum for Ethical Review Committee in Asia and the Western Pacific Region (FERCAP), outlined the ethical review systems in several south east Asian countries, including Thailand, the Philippines, Indonesia, Malaysia and Laos.

Dr. Torres noted a general trend towards centralization of research ethics review in Asia in terms of preparation of national guidelines for ethical review of researches and special types of health research. In Thailand, there are special provisions for the conduct of HIV/AIDS studies and Community Advisory Boards (CABs) have been formed in some HIV studies to liaise with the host community. The Philippines has formulated national guidelines on research ethics and specific guidelines for the conduct of and research into organ transplants, genetic engineering, HIV/AIDS, and assisted reproductive technology. Other countries like Malaysia and Singapore have adopted their own version of Good Clinical Practice to guide ethical review. In Southeast Asia, national guidelines have generally followed major international research ethics guidelines such as the Declaration of Helsinki, ICH-GCP and CIOMS, indicating acceptance of basic international standards in matters of research ethics review.

Other Asian and Western Pacific countries have also moved towards centralization. Dr. Torres cited Indonesia, Malaysia, Cambodia, Vietnam and Laos, all of which have created national ethics committees and have either developed their own research ethics guidelines or adhere to international guidelines. In the Philippines, a national research ethics committee that formerly reviewed research is being transformed into a body that oversees the work of institutional and local RECs.

FERCAP is involved in capacity building and education for RECs in Asia. It is developing models of good research ethics review in Asia and the Western Pacific. It has developed templates of standard operating procedures for RECs as well as a system for evaluating RECs developed through the assistance of the Joint Program for Tropical Diseases (TDR) of the World Health Organization. FERCAP is a member of the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) created to serve as an umbrella organization of different regional fora to improve capacity in ethical review. As with many other jurisdictions, however, the problem of enforcement remains. Research ethics guidelines do not have legal authority, only moral force.

During the discussion period, one participant wondered whether current ethical review processes were actually ensuring quality ethics review, while another asked if RECs were speaking to subjects during and after research to determine how they felt about the level of protection offered by the research ethics process. Dr. Torres noted that in some
parts of Asia, community involvement in assessing research ethics review structures is becoming increasingly common. Indeed, community involvement often stems from community initiatives to become involved. For example, in Thailand, an HIV study group has created a community advisory board to deal with these research ethics review issues.

Russia

Presentation by Dr. Asmik Asatrian

Dr. Asmik Asatrian is General Secretary of the Forum for Ethics Committees in the Confederation of Independent States (FECCIS).

Russia has a general centralized ethical review system for pharmaceutical research. Drug research protocols are reviewed for ethical approval by the National Ethics Committee (NEC), which is considered an independent ethical review body. Ethics committees in Russia are not considered part of the government. They are not government-funded, and members are not paid for their work. For non-pharmaceutical research, ethics approval is obtained through either the regional ethics committees run by the various provinces or local ethics committees, which are run by hospitals or other local institutions. In addition to the initial approval of research protocols, these regional and local ethics committees are responsible for monitoring protocols as they proceed.

The Russian government has instituted national research ethics guidelines. Regional and local committees may also have their own institutional guidelines that they follow in approving research protocols. Russia has also adopted all international research ethics guidelines, such as the Declaration of Helsinki and the ICH-GCP, into national law and these international guidelines override national laws in the case of a conflict. This gives these international guidelines the force of law, unlike the situation in many other jurisdictions we have examined. Researchers who do not comply with ethical guidelines may have their research suspended and may not receive approval for subsequent protocols.

Russia has been instituting research ethics training for those who provide ethical approval. It provides GCP courses, seminars and conferences and almost all MD programs in Russia contain an ethics requirement. There is no independent auditing system for research ethics committees, but this problem is being addressed.
India

Presentation by Dr. Partha P. Majumder

Dr. Partha Majumder is the Head of the Human Genetics Unit of the Indian Statistical Unit in Kolkata (Calcutta).

In India, research ethics review mostly occurs locally. Research involving human subjects is reviewed by the REC at the institution in which the proposed research will be conducted. If there is no REC at the institution, a protocol can be reviewed for ethical approval either by the Central Ethics Committee of the Indian Council for Medical Research or the National Bioethics Committee, Department of Biotechnology. Even though research ethics review is generally performed locally, there are national policies and guidelines that govern research ethics approval. The National Bioethics Committee has a National Ethical Policy while the Central Ethics Committee has issued National Ethical Guidelines. These documents have been harmonized.

Although the guidelines are harmonized, Dr. Majumder noted that there is significant overlap in the functions of the two national RECs. Even in cases where the national RECs are not involved, if several institutions are involved in the research, ethics approval must be granted by all institutions. This is seen as a waste of scarce resources and often results in delays in initiation of a project. Dr. Majumder noted that there are not enough trained professionals to sit on RECs and that usually no compensation is given to those who do.

Although India has policies and guidelines requiring ethics approval before any project begins, there are no legislative enforcement mechanisms. Without such legal “teeth”, some researchers can bypass the ethical review process.

If the proposed research is funded either in whole or in part by non-Indian agencies, or involves researchers or institutions located outside India, the procedure for ethics approval changes. In such a case, research ethics approval is required from the Central Ethics Committee of the Indian Council of Medical Research and from all institutions involved in the research, whether they are located in India or not. In addition, the Health Ministry Screening Committee, Government of India, has to approve all international collaborative projects on biomedical research.
South Africa

Presentation by Dr. Jerome Singh

Dr. Jerome Singh is Head of the Bioethics and Health Law Programme at the Center for the AIDS Programme of Research in South Africa.

South Africa, like Tanzania, has a heavy disease burden. However, unlike Tanzania, it also has a high level of scientific expertise and relatively good research infrastructure, which makes it an attractive place to conduct human subject research. However, despite the fact that a lot of such research takes place in South Africa, the research ethics review system remains highly fragmented. Review procedures and guidelines differ, depending on where the research is being conducted, or who is funding it.

South Africa has four statutory councils that perform or oversee research on human participants. The Council for Scientific and Industrial Research (CSIR), established in 1947, conducts a limited amount of research that could impact on human health (for example, research on genetically modified organisms aimed at human consumption), but still does not have its own REC. Instead, it relies upon the RECs of other organizations to screen its research that involve human participants. The Medical Research Council (MRC) issued the original guidelines on research ethics for South Africa, which were most recently updated in 2002. These guidelines have no legal force, but a failure by MRC researchers to follow MRC guidelines would probably result in disciplinary action by the MRC against the researcher, and the matter would be reported to the researcher’s professional association. Researchers not funded under the MRC are not bound to follow the MRC guidelines.

The Medicine Control Council (MCC) deals with regulation relating to drug research, clinical trials and drug safety. It does not have its own guidelines, but follows the Good Clinical Practice guidelines issued by the South African Ministry of Health. These guidelines are only applicable to clinical trials, and, like those of the MRC, have no statutory force. The GCP guidelines, however, do provide some guidance on how RECs should be set up, how they should function, and what their scope should be. Finally, the Human Sciences Research Council (HSRC) is a statutory body that specializes in social sciences research in South Africa. It has its own code of research ethics but like the guidelines of its statutory counterparts, the HSRC code of ethics is not legally binding.

What is different about the South African example, however, is that much of this fragmentation is about to change, with the implementation of the National Health Act, 2004 (NHA). The NHA mandates the creation of the new National Health Research Ethics Council (NHREC), which will:
• issue national research ethics guidelines
• maintain a registry of accredited institutional RECs
• set norms for human health research
• hear appeals from researchers who have been turned down by RECs
• refer those in violation of the guidelines to their respective professional associations for discipline
• discipline its own members for violations

Currently, the NHREC is in an interim stage, called the “National Interim Health Research Council,” but it has already issued national research ethics guidelines, which are the first in the country to be backed by statutory authority. However, it remains to be seen how the guidelines will be enforced, as the NHA does not legislate any enforcement body. Stakeholders are currently waiting for the Ministry of Health to institute regulations for the enforcement of NHREC guidelines, and sanctions for those in violation of such guidelines. However, while there are still uncertainties about how the NHREC will operate and how its guidelines will be enforced, it is a big step forward towards a stronger research ethics system in South Africa.

Turkey

Research Ethics in Turkey – 12 Years’ Experience

Presentation by Dr. Sefik Gorkey

Dr. Sefik Gorkey is Professor of Medical History and Ethics and Chairman of the Medical Ethics Department of Marmara University Medical School in Istanbul.

Dr. Gorkey noted that RECs had emerged in Turkey in response to several developments:
• the 1987 Zakkum case, in which a doctor announced that he had found a cure for cancer in a plant;
• the requirement of ethical approval for studies published in international medical journals; and
• the rise of multinational medical research projects and industry in Turkey.

In 1993, the Turkish government passed a law governing clinical trials, but not other research that might use human subjects. Under this law, a Central Research Ethics Committee was created within the Ministry of Health. The Central REC has the authority to oversee the approximately 80 Local Research Ethics Committees throughout
the country. All clinical trials must have the ethical approval of a Local REC before research can begin.

The Central and Local RECs in Turkey use the latest version of the Declaration of Helsinki and the ICH-GCP as guidelines for granting ethical approval. In addition, Local RECs have the legal power to stop research if these guidelines are violated.

There have been other changes since the law was passed in 1993. Turkey is currently seeking membership in the European Union. In order to be granted full membership, it must bring many of its laws, including those dealing with human subject research, into line with European standards. As a result, the Turkish government is drafting new legislation on clinical trials. The current draft includes more stringent regulations governing how research protocols are defined and the composition of RECs. Under the proposed reforms, an ethicist must sit on the Central Ethics Coordination Council, a patient representative must sit on the Central REC, and lawyers and patient representatives must be included on Local RECs.

Among the criticisms of the Turkish research ethics system are that it is too centralized and that it takes too long get ethical approval for a clinical trial. Dr. Gorkey recommended more autonomy and funding for Local RECs, in concert with more education for Local REC members.

### Session 1 Discussion

These seven presentations illustrated the immense regulatory challenges faced by developing and transitional countries. Despite centralized administrative structures and adherence to international biomedical research standards, practical challenges continue to overwhelm regulators in some countries. Funding constraints, conflicts of interest, a lack of REC expertise, and an inability to enforce standards all combine to make the work of RECs difficult. The ensuing discussion developed this theme and workshop participants also raised and discussed several other key points:

1. **Overlapping RECs:** Some countries, such as India and South Africa, require ethical approval from more than one REC for the same protocol. Is this kind of overlapping approval a waste of scarce resources? Furthermore, the requirement for more than one REC to approve any given protocol raises questions about the standards being used by each REC. How can we be sure that each REC is using the same standard? Should they be using the same standard?

   It was noted that in South Africa, one response to the requirement for multiple approvals is more informal communication between the various RECs. It also appears that within this informal communication system there is a classification of ethical
reasons for accepting or rejecting a protocol. This kind of communication between RECs appears to be crucial, especially in jurisdictions where the system is not centralized through national guidelines, as there was evidence of forum-shopping taking place.

2. **Role of private law?** Much of the focus on enforcing ethical standards appears to be through public law. Is there a role for private law in enforcing ethical standards?

Contract law could be employed to uphold ethical standards in human subject research. It could be argued that researchers are bound contractually to act in an ethical manner and that a breach of this contractual obligation could be an employment law matter. This argument was used successfully in a case where a researcher forged results in a cancer study. Because this act was outside the bounds of his employment contract, he lost his job. In this way, employment law made the researcher accountable for his actions.

3. **Monitoring.** How do we know whether review procedures and standards are actually protecting human research subjects? How are we ensuring the ethical quality of ethical review? Are we talking to research subjects to find out how they view the protection of their interests under various ethical systems?

Dr. Torres noted that in Thailand, such consultation with the community is taking place. In fact, there is a community initiative to document the subjective experiences of research participants. An HIV study in Thailand has a community advisory board that monitors the views and concerns of study subjects.

It was also pointed out that it takes time to determine whether the systems in place actually work the way we want them to. We must first focus on putting the procedures in place and making them functional before we can judge whether they are successful or not.

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**Session 2: Research Ethics Committee Oversight: Accreditation and Other Regulatory Mechanisms**

One of the main problems in the use of research ethics review systems is determining whether the review meets an acceptable standard. Are RECs using the proper guidelines in reaching their conclusions on the ethics of a research protocol? Are those who sit on the REC adequately trained? Are there conflicts of interest that could prevent the REC from providing a truly independent ethical review? Systems of accreditation are being explored as one way of assuring the public that a research ethics review is meeting certain basic standards in its operating procedures and application of ethical guidelines. Several jurisdictions have implemented systems of accreditation or have explored accreditation schemes.
United Kingdom: Central Accreditation

United Kingdom: The Central Office for Research Ethics Committees (COREC)  
Presentation by Professor Terry Stacey

Professor Terry Stacey, of the U.K. Department of Health, was inaugural Director of the Central Office for Research Ethics Committees under the auspices of the Department of Health. In 1997, he was responsible for implementing a new system of Multi-centre RECs and later advised on the modernization of the overall NHS REC system so that it could function uniformly throughout the country. (He retired in March 2006).

The accreditation scheme in the U.K. is a quality assurance tool designed to minimize inconsistencies within the REC system. It will help to ensure best practices for RECs countrywide and will assure researchers, research subjects and the public that RECs are fit for purpose, and that appropriate guidelines and policies are being used.

The accreditation tool was developed under the auspices of the Central Office for Research Ethics Committees by an Accreditation Working Group, drawn largely from Chairs, members and administrators of RECs, with expert guidance from SGS United Kingdom Ltd., a company renowned for audit systems. After the design of the audit tool was completed and piloted, the Accreditation Working Group developed an operational programme by which RECs could become accredited. A full-scale audit is an extremely rigorous process. It scrutinizes everything, from the way the members are selected, how meetings are organized and the guidelines used, to the use of standardized office procedures and correspondence, and even good management practice such as the locking of filing cabinets overnight.

The inspection of an REC is based on a “peer review system”. Chairs, members and administrators were invited to apply to be Reviewers. Reviewers are required to have considerable experience of the REC system, have good communication skills and be diplomatic. They also need to have a commitment to quality assurance, and be prepared to undertake at least two reviews per year, each lasting one or two days.

The response was very enthusiastic, and so far 87 reviewers have been identified through a formal application and interview process. Of those, 32 have signed on by formally agreeing to the terms and conditions set out by the Working Group at induction events held in January and February 2005. More induction events are already planned. So far, 40 RECs in the U.K. have been selected to undergo review to be completed by the end of 2005.

The review process begins by the REC completing a self-assessment test. This allows peer reviewers to determine its current position on practices, procedures and use of
guidelines. This is followed by an on-site inspection of office practices and procedures. Peer reviewers also attend and observe an REC meeting.

To receive accreditation, an REC must, as a minimum, adhere to the following policy documents:

- Standard Operating Procedures for Research Ethics Committees (SOPs);
- Governance Arrangements for Research Ethics Committees;
- Directive 2001/20/EC of the European Parliament and of the Council; and
- ICH-GCP.

The review process can have either of two outcomes:

- Full accreditation status for three years.
- Preliminary accreditation status, meaning that the REC needs to do more work before it can be fully accredited. Full accreditation will be awarded within six months of the completion of an agreed action plan.

The accreditation system in the U.K. is designed for quality assurance. It is not meant to regulate RECs, and there are no penalties associated with the system. Similarly, there are no economic incentives or penalties to encourage researchers and research institutions to use accredited RECs. The goal is that all U.K. RECs will soon reach the required standard, and will be re-reviewed every three years. For further information, see the COREC web site. http://www.corec.org.uk

**Lithuania**

**Establishment of RECs and Setting Standards for their Activity**

**Presentation by Gytis Andrulionis**

Gytis Andrulionis is a law professor at Mykolas Romeris and Vilnius Universities in Vilnius. His sphere of interests include the legal and regulatory aspects of REC review in Lithuania and other Baltic countries.

Situated in the Baltic region of Eastern Europe, Lithuania has a population of about 3.48 million. Lithuania was part of the USSR until 1990, when it declared its independence and in 1992 adopted its own Constitution. This is one of the reasons why Lithuania does not have broad experience in the developing of establishment of the RECs and standards for their activity. Lithuanian legislation was considerably influenced by international standards laid down in a number of documents at international level, especially since Lithuania became a member state of the Council of Europe in 1993 and a member of the European Union (EU) in 2004.
The Council of Europe and the EU have well-developed guidelines on research ethics review. They include the Convention on Human Rights and Biomedicine (1997), the Additional Protocol to the Convention on Human Rights and Biomedicine (2005) concerning Biomedical Research, the ICH-GCP (1996) and Directive 2001/20/EC of the European Parliament and of the Council 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. All have either been signed and ratified by Lithuania or have been otherwise implemented in Lithuanian law.

Although requirements of these documents define the standards for Independent Ethics Committees and their activities, they also allow each state to specify and implement these requirements in the national law at their own discretion. Therefore, while establishing standardized ethical review, national law should provide certain requirements for Research Ethics Committees, including:

- Independence
- Constitution
- Competence
- Standard Operating Procedures

There are two ways of deciding whether these standards have been met by RECs:

- Internal quality evaluation, in which RECs evaluate themselves
- External quality evaluation, i.e., an Accreditation system

Lithuania’s research ethics system is two-tiered, with the Lithuanian Bioethics Committee (LBC, a national REC) and Regional Biomedical Research Ethics Committees. The model operating procedures of the Regional Biomedical Research Ethics Committees, quotas of representation in the committees, the number of committee members and composition of the committees, the territory of their jurisdiction shall be established by the LBC. Although all biomedical research must be approved by the LBC, it can ask Regional RECs to approve research in certain situations. In such cases the LBC undertakes monitoring of the activities of Regional Biomedical Research Ethics committees. If the Regional Biomedical Research Ethics Committee fails to perform these functions in the appropriate manner, its right to issue approvals may be suspended by a reasoned decision of the Lithuanian Bioethics Committee. The LBC oversees all the activities of Regional RECs, however there is no regulation of the evaluation procedure or criteria.

On the other hand, in Lithuania the functioning of the LBC according to the above mentioned standards is not legally regulated neither in the form of self-assessment nor accreditation. There are certain rules prescribed by law which establish: the LBC, its
activities and monitoring procedures; training of LBC members; and annual reporting to the Ministry of Health about its activities. However, these rules do not ensure a proper evaluation system, like self-assessment and accreditation would. This is considered to be a weakness of Lithuania’s research ethics system.

Professor Andrluionis concluded that the system could be improved by:

- strengthening legal documents regulating research ethics review;
- implementing an internal quality assessment to be performed at both the national and regional levels; and
- implementing an external system of quality review, or accreditation.

Whereas it is difficult to establish an accreditation system in a small country like Lithuania, Professor Andrluionis suggested that a system of international accreditation could capitalize on the greater independence and competence found at the international level. One suggestion would be to institute a single accreditation system for all the Baltic states, which present some performance similarities.

Canada

National Council on Ethics in Human Research (NCEHR)

Presentation by Dr. Richard Carpentier

*Dr. Richard Carpentier is Executive Director of the National Council on Ethics in Human Research (NCEHR) where he recently participated in Canadian initiatives to promote the establishment of a system of accreditation.*

The NCEHR is an independent, non-governmental council created to advance the protection and well-being of human subjects in research and to foster high ethical standards in research involving humans. It was established in 1989 by Health Canada, the Medical Research Council and the Royal College of Physicians and Surgeons.

The NCEHR is involved in numerous activities, including:

- Education;
- Analysis of Emerging Issues;
- Quality Improvement Site Visits;
- Communications;
- Maintaining a list of RECs;
- National and International Liaisons; and a
- Task Force on Accreditation.
The NCEHR became interested in a scheme of accreditation for RECs as an extension of its site visit program to ensure the well-being of human subjects in biomedical research. The mandate of the site visit program is to identify best practices and help institutions to implement policies and procedures that protect research subjects. Despite ongoing site visits, however, problems were still apparent.

Due to the lack of regulation of RECs in Canada, it is unclear exactly how many there are. Dr. Carpentier estimated there may be 600 but it is not known where they are or what policies and practices they follow. A system of accreditation would be an efficient method of overseeing Canadian RECs, addressing an area of long-standing concern.

At the federal level, approval by a REC is required for clinical trials and for research funded by one of the three major Canadian funding councils – the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council and the Social Sciences and Humanities Research Council. Research funded by one of these three bodies is governed by the Tri-Council Policy Statement, which, however, has no legal force. Some provincial jurisdictions have also adopted provisions requiring ethics review, for example the Quebec Civil Code as well as privacy protection legislations.

Dr. Carpentier noted that the United States is a major financial contributor to health research in Canada (approximately $100 million a year by the US Department of Health and Human Services). However, there is little means to oversee the quality of any REC approval. Public concern over recent unethical research events has prompted increased calls from many quarters for oversight of Canadian RECs to ensure a minimal level of ethical approval standards in all research studies.

These calls have come from:

- Clinical Trial Regulations (2001);
- The Speech from the Throne (2002);
- The Standing Committee on Social Affairs, Science and Technology (2002);
- The Royal College of Physicians and Surgeons of Canada Task Force on Clinical Research (2003);
- CIHR’s Standing Committee on Ethics;
- The House of Commons Standing Committee on Health (2004); and
- The Canadian Biotechnology Advisory Committee (2004).

Similar calls have been made in the US, where one system of voluntary accreditation (the AAHRPP) has been established and accreditation legislation has been introduced in Senate and Congress.
In Canada, the NCEHR established the Task Force to Study Models of Accreditation for Human Subject Protection Programs in 1999. It was chaired by Dr. Henry Dinsdale, of Kingston General Hospital at Queen’s University.

The Task Force made three recommendations:

- Canada should have oversight of RECs, based on standards;
- this oversight should be based on an accreditation system conducted by an arm’s-length, non-governmental organization; and
- the NCEHR should facilitate discussions with stakeholders with the goal of creating a system of accreditation.

