DISCUSSION PAPER

Global Summit of National Ethics Committees

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Working Group on Research Ethics Committees

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I. Introduction

This paper sets out a number of issues in relation to the functioning and oversight of Research Ethics Committees (RECs) for the purposes of discussion among the delegates at the Global Summit of National Ethics Committees (NECs). The paper has been divided into several sections, highlighting some current issues and incorporating submissions made by several of the working group members.

Various international bodies have developed codes of ethics for human subjects research. These documents include the *Nuremberg Code* published after World War II, [1] and the *Declaration of Helsinki* published in 1964,[2] with the latest version published in 2008.[3] The Council for International Organizations of Medical Sciences (CIOMS) published their *International Ethical Guidelines for Biomedical Research Involving Human Subjects* in 1993, with updates in 2002.[4] Additional documents have been produced at the regional and national levels, including: the Council of Europe's *Oviedo Convention*[5], the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's *The Belmont Report*[6] and the Nuffield Council's *The ethics of research related to healthcare in developing countries*[7].

The requirement of ethical review of research projects by an independent Research Ethics Committee (REC) was introduced in the United States in 1966. The Research Grants Division of the U.S. Public Health Service linked access to government funding with this process. The requirement for the overview of research protocols by an independent committee was added to the 1975 revision of the *Declaration of Helsinki*. More recently some countries have passed legislation enforcing ethical requirements.

While guidelines for the ethical conduct of human subjects research and requirements for ethics review have been established at international and national

[1] *Nuremberg Code* (http://ohsr.od.nih.gov/guidelines/nuremberg.html, accessed 23 May 2012).
[2] *Declaration of Helsinki.* Helsinki, World Medical Association, 1964 (http://www.cirp.org/library/ethics/helsinki/, accessed 22 May 2012).
[3] *Declaration of Helsinki*. Seoul, World Medical Association 2008 http://www.wma.net/en/30publications/10policies/b3/17c.pdf, accessed 22 May 2012).
[4] *International Ethical Guidelines for Biomedical Research Involving Human Subjects.* Geneva, CIOMS, 2002 (http://www.cioms.ch/publications/layout_guide2002.pdf, accessed 17 May 2012).
[5] *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Biomedical Research*. Strasbourg, Council of Europe, 2005 (http://www.coe.int/t/dg3/healthbioethic/activities/02_biomedical_research_en/195%20Protocole%20recherche%20biomedicale%20e.pdf, accessed 16 May 2012).
[6] *The Belmont Report: Ethical Principles and Guidelines for the protection of human subjects of research*. Washington, 1979 (http://ohsr.od.nih.gov/guidelines/belmont.html, accessed 16 May 2012).
[7] *The ethics of research related to healthcare in developing countries.* Nuffield Council on Bioethics, 2002. (http://www.nuffieldbioethics.org/sites/default/files/Ethics%20of%20research%20related%20to%20healthcare%20in%20developing%20countries%20I.pdf, accessed 16 May 2012).

levels, there has been less guidance on the actual functioning and oversight of these review committees.

In 2000, the World Health Organization (WHO) produced the *Operating Guidelines for Ethics Committees that Review Biomedical Research*.[8] Following discussions at the 8th Global Summit of NECs in Singapore in 2010 the *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants*[9] document was produced by WHO.

[8] *Operational guidelines for ethics committees that review biomedical research.* Geneva, World Health Organization, 2000 (http://www.searo.who.int/LinkFiles/RPC_Operational_Guidlines_Ethics.pdf, accessed 15 May 2012).

[9] *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants.* Geneva, World Health Organization, 2009 (http://whqlibdoc.who.int/publications/2011/9789241502948_eng.pdf, accessed 09 May 2012).