The task force also outlined the characteristics of a viable accreditation program:

- Accountability;
- Transparency;
- Protection of the public interest;
- Education as an intrinsic component; and
- Sensitivity to the differing needs and experiences of a wide range of disciplines and provincial priorities.

The next step was to act upon the task force’s third recommendation and develop a system of accreditation. In 2003, the NCEHR struck the Task Force for the Development of an Accreditation System for Human Protection Programs, co-chaired by Ken Davey of York University and Michael Owen of Brock University.

In April and May 2005, the new task force held a national consultation on a system of accreditation for RECs in Canada. The consultation considered three areas, each featuring various options:

- **The accreditation entity**
  - A transformed NCEHR
  - Add maintenance of accreditation to the current mandate of the NCEHR
  - Create a new entity
  - Use another existing organization

- **The development of standards**
  - Use an expert committee
  - Use a professional standards organization

- **The funding mechanisms**
  - Fee for service for those using RECs
  - Government funding
  - Consortium of stakeholders
  - Blend of the above options
The national consultation demonstrated overwhelming support for the idea of accreditation of RECs in Canada. Of the 56 stakeholders involved in the consultation, 53 were in favour of an accreditation system, two were against it, and one was undecided. The consultation also found that stakeholders favoured the NCEHR with an enhanced mandate as the accreditation entity, an expert committee to develop standards and a blend of the funding options.

Following the national consultation, the next steps are to continue the dialogue with stakeholders, to develop standards and to compile a list of all RECs in Canada.

**Session 2 Discussion**

It is clear from the three presentations in this session that accreditation is the favoured method of overseeing RECs, at least in the countries canvassed. Regulation by legal means, on the other hand, is not as popular. Despite this, there remain stark differences of opinion about whether accreditation is a better way of protecting human research subjects. In the wake of recent scandals involving human subject research, implementing accreditation systems has been one response to calls for more control over the research ethics approval process. However, as one speaker noted during the discussion, adopting a system of accreditation as the only method of oversight risks substituting the mere appearance of more control for the stronger oversight people require.

The comment was also made that the accreditation process is most common in hospitals, where it emerged from the internal conflict between doctors, who were concerned about providing the best possible health care, and administrators, who were concerned about costs. This tension produced a measurement of the capacity for providing quality, yet cost-effective care. But the tension that exists in the context of research is not the same. In the current context, research is often part of an industrial activity. Industry practices are not usually submitted to an accreditation system. They are regulated and inspected to ensure that standards are met. Stricter regulatory standards should be considered as the appropriate method of overseeing research.

In addition, there are criticisms that accreditation is more concerned with process than with health and safety. This echoes the question posed in the first session about whether RECs are actually protecting the health and safety of research subjects. By extension, the hotly debated question in this session became: how do we know whether a system of accreditation will help to protect research subjects? Some argue that implementing an accreditation system must strengthen the protection of subjects, because thinking about process will increase the general effectiveness of the RECs and help them to run more smoothly. In addition, the act of going through the accreditation process will remind members that they have specific duties to fulfill. Others argue that an accreditation
system does not ensure ethical quality, which must be guaranteed by stricter regulation and penalties.

Other problems with using accreditation as the main means of oversight for RECs include the fact that accreditation is usually voluntary. In a voluntary system, good RECs will compete with one another while bad RECs will remain anonymous and unregulated.

Germany and Australia have systems that combine accreditation and regulation. In fact, Australia appears to be leaning towards more regulation. Canada’s Food and Drug Act allows Health Canada to visit research institutions to ensure that the Act is being followed. Health Canada has also started to conduct site visits of RECs to determine whether they respect Good Clinical Practices. A combined system of regulation and accreditation could be instituted for RECs.

**Session 3: Commercialization:**

**Challenges for Research Ethics Review**

Research Ethics Committees (RECs) face significant challenges in dealing with the increasing commercialization of biomedical research. Much of the biomedical research in both the developed and developing world is being conducted by pharmaceutical and biotechnology companies whose main goal is profit. Over the past several years, we have seen many controversies and some tragedies resulting from commercial biomedical research. As described in the presentation by Dr. Remigius Nwabueze, one of those tragedies occurred in Nigeria when 11 children died after being given the experimental drug Trovan in a clinical trial during a meningitis outbreak.

What role can RECs play in preventing such events? While many people believe that stronger research ethics approval systems will prevent many of these problems, there is evidence to suggest that relying solely upon RECs is not a complete solution. Many studies of RECs reveal that they are not immune from the commercial pressures that create conflicts of interest and compromise ethical approval.

How can we prevent such situations from arising in the future? Should RECs be the only safeguard against conflicts of interest, or are we placing too much pressure on an already strained ethical review system? Professor Trudo Lemmens examined these questions from a North American perspective and Dr. Anant Bhan discussed how the problem is affecting research in India.
North America: Commercialization of Research and REC Review

The Commercialization of Research and REC Review in North America

Presentation by Dr. Trudo Lemmens

*Dr. Trudo Lemmens is an Associate Professor at the Faculty of Law, University of Toronto, and holds a cross-appointment with the Faculty of Medicine. Much of his current research focuses on the regulation of medical research.*

Research ethics concerns have to be situated in the context of the significant commercial market for pharmaceutical products. The global market for pharmaceuticals is huge. According to the IMS Health, a corporate market research firm, worldwide pharmaceutical sales in 2003 totaled US$491.8 billion. Several classes of medicines reaped impressive sales on their own. For example, sales of cholesterol and triglyceride reducers reached $26.16 billion in 2003 with Pfizer’s Lipitor accounting for $10.3 billion of that total. Antidepressants generated $19.5 billion, with Pfizer’s Zoloft taking $3.4 billion.

There is intense commercial pressure to maintain and increase profits from pharmaceuticals. To sustain current levels of profitability, companies have to bring several new blockbuster drugs to the market each year. Consequently, there is pressure to get drugs out of research and development and onto the market as quickly as possible. However, bringing a new drug to market is a difficult and time-consuming task. Pharmaceutical companies must conduct clinical trials to convince governments that their products are both effective and safe for human consumption. Two phenomena are worth noting in this commercial context: the shift from research in academic settings to the private sector; and a significant increase in the number of clinical trials.

Up to the 1990s, the majority of clinical trials took place in university settings. In 1991, 80% of clinical trial funding still went to academia. In 1998, the figure was down to 40%, and in 2004 it reached only 26%. More and more clinical trials are being conducted by Contract Research Organizations and in the community by physicians who are often paid to enlist their patients as subjects. There has also been a significant increase in the number of clinical trials taking place. In 1998, there were 800 clinical trial submissions to the Canadian Drug and Health Products Directorate. The number of human research subjects is not only growing in North America but also in the developing countries of Eastern Europe, Africa and the Southern Hemisphere.

Connected to the increasingly commercial nature of medical research, Professor Lemmens noted some other characteristics of this new research environment.
Control of all facets of the research process is increasingly in the hands of the sponsors or specialized commercial agencies (contract research organizations) hired by the sponsors. This includes:

- Study design;
- Subject recruitment;
- Data collection;
- Data analysis;
- Preparation of report manuscripts;
- Creation of strategies with respect to the dissemination of data and publication of study results;
- Conflicts of interest between sponsors and researchers; and
- Blurring of the line between research and public relations.

Professor Lemmens discussed several examples that highlight how commercial interests impact on the integrity of medical research and how research is increasingly being integrated in the marketing campaign of a new drug. He discussed in detail an article by David Healy and Dinah Cattell, who analyzed how scientific publications on the anti-depressant Zoloft were coordinated by a medical information agency, Current Medical Directions (CMD). The agency managed to publish articles in the best journals, with the highest citation rate and the highest impact factor.

The lawsuit by the Attorney General of New York against GlaxoSmithKline also reveals how commercial interests can seriously undermine the reliability and integrity of published reports. GSK was alleged to have promoted off-label prescription for the anti-depressant Paxil for use by children and adolescents, using a publication which discussed only the selective positive results of one study, concealing the results of other clinical trials that showed lack of efficacy and negative side effects such as a marked increased risk of suicide and suicidal ideation. The Attorney General of New York State sued GSK for fraudulent misrepresentation, but the lawsuit was settled out of court.

Professor Lemmens further discussed in detail the Gelsinger case to highlight how financial interests may also affect the health and well-being of research subjects.

What can be done about such practices, that have flourished as a result of the commercialization of clinical trials? Professor Lemmens noted that there have been repeated calls for more disclosure and transparency of all potential conflicts of interest in publications, to RECs and in the consent forms to be signed by research subjects. Many have cited the issue of commercialization as one for RECs to tackle, since it is their job to review the ethics of the protocol. However, this entails a great deal of work, including:
• Reviewing clinical trial agreements between researchers and sponsors;
• Reviewing the budgets of clinical trials, including incentives for the recruitment of subjects and payment to subjects;
• Reviewing publication agreements;
• Reviewing the scientific validity of the trial;
• Monitoring access to the data; and
• Reviewing and monitoring any publications.

Should RECs be expected to do all of this work? Are RECs capable of completing these tasks? Professor Lemmens noted that RECs cannot take sole responsibility for unraveling the complex relationships between scientists and the companies that sponsor them. In fact, many RECs have their own relational issues with sponsors, such as private RECs that provide ethical approval for a fee, or RECs that are part of CROs. Institutional RECs are also affected by conflicts of interest: the institutions in which they are located have significant financial interests in research and the RECs can be under pressure not to hinder research activities that bring in money. Many members of RECs are also involved in research activities sponsored by industry, which could taint the independence or perceived independence of the REC itself.

Professor Lemmens contends that these matters might be better dealt with through strict regulation and enforcement along with enhanced REC approval. He suggested that stricter regulation of RECs seems to be required, but that it should also be part of a larger reform of the drug regulatory system and better regulation of the impact of commercial interests in academic institutions.

India

Commercialization in India

Presentation by Dr. Anant Bhan

Dr. Anant Bhan is a physician from India, and is interested in bioethics and public health. He recently completed a master’s degree in bioethics at the University of Toronto.

The commercialization of clinical research is not only a problem in high-income countries. It is also becoming a significant problem for low-and-middle-income countries. As a result of globalization, much medical research has moved out of the West and into low-and-middle-income countries where regulations are not as strict, costs are lower, and subjects can be recruited more efficiently. In addition, it is much easier in low-and-middle-income countries to find patients who are not already taking some form of pharmaceutical treatment, allowing cleaner (although not necessarily more accurate) scientific results.
Scholars have noted that the big pharmaceutical companies are fighting a “turf war” over the developing world. They are competing for subjects as well as speed in getting their products approved and on the market. Low-and-middle-income countries, in turn, are trying to make themselves attractive for clinical trial research. In many countries, clinical trials sponsored by corporations are the only way citizens can get access to expensive medical treatment and technology.

While many countries see clinical trials as beneficial, the rush to the developing world has also raised many concerns. Problems include recruitment techniques and the consent provided by subjects. The lack of research regulation in many developing countries raises the suspicion that pharmaceutical companies are attempting to get, through the back door, what they could not get through the front door in high-income nations.

There are also serious concerns about the standard of care given to subjects in low-and-middle-income nations. Is it ethical for researchers to withhold a treatment from subjects in the developing world simply because that country cannot afford it? This is a common justification for placebo-controlled trials in low-and-middle-income countries. Citizens of those nations are receiving a lower standard of care than they would in high-income nations. In addition, there are concerns about post-trial obligations. Currently, when a clinical trial ends, companies pack up and head home, with little regard for the subjects who may have benefited from the protocol. What happens to them? Should they continue to receive treatment? Who should pay for it?

India’s large and diverse population base and high disease burden makes it an attractive destination for clinical trials. A rising economy and extensive pool of scientific expertise means that local researchers can often be used, for less money than researchers from high-income countries. Many hospitals are high tech and there is a high degree of English language fluency. India also has a vibrant pharmaceutical industry consisting of around 20,000 companies. As a result, there has been a 400% increase in the number of clinical trial applications filed in India over the past few years.

The Indian government encourages clinical research because biotechnology brings the promise of food for all, health and environmental sustainability. It also brings the hope of employment for up to a million people and huge revenues for the country. Financial incentives to companies conducting research include customs duty exemptions and tax holidays. The Indian Council of Medical Research and the Department of Biotechnology are also promoting joint government/industry partnerships for the benefit of private interests.

While the government wants to promote private investment in India, there are many concerns about the manner in which research is being conducted, including whether informed consent can be obtained from the research subjects. Dr. Bhan noted that many
of the subjects are either illiterate or semi-literate. In addition, crowding in public health care facilities may induce people to turn to clinical trials to obtain basic health care. This also presents challenges in obtaining valid and truly “informed” consent.

There are also concerns about the physicians recruited to conduct research. These physicians are often required to adhere strictly to the corporate protocol and not provide input about their own unique population. They are usually not trained researchers but are rather clinicians, who may not appreciate the ethical issues involved in research. These concerns have led many scholars to observe that Indians are being used as guinea pigs by the pharmaceutical industry.

India’s research regulation system needs to be strengthened to address these concerns. Oversight of clinical trials in India is seriously lacking. The office of the Drugs Controller General of India is understaffed, with only three trained staff members, none of whom is a physician. In addition, fewer than 200 Indian investigators are trained in Good Clinical Practices (GCPs).

The National Guidelines for Biomedical Research are only binding on research funded by the government, not the private sector. In addition, many REC members in India are not properly trained in ethics and the process of ethics review, nor is there any regulation governing the activities of the RECs. This lack of regulation and the general lack of public REC resources have led to the appearance of many commercial RECs. There may be benefits to using commercial RECs, such as speedy review, but there are also many concerns that need to be addressed. Many of the commercial RECs are owned by pharmaceutical companies or the CROs that manage and implement research, producing the potential for serious conflict of interest. In addition, members of commercial RECs could have a financial investment in the company sponsoring the research. The proliferation of commercial RECs also provides sponsors and researchers with the opportunity to forum-shop in order to find an REC that will meet their needs, i.e., speedy approval. After all, commercial RECs are businesses whose aim is to meet the needs of their clients, which are not the same as the needs of human research subjects or the needs of society. Therefore, the continuing proliferation and use of commercial RECs in India should be carefully examined.

Session 3 Discussion

Although informed consent often takes centre-stage, thinking of research ethics purely as an issue of informed consent is misleading. These two presentations showed that many other ethical issues need to be examined, especially the relationships between sponsors, institutions and researchers and potential conflicts of interest arising from those relationships. These presentations also showed the many ways in which parties can be influenced. Parties are often creative in their compensation schemes—sponsors
paying for physician/researchers’ overhead costs rather than paying them directly – and we need to be more aware of these transactions.

Dissemination of research results, and often the lack of it, was also discussed. Researchers may not have the authority to disseminate the results of their research without the approval of the sponsor. As Professor Lemmens pointed out, this can lead to the suppression of negative research findings. There should be greater transparency with respect to the results of scientific research. RECs can be part of the solution, but further reforms are needed.

**Session 4: Specialized Review Bodies: Recent Initiatives, Future Possibilities**

Specialized review bodies are an important component of research ethics review. Certain kinds of human subject research raise specific ethical issues that are best determined by research ethics committees with special expertise. Specialized RECs have emerged in several parts of the world. In this session, we examined Estonia’s research ethics review boards for its genetic databanking project and Canada’s review processes for stem cell research and xenotransplantation.

**Estonia: Review of Research involving a Genetic Databank**

**Research Ethics Review of Genetic Databanking Research: An Estonian Experience**

**Presentation by Ants Nömper**

*Ants Nömper is a lawyer and lecturer in medical law at the University of Tartu in Estonia.*

The Estonian research ethics system is relatively small. Established in 1990, it is administered by the National Council of Bioethics and currently has two regional RECs located in the country’s two largest hospitals. In 1997, local RECs were instituted as well. There are no national guidelines in Estonia. Ethical review is based on the Council of Europe’s Convention on Human Rights and Biomedicine. There are no standard operating procedures, nor is there a system of accreditation. Clinical drug research accounts for about 80% of ethical reviews. Problems with Estonia’s REC system include a lack of ethical training for REC members and a lack of funding.

In 2000, the Estonian Parliament passed legislation allowing widespread collection of genetic samples from citizens. The goals of the project are to create a collection of genetic samples and health status reports of the Estonian population, to research genes that cause common illnesses and to add to existing knowledge on genetics.
The Estonian Gene Treasury (EGT), operated by a non-profit foundation, aims to collect genetic samples from about one million Estonians – 66% of the population. However, progress was stalled due to lack of money. Before funding ran out, the project collected only about 10,000 samples. The EGT is run by a supervisory board that makes high level decisions, a management board that runs day-to-day activities, a scientific advisory board and an ethics committee.

The EGT REC currently has seven members who are nominated for a five-year term by the supervisory board. REC members must be specialists of impeccable reputation in their fields of expertise. The EGT REC is guided by recognized international ethical standards, such as the Declaration of Helsinki, CIOMS and UNESCO.

The law required a special REC for the EGT for several reasons:

- Public relations;
- To secure financing for ethical review from the state;
- To ensure quality ethics review; and
- To meet the requirements of the Oviedo Convention.

In addition to the legal requirement, there were also ethical reasons for having a specialized review committee:

- The project is ongoing (i.e. there is no time limit);
- Minors are included within the scope of the project;
- The informed consent provided is not specific consent; and
- The project involves genetics.

There are some concerns about the EGT REC. Members are paid by the EGT and are not considered autonomous. The supervisory board can remove them at any time for failure to perform their duties, inability to participate in the work of the REC or causing significant damage to the interests of the EGT.

Canada: Review of Stem Cell Research

Centralized Review of Human Stem Cell Research in Canada

Presentation by Dr. Michael Enzle

*Dr. Michael Enzle is an experimental social psychologist at the University of Alberta. He is currently the Chair of the Stem Cell Oversight Committee at the Canadian Institutes of Health Research.*
The Stem Cell Oversight Committee (SCOC), an *ad hoc* working group of experts in stem cell research, ethics, law and medicine, was created in 2000 in response to the explosion of stem cell research in Canada. Its mandate was to advise the Canadian Institutes of Health Research (CIHR) on whether human embryonic stem cell research was eligible for federal research funding. The Human Pluripotent Stem Cell Research: Guidelines for CIHR-Funded Research (Stem Cell Guidelines) were unveiled in 2002 and all three federal funding agencies – CIHR, National Science and Engineering Research Council (NSERC) and Social Sciences and Humanities Research Council (SSHRC) – agreed to take a common approach in implementing the guidelines.

The Stem Cell Guidelines state:

- Only excess embryos created for reproductive services may be used;
- Consent to research must be free and informed and given at the time of donation;
- No human cloning;
- No human parthenogenesis;
- No combining of human or non-human embryonic stem cells with human embryos;
- No grafting of human or non-human embryonic stem cells to a human fetus; and
- No grafting of human embryonic stem cells to a non-human fetus.

Although the mandate of the SCOC is very similar to that of an REC, it is not an REC, as the focus of the review is to ensure adherence to the Stem Cell Guidelines and not basic ethical principles. The SCOC reviews funding applications to the CIHR, NSERC and SSHRC that deal with stem cell research as well as applications to other agencies that receive funding from the CIHR (and from other agencies where agreed upon by the parties). It gives advice about applying the Stem Cell Guidelines to RECs and Animal Care Committees and about ethical and scientific issues regarding stem cell research. It is also developing a monitoring system to ensure compliance with the Stem Cell Guidelines at all stages of research. Finally, the SCOC continually reviews and revises the guidelines themselves.

The SCOC has 12 members from different backgrounds:

- Stem cell biology and therapeutics, developmental biology or embryology
- In vitro fertilization health care
- Ethics
- Law
- Social sciences
- A health-oriented charitable organization
- International member with expertise in stem cell research policy
• In vitro fertilization patient
• Members of the public who are not advocates for any interest group but who have an interest in health research

SCOC members are appointed for one-, two- or three-year terms. Members may serve a maximum of two terms. The chair of the SCOC is selected by the CIHR’s Governing Council. The committee must meet in person at least twice a year. The SCOC’s main enforcement powers are through the Stem Cell Guidelines as well as the memorandum of understanding of the Tri-Council Policy Statement (TCPS). Those who violate the Stem Cell Guidelines or the MOU may lose funding from the three federal funding agencies.

Interestingly, the original Stem Cell Guidelines issued by the SCOC in 2002 included a recommendation that the federal government establish a National Research Ethics Review Committee that would be responsible for reviewing:
• Novel and contentious areas of research where expertise was not available at the local level;
• Multi-centre trials; and
• Large population based studies.

The suggestion was never implemented and it was removed from the guidelines.

The SCOC is coming to an end. The Assisted Human Reproduction Act, which legislates in the area of stem cell research, was passed in 2004. It mandates the creation of the Assisted Human Reproduction Agency, which will eventually replace the SCOC once its regulations have been put in place.

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**Canada: Public Consultation on Xenotransplantation**

**Public Debate as Part of Xenotransplantation Regulation**

**Presentation by Professor Thérèse Leroux**

*Thérèse Leroux is a professor and researcher at the Centre de recherche en droit public de l’Université de Montréal.*

Like many other countries, Canada has a critical shortage of organ and tissue donors. Many people die while waiting for a transplant. To alleviate the shortage, Canada considered xenotransplantation, which means transplanting an animal’s organ or tissue into a human being.

Xenotransplantation is full of promise. There is potentially an unlimited supply of animal donors, which could be bred specifically for this purpose. Pigs have been
identified as the most suitable animal because they are available in large numbers, are inexpensive to breed and maintain and are compatible with the anatomy and physiology of human beings. In addition, organs would be in better condition than those harvested from someone who has experienced brain death. Surgery could be elective, instead of the current emergency procedure.

Along with the promise, however, xenotransplantation comes with challenges and concerns that need to be addressed. Among the challenges are organ or tissue rejection – something we already deal with – and cross-species infection – something we don’t. The biggest hurdles, however, are the ethical, legal, social and economic implications of xenotransplantation. Does transplanting a non-human organ or non-human tissue into a human threaten human identity, solidarity or autonomy? The question persists and has no easy answer.

To address these concerns, the Canadian government decided to launch a widespread consultation to canvas public opinion on the issue. The consultation was announced in August 2000 and was completed by September 2001. The results were published by the Canadian Public Health Association in a report entitled “Animal-to-human Transplantation: Should Canada Proceed?” The consultation was comprehensive and used various methods of gathering opinions – citizen forums, telephone surveys, website surveys and mail-in surveys – to reach a wide cross-section of the Canadian public. The consultation revealed that Canadians are not in favour of using xenotransplantation at this time, although some who were against using it now would favour using it in the future if some of the challenges and concerns could be addressed satisfactorily.

In light of these results, the Xenotransplantation Public Advisory Group recommended that Canada not proceed with xenotransplantation because of the issues that need to be resolved. However, it praised the public consultation model and recommended its use for other complex policy issues. The Public Advisory Group found that when citizens are given the appropriate information, they can grapple with complex policy issues and provide informed opinions.

**Session 4 Discussion**

The discussion after the presentations focused on the issue of xenotransplantation. While ethical discussion surrounding the issue was generally deemed to be necessary, participants wondered why Canada, and other countries, have spent so much time on issues such as xenotransplantation, when there are so many more pressing issues with more obvious solutions, such as preventable diseases. It shows that we are not necessarily focused on health, but that commercial interests often shape the debate. Part of the problem is seen to be the societal focus on the individual, not the community.
People want to be able to access all technologies that are available and feasible. A fortunate result of the public consultation on xenotransplantation, was a renewal of focus on raising awareness about human organ donation.

This led to a discussion of how priorities are set in health research. It was noted that there is a disparity between high-income countries, which focus on issues such as xenotransplantation, and low-and-middle-income countries, which focus on research connected to mortality and morbidity rates.

**Session 5: Specialized Review for Public Health Research**

Public health research creates unique challenges for the research ethics system because it often arises from an emergency situation, like Toronto’s SARS outbreak. Should we follow standard research ethics procedures during public health emergencies or should we establish specialized practices that take both the emergency and public health concerns into account? To help answer this question, we had presentations from Robert S. Williams, a bioethicist from the hospital that was at the centre of the 2003 SARS crisis, as well as from Dr. Bernard Dickens, who proposed a public health model for dealing with research in emergency situations like SARS.

**Canada: Research Review during the SARS Crisis**

**Severe Acute Respiratory Syndrome (SARS): Challenges for Research Ethics Committees**

**Presentation by Robert S. Williams**

Robert Williams is a bioethicist at The Scarborough Hospital (TSH) and has served on its research ethics board since 1998. He is currently a Ph.D. candidate at the University of Toronto’s Institute of Medical Science and the Joint Centre for Bioethics. His dissertation focuses on the experiences of TSH staff during the SARS outbreak.

The Scarborough Hospital (TSH) was the epicentre of the Canadian SARS outbreak of 2003. The Scarborough Hospital is one of Canada’s largest community hospitals, providing comprehensive health care services to this large eastern part of Toronto.

On February 14, 2003, the World Health Organization (WHO) reported that an unusual respiratory illness, later named Severe Acute Respiratory Syndrome (SARS), had infected 300 people, including 100 health care workers, in Guangdong Province, China. Five of those infected had died. On February 23, 2003 a woman and her husband returned to Toronto from a trip to Hong Kong, where they had stayed on the same floor as a physician from Guangdong Province who had SARS. On March 5th, the woman died at home from the disease.
Between March 7th and 9th, her son was admitted to the emergency room of the Grace site of TSH before he was transferred to the Intensive Care Unit, where he died on March 13th from SARS. On March 23rd, 2006, with 24 staff members at the Grace site of TSH infected with SARS, the emergency and intensive care units were closed to all patients, except those with the disease. New admissions and transfers were refused and all outpatient clinics were closed. Staff members were prohibited from working at any other hospitals and anyone who had been to the hospital after March 16 was put in a ten-day quarantine. On March 29th, the hospital was put on Code Orange, which meant that it was closed except for essential services. The Code Orange was not lifted until August.

In total, 106 staff members and physicians at TSH contracted SARS during the outbreak. Many of them experienced lingering problems including psychological trauma and were forced to remain off work or accept modified duties. A few people went on permanent disability. Moreover, some decided either to resign from the hospital or to leave the health care altogether.

In addition to the obvious toll from SARS on the hospital in general, the outbreak had a serious impact on the functioning of the hospital’s REB. In normal times, the TSH REB reviews between 60 and 80 protocols a year. During the crisis, however, 15 SARS-related protocols were brought before the REB in a relatively short time frame, the first being submitted on March 31. The first problem faced by the REB was its inability to meet with a properly constituted quorum, because regular staff meetings had been suspended, the Code Orange prevented the community members from entering the building, and most staff members on the board had been given outbreak duties elsewhere or were quarantined. To circumvent this problem, the REB obtained permission from the administration to hold ad hoc meetings to review any SARS research protocols brought to it. It also instituted new criteria and terms for expediting what was called “crisis review”, including a reduced quorum of five key members and the use of conference calls. One of the problems with this method of crisis review was that approval had to have been unanimous amongst the five REB members and there was no way that a refusal could be appealed expeditiously.

A second problem faced by the REB members was the overwhelming pressure – including intimidation and threats – to approve any and all SARS research protocols quickly, regardless of possible or potential flaws in the science, the design or the ethics of the project. This pressure, primarily exerted by Public Health authorities and the government through the hospital’s administration, was diametrically opposed to the REB’s obligation to follow applicable laws and guidelines (such as the Tri-Council Policy Statement, CIOMS and Good Clinical Practice), long-to follow established principles of research ethics and meet the expectations of potential participants. Some of the studies submitted clearly did not adhere to the guidelines or principles of research ethics.
In view of the challenges faced by the REB during the SARS crisis, Mr. Williams asked how REBs can be protected from such pressures and threats to their independence when facing a similar health crisis in the future. Should research carried out in such crisis conditions be characterized as a Public Health investigation rather than research, as some Public Health officials maintained at the time? How and by whom should it be determined that a study is an emergency Public Health investigation rather than a research protocol? If a study is identified as a Public Health investigation, do REBs still have the authority and obligation to review such investigations in their own institutions? Such issues as these arose during the SARS crisis, and need to be addressed to prevent a similar situation from occurring in the future.

**Emergency Preparedness and Human Subjects Research**

**Presentation by Dr. Bernard M. Dickens**

_Dr. Bernard M. Dickens is the Dr. William M. Scholl Professor Emeritus of Health Law and Policy at the Faculty of Law, the Faculty of Medicine and the Joint Centre for Bioethics at the University of Toronto._

The SARS crisis beginning at Scarborough General Hospital should be a warning to healthcare systems to be better prepared for future health emergencies. The threat of bioterrorism and illnesses like avian flu seems to be in the newspaper headlines almost every day. But what happens when the next health emergency strikes and public health authorities and researchers again want to start studying and implementing new treatment methods?

The clinical research model mandates that any protocol go through the normal course of ethical review for approval before any research begins. In a crisis, however, this review may be too cumbersome, both for those wanting to use new treatments and for research ethics boards that feel that they have a duty to review such protocols under the clinical research model. Robert Williams’s example of the struggles of the Scarborough Hospital’s REB illustrate how the clinical research model failed to serve the interests of all parties, including the REB and its members, who were coerced and even threatened into fast-tracking approval.

Instead of continuing to rely upon the clinical research model in emergency situations involving novel pathogens such as SARS, Professor Dickens argued that we should look to the public health model for guidance on ethical approval. He said that the public health model is much more in tune with what is actually taking place during a health crisis such as SARS. Physicians and researchers are looking for ways to cure patients who have contracted the illness, to protect other members of the community from contracting it and to stop such crises from happening again. In many cases, the illnesses
do not respond to conventional treatment. Under the traditional clinical research model, using therapeutic innovations where standard treatments have failed may be classified as human subject research, requiring research ethics approval. Looking at the issue in a different way, however, we can see that much of what happens during a health emergency is more like public health practice – trying to cure those affected and to contain an epidemic – and less like traditional human subject research, where the effectiveness of one treatment is tested against another.

Public health practice is modeled upon principles of legal authorization made by the state in place of individuals. The authorization may be given by the state to protect the health and safety of the public. It is a type of coercion and people cannot opt out of the authorization once it is made. While the power given to the state to authorize consent for individuals may seem drastic, it is actually a common kind of state power, where the common law of necessity overrides normal individual rights and liberties. There are many laws that override individual rights to protect the common good, such as policing powers, war measures powers, military conscription powers and quarantine power.

Using the public health model, it may then be permissible to dispense with the traditional research ethics approval model through REBs in some health emergencies, such as dealing with novel pathogens that may not respond to conventional treatment. This is not to say that such a classification is not controversial. During the Gulf War, the U.S. government waived consent for American soldiers to be treated with untested products to protect them against anthrax, setting off a debate about whether this consent waiver was justified. Indeed, the nature of the illness may well determine whether the use of public health standards is justified. However, there are likely to be cases where the interests of society as a whole could outweigh the interests of individuals. In the SARS case, the interests of the health care professionals who treated and cared for SARS patients could have outweighed the interests of individuals affected.

Following the public health model in health emergencies does not mean that ethics are dispensed with completely. The public health field has its own system of ethics and guidelines that must be adhered to. What Professor Dickens suggested is that the ethical practices of the clinical research system, including the traditional REB approval, should be replaced by the ethical practices of the public health field. If we were to determine that health emergencies involving novel pathogens, like SARS, fit the public health model, we would need to look to that model to determine what ethical restraints and requirements need to be adhered to. Where public-health-trained REBs are not available, the local REB at each institution should review protocols using public health guidelines such as the CIOMS Guidelines for Ethical Review of Epidemiological Studies, now in revision.
Session 5 Discussion

Workshop participants acknowledged that setting special guidelines for dealing with emergency situations involving novel pathogens is important. They believed that emergency research entailed a different underlying rationale for innovation, which is to protect the health of others. However, they were also careful to point out that the proposed research should be directly related to the outbreak and not merely disguised as outbreak-related in order to evade REB approval.

It is also important to make a clear distinction between traditional research and experimental, innovative therapies that theoretically could help victims of the outbreak and/or protect society-at-large. It was pointed out that some of the protocols brought to The Scarborough Hospital during the SARS crisis were not intended to benefit patients directly, but were identified as public health investigations of the disease outbreak thereby avoiding the due diligence and scrutiny of the hospital’s REB.

Session 6: The Role of International Bodies

International bodies play an important role in setting ethical norms and standards for sound and scientific clinical research. They organize discussions and issue publications on various issues and develop guidelines for ethical review and ethical conduct of research. Yet organizations such as the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS) encounter many challenges when they attempt to develop advice and policy. They must address the issue of research conducted in low-and-middle-income countries, where it may be necessary to interpret or even modify generally accepted norms and standards to ensure that all participants are adequately protected. These organizations also have the power to influence the type of research conducted worldwide when they commission studies on emerging or neglected health areas. The challenge is to find common ground between high-income countries who are often sponsors of the research and low-and-middle-income countries who host the studies, in order to undertake research that is relevant to both.

Role of the World Health Organization

The Role of International Bodies: Triple Burden or Triple Opportunity? WHO and the Ethics of Research

Presentation by Professor Alexander Capron

Prof. Alexander Capron is the first Director of the Department of Ethics, Trade, Human Rights and Health Law at the World Health Organization. He is on extended leave from his position as co-director of the Pacific Center for Health Policy and Ethics and professor of law and medicine at the University of Southern California, Los Angeles.
Professor Capron discussed particular health problems that mainly affect people in poorer countries and introduced the phenomenon known as the 10/90 Gap, where only 10% of the world’s output of medicines responds to the needs of 90% of the global population. The 10/90 Gap is a reflection of the “triple burden” of disease that affects the poorest populations in the developing world, including:

- Non-communicable diseases – illnesses resulting from chronic conditions (diabetes, cardiovascular disease, cancer), mental health disorders, injuries and poor nutrition;
- Communicable diseases;
- The neglected (mostly tropical) diseases that do not threaten life in high-income countries;
- Diseases such as AIDS and TB that occur at a much higher rate in the developing world; and
- Socio-behavioural conditions – the diseases of modern life (e.g., tobacco use, diet, road injuries and substance abuse).

Even though many of the health problems arising from the triple burden of disease are related to health systems and social infrastructure, pharmaceutical research can help to treat many of the conditions caused by communicable diseases. But in order to do so, companies must direct research towards neglected diseases and must adapt treatment to the health care conditions in low-and-middle-income countries.

At one time, “neglected” diseases threatened populations all around the world and the need to treat them led to considerable knowledge about their biology and epidemiology. As living conditions in high-income countries improved, however, rates of transmission were greatly reduced and eventually eliminated there through access to health care and a reasonable standard of living, rather than by specific medications. Consequently, there has been little research to develop better and more modern treatments. However, neglected diseases are still very prevalent and can be disabling as well as stigmatizing. They include Chagas’ disease, leishmaniasis and trypanosomiasis. The WHO estimates that these three diseases alone affect 510 million people in Africa, Asia and Latin America. There are no vaccines or drugs to prevent them.

For communicable diseases that affect all populations, such as HIV/AIDS, a considerable amount of research is being conducted. However, there needs to be more research into how to make treatments, such as antiretroviral medicines, more effective in resource-poor settings. Research also should be directed towards measures to prevent transmission where the prevalence of a communicable disease is high.

The heavy burden of disease facing people in low-and-middle-income countries concerns everyone and has ethical implications for the future of research. High-income
countries have a moral imperative to improve conditions in poor countries to the extent that it is possible to do so through research. This should involve more health research (both biomedical and systems research) adapted to the needs of low-and-middle-income countries. This would mean an increased volume of research being undertaken in poor countries, which in turn will require that these countries have the capacity to undertake ethics review of research projects to protect vulnerable populations.

Although challenging, Professor Capron argues that research focused on the needs of low-and-middle-income countries presents an opportunity to:

- Narrow the 90/10 Gap by creating capacity in health systems as well as the regulation of health research;
- Move away from using professionally-based standards for research to principles settled by governments; and
- Provide more refined resolutions to issues that impede research progress.

International bodies such as the WHO can play a large role in realizing this triple opportunity. The WHO currently undertakes various activities directed at building research capacity in low-and-middle-income countries. It provides technical assistance through country consultations and capacity building workshops (working with groups such as FLACEIS, FECCIS and FERCAP). The organization also establishes international normative ethical standards to guide national regulation of research and promotes knowledge development through associations such as the Global Forum for Bioethics Research and Networking for Ethics in Biomedical Research in Africa.

Regarding the issue of governmental agreement on principles, the WHO has already produced some technical documentation, such as Training in Tropical Diseases guidance for research ethics committees. It is hoped that eventually low-and-middle-income countries will be able to implement their own research guidelines, preferably enacted through legislation to ensure that the guidelines are followed. However, government regulation (and law generally) is better at structure and process than substance and ethical commitment; behaviour and conduct can not easily be changed through the law.

But even with internationally approved research guidelines, improvements in the conduct of research have been modest. To make real progress, we need to spend more time addressing failures and confusion. As a global community, we need to re-examine the moral legitimacy of the research enterprise and its framework. For all research, there must be greater uniformity in rules and procedures, more attention to conflicts of interest and more focus on building the capacity for adequate ethics review in both high-income and low-and-middle-income countries.

Improving the research enterprise involves more than just better-drafted consent forms. To address failures, it is vital to question the implications of the basic principles of autonomy, beneficence and justice and ask whether the research enterprise truly
respects and promotes autonomy through informed and free choice, acts beneficently
towards subjects and ensures just distribution of resources and power. We must also
ask whether research subjects participate voluntarily. Undue incentive plagues research
in both high-income and low-and-middle-income countries. In both cases, research may
be the only way to receive care. To mitigate the problem, broad involvement of the
population is needed, along with assured benefits.

More work is also required to address unresolved international issues such as:

- Is there a single or multiple standard of care?
- What is the appropriate use of placebo?
- How can we ensure that research is relevant to health needs?
- What are the means and limits of benefit-sharing for research participants,
  communities and nations?
- How can we co-ordinate and harmonize review within and between countries?

The WHO and other organizations and individuals involved in research can develop
global standards to implement universal expectations and discourage “forum shopping”.
Guidelines that explicitly address sponsors’ obligations are also needed. Finally, those
who conduct research must be willing to limit research to situations where participants
have a reasonable expectation of care.

The Council for International Organizations
of Medical Sciences (CIOMS)

CIOMS: Current Activities Related to Ethical Issues

Presentation by Professor Juhana E. Idänpään-Heikkilä

Dr. Juhana E. Idänpään-Heikkilä, a former physician and pharmacology professor, has been
Secretary-General of the Council for International Organizations of Medical Sciences (CIOMS)
since 2000. His extensive background in drug regulation includes acting as Director of WHO’s
Pharmaceutical Division in Geneva and Chief Medical Officer at the National Medicines
Control Agency in Finland for almost 30 years.

CIOMS is an international, non-governmental, non-profit organization established in
1949 by the WHO and UNESCO. It is a forum where senior scientists from drug
regulatory authorities (public health) and the pharmaceutical industry (private sector),
as well as academics, can consider and prepare advice on contentious issues in clinical
research ethics and the safety of pharmaceuticals. The organization’s publications are
read by a wide audience, including the WHO, public health authorities, academics,
investigators, the pharmaceutical industry and others.
CIOMS has published several ethical guidelines on clinical research, including:

- CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002 (available on www.cioms.ch)
- CIOMS International Guidelines for Ethical Review of Epidemiological Studies, 1991, currently being revised (see www.cioms.ch for a draft) to include three new guidelines on the following:
  - Informed consent in the use of stored biological samples
  - Use of the Internet in epidemiological research
  - Disclosure and review of potential conflicts of interest

The CIOMS ethical guidelines recommend how fundamental ethical principles, such as those contained in the World Medical Association’s Declaration of Helsinki, can be applied effectively in medical research worldwide. These guidelines are meant to be adaptable to different cultures, religions and traditions, and account for a variety of socioeconomic circumstances, national laws and situations unique to low-and-middle-income countries.

In addition to research guidelines concerning human subjects, CIOMS also co-ordinates working groups to discuss drug development and drug safety as well as publish information on their respective topics. Working groups (WGs) include:

- WG VI – Managing Safety Information from Clinical Trials (2005 Publication)
  - Focuses on clinical trial phases II and III
  - Safety of patients during drug development
- Pharmacogenetics (published its report in January 2005)
- Standardized MedDRA Queries (SMQs) (publication available at CIOMS)
- WG VII – Developmental Safety Update Report (in development)
- WG on Vaccine Pharmacovigilance (ongoing)

Dr. Idänpään-Heikkilä provided examples of certain research issues that the CIOMS’s working groups have discussed and the recommendations they have issued.

The first example involved the role of Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs) in fostering ethical drug trials. Several international documents provide guidance on this topic, including the Declaration of Helsinki, the EU Clinical Trials Directive and the CIOMS Ethical Guidelines on Biomedical Research (2002). All agree that IRBs/IECs:
• are responsible for protecting the safety and well-being of clinical trial subjects;
• are required to monitor ongoing clinical trials; and
• must collect serious adverse event/reaction reports from researchers.

In its 2005 publication, “Managing Safety Information from Clinical Trials”, CIOMS WG VI made two recommendations on how to better communicate safety data to IRBs/IECs. The first is for IRBs/IECs to establish periodic ad hoc communication with investigators to receive regular updates about safety information and evolving risk-benefit profiles (instead of researchers sending large numbers of individual case reports to IRBs/IECs). The second recommendation is for expedited communication of significant new safety information.

The next example in the presentation involved ethical issues documented by the CIOMS Working Group report on pharmacogenetics. These included confidentiality and informed consent when categorizing genetic data in clinical research and medical practice. Applying the four principles of bioethics, the report also indicates that researchers must be aware of the non-malefice aspects of pharmacogenetics, such as privacy and how to protect against discrimination in pharmacogenetic testing. Justice issues can arise when disease populations are genetically defined and, as an extension of genetics, ethnically defined. This is a particularly sensitive issue in low-and-middle-income countries.

The draft report of the CIOMS WG on Drug Development Research in Resource-poor Countries says that applying good clinical practice to research conducted in resource-poor settings requires capacity to establish ethics committees, drug regulatory authorities (government responsibility), adverse drug reaction surveillance systems and duties to which researchers and sponsors must adhere.

**Session 6 Discussion**

These two presentations highlighted the importance of international agencies in developing research standards, as well as revising research protocols or particular practices to account for new technologies and to improve the protection of research subjects. This session also made it clear that the need for improved guidelines is greatest in low-and-middle-income countries. Research being conducted on poor populations emphasizes the responsibility of researchers to respect the four principles of bioethics as well as to perform research that is relevant and useful for the majority of the population.

Both speakers emphasized the importance of updating the research enterprise to reflect today’s moral and ethical norms. The four principles of bioethics are as relevant as ever, but it is now recognized that values are not uniform across different research settings.
and projects. A participant added that there is a need to make research projects and results more transparent, so that the whole community, not just the researchers, can evaluate them.

In addition to improving research conduct and objectives, the presentations also made the point that health systems’ capacity must be enhanced to conduct ethical research. A discussion among participants about the “brain drain” of health professionals from low- and-middle-income countries to high-income countries underscored the importance of creating sustainable health systems worldwide. Moreover, now that health research is a strategic trade interest, ethical considerations are given more respect, allowing health to trump trade interests to achieve equality.