II. Analysis of the RECs questionnaires sent to NECs

In preparation for the 9th Global Summit, a questionnaire was sent to all NECs. It was hoped that responses would allow for a better understanding of:

- current practices by RECs and their oversight by NECs;
- assistance required for the implementation of WHO Standards;
- practicality of WHO Standards, in particular in relation to implementation of a quality management system for RECs;
- future prospects that the Global Summit could develop.

The resulting report (Annex 1) contains data from the respondent NECs (22%) and from other sources.[10,11,12] Information in the report includes data from approximately 40% of the existing NECs .

Existing norms governing ethics review of research and the enforcement of these norms is heterogeneous. In many surveyed countries, particularly in Latin America, there are no specific laws on ethics review, but rather provisions, which are not always being enforced. In most of these countries, there is no penalty for violating these norms and there is no mechanism to oversee the current regulations.

With regard to the establishment of RECs, the majority of the respondents have indicated that their RECs have common standard operating procedures (SOPs) and policies.

RECs are very rarely accredited or certified. This is particularly evident in the regions for which more data are available (i.e. AMRO and EURO). Where systems exist, some of the most common criteria for accreditation have to do with the structure and membership of the REC. A national agency responsible for overseeing health research and the protection of human subjects is rarely in place.

The majority of the respondent countries reported that they do not have registration systems for RECs, but many have plans to create them. About a quarter of the respondents, all in EURO, stated that there is no need for registration, as RECs are not formed on a voluntary basis, but, rather, are established by law. For almost all the countries that have systems for registration or plans to create such systems, the REC registry is operated (or will be operated) by the NEC. These REC registries are

[10] *Report on Data on Research Ethics Committees in Seven Countries Outside Europe.* EFGCP, July 2010 (http://www.efgcp.be/Downloads/Library/EFGCP%20-%20NRES%20Report%20on%20RECs%20Vol%202%202%20PP.pdf, accessed 05 June 2012).

[11] *The EFGCP Report on The Procedure for the Ethical Review of Protocols for Clinical Research Projects in Europe.* EFGCP, April 2011 (http://www.efgcp.be/EFGCPReports.asp?L1=5&L2=1, accessed 05 June 2012).

[12] *Research across borders.* US Presidential Commission for the Study of Bioethical Issues, International Research Panel, September 2011 (http://bioethics.gov/cms/sites/default/files/PCSBI-IRP_Research-Across-Borders_0.pdf, accessed 06 June 2012).

mostly funded by governments and ministries of health. One respondent stressed that registration of RECs is important for the enforcement of norms governing research ethics review, especially when the countries do not have laws for ethics review (only provisions).

Concerning the operations of RECs, about half of the respondent countries have full time staff in their RECs' secretariats, with an average of two staff members per REC, generally secretaries, lawyers, nurses, social scientists. The size of REC membership is on average ten. The majority of the respondent countries do not carry out any joint review of protocols and about half have declared that their RECs do not accept ethics review from other RECs.

In many respondent countries, RECs are not regularly monitored. The scenario seems to be problematic, particularly in the AFRO and AMRO regions. In EURO, the situation is more favourable. REC performance is usually monitored by a NEC and sometimes by a Ministry of Health.

The respondent countries also reported on some measurements on the quality of ethics review. The average time RECs take to reach a final decision about a research protocol is six weeks. Just a few respondents declared having an electronic system to track submissions and review protocols. In addition to ensuring the quality of procedures, it is important to ensure the competence of REC members. More than ¾ of the NECs stated that they do not have requirements for the continuing education of their members, but many of them do have incentives to encourage training. In most of the countries, there is no assessment of the quality and the impact of training and networking activities.

In the majority of the respondent countries, RECs monitor studies after their approval. Generally, monitoring is carried out annually and in very rare cases more frequently. It should be noted that in almost 30% of the respondent countries, RECs carry out monitoring, but not in a systematic way.