**Session 7: The Role of International Instruments in Research Ethics Review**

**Europe**

*Presentations by Prof. Dr. Elmar Doppelfeld*

*Prof. Dr. Elmar Doppelfeld is Chair of the Council of Europe Steering Committee on Bioethics.*

**The Council of Europe: Steering Committee on Bioethics and the Oviedo Convention**

Dr. Doppelfeld’s first presentation described legal instruments promulgated by the Council of Europe (COE) dealing with biomedical research. The two main instruments are the 1997 Oviedo Convention and the 2005 Additional Protocol to the Convention concerning biomedical research.

The COE was formed in 1949. It currently has 46 member states, with a population of about 800 million. Its basic aims are to promote human rights and democracy in Europe through the use of legal instruments and other measures. The COE promulgates conventions and protocols. Conventions are like multilateral treaties between nations and express general principles. Protocols are specific and detailed applications of these principles, which can only be signed and ratified by countries that have already ratified the conventions.

The Oviedo Convention on Human Rights and Biomedicine, adopted in 1997 by the Committee of Ministers of the COE and now signed by 31 and ratified by 19 member States, is the only legally binding international instrument for biomedical research. It becomes the basis and framework for national legislation in the acceding states. It creates basic minimum standards, including a central role for REC review, and binds researchers without regard to their profession.
Its key provisions protect a range of values:

- Primacy of the human being (Article 2);
- Consent and protection of persons not able to consent (Articles 5, 6 and 17);
- Private life and right to information (Article 10); and
- Protection of persons undergoing research (Article 16).

The Convention also requires that a research project be “. . . approved by the competent body after independent examination of its scientific merit, including assessment of the importance of the aim of the research, and multidisciplinary review of its ethical acceptability” (Article 16, iii). This requirement emphasizes the role of RECs in determining the ethical acceptability of the research.

In particular, the protocol sets out the following basic research standards:

- Primacy of the human being and an absence of alternatives to using humans in research (Articles 3 and 5);
- A careful weighing of risks and benefits (Article 6);
- Appropriate informed consent (Chapter IV); and
- Protections for persons who lack or lose capacity to give consent (Chapter V).

In addition, research must meet “generally accepted criteria of scientific quality” and be carried out under the supervision of a qualified researcher (Article 8). Ethics Committees (RECs) are required to carry out an assessment of proposed research to “protect the dignity, rights, safety and well-being of research participants” (Article 9). RECs must provide opinions with reasons for their decisions.

Under the Protocol, member states are required to “. . . take measures to assure the independence of the ethics committee” (Article 10). RECs “. . . shall not be subject to undue external influences” and REC members must declare “. . . all circumstances that might lead to a conflict of interest. Should such conflicts arise, those involved shall not participate in that review.”

The protocol also requires researchers to provide detailed information relevant to the assessment of the project. Descriptions must name the principal researchers and their funding arrangements, the purposes and methods of the research, and declare earlier or other submissions for approval.

In relation to consents and participation, researchers must also include in their descriptions:

- justification for involving human beings in the research project;
- the criteria for inclusion or exclusion of the categories of persons for participation and how those persons are to be selected and recruited;
• reasons for the use or the absence of control groups;
• a description of the nature and degree of foreseeable risks that may be incurred by participating in research;
• the nature, extent and duration of the interventions to be carried out on the research participants, and details of any burden imposed by the research project; arrangements to monitor, evaluate and react to contingencies that may have consequences for the present or future health of research participants; and arrangements to protect the privacy of research subjects.

The protocol also requires researchers to provide RECs with financial information that may relate to the independence of researchers. All payments and rewards to be made during the project must be disclosed, as must “. . . details of all circumstances that might lead to conflicts of interest that may affect the independent judgment of the researchers.” In addition, researchers must detail any “foreseen potential further uses”, including potential commercial uses, of the research results, data or biological materials.

**The European Directive on Clinical Trials**

In his second presentation, Dr. Doppelfeld shifted the focus from the COE to the European Union where EU Directive 2001/20/EC, regarding good clinical practice in clinical trials, is the most prominent instrument to date. The EU has 25 member states. EU directives require member states to comply by reforming domestic laws within a given period.

Directive 2001/20/EC covers only clinical trials, not all kinds of research involving humans. Article 2 defines a clinical trial as “. . . any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.”

The Directive requires researchers to obtain REC approval before beginning a clinical trial (Article 9). Similar to the requirements in the Oviedo Convention and Protocol, member states must take steps to set up RECs, and RECs must give opinions before research starts (Article 6). The Directive also sets standards for the protection of subjects, particularly minors and persons incapable of consenting. RECs must assess the risks and benefits of the research, information provided by the researchers, the measures taken for informed consent and measures taken to address participation by incapable persons or minors. In particular, an REC shall retain experts in pediatrics or other fields to advise them about such issues.
The Directive addresses multi-centred clinical trials as well. Where such trials occur entirely within a member state, the state must “…establish a procedure providing, notwithstanding the number of ethics committees, for the adoption of a single opinion for that member state.” Where a clinical trial is spread over more than one member state, each member state shall have a single REC opinion on the research (Article 7).

The Directive has been supplemented by Directive 2005/28/EC, which adds requirements for RECs to establish rules of procedure, to retain documents for three years and to foster more efficient communications between RECs in member states.

Latin America: A Need for International Instruments?

Latin American Forum for Ethics Review Boards
Presentation by Dr. Andrés Peralta

Dr. Andrés Peralta is vice-chairperson of the Latin American Forum for Ethics Review Boards

The absence of unified multinational institutions in Latin America and other Southern regions is a problem that is magnified by the myriad challenges for RECs operating at the national or local levels in these regions. Dr. Peralta’s presentation focused on these problems, as well as some successes, with an emphasis on conditions in the Dominican Republic.

International instruments play a central role as standards of REC review. These include the Helsinki Declaration, ICH/GCP, and WHO Operational Guides for RECs. But a three-year survey concluded in 2002 by a group of National Organizations for Science and Technology (ONCYT) in Latin America provided more detailed information about the region’s RECs. Thirty-three countries were questioned and 21 responded.

The results showed that ONCYTs in 14 countries required research review. In five countries, research protocols were not evaluated by RECs, or their evaluations were deficient. In most other responding countries, however, research was overseen by government agencies and reviewed by independent academic or clinical RECs.

As for the funding of research, a major ONCYT concern in most countries, both public and private sources are involved. RECs use researcher certifications, transparency in accounting and the “excellency criteria” to complete ethical and methodological evaluations.
The report by the ONCYTs concluded that:

- research review was deficient due to the lack of qualified REC personnel;
- there are also clear deficiencies regarding national regulations for biomedical research; despite improvement between 1999 and 2002, there are still very few RECs at the national level to monitor local RECs and research in general; and
- training is urgently needed to qualify REC members to evaluate the science and ethics of biomedical research.

Dr. Peralta reviewed a report by the Pan-American Health Organization (PAHO) Bioethics Unit on the regulation of research review in Latin America. This report examined 28 Latin American countries between 1995 and 2002 and found some interesting trends. Key among these were an increase in the number of national bioethics committees (from 5 in 1995, to 13 in 2002) and a dramatic upsurge in the number of RECs (from 15 to 489). In Argentina, Brazil, Chile, Colombia and Mexico, the number has doubled in the past eight years. In Bolivia, Dominican Republic, Nicaragua, El Salvador, Guatemala and Uruguay, however, there are still very few RECs. Dr. Peralta noted that half the countries in Latin America still lack a national bioethics commission, although in four (Chile, El Salvador, Honduras and Paraguay) there are projects to establish NBCs with PAHO’s guidance.

Reviewing the legislative situation in Latin America as a whole, Dr. Peralta noted that only recently have many countries enacted legislation on biomedical research and REC review, if they have moved at all. Constitutional norms concerning the dignity of the person and basic human rights go some way toward protecting clinical trial subjects, but that is where it ends.

Turning to the legal and regulatory framework for REC review in the Dominican Republic, Dr. Peralta showed how the Latin American Forum for Ethics Review Boards (FLACEIS), currently a multinational NGO, advises and oversees national bioethics committees, which in turn oversee RECs and other bodies responsible for research review. The Dominican Republic enacted legislation in 2001 setting up the National Council on Health Bioethics (CONABIOS) to regulate research centers and RECs. Institutional RECs function at public and private health institutions, but CONABIOS has the final word in approving biomedical research. Once the clinical trials are reviewed, they must be sent to CONABIOS for a final decision. To date, there is no REC accreditation body in the country, although a national REC network is being contemplated and monitoring is being done in some specific trials to ensure on-going scientific and ethical compliance.
Alternatives to International Law: Promotion of Equivalent Standards

The ‘Equivalent Protection’ Doctrine

Presentation by Dr. James Lavery and Dr. Michael McDonald

Dr. James Lavery is an associate professor of public health sciences at the University of Toronto. Dr. Michael McDonald is co-chair of the Standing Committee on Ethics, Canadian Institutes of Health Research, Ottawa.

The final presentation of the session focused on an innovative way to regulate cross-national research, even in the absence of formal international bodies or legal instruments. Dr. James Lavery described how the “equivalent protection” mechanism adopted in U.S. legislation can function as an incentive toward harmonization of REC standards internationally with those adopted in the U.S. The result, in theory, is the indirect extension of higher standards of research review to foreign countries.

Dr. Lavery explained the equivalent protection doctrine in detail. The starting point is the U.S. Federal Policy for the Protection of Human Subjects (the “Common Rule”). The Common Rule aims to protect research subjects in studies funded by the U.S. but carried out in other countries. It sets out broad standards for approval of research. The purpose of the Common Rule’s “equivalent protection” provision (s. 46.101(h)) is to recognize approvals by RECs in other countries where those RECs offer equal or greater protections than those that exist under the Common Rule. It operates as a kind of exception to the usual rule that all U.S.-funded research undertaken abroad must pass the Common Rule’s requirements.

The equivalent protection rule arose from a series of reports that researchers were frustrated with Common Rule procedures and that the U.S. was too forceful in imposing standards. One report concluded that it would be prudent to enact a rule that recognized and accounted for “. . . whether other nations’ laws and practices afford equivalent protections to those that apply to human subjects participating in clinical trials in the U.S.” The culmination of this study was the OHRP’s Report of the Equivalent Protections Working Group, in July 2003.

In addition to the equivalent protection doctrine, the Director of the Office of Human Research Protections is now required by the Research Revitalization Act (2002) to publish a list of countries “. . . in which protections for human research participants are substantially equivalent to those of the United States.” Thus, administrative mechanisms are already in place to allow for appropriate and informed application of the equivalent protection exception.
The working group set out a framework for applying the equivalent protection doctrine. This involved articulating the specific protections embodied in the Common Rule, assessing the protections provided by the foreign institution’s procedures and determining equivalence.

Dr. Lavery gave several reasons why Canadian institutions should increase their use of equivalent protection:

- the potential for reduced administrative burden following the initial process for determining equivalent protection;
- the symbolic value of equivalent protection for Canada – a recognition that the same ends achieved can be met by different means;
- the potential for enhancing investment in Canadian research by reducing administrative costs and burdens; and
- the opportunity for the U.S. to establish “proof of principle” of equivalent protection in a familiar system before tackling that challenge in other countries.

Session 7 Discussion

There was discussion on the potential role of each country’s National Bioethics Councils or similar organizations. It was suggested that they are well situated to act as accreditation bodies. More involved discussion arose over the issue of transparency in REC deliberations. The presentations highlighted several instances where RECs were required to provide reasons for their decisions. This idea was endorsed in principle because these explanations could be useful to subsequent RECs. However, intellectual property and confidentiality concerns were serious issues, particularly in Germany and the U.K. It is not easy to review a research protocol, and how another REC reviewed it, without revealing the protocol itself. Legislation is the only way RECs can have the freedom to disclose reasons for a decision without compromising the confidentiality of the sensitive information they encounter. In broader terms, transparency in REC proceedings was not seen as an unqualified good. In some contexts, lay members of RECs are more reluctant to speak freely when the public or media are present.

Session 8: Promotion of Equitable Research Practices

The promotion of equitable research practices responds to the vulnerability of research participants arising from, among other things, high disease burden, poverty, lack of education and minority status. As the presentations in this session reveal, there are vulnerable populations everywhere. This could be because they live in a low-or-middle-
income country or because they are a marginalized group in a high-income country. Although many vulnerable populations have legitimate reasons for accepting an offer to participate in medical research, their interests usually are not the focus of the study. Researchers have an ethical duty of care not to treat research participants as a means to an end but commercial interests often take priority. The presentations in this session show how universal research guidelines can be adapted to incorporate the research location and subjects to ensure that vulnerable populations are treated fairly.

South Africa: The Concept of an International Duty of Care

Presentation by Dr. Solomon Benatar.

Dr. Solomon Benatar, professor of medicine at the University of Cape Town, Director of the UCT Bioethics Centre and Visiting Professor in Public Health Sciences and Medicine at the University of Toronto, is a member of several international medical organizations and has served as President of the International Association of Bioethics.

Dr. Benatar reviewed global health research, which exacerbates disparities in wealth and health between high-income countries and low-and-middle-income countries. Statistics show that 87% of annual expenditures on health is applied to 16% of the world’s population and 90% of medical research expenditure is devoted to diseases responsible for only 10% of the global burden of disease.

Citing the urgent needs for prevention and treatment of HIV/AIDS in Africa, Dr. Benatar said that research undertaken in low-and-middle-income countries has stimulated the concept of an international standard of care, sensitive to contextual considerations and of potential value in improving health care in resource-poor areas. Promotion of an international standard of care for clinical trials, a standard that was limited to the drug used in the control arm in HIV transmission studies, set off a debate about whether a “universal standard of care” extended beyond considerations on the use of placebos.

Dr. Benatar and Peter Singer proposed a broader international standard of care that goes beyond merely consideration of whether placebos can be used, with each study evaluated according to its merits in relation to perceived harms and benefits and with due regard to the moral relevance of local factors when applying universal principles.¹

The new standard strives to achieve equality through protection of vulnerable participants, creation of partnerships, improvements to overall health care and benefit sharing. Such a feasible international standard of care would promote:

- respect for the dignity of subjects – treating subjects as ends in their own right;
- meaningful informed consent – linguistically and culturally appropriate;

• research in the best interests of subjects – relevant to their needs and combined with medical care; and
• fairness – in distribution of risks and benefits to participants and communities.

Such an international standard of care would allow for morally legitimate different standards that would not be “double standards”. By broadening the scope of the standard of care provided and addressing the needs of the participants, research could help low-and-middle-income countries progressively improve their health care systems, leading to a time when research would be conducted according to a single universal standard.

A broader international standard, as opposed to a single universal standard of care – based merely on consideration of which drugs can be used – could be justified on several grounds: 2

At the moral level, the principles of beneficence, non-maleficence and justice require that scientific progress be linked to moral progress. At the cultural level, an international standard of care acknowledges that research invades local customs and imposes external norms. In low-and-middle-income countries, such an expanded international standard could also accommodate the cultural expectation that researchers are physicians and that research has a medical care component. Justification is further provided at the strategic level, because it can be argued that an improved standard of care along with collaborative work will enhance participation in research and the self-interest of all those involved over the long term. At the operational level, an international standard of care is linked to improvements in care delivery by being part of a capacity building process.

It is also important to note that the standard of care is an extension of the duty of care, and that, as such, researchers owe a duty of care to participants. The real issue is the extent of this duty of care. Dr. Benatar suggests that the duty should be expanded to become an international duty of care, so that researchers would have to provide medical treatment when conducting research in situations where no other medical treatment is available. The role of the physician in many communities is seen as one in which research is not considered to be separate from medical practice but rather as one of its components. An international duty of care would accommodate such a worldview of medical responsibility and help to ensure equitable research practices.

Beyond the rationale for an international duty and standard of care, practical steps are needed to improve care. These involve ethical, economic and operational factors such as incorporating the community in study designs to determine contextually relevant specifics of the standard of care, as well as encouraging partnerships and collaborations. Along with participation, trials should provide preventative measures and treatment

(such as ARVs) and aim to strengthen health infrastructure by gradually building capacity so that participants and communities will be guaranteed benefits.

Dr. Benatar emphasized the importance of partnerships with donor aid organizations and the host government to promote multidisciplinary strategic alliances and systems approaches. Partnerships are an essential component in addressing the upstream causes of poverty because they build researcher and health system capacity, driving the transition from research to sustainable health care practice.

An international standard of care could also contribute to a new research paradigm – a reasoned middle ground between unprincipled practice (low local standards) and unachievable utopias (highest universal global standard).

Since the Western world has taken the lead in research, the tendency has been to impose Western ethical views and guidelines on others, without adequate consideration of contextual features and values. Ethical guidelines tend to be seen as instruction manuals. There is a need to encourage moral reflection on substantive moral issues and to be able to reason about how to best apply universal principles in varied local contexts.3

**Cameroon: Promotion of Equitable Research Practices**

**Presentation by Dr. Godfrey B. Tangwa**

*Dr. Godfrey B. Tangwa is head of the Philosophy Department at the University of Yaounde 1 in Cameroon. He is an expert in African philosophy and bioethics and a member of the International Association of Bioethics as well as the Pan-African Bioethics Initiative.*

Distributive justice is concerned with the fair distribution of goods, benefits and advantages resulting from collaborative ventures. Medical research is a type of collaborative venture but increasing commercialization is resulting in less equitable division of its benefits.

Although a high proportion (90%) of the global disease burden affects low-and-middle-income countries and especially those in sub-Saharan Africa, just 10% of global health research is targeted towards diseases in these countries. This is known as the 10/90 gap. Increasing research activity is occurring in the developing world, but it is difficult to determine whether the gap is narrowing or widening. Africa, in particular, is plagued by a formidable disease burden that includes the highest rates of child mortality and maternal morbidity/mortality and the lowest life expectancies, resulting from epidemics such as HIV/AIDS as well as violent conflict.

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3 Benatar S R (2004). Towards progress in resolving dilemmas in international research ethics. *Journal of Law, Medicine and Ethics*. 32: (4) 574-582
The triple disease burden that affects developing world populations triples the extent of vulnerability. Research subjects in developing countries are exploitable because they are members of economically and medically disadvantaged groups, given their high burden of disease. Minors from these populations are increasingly being used as research subjects. In Africa, in particular, vulnerability applies equally to researchers, scientists, institutions, and even governments.

According to Article 5 of the Helsinki Declaration, “... considerations related to the well-being of the human subject should take precedence over the interests of science and society”. Yet medical research in the industrialized world – which is market-oriented, profit-driven and susceptible to morally blind economic forces – fails the ethical duty of care established by Article 5.

Considering the crucial need for medical research in the developing world and also the high degree of vulnerability of research patients, Dr. Tangwa posed several questions about developed-world medical research that is conducted in the developing world:

- Can commercial motives be combined with altruistic philanthropy?
- Can such research be non-exploitative?
- Can it avoid harming the vulnerable?
- Can it avoid undue inducement and double standards?
- Can it respect the autonomy of research participants?
- Can it separate ethical imperatives from culture and ideology?

To achieve distributive justice, there is a need for clear distinctions and explanations of the following issues:

- treatment or research? Or treatment combined with research?
- discovery of scientific knowledge or the art of treatment and healing?
- business/commerce or altruistic philanthropy? Or business/commerce combined with philanthropy?

To achieve equitable research practices, there are four indispensable preconditions:

- good science and research design;
- adequate resources and funding;
- well-informed, free and willing subjects; and
- appreciation for the role of the research participant.

Distributive justice cannot be achieved without recognition of the important role of the research subject and without evenly distributing risks and benefits between the research subject and other participants.
Canada: CIHR Guidelines for Health Research Involving Aboriginal Peoples
Presentation by Dr. Geneviève Dubois-Flynn

Dr. Geneviève Dubois-Flynn is a senior ethics policy advisor at the Canadian Institutes for Health Research where she has worked on governance of research ethics, including research involving Aboriginal Peoples.

CIHR is composed of 13 institutes, one of which specializes in Aboriginal Peoples’ health. The mandate of the CIHR is to create new scientific knowledge and translate it into improved health for Canadians, more effective health services and products and a strengthened Canadian health care system. With respect to ethics, CIHR is concerned with promoting and undertaking ethical health research, fostering the discussion of ethical issues related to health research and monitoring these health related ethical issues.

CIHR has recently drafted the Guidelines for Health Research Involving Aboriginal Peoples. The rationale for these distinct guidelines relates to the particular vulnerability of First Nations Peoples in Canada, who have been exploited in several research projects (e.g., arthritis research in the Nuu-chah-nult Community) and continue to be abused through the use of data obtained from that research. In addition, Aboriginal Peoples experience profound health disadvantages compared to the general population, and their burden of disease is not often prioritized.

The Canadian Tri-Council Policy Statement (TCPS) on research ethics was developed in 1998 without Aboriginal involvement. Since the TCPS provided the only protection for Aboriginal research participants, more specific guidelines had to be introduced. The development of the new guidelines is intended to be an inclusive process, involving researchers and members of Aboriginal communities. In particular, the guidelines must balance researcher and Aboriginal interests and be a product of collaboration with other partners such as the Interagency Advisory Ethics Panel.

To make the process more inclusive, eight Aboriginal Capacity and Developmental Research Environment (ACADRE) centres were created within research institutions. ACADRE centres are designed to help build research capacity (including research ethics) as well as develop specific reports on Aboriginal health status and stimulate debate on Aboriginal health issues. The Aboriginal Ethics Working Group (AEWG) was also created to assist in the drafting of the guidelines and build on ACADRE reports as well as community and elder dialogues. At this stage in the process, the guidelines are being vetted by ACADRE centres and then will be reviewed further by different CIHR committees, including the thirteen institutes.