Almost 70% of the respondent countries have declared that their RECs charge fees for reviewing protocols. If no policies regulating conflicts of interest are in place, payment could raise concerns. Most surveyed NECs reported having policies on conflicts of interest, but the situation is sometimes heterogeneous within a country (some RECs have policies, while others do not). In some countries, including in EURO, there are no specific policies for conflicts of interest, but, nevertheless, there are general measures related to official liability.

With regard to transparency, in about half of the respondent countries, there are systems for documenting complaints regarding RECs decisions.

Finally, most of the responding countries indicate that they require clinical trials registration, usually in their national clinical trials registry or in regional clinical trials registries. In many countries, clinical trials are required to be registered when the application is submitted to the REC. Many of them indicate that they have a publically accessible registry. In more than a half of the countries which have answered the question, information about ethics review is disclosed in the clinical trials registry.

A more complete analysis of the responses, along with information gathered from other sources, can be found in Annex 1. Tables containing raw data from specific countries are also available on request to the Global Summit Secretariat.

Case Study 1: Accreditation in Kenya

In 2011, Kenya's National Commission on Science and Technology (NCST) published the *Guidelines for the Accreditation of Ethics Review Committees in Kenya*. The accreditation process laid out in the *Guidelines* strives to standardize the "structures, capacities, and operational framework" of ethics committees in Kenya. The Guidelines require that each ethics committee (IERC) submit SOPs and a list of membership to the NCST. The NCST reviews these documents and determines whether the IERC meets the requirements for accreditation. The IERCs must meet membership criteria that are specified in the Guidelines, with regards to the number of committee members, gender distribution, and areas of expertise. IERCs are accredited for three years. Accreditation can be terminated if a committee fails to meet the standards set out by the NBC. IERCs must also submit an annual report to the NCST with information about changes in membership, protocols reviewed, questions about policy, areas of difficulty, and summary of other committee activities. [1]

[1] *Guidelines for Accreditation of Ethics Review Committees in Kenya*. National Council for Science and Technology, February 2011 (http://www.ncst.go.ke/index.php?option=com_rokdownloads&view=file&task=download&id=112%3Aguidelines-for-accreditation-of-ethics-review-committees-in-kenya&Itemid=90&lang=en, accessed 25 June 2012).

Case Study 2: Accreditation in the United Kingdom

The UK's National Research Ethics Service (NRES) oversees a three stage accreditation process for research ethics committees (RECs) in the UK. RECs first complete the Self-Assessment Tool (SAT), which reviews RECs' compliance with Standard Operating Procedures for Research Ethics Committees in the UK (SOPs) and the Governance Arrangements for NHS Research Ethics Committees (GAfREC). The second step of the accreditation process involves on-site review by the NRES. Training records, membership records, sample study files, accommodation, equipment, and office procedures are reviewed and the SAT is reviewed with Coordinator. Finally, the auditor conducts an observation of an REC meeting. An REC either receives Full accreditation or Provisional accreditation. RECs that receive Provisional accreditation must complete an action plan to receive full accreditation. Audit and accreditation are repeated every three years. [1]

[1] *Quality Assessment Accreditation Scheme for National Ethics Research Service*. NHS, May 2008.

Case Study 3: Quality assessment in the Netherlands

The Netherlands' Central Committee on Research Involving Human Subjects (CCMO) recently released the *CCMO Annual Report 2010,* which describes measures that have been instituted for assessing the quality of ethics review in the Netherlands. The CCMO oversees all accredited Medical Research Ethics Committees (MRECs) in the Netherlands. The CCMO monitors the MRECs through three different types of oversight: a priori oversight (assessment of regulations and committee membership); for cause oversight (response to incidents, reports, and signals); and continuous oversight (monitoring quality and continuity of MREC improvement). The CCMO implemented the continuous oversight system in 2010. Unlike the other oversight mechanisms, this new system is not based on regulatory oversight. Instead, it focuses on principles of ethical review, identifying problem areas, and encouraging MRECs to self-reflect.

The CCMO has adopted several mechanisms for enforcing oversight. If the CCMO identifies errors in the functioning of a MREC it may withdraw its accreditation, suspend its activities, or issue a warning. The CCMO has employed all of these measures. In 2010, the CCMO suspended the activity of two MRECs and later withdrew the accreditation of one of these MRECs.

The Netherlands also reformed its system for auditing ethics committees in 2010. Previously, the Netherlands Association of MRECs (NVMREC) audited MRECs. Beginning in 2010, this old audit system was replaced with a new intervisitation system whereby the CCMO and the NVRMEC audit MRECs through a coordinated effort.

In an effort to increase transparency, the CCMO began to publish annual reports of MREC activity on its website beginning in 2009. Since 2011, the CCMO has also published updated documents for complaints reporting on its website to facilitate companies and researchers in filing complaints with accredited MRECs.[1]

[1] *CCMO Annual Report*. Central Committee on Research Involving Human Subjects, 2010 (http://www.ccmo-online.nl/hipe/uploads/downloads_catc/CCMO%20jaarverslag%202010_Engels(1).pdfM, accessed 25 June 2012).

Case Study 4: Strengthening research ethics in Mexico through policy instruments

Since 2009, with the publication of the *National Guidelines for the Integration and Operation of Research Ethics* by the National Bioethics Committee *Committees* began a series of events that indicate a stage of significant development in this field.

The main objective of the *Guidelines* is: "to propose uniform criteria for the integration and operation of the Committees." From that stand, the CONBIOÉTICA intends to conduct a constructive dialogue with RECs and establish a process of continuous updating on bioethical issues that have particular relevance to research. The *Guidelines* were updated the following year, and minor modifications were made with respect to electronic references and biographical information about the CONBIOÉTICA[1].

In 2011, another element that strengthened the development of RECs and their standardization were amendments to the law. This reform, among other things, required that all medical care facilities in which research is carried out with humans establish RECs according to the criteria for operation laid out by the CONBIOÉTICA[2].

Also, during 2012 the CONBIOÉTICA has been dedicated to developing such criteria, as well as an update for the *Guidelines*, which will present significant changes for the harmonization of their ethical standards to the WHO guidelines.[3] These amendments include the addition of a specific section that will serve as guidance for researchers.

It is important to acknowledge the efforts to strengthen research ethics. Mexican law provides penalties for institutions that fail to comply with the provisions, so that there is a legal guarantee for the protection of human subjects involved in research and the existence of spaces to discuss the ethical dilemmas generated.

[1] *National Guidelines for the integration and operation of Research Ethics Committees.* Mexican National Bioethics Commission (http://cnb-mexico.salud.gob.mx/descargas/pdf/publicaciones/docutec/guiaceifinal.pdf).
[2] *Official Journal of the Federation* (http://www.dof.gob.mx/nota_detalle.php?codigo=5224260&fecha=14/12/2011).
[3] *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants*. WHO, 2011 (whqlibdoc.who.int/publications/2011/9789241502948_eng.pdf accessed 25 June 2012*).*

Case Study 5: Harmonization in Australia

The National Health and Research Council (NHMRC) is implementing a harmonized approach for ethical review through the Harmonisation of Multi-centre Ethical Review (HoMER) Initiative. Researchers who are conducting multi-center trials in Australia will only be required to submit their research protocol to one certified Human Research Ethics Committee (HREC) for review.[1] The HREC will evaluate the project's compliance to the National Statement on Ethical Conduct in Human Research (2007).[2] After a project is approved by an HREC, each participating institution will need to conduct a site-assessment and authorize the project.[1] Researchers will no longer need to seek ethical approval separately from each participating institution, which can be costly and time consuming.[3] During the initial development stage of HoMER, tools were constructed to support the National Approach to Single Ethical Review, including the National Certification Scheme, standardized participant information and consent forms, HREC template letters, and information on the roles and responsibilities of key stake holders in the new review system.[3]