Dr. Dubois-Flynn noted that the guidelines had to accommodate particular concerns of Aboriginals because their values are different than those of other Canadians. These
include the concept of an Aboriginal community, Indigenous worldviews (such as non-homogeneity between different Aboriginal populations in Canada), complex authority structures and challenges to formal community authorities. Other important Aboriginal concepts include sacred space, traditional knowledge and ethical space.

Substantive principles that helped to guide the drafting involved:

- recognizing community jurisdiction and approval;
- acknowledging research partnership methodology;
- allowing collective and individual consent;
- considering typical research issues such as confidentiality, privacy and personal autonomy;
- including indigenous knowledge in research; and
- protecting cultural knowledge.

Other substantive principles that were addressed were:

- benefit sharing, empowerment and capacity development;
- the right to control collection, use, storage and potential use of data; and
- interpretation and dissemination of results.

Additional features of the guidelines include the ability to create a memorandum of understanding (and research agreements) between the community and the researcher, and the rule that, in the event of conflict between the guidelines and community guidelines, the latter will prevail. Ultimately, the guidelines are intended to ensure that Aboriginal research is based on equity and respect.

One participant asked how ethical review procedures could be improved to achieve better accountability for vulnerabilities. Could accreditation help, or is there a special body that deals with research with Aboriginal peoples? Dr. Dubois-Flynn replied that institutional REBs will look at research protocols but local REBs are reviewing them more frequently now. There are even some regional Aboriginal REBs, but it is not mandatory that they approve studies, as only some communities have them. Some communities also insist that institutions enter into agreements with them before studies are approved. One community, for example, requires that researchers take a course in cultural sensitivity before any research takes place.

**Session 8 Discussion**

The presentations in this session challenge existing research practices that exploit vulnerable populations and describe how research can become more equitable through more adaptable research standards and a commitment to distributive justice. The discussion focused on the issue of vulnerability, specifically, how to ensure that
researchers are sensitive to cultural or local conditions. A contextual approach to research is very important because researchers and REBs often do not understand the specific vulnerabilities of research subjects. Guidelines will point researchers in the right direction but, as Dr. Benatar acknowledged, the idea of empowerment and capacity building is not being implemented correctly. Researchers should understand the basic social structures of the communities in which projects are undertaken and consult community members about how this work can benefit them.

Another participant said that focusing on the community might make it difficult to balance the needs of groups with those of individuals. According to some perspectives, the rights of the individual are primary. Alternatively, problems arise when individual opinions differ from that of the group, or there is disagreement over what is considered acceptable. Considering these issues, how can the notion of community consent be accepted?

On one hand, community consent can help to empower an individual. Looking to the community may be a way of overcoming vulnerabilities of individual research subjects and achieving self-determination through a group. On the other hand, community consent can also accommodate the preferences of the individual. One way to achieve informed community consent is through community REBs. Then it will not simply be traditional band or tribal leader consent – one person who decided for the group – but a more balanced consent. It is an epistemological question: are we individuals first or members of groups? The answer seems to be neither, and this is the problem.

Certainly there is a tension between collective dissent and collective assent. Furthermore, just because a community is involved does not mean that community consent is required. One participant suggested that in Africa, for example, the elders are often the gatekeepers of the society. You need to approach the elders to have the gates opened to the individuals. This does not detract from individual consent.

But when trying to promote equitable research and minimize exploitation, it is important to remember that the language of vulnerability can be patronizing. Aboriginal communities, such as those in Australia, New Zealand and Canada, are strong and should be treated with respect. There should be no suggestion that they are incapable of looking after themselves. The focus should be on values, not necessarily procedures. This reasoning supports an international standard of care, through which local values, needs and conditions will shape individual research projects and ensure that research can always be beneficial for all parties involved. Furthermore, this argument does not preclude specific guidelines such as those drafted by CIHR for research involving Canadian Aboriginal groups. It does, however, reinforce the importance of being sensitive to the needs of others, an imperative that can only be learned through communication and interaction with others and a willingness to accept different points of view.
Session 9: Liability in the Context of Research Review

The previous sessions discussed how to minimize participant harm in clinical research – be it physical harm or other types of injury such as mental suffering or violation of a person’s dignity. But the unfortunate reality is that harm does occur in clinical trials, despite appropriate guidelines, because of many inherent risks involved in research. The presentations in this session review the legal mechanisms available for research participants who claim monetary compensation for injuries incurred through clinical trials. In particular, the speakers focused on the procedural difficulties that research patients face in low-and-middle-income countries, common law countries and civil law countries, when seeking pecuniary redress.

Nigeria: Litigating The “Trovan” Tragedy

Nigeria: Abdullahi v. Pfizer:
Ethical Review of Research Involving Human Subjects in Nigeria
Presentation by Dr. Remigius N. Nwabueze

Dr. Remigius Nwabueze is a law professor, then at the University of Ottawa, now at the University of Southampton in England. He specializes in the areas of tort, conflict of laws, health law, intellectual property law, biotechnology and bioethics.

Clinical trials are becoming increasingly globalized, as statistics show that the number of countries where clinical research is conducted increased from 28 in 1990 to 79 in 1999. Although the incidence of research being undertaken in low-and-middle-income countries is growing in number, there is often inadequate ethical review of the research protocols. Furthermore, much of the research in low-and-middle-income countries is used to generate evidence for medication predominantly marketed in high-income countries. National research institutions such as the FDA in the United States have observed that to ensure the safety of patients in low-and-middle-income countries, sponsors need to better monitor the research and researchers, and outside sources must assist foreign ethics review boards to gain the required capacity.

Research in low-and-middle-income countries may be undertaken for altruistic reasons such as improving health care systems and providing access to necessary medicines and treatment. However, there are many conditions that exist in low-and-middle-income countries that allow for exploitation to occur during foreign drug trials. They include abundant and vulnerable research subjects, high rates of poverty and disease, low levels of drug regulation and less expensive costs for conducting the trials. Foreign trials are also exploitative if their studies are used to generate evidence for drug registration in a high-income country, or if they distort health priorities in low-and-middle-income countries by diverting already limited medical resources.
Nigeria has been the scene of a particularly controversial drug trial which was run by Pfizer in the city of Kano after an outbreak of an epidemic of meningitis in 1996. Pfizer’s medical scientist at the time, Juan Walterspiel, raised objections to the study but his employment was terminated shortly thereafter. The research participants were children and the study compared a new drug developed by Pfizer called Trovafoxacin (Trovan for short) with the gold standard drug Ceftriaxone. Equal numbers of children were given each drug, and six children treated with Ceftriaxone and five with Trovan died of meningitis, while many other children suffered brain damage, paralysis or deafness.

The Trovan trial raised many ethical issues. For instance, Pfizer was accused of giving children in the control group a low dose of Ceftriaxone in order to produce evidence of the efficacy of Trovan. The parents of the children in the study did not provide informed consent on behalf of their children, as many of the guardians could not speak English and many also had the expectation that their children would be receiving treatment instead of participating as research subjects. There was no ethical review conducted by Nigerian authorities (because there was no Research Ethics Board in existence at the hospital where the trial occurred), and therefore no one but the researchers had reviewed the protocol. Not surprisingly, Pfizer denies all of the above allegations. The Trovan study is now the subject of litigation in Nigeria as well as the United States, where the decision of the United States District Court for the Southern District of New York, dismissing the case for *forum non conveniens*, was vacated by the Court of Appeals and the case was remanded for further proceedings in the District Court.

The Trovan study drew significant attention to the overriding importance of ethical review of research in low-and-middle-income countries. Also brought to attention by the study was the almost non-existent ethical review framework in Nigeria. At the time, there was no formal regulatory system of ethics review, nor a set of national biomedical research guidelines. Furthermore, only a few Nigerian research institutions had ethical review committees, and these had to rely on international guidance standards for insight.

Since the Trovan tragedy, substantial progress has been made in Nigeria to develop better ethical review frameworks in different regions of the country. However, there still exists only a small number of research ethics committees in comparison to the number of research institutions, and where committees do exist, many members lack adequate training in bioethics.

Dr. Nwabueze pointed out that Nigeria is not the only low-or-middle-income country that has limited research review capacity. He mentioned a 2004 study by Hyder that found that 25% of research undertaken in low-and-middle-income countries did not undergo any ethical review.
In conclusion, Dr. Nwabueze provided several suggestions as to how to make research safer and more accountable to its participants. He recommends that:

- Nigeria enact a research guideline that is legally enforceable, in order to remove any questions about legal accountability;
- Sponsors of foreign clinical trials, institutions from high-income countries and international organizations should assist low-and-middle-income countries in improving capacity for the ethical review of biomedical research;
- Nigerian ethics review committees should charge fees for reviewing international research protocols. To avoid conflict of interest and protect committee independence, any fees should be paid to a central fund and devoted to financial support of ethics committees in Nigeria; and
- There should be stiff penalties and damages for research injuries that result from unethical research.

In the discussion that followed, the recommendation that REBs charge user fees drew many comments. Some conference participants were uncomfortable with the idea of charging for ethical review. For instance, some researchers are low-income graduate students who have already paid their tuition for studies, of which the research is part. This point prompted a comment that there should be a discriminatory system of charging for REB approval, where only those who can afford to pay will be charged: i.e., biotechnology companies and other commercial enterprises. However, there is trouble with differential charging when the regulations are not the same for everyone. Since the issue here is the health and safety of the public and not commercial interests, another participant argued, there should be no charges for independent review.

Australia: Common Law Liability

Common Law Liability in Research – an Australian Perspective
Presentation by Professor Colin Thomson

Colin Thomson, a law professor at the University of Wollongong has been a member and chair of the University's research ethics committee and a member of similar committees for other Australian universities and health research agencies. He is presently the consultant in health ethics to the Australian National Health and Medical Research Council. Professor Thomson discussed potential common law actions that could be used to seek compensation for research harm.

In Australia, although research guidelines are non-statutory, they are legislatively applicable to drug and device clinical trials and contractually applicable to recipients of public research funds. Thus, if there is a failure to meet the requirements of disclosure under the National Statement, a trial can be suspended under the Therapeutic Goods
Act. A breach of the ethical research guidelines will result in a breach of contract between an Institution and a funding agency.

However, there are no legislative provisions that enable research participants to claim damages for research harm; therefore, participants must rely on the common law and actions such as negligence. However, it will be more difficult for a complainant to plead a successful case of negligence now, because negligence law has been reformed by statute, in response to a public liability crisis. Because of liability reforms, defendants are no longer liable for obvious risks.

In order to determine how a negligence claim based on injury from a research trial would proceed, Professor Thomson provided a hypothetical case. Suppose that a research participant suffers harms from research risk, but that the researcher and REC breached the guidelines because the researcher should have avoided this risk and the REC should have identified it and required that participants be warned more clearly. Using this example, Professor Thomson tested the participant’s chance of obtaining recourse against the researcher, the REC/Institution and the sponsor.

To obtain compensation under the common law, the participant’s injury must be able to meet the four components of a negligence action:

1. Duty of Care: The defendant must have been able to foresee the risk of harm, and the relationship between the defendant and participant must have been close (proximate);

2. Standard of Care: The defendant must have failed to meet the relevant standard;

3. Harm: In the hypothetical case, harm (injury) is taken to have occurred; and

4. Causation: the breach of the standard of care caused the harm.

In a case against the researcher, the researcher automatically accepts a duty of care to conduct the research with care. The standard of care is based on the type of conduct that would be necessary to meet the national and international ethical guidelines. It also depends on the magnitude of risk, the degree of probability of its occurrence and the expense and difficulty required to take alleviating action. In the hypothetical situation, the standard of care would probably have been breached because the researcher failed to inform the participant about the risk in accordance with the guidelines. The harm is a given, but the last component – causation – is the most difficult test to meet. Even though the participant would not have consented to the research if he had known the risk (be careful of hindsight), by statute, there can be no liability for an “obvious” risk in Australia. Therefore, it would be difficult to argue a successful negligence claim.
It will also be difficult to bring a successful negligence claim against an REC or institution. (In Australia, many RECs are institutional, and therefore the institution is subject to vicarious liability – i.e., being responsible for the actions of its own committee. It will be difficult to show that the REC or institution owes the participant a duty of care. Foreseeability is probably satisfied, but the relationship may not be sufficiently proximate because the REC has a duty to advise the institution or the researcher, but not the participants. To breach the second component involving the standard of care, the REC must have failed to consider a relevant issue (which is the case in the example) or must have reached the wrong conclusion. Harm is a given, but it will be difficult to prove that the REC advice, “as a matter of ordinary common sense and experience, should be regarded as a cause” of harm.

Against the clinical trial sponsor, the participant should have more recourse to monetary compensation. Sponsors of clinical trials have a duty of care in relation to the design of the trial. In addition, sponsors of clinical trials accept an obligation to indemnify a participant for trial related harm or loss. But the standard form of indemnity excludes harm caused by negligent or wrongful acts, breach of statutory duty, or by failures to meet National Statement and common law defects. Therefore, it is very difficult for a claim against the trial sponsor based on the indemnity to succeed.

Should the participant be successful against the researcher or REC, the participant should be able to receive compensation from insurance. Institutions carry insurance for employees’ negligence, but the insurance would not normally apply to researcher negligence if it is beyond the scope of employment.

Aside from negligence, there are several other common law actions that the participant may consider. For example, a participant can claim fraud if the participant was not informed that a researcher would receive financial rewards, is required to compete for access to funding, has a desire to profit from intellectual property, is involved in a conflict of interest and/or used a therapeutic misconception. Alternatively, the participant may claim unjust enrichment if the participant contributed significantly to the research, provided family histories and a tissue sample, and the researcher or sponsor made a significant profit but failed to disclose this information to the participant. Administrative law principles may also apply to clinical trial research and review. It is important to note, however, that no cases have been tried under these additional remedies, and so it is not possible to know if they will offer monetary relief.

As a caveat, it is also argued that risk of liability will promote researchers and institutions to comply with ethical guidelines. However, researchers may begin to implement defensive practices and ethics committee members may promote a conservative compliance mentality. Ethical deliberation may then become distorted.
Hungary: Civil Law Liability

Hungary: Civil Law Liability in Hungary
Presentation by Dr. Dorottya Mogyorósi

Our final presenter was Dr. Dorottya Mogyorósi, the deputy head of the Secretariat of the Medical Research Council of Hungary, as well as the Secretariat of the Human Reproduction Committee of Hungary. She is a rheumatologist and lawyer, and lectures on medical law at Pázmány Péter Catholic University.

In Hungary, medical research is governed and organized according to several Parliamentary Acts, which incorporate European Union ethical research guidelines. Parliamentary Act No. CLIV (1997) on Health also establishes national regulatory guidelines that provide directions for research conducted on human beings. Act No. CLIV sets out standards for informed consent, provides state compensation for a participant that suffers or dies from research (if the research was performed properly and in compliance with professional rules) and requires that a research institute must contractually agree to provide insurance for trial-related damages (committed by a researcher or the institution).

The criminal law may also have a role in regulating clinical trials, but applies only to medical research that violates Parliamentary Act No. IV (1978), or specifically “Crimes Against the Order of Medical Interventions and Medical Research, and Against Self-determination Related to Health Issues.” Criminal activity includes human genome interference, sex selection techniques and transplantation sale of human body parts and cadavers. Violation of the rules can result in up to five years of imprisonment.

The review of more general clinical trial issues falls under the domain of central research ethics committees, of which there are three specific types in Hungary. There are Scientific and Research ethics committees, Clinical Pharmacology ethics committees and Human Reproductive ethics committees - all of which operate independently of government, although membership is through appointment by the Minister of Health. RECs follow standard operating procedures that are recommended in the various Guidelines. Although only recommendations, they are referenced in the regulations and therefore must be followed. The Guidelines detail REC procedures for ethical examination as well as decision-making and state that an REC shall also examine the research contract for the existence of responsibility insurance.

Professional liability of researchers, physicians, REB members and institutions is enforced through legal sanctions provided in the Civil Code. The primary purpose of the sanctions is to compensate an injured patient, but they also act as a method of deterrence. In the Hungarian civil system, it is important to note that the civil law distinguishes between damages that occur outside a contract (delictual liability) and
damages that arise from contractual responsibilities. In Hungary, the majority of civil litigation initiated against health institutions involves delictual liability. Under §339 of the Civil Code, anyone who causes unlawful damage to another is required to compensate for that damage. However, if the defendant can prove that he lived up the expectations in a given situation, he will not be held liable.

If a participant brings a civil law claim for damages arising from contractual responsibilities, four elements must be satisfied in order to establish liability:

1. Damage
2. Causation
3. Medical Intervention contra legem artis (fault)
4. Unlawfulness of the damage

The defendant and the claimant are each responsible for disproving or proving some of the factors listed above. For example, medical liability in a civil law system is also based on fault, or negligence. In a civil law system, however, it is the defendant who must prove that he or she was not at fault by showing that he or she did everything that was prescribed by the professional rules. Generally, unlawfulness refers to all forms of behaviour (active or passive) or results from behaviour that violates legal standards. The complainant is responsible for establishing causality. In cases where there is lack of sufficient information and there are no medical protocols, it is difficult for the patient to prove the link between the symptoms and the medical intervention.

The damages (or harm) can be either non-material (pain, mental suffering or violation of an individual’s dignity or honour), or personal. If a victim is entitled to compensation for losses suffered, the compensation must match the extent of damage suffered and cannot exceed it (so that it cannot be a source of revenue). However, the victim must be fully compensated for all damages suffered, and therefore there is no limit on restitution.

As opposed to claims against research institutions, there have still been no lawsuits against any researcher in Hungary. Several factors contribute to the dearth of legislation, including the fact that the researcher can evade paying compensation, research subjects are uninformed about legal actions, and there have been few successful legal actions by patients in general.

Session 9 Discussion

It is clear from the three presentations in this session that it is difficult for research subjects to hold researchers and research institutions accountable for ethical infringements. In high-income countries, research participants may be monetarily compensated for physical harms that they suffer through institutional insurance.
However, many research contracts now exclude payment for damages caused by negligence. Both common and civil law systems provide an action for negligence, but as the presentations revealed, it can be difficult to prove causation. Furthermore, most research guidelines are not legislative instruments, and research participants have no statutory recourse against those who conduct research.

One topic that was absent from the presentations was whether researchers have a fiduciary duty to their subjects. In the discussion, Professor Thomson explained that in Australia researchers and patients are likely in a contractual relationship. Many would argue that the researcher/subject relationship is not like that of the doctor/patient relationship and that it should not be considered the same.

There was some discussion about how other jurisdictions approach this issue. In Canada, the SCC has ruled that the doctor/patient relationship is fiduciary in nature. Doctors influence patients and patients are in a relationship of dependency toward doctors, who owe them a higher obligation of care. However, does this also apply to researchers? In a civil law case in Quebec, a court rejected the argument that a doctor who enrolls a patient in a research study in an academic hospital is not acting as a physician but as a researcher. It held that a researcher-physician could be held accountable as physician for his conduct in a study. There is no equivalent case under Canadian common law.

In other civil law jurisdictions, the relationship between researchers and patients is better characterized. In Germany, a doctor is in a position of power over the patient. Even if that doctor is a researcher, he or she still has full responsibility for the entire medical needs of the patient.

It was argued that it should be morally wrong for researchers not to owe any clinical duties towards their subjects. For example, there was a case in the US during the Vietnam War where a man was disqualified from service. It was originally thought that he was disqualified due to a leg injury, but he was actually ineligible due to having cancer; however, the army medical officials failed to inform the man’s physician of this fact. The US courts held that the army was liable to the man, even though there was no therapeutic relationship. They found that there was a fiduciary relationship in this case.

The American case raises the issue about the situation where a patient may not want to be informed about certain knowledge. The default position seems to be to tell the participant everything, although, again, it depends on the jurisdiction. In Ontario, Canada, there is no civil claim for disclosure of unwelcome truths. However, in the US there is the tort of outrage.

As mentioned in the presentations, there is a cause for concern that fear of liability is prompting researchers to adopt certain behaviour. However, no researchers have
actually been sued, and it is hoped that researchers are being driven instead by a desire to do their work well so that they are not affected by the threat of liability. The same concerns affect Research Ethics Board members. In Quebec, Canada, for example, there is one court case in which an institution was held liable for the negligent work of the REB. In the wake of this case, REB members have become concerned about liability and started inquiring about insurance. In some institutions, REBs are linked to the board of directors of the institution and therefore are covered by the board’s insurance.

SECTION D. Synthesis of International Surveys

Introduction

Before the workshop, a questionnaire was distributed among participants of this workshop to obtain detailed information about each country’s legal and administrative framework for research review. From the resulting information – for which we thank all participants who completed questionnaires – we have prepared this synopsis. It provides a quick glance at each country’s ethics review system, points out similarities and differences among countries, identifies trends and highlights outstanding achievements.

Countries covered in this analysis to date are Australia, Canada, Costa Rica, Cuba, Estonia, Germany, Hungary, India, Lithuania, Mauritius, Mexico, Russia and Tanzania. A report from the Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP) allowed us to include information from China, India, Indonesia, Japan, Korea, Laos, Malaysia, Mongolia, Nepal, Philippines, Singapore, Sri Lanka, Taiwan and Thailand. Two earlier studies on the research review structures of Nigeria and South Africa were also incorporated.

In an addendum to this publication, a synoptic chart describes the main characteristics of the research review structures in countries that answered the questionnaire. This section, then, describes and discusses similarities and differences between countries’ regulatory models, which are as varied as the social, cultural, economic and political characteristics of the countries in question. Some already have strong research review structures while others are still working to design review structures, establish appropriate bodies and prepare guidelines and/or legislation on research involving human subjects.

We have organized our analysis under the following topics:

- Research Review Structures;
- RECs – Governance and Oversight;
- Specialized Review Bodies and Guidelines;
• RECs – Conflicts of Interest and Commercialization of Research;
• Citizen Participation in Research Review;
• Transparency of Research Review;
• Liability and Health Care Coverage;
• International Research;
• Benefit-Sharing; and
• Current Challenges.