[1] *Framework for Monitoring. Guidance for the national approach to single ethical review of multi-centre research*. National Health and Medical Research Council, January 2012 (hrep.nhmrc.gov.au/_uploads/files/Framework_for_Monitoring.pdf, accessed 25 June 2012).
[2] *The National Approach to Single Ethical Review*. National Health and Medical Rseearch Council (http://hrep.nhmrc.gov.au/national-approach, accessed 25 June 2012)
[3] *Harmonisation of Multi-centre Ethical Review (HoMER).* National Health and Medical Research Council (http://www.nhmrc.gov.au/health-ethics/harmonisation-multi-centre-ethical-review-homer, accessed 25 June 2012).

III. Summary of the reports by the U.S. Presidential Commission for the Study of Bioethical Issues

The Presidential Commission for the Study of Bioethical Issues released two reports on research ethics in 2011*: "Ethically Impossible": STD Research in Guatemala from 1946 to 1948* and *Moral Science: Protecting Participants in Human Subjects Research*. The first report discussed research on sexually transmitted diseases that was conducted in Guatemala during the 1940s with U.S. support. The researchers intentionally exposed 1,308 research participants to syphilis, gonorrhoea, and chanchroid without their consent. The research subjects included prisoners, soldiers, and psychiatric patients.[13] In October 2010, President Barack Obama apologized to the Guatemalan people for the research. He subsequently asked the Commission to conduct a historical and ethical assessment of the experiments conducted in Guatemala.[13] He also asked the Commission to investigate "if federal regulations and international standards adequately guard against the health and well-being of participants in scientific studies supported by the federal government."[13] This second topic was explored in *Moral Science: Protecting Participants in Human Subjects Research.*

Ethically Impossible: STD Research in Guatemala from 1946 to 1948

In its report, *"Ethically Impossible": STD Research in Guatemala from 1946 to 1948* the Commission concluded that the experiments in Guatemala were "gross violations of ethics as judged against both the standard of today and the researchers' own understanding of applicable contemporaneous practices."[13] In addition, the Commission reported that some of the researchers were "morally culpable and blameworthy for these wrongs" since there is evidence that the research team recognized the ethical considerations that applied to their work.[13] The Commission believes that the U.S. researchers had "ample authority, experience, and opportunity to have prevented moral wrongs from occurring."[13]

The standards for ethical human subjects research that are expressed in the bioethics literature, government documents, and international standards today include "informed consent… minimization of risks, a reasonable balance of risks and benefits, sound scientific justification, protection of privacy and confidentiality, and special protections for those who are particularly vulnerable, including minors, prisoners, and those with impaired decision making."[13] The researchers in Guatemala did not follow any of these standards, even though they were aware of at least some of them.[13] The experiments in Guatemala demonstrate that "the quest for scientific knowledge without regard to relevant ethical standards can blind researchers to the humanity of the people they enlist into research." [13]

[13] "*Ethically Impossible" STD Research in Guatemala from 1946 to 1948.* Washington, D.C., Presidential Commission for the Study of Bioethical Issues, 2011 (http://bioethics.gov/cms/sites/default/files/Ethically-Impossible_PCSBI.pdf, accessed 25 June 2012).

Moral Science: Protecting Participants in Human Subjects Research

In the Commission's second report, *Moral Science: Protecting Participants in Human Subjects Research*, the Commission reviewed regulations for human subjects research supported by the U.S. government that is conducted in the U.S. and abroad.[14] The Commission convened an International Research Panel—a panel of experts from ten different countries—to discuss international research standards and practices. The Panel's findings and recommendations are documented in *Research Across Borders: Proceedings of the International Research Panel of the Presidential Commission for the Study of Bioethical Issues*, and they also informed the recommendations in the *Moral Science* report.[14] In *Moral Science: Protecting Participants in Human Subjects Research*, the Commission concludes, "the current US system provides substantial protections for the health, rights and welfare of research subjects, and in general, serves to 'protect people from harm or unethical treatment.'"[14]