These topics incorporate most of the responses and information provided by participants. It must be noted that generalizations were made where necessary and appropriate. Finally, notwithstanding our efforts to be as accurate as possible when describing each country’s general research review structure, we urge those interested in specific jurisdictions to obtain additional information directly from the relevant agencies or organizations in each country.

I. Research Review Structures

Research review structures vary considerably from country to country. Although all countries contemplate the existence of RECs, there are marked differences in the scope of research that is subject to ethical review, the nature of the instruments mandating or requiring such review and the organization of RECs, among other things.

In looking at the scope of research to be reviewed, we must differentiate clinical trials from other types of health research. Clinical trials are more strictly regulated in all countries. In general, health authorities – whether health ministries directly or drug regulating agencies – have to authorize clinical trials that require testing new substances and/or devices on human subjects, or that intend to vary their approved indications.

In most cases, health authorities do not review ethical aspects of clinical trials in depth but require REC review and approval as a condition for authorization. REC review of clinical trials is, therefore, generally mandated in binding regulatory instruments.\(^4\) In some countries, REC review is not specifically mandated in legislation but regulations may require that clinical trials should be conducted in accordance with set guidelines – national and/or international – that in turn require such review and provide more detailed information.\(^5\) Compliance with guidelines – soft law – is more or less

\(^4\) Some of these binding instruments include: the Medicinal Products Act in Estonia; the General Health Law and the Health Research Regulations in Mexico; and the Federal Drug Law and the Federal Law on Medicinal Products in Germany.

\(^5\) In Canada, for example, Health Canada (a federal department) regulates clinical trials and mandates that these comply with the International Convention on Harmonization of Good Clinical Practice (ICH-GCP), which requires mandatory REC review.
compulsory in these countries. Overall, the tendency is to mandate REC review of clinical trials either directly in legislation or by reference in legislation to specific guidelines. More specific information on how RECs should review clinical trials is usually contained in non-binding instruments, such as national and/or international guidelines, rather than legislation.6

Apart from clinical trials, the scope of health research subject to REC review varies widely among countries. Some countries have extensive guidelines that cover all research involving human subjects, whether it is health-related or not (research in the social sciences, for example) and require that all such research be reviewed by an REC.7 Most countries, however, have specific laws or guidelines for health research – especially biomedical research – irrespective of whether they regulate other types of research involving human subjects.8

It should be noted that some countries have voiced concern about research on traditional medicine.9 Apparently, little or nothing is mentioned in legislation and/or guidelines regarding traditional medicine, even though it is the most accessible option for people in many of the countries included in this report. It has been suggested that one of the challenges faced by certain countries is to promote and regulate traditional medicine research.10

In most countries, REC review of biomedical research is mainly required by governmental authorities although in some countries it is required by funding institutions.11 Even in countries where REC review is mainly required by governmental authorities, funding institutions play an important role in the research ethics review system because REC review is usually a precondition for funding. In countries where REC review is principally required by funding agencies, the research ethics guidelines

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6 Australia’s Therapeutics Goods Legislation regulates clinical trials and mandates REC review in accordance with the National Statement on Ethical Conduct in Research Involving Humans (NSECR). The NSECR is a set of non-binding guidelines issued by the National Health and Medical Research Council of Australia that provide detailed information on how RECs should be formed and operate.

7 For example Canada. In Australia, the NSECR also applies to several types of research as it has been endorsed by varied organizations in Australia. Coincidentally, in both countries REC review is principally required by funding institutions.

8 Some countries provided additional information about other types of research subject to ethical review. For instance, in Laos, behavioral and social sciences research – including educational research and epidemiological research – is subject to review.

9 For instance, India and Nepal. The issue has also been discussed in Indonesia.

10 Tanzania and South Africa have provided certain information on traditional medicine-related research. In Tanzania, one of the objectives of the National Institute for Medical Research (NIMR) is to conduct and promote research into various aspects of local traditional medical practices with the aim of facilitating the development and application of herbal medicine. The institutional REC in NIMR might review ethical aspects of this type of research. South Africa’s Medicine Control Council (MCC), a drug regulating agency in charge or reviewing all clinical trials in South Africa, is comprised of several committees, of which one is the African Traditional Medicines Committee. As suggested, committees of the MCC – although not RECs – review research to determine regulatory and ethical compliance with national standards.

11 For example, Canada and Australia. In South Africa, until recently REC review was only required by the major federal funding agency, the Medical Research Council, through its guidelines. New legislation is already in place that regulates research in detail and mandates REC review.
used by those institutions are generally endorsed by other institutions and even by governmental authorities.

The organization of RECs, and research review systems in general, varies from country to country. All countries have mixed structures that combine national, regional and local RECs and many of these are worthy of comment. The most popular structure seems to include a national oversight and/or advisory body – for example, a national research council, national REC, or national bioethics commission – to which local RECs report and which is entrusted with, among other functions, setting national standards and guidelines. There is a tendency for countries to promote local ethical review – through the establishment of institutional RECs – and to establish central bodies with advisory and/or monitoring functions. These central bodies may or may not have jurisdiction over local RECs.

Describing every research review structure is beyond the scope of this report. Each is unique and complex enough to warrant independent, in-depth analysis and we do not have enough information to attempt such an exercise. Instead, we will describe some of the systems that exist in specific countries.

Russia and Hungary have three levels of review: national, regional and local. In Russia, while the National Ethics Committee reviews and approves clinical trials, regional and local RECs review other types of research and follow-up trials approved by the national REC. In Hungary, there are three national RECs, 12 regional RECs and a local REC for every institution that conducts research involving human subjects. Different types of RECS review different types of research with the stipulation that institutional RECs should always review projects conducted at their institutions.

Lithuania has a national-regional ethical review system comprised of the Lithuanian Bioethics Committee – the national REC in charge of reviewing clinical trials, among other types of research – and Regional Biomedical Research Ethics Committees, whose functions and competence are determined by the national REC. India and Tanzania also have two-tier review systems. In India, most institutions that conduct biomedical research involving human subjects have their own RECs. In addition, two national committees – the REC of the Indian Council of Medical Research and the National Bioethics Committee of the Department of Biotechnology – review research projects of national importance or those conducted in institutions lacking their own REC. In Tanzania, local RECs report to a national REC within the National Institute for Medical Research. Canada also has two types of RECs, mostly local, with some regional RECs for community-based health research. Australia’s structure is similar.

As stated earlier, our description and analysis of each country’s review structure is based on information provided by participants, country reports and our understanding, often limited, of each system. We recommend that specific aspects of national review
systems be investigated further by consulting local experts. Overall structures may be much more complex than indicated here.

As a final word on this topic, we want to mention efforts in several countries to transform soft law into hard law. In many countries, research involving human subjects is regulated through guidelines and/or other types of non-binding instruments. In countries where ethical review is voluntary, there may be a significant rate of compliance with guidelines, but detailed and reliable information on what happens in practice is generally lacking. The absence of legislation and/or any other binding instruments is a cause for concern. In light of this, many countries with systems that rely on the observance of soft law are promoting the enactment of legislation. India’s Ethical Guidelines for Biomedical Research on Human Subjects, prepared by the Indian Council of Medical Research in 2000, have been drafted as legislation and might be sent to parliament soon. Malaysia is also drafting legislation and South Africa recently did so. These initiatives, and others that might be taking place in other countries, will no doubt strengthen the research review systems for the benefit of participants.

II. RECs: Oversight and Governance

Irrespective of whether the need to establish RECs is contemplated in legislation or non-binding instruments, in most countries more detailed information about RECs – how they should be formed and funded, requirements for membership, criteria for assessing risks and benefits, elements to be considered during review, etc. – is provided in national guidelines and/or similar documents. RECs, therefore, have a lot of flexibility in their internal structure and operation. Indeed, in most countries RECs may create their own internal regulations.

There was little information about commercial RECs. Most respondents emphasized their countries’ institutional RECs. Institutional RECs can be funded by the institutions to which they belong and RECs within a governmental entity are generally funded by the government. Depending on the type of research, institutional RECs in some countries charge fees. It was noted that RECs are generally under-funded and that this has had a negative impact on their performance.

Little is mentioned about specific requirements for REC membership. Committees are usually required to have members of both sexes with expertise in the area of research under review, some of whom are not affiliated with the institution. As noted earlier, guidance on the composition and operation of RECs is usually contained in non-binding instruments that serve as a general framework and this gives RECs a lot of flexibility. Several countries said that trained bioethicists are not common and that REC members often lack the expertise to participate in research review activities. Several countries have designed programs to meet the need for qualified individuals. India is currently planning and implementing several education programs, including virtual programs, on
research ethics. Medical colleges and universities are preparing curricula that include courses in bioethics and a new textbook on research and research ethics will be widely circulated. Indonesia’s recently created National Commission on Health Research Ethics will play a leading role in education on the importance of research ethics.

The regulatory instruments or guidelines used by RECs when carrying out research review are generally those that establish the need or obligation to have research ethically reviewed. As we have explained, some countries have hard law, others have soft law, but most countries have a combination of the two. The review of clinical trials is usually governed by stricter legislation and/or guidance and RECs must refer to such legislation and guidance when reviewing the ethical aspects of clinical trials. RECs might also have their own internal regulations and, in the case of institutional RECs, they might have to observe institutional guidelines and operating procedures as well. RECs in most countries not only apply national legislation and guidelines but also consider the international documents to which the legislation and guidelines refer. These international documents include: the International Conference on Harmonization for Good Clinical Practice; the World Health Organization Operational Guidelines for Ethics Committees that Review Biomedical Research; the Belmont Report; the Declaration of Helsinki; and the Council for International Organizations of Medical Sciences’ International Guidelines for Biomedical Research Involving Human Subjects.

To the best of our knowledge, only a few countries – such as Costa Rica\(^{12}\) and the United Kingdom – have formal accreditation systems for RECs. Although some countries have signaled their intention to establish accreditation systems soon,\(^{13}\) performance review of RECs, if any, is mainly carried out by health authorities in some countries, and by funding institutions or RECs of superior hierarchical levels in others. In Mexico, for example, RECs must register with, and submit annual reports to, the Federal Commission for the Protection of Sanitary Risks, which is the drug regulating agency recently created within the Ministry of Health. In Australia, RECs should be registered with, and submit annual reports to, the National Health and Medical Research Council in order for institutions to remain eligible for funding. In Lithuania, Regional Biomedical Research Ethics Committees report annually to the Lithuanian National Bioethics Committee, which in turn reports to the Ministry of Health. In South Africa, legislation requires RECs to be accountable to the soon-to-be-created National Health Research Ethics Council. Local RECs in Tanzania must report to a national committee within the National Institute of Medical Research.

Many countries have emphasized the need to strengthen monitoring mechanisms following REC review and approval of research projects. Although practically every

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\(^{12}\) In Costa Rica, as established in Decree N° 31078-S, the National Council for Health Research should accredit RECs established in public and private institutions that conduct research involving human subjects. Accreditation may be suspended or withdrawn if RECs do not abide by national legislation.

\(^{13}\) For example, Cuba, India and Singapore. In Canada, it is also an issue that has received attention and discussion.
country has some kind of follow-up mechanism in place, participants from some countries suggested that, in practice, these mechanisms are virtually “non-existent.” In general, monitoring of research projects after REC review and approval relies on periodic reports that researchers submit, not necessarily to RECs, but often to the directors or heads of research departments within institutions. Because monitoring mechanisms may vary across institutions, monitoring is generally inconsistent. Most countries mention that RECs should at least be informed of amendments to approved research protocols, as well as adverse events. According to most countries, monitoring is not necessarily the role of RECs alone, but of all those involved in research – institutions, RECs, researchers, etc.  

In some countries, health authorities, such as health ministries, drug regulating agencies or other bodies, may have specific monitoring functions in addition to those of RECs. The Lithuanian National Bioethics Commission can visit trial sites to contact researchers and participants. In Mexico, the Federal Commission for the Protection of Sanitary Risks can inspect research to verify the safety of participants. If irregularities are detected, the Commission can enforce safety measures and impose administrative sanctions. In Canada, the Inspectorate of the Health Products and Food Branch also has started to conduct site visits of RECs to determine whether they comply with good clinical practice standards.

As explained above, neither monitoring nor enforcement of ethics standards are necessarily the role of RECs alone. In most countries, RECs can only withhold approval for a project before it starts. If subsequent events concern REC members, approval can be withdrawn and the REC can recommend that the project be suspended or terminated. Initially, it may seem that RECs do not take specific enforcement measures against non-compliant researchers, but, by withholding or withdrawing approval, an REC can have a significant impact depending on the country’s research review system. As we have seen, some countries make REC approval a condition for funding and, therefore, for the conduct of research. An REC’s withdrawal of approval can mean withdrawal of funding. In other countries, doing research without REC approval may be considered misconduct or even a criminal conduct, and will be sanctioned accordingly. In the case of the more strictly regulated clinical trials, protocols without REC approval may not be cleared by health authorities and/or drug regulating agencies.

Besides RECs, other bodies can have an important role in enforcing research ethics standards. Their functions may also depend on the country’s review system.

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14 In Costa Rica, for example, it is suggested that in addition to RECs, data safety monitoring boards may be established if appropriate. We found no additional information, however, on how these boards should be composed or operate.
15 For instance, in Canada, Australia, Germany and India.
16 This would happen in countries – e.g. Mexico, Lithuania and perhaps Hungary and Korea – that have legislation (not soft law) that requires REC review and approval. Conducting or continuing research would be in breach of such legislation.
Considering the general descriptions provided under the previous topic, it could be said that the most common are health authorities and/or drug regulating agencies, particularly in the case of clinical trials. Other relevant bodies include funding agencies – as explained in connection with denial or withdrawal of funding\(^\text{17}\) – other governmental bodies,\(^\text{18}\) and professional associations. In Mexico, for example, medical colleges and even federations of colleges have their own ethics codes in which there may be provisions dealing with research. Members of colleges who do not comply with ethics codes may be sanctioned and even expelled from their organizations. If there is criminal misconduct, college representatives may report it to the authorities.

Some countries have expressed concerns that there is not enough communication among RECs and have suggested that mechanisms be created allowing RECs to learn from the experiences of other review boards, both at national and regional levels. This is not a problem in countries like Estonia, which has only two regional RECs that seem to be very much aware of each other’s activities. However, most countries have complex structures involving a large number of RECs at different levels. The only significant interaction between RECs is usually between a local REC and the national REC to which it reports.

### III. Specialized Review Bodies and Guidelines

Recent scientific advances have prompted countries to introduce legislation, guidelines or administrative regulations establishing specialized review committees or other bodies. Most of these bodies, irrespective of their origins, provide advice and assessments and issue non-binding guidelines. Many countries have specialized committees within funding institutions, national health research councils or other bodies, which have several functions. In Canada, for example, the Canadian Institutes of Health Research – one of the three major federal funding institutions that issued the Tri-Council Policy Statement – has established the Stem Cell Oversight Committee. This committee will conduct an ethics review of human stem cell research funding applications submitted to any of the three agencies, as well as applications submitted to any institution that receives funding from the three agencies.\(^\text{19}\) The new Assisted Human Reproduction Act in Canada also introduces a new national review structure for research involving human reproduction. In Australia, the National Health and Medical Research Council has specialized advisory committees such as the Gene Therapy and Related Therapies

\(^{17}\) For example in Canada and Australia. In Canada, funding may be withdrawn not only from individual researchers but also from entire institutions. This puts pressure on institutions to ensure that ethics standards are observed.

\(^{18}\) In Australia, for example, the Office of the Federal Privacy Commissioner can receive complaints about researchers’ and even RECs’ failure to protect privacy. The Commissioner can then conduct an inquiry to determine whether the National Statement on Ethical Conduct in Research Involving Humans was complied with.

\(^{19}\) Also in Canada, a federal agency may be established shortly under the Assisted Human Reproduction Act that will be responsible for the ethical review of certain types of human reproduction research.
Research Advisory Panel that reviews proposals involving gene therapy and xenotransplantation and advises RECs about factors to be considered in their ethical reviews.

Hungary, Germany, Russia and India also have specialized review committees or commissions. Hungary’s Human Reproduction Commission operates within the Health Science Council to review research on the human genome and human reproduction. In Germany, a federal REC has been established to review human embryonic stem cell research. Russia has a national REC within the Russian Academy of Science that reviews research and recommends guidelines for research on matters of national concern such as stem cells, gene transfer and xenotransplantation. In India, a Bioethics Cell has been established within the Indian Council of Medical Research.

In other countries, including Mexico, Estonia and Korea, there are bodies with a broader mandate in bioethics. They may also review certain types of research – controversial research or research of national importance, for example – and issue specialized guidelines. They may also exercise other functions. The Estonian Council of Bioethics develops policies on topics such as human reproduction, euthanasia and transplantation. In Mexico, the National Bioethics Commission may review research protocols and develop policies on specialized topics in bioethics. Korea’s National Bioethics Review Committee, established by the Bioethics and Biosafety Law, determines who can conduct specific types of research such as human embryonic stem cell research.

Although most specialized bodies have been established to respond to ethical issues raised by new technologies, some countries have them for other purposes. One that caught our attention is India’s Health Ministry Screening Committee, which reviews research involving human subjects that involves international collaboration.

Just as there is a tendency for countries to establish specialized review bodies, there is a tendency for these bodies to issue specialized guidelines, usually related to certain technologies. Most of these guidelines are non-binding and serve as a general framework for relevant actors, including researchers, RECs, health authorities and participants. There are many interesting examples of specialized guidelines. India has ethical guidelines for stem cell research and gene therapy. In Japan, there are guidelines for research on the human genome, embryonic stem cells and human cloning. China has also issued Ethical Guidelines on Human Embryonic Stem Cell Research. Australia’s National Health and Medical Research Council has issued, among others: Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research; Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies; and Guidelines for Genetic Registers and Associated Genetic Material.
In addition to specialized guidelines for research related to certain technologies, some countries have also issued specialized guidelines on particular topics such as specific populations or diseases. India has issued Ethical Guidelines for Biomedical and Behavioral Research on HIV/AIDS. As for specific populations, Australia’s National Health and Medical Research Council has issued Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research.

**IV. RECs: Conflicts of Interest and Commercialization of Research**

Most countries have similar mechanisms to safeguard against a lack of impartiality on the part of REC members. In general, it is mandated that REC members declare any conflicts of interest and refrain from participating in the ethics review process in those cases. In some countries, REC members must sign no-conflict-of-interest statements, such as Lithuania’s Statement of Impartiality. In many countries, researchers and even external advisors have the same obligation. In Australia, for example, the National Statement on Ethical Conduct in Research Involving Humans requires researchers, REC members and expert advisors to disclose any commercial or business interests in research. In Lithuania, researchers are required to declare their interests in an Ethical Assessment Form that is submitted to RECs. In Russia, REC members and external consultants must sign an Agreement concerning Conflict of Interest.

In general, RECs do not take a very active role in tracking down conflicts of interest on the part of researchers, institutions and sponsors involved in research proposals. REC members seem to rely on the declarations of researchers, expert advisors and others involved. Some country reports suggested that REC members could play a more active role, but few said what that might be. In Lithuania, for example, in addition to requiring researchers to submit an Ethical Assessment Form, RECs may review any arrangements between sponsors and researchers, participants and trial sites. In Costa Rica, RECs may review the amount and sources of funding, as well as detailed information including, for instance, salary information. As for the factors or circumstances that could give rise to conflicts of interest, the Australian representative cited the amount and sources of funding, personal involvement in the research (external advisors, for example) and financial interests in the outcome or involvement in competing research. No country report mentioned the existence of specialized committees to deal with conflicts of interest.

The independence of RECs from government agencies, commercial entities, researchers and supporting institutions, among others, varies depending on the country’s research review structure, the types of RECs and their sources of funding. In general, there seem to be no specific safeguards to address this issue. Most country reports have identified the need to adopt measures to protect the independence of their RECs. Suggested mechanisms include: establishing appeal procedures within institutions to appeal RECs’
decisions; ensuring the financial and administrative independence of RECs to perform their duties; and promoting continued collegial vigilance. In the case of RECs that belong to governmental entities, legislative safeguards may be established to guarantee independence from governmental bodies.

Participants did not provide much information about conflicts of interest and commercialization of research issues. Many countries provided no information and others said that these issues are outside the scope of RECs or have not received much attention. In the context of the current global trend towards commercialization of research, several participants at the workshop suggested that conflicts of interest affecting researchers, institutions, sponsors and even REC members may compromise their duty to ensure participants’ safety and well-being. It seems somewhat surprising that not more measures have been implemented to counter these conflicts of interest.

V. Citizen Participation in Research Review

Most countries have legislation or guidelines requiring that at least one lay person sit on each REC although there were few details about the person’s qualifications. Australia requires that lay persons not be affiliated with the institution or the scientific work and preferably belong to the community in which research is to be conducted. In Russia, RECs must include representatives of the community or of different religious groups. In general, the participation of lay persons on an REC is designed to promote the committee’s independence.

Regarding citizen participation in the development of research ethics standards in general, few countries provided specific information. Some explained how the general public may participate to some extent in RECs’ standard setting. In Canada, for example, amendments to the Tri-Council Policy Statement, the main set of guidelines issued by the three major federal funding institutions, involve public consultation. In Mexico, Mexican Official Norms – regulatory instruments that detail general provisions in legislation – follow different stages before approval and promulgation by authorities. Such a norm regulating RECs according to the Health Research Regulations may soon be open for public consultation.

Overall, citizen participation depends on the country’s research review system. In countries in which research involving human subjects is regulated by hard law, there may be opportunities for citizens to participate through political channels. In countries where soft law is the rule, certain mechanisms may also be in place to promote public discussion and consultation on guidelines. Citizen participation should be actively encouraged. Some countries report that civil society organizations have made significant
achievements in recent years. These organizations have an important role in strengthening research review systems and setting REC standards.

VI. Transparency of Research Review

General information on RECs’ decision-making processes as well as specifics like members’ names and profiles, workload and the type of research projects that are subject to review, could be useful for many purposes, not only at the national level but also at the international level. Yet there seems to be little, if any, access to information on the characteristics and performance of RECs.

Most countries report that REC records and decisions are usually confidential. In some countries, reports are published either by RECs themselves or by the health authorities or bodies to which they report. However, these reports contain general information such as the names of projects reviewed and a general statement summarizing their decisions rather than detailed information about decisions. Data protection, particularly in light of the growing commercial interest in research, as well as third-party rights such as privacy and intellectual property rights are cited as the main reasons for keeping information about RECs’ decisions confidential. It is also suggested that in some countries there is little public interest in the decisions of RECs.

Whatever the reason, most countries publish little, if any, information about their RECs and most of the information that is available is quantitative rather than qualitative. This means that little is known about how RECs are made up, how they work, what criteria they use in ethical assessments, their most frequent challenges, their relationship with researchers, external advisors, and sponsors, etc. Information on these issues would be very useful in designing effective policies and strengthening review systems.

20 In Canada, the National Council on Ethics of Human Research is a non-governmental organization supported by the Canadian Institutes of Health Research; Health Canada; and the Royal College of Physicians and Surgeons of Canada. Its mission is to advance the protection and well-being of human participants in research and promote high ethical standards in research involving human subjects. Some of its activities include: site visits to RECs; continued training for REC members; analysis of emerging issues; organization of national and international workshops; and, strategic planning to promote compliance with ethical standards. In Japan, the Japanese Forum for Members of Institutional Review Boards is a non-profit organization dedicated to the enhancement of ethical review in health research. It promotes the exchange of information, educational programs and general discussion of research ethics issues. National chapters of regional organizations focused on research ethics have also been established in many countries. For instance, many of the FERCAP countries now have their own organizations. In Thailand, the Forum for Ethical Review Committees (FERCIT) has been promoting major developments in ethics review. Other FERCAP countries that have established national chapters include: India (FERCI) and Taiwan (FIRST).

21 We have avoided using terms like “all” and “none” because not all countries provided information on every topic.

22 For example, in Germany.

23 The Lithuanian Bioethics Committee, to which local RECs report annually, issues annual reports although the information they contain is rather statistical.

24 In fact, several countries have conducted surveys recently to gather specific information on RECs. Response rates have been very low, indicating that information systems are inefficient and that many RECs are unwilling to participate.
For this reason, some countries have undertaken interesting initiatives to put health information systems in place that might have a positive impact on research review structures. In the Philippines, the Department of Health and the Department of Science and Technology are working together to create the Philippine National Health Research System. Mexico’s National Council of Science and Technology and its Ministry of Health are also collaborating to create a nodal system for health information, which will include a registry of all institutions conducting health research, as well as the names of researchers, a description of their projects, etc. These systems may facilitate the work of RECs and promote a more effective approach to issues such as conflicts of interest. RECs, for example, will be able to find out who the researchers are, their institutional affiliations, and people with whom they worked. Health authorities and other bodies entrusted with enforcing ethics standards could have up-to-date information on which institutions are conducting research involving human subjects, and require them to comply with research ethics legislation and guidelines.

Besides information systems, some countries have come up with other measures to enhance transparency and accountability in health research, principally in clinical trials. Health Canada, for example, requires all clinical trials to be registered and this information to be available to the public. In South Africa, legislation entitles trial participants to a written “discharge report” at the end of the study.

**VII. Liability & Health Care Coverage**

Few countries provided information on legal or regulatory remedies for research misconduct and in all of them the remedies are similar. It must be noted that the countries included in our analysis have different legal systems, some based in common law, others in civil law and some in a mixture of the two. Remedies may be pursued differently and have different characteristics in each system. The descriptions that follow should be understood in this context. One participant also pointed out that the legal basis for the liability of researchers and others involved in research will depend on the type of liability alleged. Because most countries only provided information about the liability of researchers – and in some cases, institutions and RECs – arising from harm to research participants, we will focus on this type of liability.

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25 Some countries might already have health research information systems. For instance, in Costa Rica, according to Decree Nº 31078-S, the National Council for Health Research should have a database with the following information: research projects involving human subjects; institutions and professionals authorized to conduct research involving human subjects; and, existing RECs. Also, information on researchers sanctioned for breaching provisions on research involving human subjects should be included in the registry. Unfortunately, we have no additional information on how – and if – the system is working properly.

26 Australia.

27 Liability could be alleged for the misuse of public funds, where researchers and/or institutions receive public funding, or violation of privacy rights. In Australia, privacy complaints can be filed with the Privacy Commissioner, who may order compensation.
In general, research participants who are harmed in research have remedies in civil and criminal law. In common law countries, the most likely basis for liability of researchers and institutions is the tort of negligence for lack of reasonable care in the conduct of research.\(^{28}\) In civil law countries, research participants also have an action for civil damages – material and/or moral – on the basis of professional liability on the part of researchers. In both systems, contractual breach may be the legal basis of liability of researchers and institutions.\(^{29}\) Institutions may also be held liable – vicarious liability – for researchers’ negligence, depending on the relationship between researchers and institutions as well as local regulations.

Research subjects may also have remedies in criminal law. Although our respondents did not provide much information, we assume that in many if not most countries, research participants must be able to accuse researchers of criminal conduct to obtain compensation for physical and psychological injuries in the most egregious cases of research misconduct. For instance, assault and battery may be alleged for harms resulting from a lack of informed consent of participants.\(^{30}\) Researchers may also be liable for injuries caused as a result of research.

Besides remedies in civil and criminal law, researchers who harm participants may face disciplinary procedures before their own professional associations, which could sanction or expel them. In addition, professional associations may strengthen guidelines and require higher ethical standards from their members. In South Africa, for example, it is suggested that the Health Professions Council, established under the Health Professions Act, No. 56 of 1974, can play an important role in protecting research subjects by using its powers to investigate accusations of research misconduct. In Mexico, members of medical colleges may be sanctioned and even expelled for not complying with ethical codes of conduct. If misconduct is considered a crime, college representatives may report it to the appropriate authorities.

Respondents provided little information about the liability of RECs. German RECs have special liability insurance coverage and in Lithuania, the National Bioethics Committee can suspend the right of regional RECs to issue approvals if they fail to perform their duties. Not much is mentioned either about the relationship between RECs, collegial bodies and health or other authorities. RECs do not seem to have special status within jurisdictions and we assume that their members may be held individually liable where appropriate.

\(^{28}\) It has been suggested that RECs could also face this claim for not reviewing research adequately.

\(^{29}\) Some countries have specifically mentioned this, e.g. South Africa.

\(^{30}\) In South Africa, failure to obtain consent is considered assault. In other countries, such as Canada, lack of informed consent may be battery and inadequate informed consent may be assault.
Only a few country reports provided specific information about actions for liability against researchers. Recent cases of researcher misconduct in Australia include: fabrication of research results; use of manipulated results in grant applications; and misrepresentation of historical control of data as current. There was no information on the remedies applied in these cases. Nigeria provided an interesting example of research misconduct in the case of an externally funded study conducted in 1996. Known as the Trovan case, it involved a U.S. pharmaceutical company that took advantage of a meningitis epidemic to test its new drug, trovafloxacin, on children. The company conducted a double-arm clinical trial which resulted in the death of several children and harmed many others. It is alleged that the company did not obtain informed consent from the children’s parents or ethical approval from Nigerian authorities. The Trovan case has been the subject of an administrative inquiry in Nigeria and has been litigated in Nigeria and the U.S. No additional information was provided about the remedies used or the legal basis for the alleged liability.

Regarding health care coverage in case research participants need medical care, it must be noted that each country’s health system is unique. Some have publicly funded systems and others have mixed public/private schemes. A description of every system is beyond the scope of this analysis, which limits itself to information provided by participants. It must be noted, however, that in countries with publicly funded health systems, the issue of health care coverage is not a pressing concern, unlike the case of countries with private or mixed public/private systems.

In general, health care coverage should be guaranteed to all participants injured as a direct consequence of research. Some countries have interesting mechanisms to safeguard participants. In Estonia, research sponsors must demonstrate that subjects are insured and will receive necessary treatment before health authorities will approve research projects. Under Lithuanian law, sponsors and principal researchers in biomedical research involving human subjects must obtain third-party insurance against research-related damage. In other countries, guidelines require RECs to look into these issues. In South Africa, for instance, the Guidelines for Good Practice in the Conduct of Clinical Trials on Human Participants require RECs to consider the mechanisms in place to guarantee compensation and/or treatment in the case of injury or death of participants, as well as the insurance or indemnity schemes designed to cover liability costs.

Other countries only have mechanisms for biomedical research involving clinical trials. Tanzania and Germany require liability insurance. In Australia, it is common for pharmaceutical companies to obtain insurance for participants’ research-related injuries.

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31 As explained, responses have been mainly institutional.
32 We will return to this example in the International Research section.
33 For instance, in countries with publicly funded health systems such as Cuba, injured participants would necessarily have access to health services.
34 The 2000 Rules of Compulsory Civil Liability Insurance for the Principal Investigator and the Sponsor establish that the insured sum can be no less than €29,000 for damages inflicted during, or resulting from, research participation.
However, coverage is limited to the effects of trials and does not cover injuries caused by the negligence of researchers and/or institutions or the inappropriate conduct of trials.

**VIII. International Research**

Some respondents indicated that the international component of research involving human subjects in their countries was relatively small while others said that most of the projects were being undertaken by international researchers.\(^{35}\) In general, international research tends to be more prominent in Africa and some Asian countries.\(^{36}\) Some of these countries might have similar characteristics in terms of medical infrastructure, population, diminished access to health care and, in some cases, the lack of a regulatory framework for research involving human subjects. International research seems to be increasing in some countries. The Lithuanian Bioethics Committee reports that the number of international research projects reviewed went from 51 in 2001 to 87 in 2004.

Although international research is not a pressing issue for many countries, others are concerned about the lack of safeguards for participants. As mentioned earlier, a Nigerian representative described how the lack of a formal regulatory system of ethics review endangered the safety and well-being of many participants in international research projects. The Trovan Case may be the tip of the iceberg.

Other country reports that provided information on claims or complaints involving international researchers included India and Mauritius. The report on India mentioned a collaborative research project involving Johns Hopkins University and a cancer hospital in Kerala.\(^{37}\) The Indian Council of Medical Research has also been investigating other cases. In the report on Mauritius, complaints were brought against researchers in a study involving an Australian company, Autogen. Originally, the study focused on the genetics of diabetes and heart disease in the Mauritian population but blood samples were later used for purposes such as DNA testing and banking.

In general, there are no special liability regimes for international researchers. Researchers may be subject to the laws of the countries in which they conduct research. In any case, international research is often conducted by local companies – either subsidiaries of transnational companies or funded by them – and, therefore, the laws of the countries in which they are based should apply. Some countries, however, have specific policies. In India, Ministry of Health authorization is required before a local company can accept external funding for research and a specialized body, the Health

\(^{35}\) The term “international researchers” describes researchers, companies or other entities based outside a particular country.

\(^{36}\) For instance, India, Malaysia, Nigeria, and South Africa.

\(^{37}\) Apparently, the case involved the use of an experimental drug on cancer patients without clearance from Indian health authorities and without approval by an REC.
Ministry Screening Committee, has been established for this purpose. Sri Lanka’s Medical Association has recently developed Guidelines on International Collaborative Research. South Africa’s “Medical Research Council Guidelines on Ethics: General Principles” also provide guidance to researchers on international collaborative research, among other issues.

IX. Benefit-Sharing

Benefit-sharing takes many forms. According to UNESCO’s Universal Draft Declaration on Bioethics and Human Rights, these include: access to quality health care; provision of new diagnostic and therapeutic modalities or products stemming from research; access to scientific and technological knowledge; and capacity-building facilities for research. Unfortunately, most of the countries included in our analysis do not have mechanisms to promote any of these forms of benefit-sharing. Among those that have are Estonia, Lithuania, Australia and Costa Rica. Estonia attached benefit-sharing measures to the Estonian Genome Project. Investors and health authorities signed an agreement, but this was terminated when the project was interrupted. In Lithuania, the sponsors of a few projects were asked to provide patients with the medication used during clinical trials after they ended. Australia’s Pharmaceutical Benefits Scheme (PBS) applies the findings of research about the efficacy and safety of pharmaceutical products against their cost and offers Australians subsidized prices for listed drugs. In Costa Rica, national legislation requires that protocols submitted for review explain how access to medication used in research will be continued after the research is terminated. Also, protocols should explain how sponsors will strengthen local capacity. Moreover, a Letter of Undertaking by sponsors must accompany every protocol outlining the obligation of sponsors to provide participants with free treatment – if proved efficient – until its subsequent approval and marketing.

In general, RECs do not seem to have an active role in promoting benefit-sharing, nor the power to do so. In fact, several countries stated that although there may be certain measures in place to promote the equitable distribution of economic and medical benefits of research to the subject population, this work is beyond the scope of RECs. RECs are hardly in a position to promote benefit-sharing, especially as it does not depend solely on the good will of researchers or institutions but on multiple factors, such as the local economy, the health system and intellectual property rights. However, some RECs may be able to contribute. In countries where there are national and/or

39 For example, in Germany and India.
40 In Canada, for example, the Tri-Council Policy Statement says that research conducted in other countries should ensure that benefits be available in the host country, on the understanding that RECs should not force or expect researchers to act as aid agencies.
regional RECs, they have greater authority, either regulatory or moral, to work with national authorities in analyzing the feasibility of benefit-sharing. Regional RECs may also be able to collaborate with local authorities to analyze national schemes and apply them locally.

RECs have a limited role not only in promoting benefit-sharing, but also in promoting public access to research data at the conclusion of studies. As with benefit-sharing schemes, most country reports explain that such promotion is beyond the scope of RECs. In some countries, for instance, Australia and Germany, RECs may recommend or even insist that mechanisms be in place to guarantee that research findings will be published. However, there are no enforcement measures for non-compliant researchers. Little was mentioned about RECs’ role in the ethical review of agreements between researchers and institutions and/or sponsors, a common source of confidentiality obligations preventing researchers from making their findings public. RECs should have access to this information as part of the ethical review of research projects, because it involves conflict of interest issues as well as potential barriers to the publication of research findings. Although RECs would still not have the power to mandate publication, confidentiality obligations should be carefully scrutinized for their effect on research participants.

Finally, the promotion of benefit-sharing schemes and access to research findings should not be the task of RECs alone. All relevant actors need to be involved in the protection of research subjects. Benefit-sharing schemes may not be a priority in countries where research is mainly internally-funded and public health systems provide coverage for all. In countries where access to health care is limited and the population is of interest to international researchers, however, benefit-sharing could be a window of opportunity. As for public access to research data at the conclusion of research, all countries – irrespective of their socioeconomic conditions – could benefit. Transparency would be enhanced and research review systems in general would be strengthened.

X. Current Challenges

Each country included in our analysis faces different challenges depending on its research review system. Most countries, however, share certain challenges and could learn from one another in trying to solve them. The information in this section comes mainly from FERCAP's report on countries of the Western Pacific region, but most of it applies to many of the countries surveyed.

The most common concern about review systems in general is the lack of binding instruments to deal with research involving human subjects. In the absence of legislation, many countries’ reports note that ethical guidelines are rarely followed. In addition, there are countries that don’t even have guidelines. The need to legislate
and/or establish indirect enforcement mechanisms through guidelines has, therefore, been identified as a priority. There has also been considerable discussion about the need to expand the scope of existing legislation and/or guidelines to mandate ethical review not only of clinical trials, but of all biomedical research – and perhaps all research – that involves human subjects.

Most country reports indicated that training is needed for REC members. Although capacity development in some countries may be hampered by geographical, social, cultural and economic characteristics, designing formal training programs for REC members is a priority. Lack of expertise compromises RECs’ efficiency.

Establishing new RECs and reducing the workload of those already in operation were also cited as priority issues. Lack of adequate resources is also considered a major challenge to the effective operation of RECs in most countries. Many countries suggest that charging fees could be an option but the associated conflict of interest issues would have to be addressed.

Other challenges currently faced by many countries include the need to develop quality assurance systems by building partnerships with REC oversight bodies in government, or creating them, as well as by strengthening international collaboration. The need to promote communication among national RECs – through national fora and workshops, for instance – is also recognized. Most countries have emphasized the need to raise awareness about the importance of ethical review of research.

**Conclusion**

This analysis of the information provided by participants has helped us to understand some of the features of each country’s research review structures and to identify similarities and differences in approaches to research involving human subjects. The exercise suggests that countries have much more in common than they realize.

Each country has a unique research review structure based on its social, cultural, economic and political characteristics. While some countries already have strong structures, many are still struggling to design them. Even so, most countries share concerns and challenges and agree about the need to promote the development of appropriate administrative structures to protect research participants.

One of the aims of the workshop was to provide the opportunity for representatives of diverse countries to discuss and compare their review structures. The information provided by participants in their responses to our questionnaire certainly contributed to this dialogue. It is a dialogue that must continue if countries are to learn from each other and coordinate efforts to protect the human subjects of research.
SECTION E. Participant Biographies

Gytis Andrulionis

LL.B., magister iuris at Faculty of Law, Law University of Lithuania, Ph.D. Candidate at the Faculty of Law, Mykolas Romeris University, Vilnius.

Since February 2005 he is the Chairman of the Lithuanian Bioethics Association. Mr. Andrulionis teaches Health Law and Economics, Public Health Law and Medical Law in Vilnius University. He is an active expert in the legal and regulatory aspects of REC review in Lithuania. His doctoral dissertation focuses on human rights in biomedicine. His research interests also include regulations regarding stem cell research, and in particular the status of the embryo in various countries as well as at the international level.

Tom Archibald

Research Associate, S.J.D. (doctoral) Candidate at the Faculty of Law, University of Toronto

Tom Archibald worked with Professor Trudo Lemmens as a research associate in the fields of biomedical research regulation and the regulation of genetic databanking. His current research focuses are on privacy issues in biomedical research, including genetic-based research. He has taught in the areas of administrative law, labour law and health law, and published articles on labour law and health law in Canada. Tom is now completing his S.J.D. (doctorate in law) at University of Toronto.

Dr. Asmik Asatrian

General Secretary, Forum for Ethics Committees in the Confederation of Independent States (FECCIS)

Dr. Asmik Asatrian is the General Secretary of the FECCIS Secretariat, which acts as a co-ordinating research ethics review body for the Commonwealth of Independent States. Together with Prof. Dr. Olga Kubar, the Chair of FECCIS, Dr. Asatrian has written and spoken frequently on research ethics review issues. Most recently, Dr. Asatrian gave a lecture on the role of ethics committees in the implementation of principles and provisions of international documents at the Regional Expert Consultation on Networking in the Sphere of Ethics and Bioethics, held by the FECCIS, March 2005 and participated in the Workshop FECCIS/SIDCER/IEC/IRB Recognition Program, Chisinau, Moldova, March 2006. (available online at http://www.feccis.net/cgi-bin/generator.pl?id=3.9eng)
Dr. Solomon Benatar  
*Department of Medicine, University of Cape Town, South Africa and Joint Centre for Bioethics, Toronto*

Dr. Solly Benatar is Professor of Medicine at the University of Cape Town, Director of the UCT Bioethics Centre, and Visiting Professor in Public Health Sciences and Medicine at the University of Toronto. He is past President of the International Association of Bioethics, ethics consultant to the HIV Prevention Trials Network (USA) and elected Foreign Member of the US National Academy of Sciences’ Institute of Medicine and the American Academy of Arts and Sciences. His research interests include International Research Ethics, International Health and Global Health Ethics.

Dr. Anant Bhan  
*Independent Researcher, Bioethics and Public Health, Pune, India*  
*University of Toronto Joint Centre for Bioethics*

Anant Bhan is a physician from India. Besides an undergraduate degree in medicine from Bangalore, he has received additional training in medical law and ethics. He has worked with a voluntary organization on a fellowship in community health, and with the global secretariat of the Peoples Health Movement. Later, he worked with a central government public health educational institution on a project focusing on ‘Mainstreaming Gender in Medical Education’. He recently completed graduate masters training in bioethics in Toronto on a Fogarty International Fellowship. His fields of interest lie in public health, bioethics, global health, poverty and health, gender and health, human rights, the role of media in health, and young people’s sexual and reproductive rights. Anant is a member of the International Steering Committee of the International Youth Parliament. He worked briefly at a centre focused on bioethics and human rights in Mumbai, India and as the Assistant Executive Editor of the *Indian Journal of Medical Ethics*. Presently he is based in Pune, India and works as an independent researcher in bioethics and public health.

Dr. Corina Bontempo Duca de Freitas  
*Executive Secretary, National Commission for Research Ethics (CONEP)*

Corina Bontempo Duca de Freitas is a medical doctor specializing in Public Health. She is Executive Secretary of the Brazil National Commission for Ethics in Research (CONEP), and also Consultant to the Brazil National Health Council. She has been working with research regulation since 1995, when the National Health Council decided to review national norms, working with the multi-disciplinary group that established Resolution No. 196/96, the main guideline for ethical review in Brazil. She is currently working on a monitoring proposal to evaluate the ethical review system, eight years after its initial implementation. She is also nearing completion of her Ph.D. degree at the University of São Paulo, where her doctoral dissertation is on evaluation methodology to the research ethical review system.
**Prof. Alexander M. Capron**

*Director, Department of Ethics, Trade, Human Rights, and Health Law*  
*World Health Organization, Geneva*

Alexander Morgan Capron is the first Director of Ethics, Trade, Human Rights and Health Law at the World Health Organization, Geneva, Switzerland. He joined the WHO in October 2002 to launch the Ethics and Health Initiative in the Director's General Office. He has previously taught law, medicine, and ethics at Georgetown, Pennsylvania, Yale and most recently at the University of Southern California.