The Commission identified several areas for improving human subjects research protections. Their recommendations are targeted towards governments, research investigators, scientists, and other parties that are involved with research.[14] The Commission's fourteen recommendations broadly discuss:

- Recommendation 1: improving accountability through public access to ongoing study information;
- Recommendation 2: supporting more studies on the effectiveness of human subjects protections, and ethical and social considerations of protections;
- Recommendation 3 and 4: constructing a framework and programme to compensate or treat individuals who suffer research related injuries; the Commission also recommended that the US Federal Government report on their decision to create a system for compensation or their decision to maintain the status quo;
- Recommendation 5: creating a culture of responsibility by clarifying and making the ethical foundation of regulatory requirements explicit—so that the rationale and context of applicable guidelines are clear;
- Recommendation 6: clarifying responsibilities of investigators in the US Common Rule (the US policy and legislation for human subjects research);
- Recommendation 7: supporting more research ethics education and discourse;
- Recommendation 8: instituting a mechanism to recognize equivalent protections in other countries based on the procedural requirements of the Common Rule;
- Recommendation 9: promoting community engagement as a way to understand and take into account the community norms, beliefs, customs and cultural sensitivities in the research process;
- Recommendation 10 and 11: justifying site selection; sites where studies are to be done should have or be assisted to acquire capacity for human subjects protection, and responsiveness of research to local needs should be a consideration in selecting a study site;
- Recommendation 12: ensuring ethical study designs for control trials;

[14] *Moral Science: Protecting Participants in Human Subjects Research.* Washington, D.C., Presidential Commission for the Study of Bioethical Issues, 2011 (http://bioethics.gov/cms/sites/default/files/Moral%20Science%20%28Updated%202012%29.pdf accessed 25 June 2012).

- Recommendation 13: promoting the US Federal Government's current reform efforts;
- Recommendation 14: requesting that the US government to follow up on the Commission's recommendations and justify changes they make in response to the recommendations or maintenance of the status quo.[14]

IV. Discussion on conflicts of interest in research

A financial relationship[15] is the clearest example of an interest that could potentially compromise judgements and decisions that need to be made impartially. However other conflicts may arise, for example, from personal or professional relationships, opportunities for career advancement or desire for recognition of achievements. Such conflicts apply equally to an individual researcher, research teams, and institutions in which research is undertaken. Additionally there is recognition that a *perception* of a conflict of interest may be just as serious a challenge to the integrity of those conducting research. Conflicts of interest in the research area are common and it is important that they are disclosed and dealt with properly.

Guidance should be provided to RECs in regards to identifying conflicts of interest and appropriate measures to minimize their impact on research. For example, in Australia such guidance is provided by the *National Statement on Ethical Conduct in Human Research*.[16] This document includes information on:

1. Where conflicts exist:

   "A conflict of interest in the context of research exists where:

   - a person's individual interests or responsibilities have the potential to influence the carrying out of his or her institutional role or professional obligations in research; or

   - an institution's interests or responsibilities have the potential to influence the carrying out of its research obligations."[16]

2. Adopting measures to manage conflicts of interest involving researchers, which may include requiring that:
   a) "the information be disclosed to research participants;
   b) a person other than the researcher make the initial approach to participants;
   c) the information be disclosed in any report of the research;
   d) the research be conducted by another researcher; or
   e) the research not be conducted."[16]

3. Levels at which conflict may occur:
   "Institutions should establish transparent process to identify and manage actual and potential conflicts of interest involving:
   a) the institution itself;
   b) researchers; or
   c) ethical review bodies, their members or advisors."[16]

[15] For a review on this subject see Trudo L paper (Annex 1) in *Research ethics committees Basic concepts for capacity building*. Geneva, World Health Organization, 2009.
[16] *National Statement on the Ethical Conduct of Human Research.* Canberra, National Health and Medical Research Council, 2007 (http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e72.pdf, accessed 29 May 2012)

The final point is important to emphasize, while it is generally acknowledged that researchers and research institutions may have conflicts of interest, there is sometimes less consideration given to the potential conflicts of interest that may exist for a REC as a whole, or for individual members.