Professor Capron, who earned his LL.B. at Yale University and B.A. (High Honors) from Swarthmore College, specializes in health policy and medical ethics. He has written or edited eight books, including *Law, Science and Medicine* and the *Treatise on Health Care Law*. His recent articles and chapters treat such issues as brain-based determinations of death, current controversies in human gene therapy, genome mapping, human cloning, and research with human beings.

He is a Trustee of The Century Foundation and Vice President of the International Association of Bioethics, for which he served as President of the III World Congress on Bioethics in 1996. He is a member of the Institute of Medicine (US National Academy of Sciences), on whose Council he served for two terms; a Founding Fellow of the Hastings Center, where he was also a long-time Board Member; and a Fellow of the American Association for the Advancement of Science and of the American College of Legal Medicine.

Professor Capron has also served as President of the American Society of Law Medicine and Ethics, as Vice President of the Council for International Organizations of Medical Sciences, and as chairman of the Biomedical Ethics Advisory Committee of the U.S. Congress (1987-90). He has been a member of NIH’s Recombinant DNA Advisory Committee (1984-92), and of the National Bioethics Advisory Commission (1996-2001). His biography appears in *Who's Who in America* as well as other national and international reference works.

**Dr. Richard Carpentier**

*Executive Director, National Council on Ethics in Human Research (NCEHR), Ottawa*

Dr. Carpentier is Executive Director of Canada’s National Council on Ethics in Human Research. In this capacity, he has been directly involved with the many initiatives of the NCEHR related to the promotion of research ethics in Canada. He recently participated in initiatives promoting the establishment of accreditation procedures in Canada.
Dr. Bernard Dickens
Faculty of Law, University of Toronto

Professor Dickens, a member of the English Bar and the Ontario Bar, is the Dr. William M. Scholl Professor Emeritus of Health Law and Policy in the Faculty of Law, the Faculty of Medicine, and the Joint Centre for Bioethics at the University of Toronto. He is legal articles co-editor of the Journal of Law, Medicine and Ethics, co-editor of ethical and legal issues of the International Journal of Gynecology and Obstetrics, and a member of editorial boards of several journals including the American Journal of Law and Medicine and Medicine and Law. His writing includes about three hundred and fifty publications including books, chapters in books, articles and reports, primarily in the field of medical and health law. He was a member of the Board of Governors of the American Society of Law, Medicine and Ethics, and is a former Society President. He is now a member of the Board of Governors of the World Association for Medical Law, and an Association Vice President. He is a Fellow of the Royal Society of Canada. His most recent book, co-authored with Rebecca J. Cook and Mahmoud F. Fathalla, Reproductive Health and Human Rights: Integrating Medicine, Ethics and Law, was published in 2003 by Oxford University Press.

Prof. Dr. Elmar Doppelfeld
Chair, Steering Committee on Bioethics (CDBI), Council of Europe

As a MD and Professor of Nuclear Medicine at the University of Bonn, Elmar Doppelfeld in 1982 joined a group of German academics interested in research ethics. They started a forum for exchange of information and harmonisation for the work of ethics committees, as established by the Faculties of Medicine and the Medical Associations in the German States since the late 1970s. Prof. Doppelfeld became Secretary General and has been elected chairman of this permanent working group of ethics committees in 1994.

In 1992, Prof. Doppelfeld, scientific editor of the Deutsches Ärzteblatt (1988-2004), was appointed by the German Government as a member of the German delegation to the Council of Europe’s Steering Committee on Bioethics (CDBI). He was a member of the Working Party which prepared the additional protocol on biomedical research adopted by the Committee of Ministers on 30 June 2004 and opened for signature on 25 January 2005. He has been chairman of a Working Party developing an instrument on research using biomaterials of human origin which was completed in 2005 and on 15 March 2006 was adopted by the Committee of Ministers of the COE.
Dr. Geneviève Dubois-Flynn  
*Senior Ethics Policy Advisor, Canadian Institutes of Health Research*

Dr. Geneviève Dubois-Flynn has a background in international law (Licence from the University of Paris XI in France) and in philosophy (PhD from Laval University in Canada). After teaching several courses, including bioethics, at the University of Ottawa, she joined the National Council on Ethics in Human Research in 2000. There, she was in charge of evaluation activities and participated in 25 site visits to university and hospital ethics committees across the country.

Dr. Dubois-Flynn now works at the CIHR as Senior Ethics Policy Advisor in the areas of governance of ethics in research involving humans, conflicts of interest and commercialization. She has also been involved in policy work including in the area of research involving Aboriginal Peoples. She has also been a member of a Research Ethics Board of the University of Ottawa as person knowledgeable in ethics and as member of the community for the last 5 years (in turn for the Social Sciences and Humanities REB and the Health Sciences and Sciences REB).

Dr. Michael Enzle  
*Chair, Stem Cell Oversight Committee, Canadian Institutes of Health Research*

Michael Enzle, PhD, is an experimental social psychologist at the University of Alberta. His academic research areas include privacy, moral evaluation, self-regulation, and motivation. He has published many articles in the major journals in his field, and frequently reviews submissions for journals and granting agencies. He is a co-author of the introductory psychology text, *Psychology: The Science of Behavior* (Allyn & Bacon, 2002, 2d. ed.), and is an appointed member of the Society for Experimental Social Psychology.

Dr. Enzle has been involved in the development and implementation of human research ethics policies at the University of Alberta since 1975. He has been chair and member of several research ethics boards, and has been seconded to the Office of the Vice-President (Research) as Research Policy Coordinator since 1992. In the Spring of 2003, Dr. Enzle was appointed as full-time Director of the newly created Human Research Protections Office at the University of Alberta. Dr. Enzle is a member of the National Council on Ethics in Human Research, and Chairs its Education Committee.
Dr. Şefik Görkey

Professor of Medical History and Ethics and
Chairman, Marmara University Medical School, Medical Ethics Department, Istanbul

Dr. Görkey has published widely in the field of medical ethics and ethical issues in dental practice and research. He is presently the Chair of the Marmara University Medical School Ethics Department, and sits on the Istanbul Chamber of Physicians Ethics Committee, Marmara University Medical School, and is a founding member of the International Dental Ethics and Law Society (IDEALS). Dr. Görkey also sits on the editorial board of the Türkiye Klinikleri Journal of Medical Ethics.

Professor Dr. Juhana E. Idänpään-Heikkilä

Secretary-General, CIOMS

Professor Juhana E. Idänpään-Heikkilä holds an MD and PhD (in pharmacology) from the University of Helsinki in Finland. He practised medicine as a health center and hospital physician before moving to clinical research and teaching pharmacology at various universities. After a Visiting Professorship at the University of Baylor in Houston, Texas, in 1968-1969 and a post of Assistant Professor at the University of Oulu, Finland, he worked from 1971 to 1990 as a Chief Medical Officer at the national medicines control agency in Finland. In 1982-1983, he was an adviser in drug regulation at the US Food and Drug Administration in Rockville, Maryland, USA and in 1988-1989 served as an adviser at the United Nations Office in Vienna, Austria.

In 1990, he was appointed Deputy Director, and subsequently in 1995 Director, of the Division of Drug Management and Policies of the World Health Organization in Geneva, Switzerland. He also acted as Secretary of the WHO research ethics committee. In 2000, he received the honorary title of Professor from the President of Finland. He is the author of more than 200 scientific and other publications. Since 2000, he has been the Secretary-General of the Council for International Organizations of Medical Sciences (CIOMS), which is based at the WHO in Geneva.

Dr. James Lavery

Associate Professor, Public Health Sciences, University of Toronto
and Research Scientist, Centre for Research on Inner City Health
and the Centre for Global Health Research, St Michael’s Hospital

Before joining St. Michael’s Hospital in Toronto, Dr. Lavery was a bioethicist in the Division of Advanced Studies and Policy Analysis at the Fogarty International Center of the U.S. National Institutes of Health. In his current role, Dr. Lavery continues his interests in international research ethics, global health and health policy. He has expertise in qualitative research methods and his current research activities include projects on ethics in health research systems in developing countries in collaboration
with colleagues at Johns Hopkins University, the Tanzania Food and Nutrition Centre, the Bangladesh Medical Research Council, and the World Health Organization. He is also leading the development of a cross-border comparison of research protections between Canada and the United States with Canadian and U.S. collaborators. Dr. Lavery’s other main research interest is in HIV/AIDS-related stigma and discrimination. He is currently developing research projects in Ontario and India on the relationship between stigma and health.

**Trudo Lemmens**  
*Faculty of Law, University of Toronto*

Trudo Lemmens is Associate Professor in the Faculty of Law at the University of Toronto, with cross-appointments in the Faculty of Medicine. He is associated with the Centre for Innovation, Law and Policy and with the Joint Centre for Bioethics. His research currently focuses on regulatory and ethical issues of medical research and on legal and ethical issues raised by genetics and biotechnology. In addition to various other publications in health law and bioethics journals, he edited with Duff Waring _Law and Ethics in Biomedical Research: Regulation, Conflict of Interest and Liability_ (forthcoming 2005, University of Toronto Press).

Professor Lemmens was invited to spend the year 2003-2004 at the Institute for Advanced Studies in Princeton to conduct research on the ethical and regulatory challenges of the commercialization of medical research. He currently leads a research group at the Faculty of Law on Research Ethics and Regulation, funded by Genome Canada (through the Ontario Genomics Institute). Trudo Lemmens has been a member and chair of various ethics and advisory committees in his areas of specialization. He teaches courses on Research Ethics and Regulation; Privacy, Property and the Human Body; Public Health Law; and Legal Ethics and Professionalism.

**Professor Thérèse Leroux**  
*Centre de Recherche en Droit Public, Faculté de Droit, Université de Montréal*

Thérèse Leroux is professor and researcher at the Centre de recherche en droit public de l’Université de Montréal since 2000. From 2001 to 2003, she was Director of Ethics at the Canadian Institutes of Health Research. In 2003, she was special advisor to the President of the CIHR as member of an advisory group on the use of Placebos in Clinical Research. Before undertaking her studies in law, Professor Leroux obtained a Bachelor’s degree in Biology and a Certificate in Psychology of Human Relations at the University of Sherbrooke. She also obtained a doctorate in medical biochemistry of the Université du Laval. She is also a member of the Quebec Bar.

Professor Leroux’s research focuses on legal and ethical issues of human subjects research, organ transplants, public health, and consumer protection related to new biotechnology and biodiversity. In the coming years, she will be working on three
different themes: (1) Genomics and Society: rights and responsibilities of researchers with respect to sharing and storing information; (2) Xenotransplantation, which illustrates the tension between individual rights and public health; and (3) the authority and duties of the State in the face of scientific uncertainty related to the protection of the environment and public health.

**Dr. Partha Majumder**  
*India Statistical Institute, Kolkata*

Dr. Partha Majumder is Professor and Head of the Human Genetics Unit of the Indian Statistical Institute, Kolkata (Calcutta), India. His major scientific contributions are in the areas of human population genetics, statistical genetics and genetic epidemiology. He has published over 150 papers in scientific journals. He has served on the Board of Directors of the International Genetic Epidemiology Society (IGES) and was the Founding Chair of the Ethical, Legal and Social Implications Committee of IGES. Dr. Majumder is a Member of the Indian National Bioethics Committee, and the Human Genome Organisation (HUGO). He is a Fellow of the Indian National Science Academy.

**Dr. Michael McDonald**  
*Co-Chair, Standing Committee on Ethics, Canadian Institutes of Health Research*

Dr. Michael McDonald occupies the W. Maurice Young Chair of Applied Ethics, and is the founding Director of the W. Maurice Young Centre for Applied Ethics (1990-2002). He received an Honours BA in Philosophy from the University of Toronto and an MA and PhD in Philosophy from the University of Pittsburgh. He is the Program Director of the CIHR Ethics of Health Research and Health Policy Training Program, which offers opportunities for doctoral and post-doctoral training and research at the University of British Columbia and Dalhousie University.

McDonald’s work is located at the intersection of theory and practice in health care, business and professional life, politics, and other aspects of everyday life. McDonald was the Principal Investigator on a CIHR-supported project, “Towards the Ethical Governance of Canadian Research Involving Humans: Principles, Policies, Practices and Outcomes”. This follows on the work done by McDonald and his colleagues in a report, *The Governance of Health Research Involving Human Subjects*, to the Law Commission of Canada in 2000. This report was the first in-depth description and analysis of Canadian public and private sector oversight of health research involving human subjects.

McDonald has served Chair of the Standing Committee on Ethics for the Canadian Institutes for Health Research (CIHR) since 2001. Previously, McDonald served as a member and Deputy-Chair of the Tri-Council Working Group on Ethics – the Working Group that prepared the document that eventually became the basis of the *Tri-Council Policy Statement on the Ethical Conduct of Research Involving Humans*. McDonald is Guest Editor of a special double issue of *Health Law Review* on Canadian Governance for
Ethical Research Involving Humans (Vol. 13, 2-3) which will be published in late June 2005.

**Dr. Dorottya Mogyorósi**  
*Medical Research Council of Hungary*  

Dr. Mogyorósi is deputy head of the Secretariat of the Medical Research Council of Hungary. She is also head of the Secretariat of the Human Reproduction Committee of Hungary. She has spoken and presented widely on the legal and ethical aspects of human subjects research including recently at the European Commission’s “Research Ethics Committees in Europe: facing the future together” conference in January 2005. She is a rheumatologist and a lawyer, and lecturer of medical law at Pázmány Péter Catholic University.

**Dr. Godwin D. Ndossi**  
*Tanzania Food and Nutrition Centre, Dar es Salaam*  

Godwin D. Ndossi, PhD, is Managing Director of the Tanzania Food and Nutrition Center (TFNC), in Tanzania. Previously he was Director of Food Science and Nutrition in the same institute for nearly ten years. He is also a Fogarty Fellow of the Bioethics Institute, Johns Hopkins University. He received his B.Sc. in Botany, Zoology and Education and M.Sc. in Biology from the University of Dar es Salaam, and his PhD in International Nutrition from Cornell University.

He has worked on a variety of collaborative research projects with scientists and professionals in industry, universities (Institute of Child Health-London, Harvard School of Public Health, Cornell University and Muhimbili University College of Health Sciences), non-governmental organizations, bilateral and UN organizations.

Dr. Ndossi is also the Executive Secretary of the TFNC Research and Ethics Committee, a past member of the ethics committee of the Tanzania National Health Research Forum and a member of several editorial boards. Currently he is focal point of the WHO pilot on Health Research System Analysis in Tanzania as well as being the local investigator of the WHO Ten Country Study on Knowledge Transfer and Exchange in the Health sector.

**Ants Nömper**  
*Faculty of Law, University of Tartu, Tartu, Estonia*  

Ants Nömper is Attorney at Law, *dr. iur.*, and Lecturer in Medical Law at the University of Tartu, Estonia. He is a member of the Council of Europe Working Party on Stored Human Biological Materials and was a member of the Working Party on the *Estonian Human Gene Research Act*. Ants has been closely involved with the Estonian Genome
Project since its inception, and his research interests include the idea of open consent for population-based genetic databanks.

**Dr. Remigius Nwabueze**  
*LL.B. (Nigeria), B.L. (Nigeria), LL.M. (Lagos), LL.M. (Manitoba), S.J.D. (Toronto)*  

Remigius (Remi) Nwabueze was a Professor of Law at the Common Law Section of the Faculty of Law, University of Ottawa. Prior to joining the University of Ottawa, he was a fellow at the Centre for Innovation Law & Policy at the Faculty of Law, University of Toronto and a Genome Regulation post-doctoral fellow on projects relating to international and comparative perspectives on the regulation of genomics research. Dr. Nwabueze is now the City Solicitors’ Educational Trust Lecturer in Property Law at the School of Law, University of Southampton, U.K.

Dr. Nwabueze has practised law in all the courts within the judicial hierarchy, and between 1996 and 1998 he was invited by the Nigerian Federal Government to represent it and prosecute some cases under its then newly enacted Failed Banks Decree. His research and teaching interests are in the areas of tort, conflict of laws, health law, property law, intellectual property law, biotechnology, and bioethics. Dr. Nwabueze has published articles in reputable and peer-reviewed law journals in the U.S.A. and Canada.

**Dr. Andrés Peralta-Cornielle**  
*Vice-Chairperson, Latin American Forum for Ethics Review Boards (FLACEIS)*  

Dr. Andrés Peralta-Cornielle is radiologist and radiotherapist by training. He is currently working both in the areas of Oncology and Bioethics, as Vice-Chairperson of the Latin American Forum for Ethics Review Boards, Vice-Chairperson of the National Bioethics Commission Dominican Republic and as Medical Director of the Cibao Cancer Hospital in Santiago, Dominican Republic.

**Dr. Jerome A. Singh**  
*Howard College School of Law, University of KwaZulu-Natal, Durban*  

Jerome Amir Singh, BA, LLB, LLM, PhD (Natal), MHSc (Toronto), is Head of the Bioethics and Health Law Programme at the Center for the AIDS Programme of Research in South Africa (CAPRISA), Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa; Adjunct Professor in the Department of Public Health Sciences and Joint Center for Bioethics at the University of Toronto, Canada; and, Honorary Research Fellow and Course Director for Bioethics and the Law at Howard College School of Law, University of KwaZulu-Natal, Durban, South Africa.

He co-directs the Ethical, Social, and Cultural Issues Advisory Service for the Grand Challenges in Global Health initiative, sponsored by the Bill and Melinda Gates Foundation.
Foundation. He also serves on the International Research Ethics Board of Médecins Sans Frontières (MSF), the United States National Institutes of Health International Therapeutic Data Safety Monitoring Board (Africa), the Research Ethics Committee of the South African Human Sciences Research Council, the Scientific Advisory Board of the Aurum Institute of Health Research, the Ethics Committee of Resolution Health and Docline Medical Aid Scheme, and the Executive Committee of CAPRISA.

Dr. Singh has previously served as a member of the Research Ethics Committee of the Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, and currently acts as an *ad hoc* clinical ethics advisor to several provincial hospitals in Kwazulu-Natal. He has facilitated numerous workshops on the medico-legal aspects of HIV/AIDS for several provincial governments in South Africa and has served as an *ad hoc* trainer on HIV/AIDS Management for the South African Medical Association (SAMA) and for HIV/AIDS training initiatives sponsored by the Global Fund for AIDS, TB and Malaria. He has also facilitated numerous workshops on forensic medicine for the Independent Medico-legal Unit (IMLU). He has presented numerous papers nationally and internationally on issues pertaining to law and bioethics, and has published several works on issues pertaining to these fields.

**Professor Terry Stacey**  
*U.K. Department of Health*  
*Formerly Director, Central Office for Research Ethics Committees*

Professor Stacey recently returned to the U.K. Department of Health after serving as the inaugural Director of the Central Office for Research Ethics Committees, which advises on policy and operation of Research Ethics Committees in the National Health Service. In 1997, Professor Stacey was charged with implementing a new system of Multi-centre RECs in England, and in 2004 led the re-organization of RECs necessary for the implementation of the European Directive on Clinical Trials. He retired in March 2006.

**Dr. Godfrey B. Tangwa**  
*Professeur de Philosophie, Université de Yaoundé 1*

Godfrey B. Tangwa is Professor of Philosophy and current Head of the Philosophy Department at the University of Yaounde 1 in Cameroon. He has a B.A. (Honours) in Philosophy from the University of Nigeria, Nsukka, an M.A. in Philosophy from the University of Ife (now Obafemi Awolowo University), Nigeria, and a Ph.D. from the University of Ibadan, Nigeria. His doctoral specialization was in epistemology and metaphysics but he has also acquired considerable competence in bioethics, African philosophy, and social-political philosophy. His main interest is in practical and applied philosophy, that is, the application of philosophy to practical human problems. He is one of the leading contemporary bioethicists of sub-Saharan Africa who has gained international recognition.
Dr. Tangwa has been a member of the International Association of Bioethics (IAB) since it started in 1992, was on its Board of Directors from 1997 to 2003 and served as Vice-President of the association between 1999 and 2001. He was instrumental in the proposal for the formation of the Pan-African Bioethics Initiative (PABIN) in 2001 and has recently been elected the chairperson of CAMBIN, the PABIN chapter in Cameroon. He has published widely in international philosophy and bioethics journals.

**Professor Colin Thomson**  
*Faculty of Law, University of Wollongong, New South Wales, Australia*

Professor Thomson has been a member and chair of the University of Wollongong’s research ethics committee and a member of similar committees at the Australian National University, the ACT Board of Health and the Australian Institute of Health and Welfare. He was appointed to the Medical Research Ethics Committee of NHMRC from 1987-1991, the transplantation ethics working party of the Australian Health Ethics Committee (AHEC) from 1995-1996 and a member of AHEC from 1998-2002. He is presently the consultant in health ethics to the National Health and Medical Council.

**Dr. Cristina E. Torres**  
*Regional Coordinator, Forum for Ethical Review Committees in Asia and the Western Pacific Region (FERCAP).*

Dr. Torres is a Social Science Professor and Chair of the Ethics Review Board of the National Institutes of Health at the University of the Philippines. Her fields of interest include health systems research and bioethics.

**Robert S. Williams**  
*Bioethicist, The Scarborough Hospital, Toronto*

Robert S. Williams has been on staff as the Bioethicist of The Scarborough Hospital since 2000 and has served as the Research Ethicist on its Research Ethics Board since 1998. In March of 2003 The Scarborough Hospital was the epicentre of the Toronto SARS outbreak.

He is also a Ph.D. candidate at University of Toronto’s Institute of Medical Science and Joint Centre for Bioethics. His doctoral dissertation is a phenomenological study of the experiences of the staff of The Scarborough Hospital during the SARS outbreaks. Specifically, his work focuses on their experiences related to reporting for work during the outbreak.