Such conflicts may rise from the setting of the REC. Those established within a research institution, to review applications from that institution have a potential conflict of interest. There may be, or at least the perception may be, that the REC is under some pressure to approve research in the organization— research that may bring large amounts of funding, or prestige to the institution. Similar concerns have been raised in relation to for-profit RECs[17] and whether a fundamental conflict of interest exists with these groups, given that their continued existence and financial well-being may depend upon payment from organizations whose applications they review. Pressure to approve research applications may also come from government bodies eager for research to be undertaken in their jurisdiction.

Conflicts of interest may also occur for committee members within a REC. Within a research institution REC members may have working collaborations with applicants. They may benefit from research being approved through access to equipment purchased from research funds, or from the institutional prestige that accompanies some research projects. Members may feel that their own career may be jeopardized if they hinder research being undertaken by senior colleagues.

Concerns over conflicts of interest involving RECs, or committee members, can be addressed through:

- composition of committees— ensuring adequate representation by those who have no affiliation with organizations that sponsor, fund or conduct research reviewed by the REC and
- policies ensuring the independence of the committee.[18]

When establishing new RECs, or in the oversight and quality assurance of current RECs, these issues should be taken into consideration.

[17] Emanuel, E.J., T. Lemmens, and C. Ellio (2006)t, Should Society Allow Research Ethics Boards to Be Run As For-Profit Entrprises. *PLoS Med*,. **3**(7:e309):0941-0944.
[18] *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants.* (Standard 4) Geneva, World Health Organization, 2009 (http://whqlibdoc.who.int/publications/2011/9789241502948_eng.pdf, accessed 09 May 2012).

Case Study 6: Conflicts of interest regulations in Canada

The *Tri-Council Policy Agreement on the Ethical Conduct for Research Involving Humans* (2010) addresses conflicts of interests that arise within Research Ethics Boards (REBs). It provides examples of conflicts of interests and describes REB members' obligations when conflicts of interest arise. REB members must disclose conflicts of interest and withdraw from discussions and decisions about the projects with which they have a conflict of interest. If the REB member in question is the only person with relevant scientific expertise, the REB may seek his expertise. However, the interaction must be recorded and the REB member should not be present when the REB makes a decision about the project.[1]

[1] *Tri-Council Policy Statement: Ethical conduct for Researching involving Humans*. Canadian Institute of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, 2010 (www.pre.ethics.gc.ca/pdf/eng/tcps2/TCPS_2_FINAL_Web.pdf, accessed on 25 June 2012).

Case Study 7: Conflicts of interest regulations in the Netherlands

In 2010, the Netherlands' Central Committee on Research Involving Human Subjects (CCMO) modified the directive for Expertise requirements (WMO) for members of MRECS (February 2007). The CCMO no longer considers it acceptable for employees of an MREC secretariat to be members of the MREC for which they work. Since employees of an MREC secretariat are in close contact with applicants of medical research their ability to act as independent committee members may be compromised.[1]

[1]*CCMO Annual Report*. Central Committee on Research Involving Human Subjects, 2010 (http://www.ccmo-online.nl/hipe/uploads/downloads_catc/CCMO%20jaarverslag%202010_Engels(1).pdfM, accessed 25 June 2012).

V. Discussion on special consideration for the involvement of vulnerable populations in research

When conducting research with 'vulnerable groups' researchers should clearly demonstrate how they will respect participants. The central concern here is respect for individual as well as individual decision-making. These ideas are related to a range of ethical concerns, including the recognition of, and respect for, the inherent value of persons, recognition of the value of self-determination to the well-being, happiness and moral development of individuals, and respect for individual freedom, including freedom of choice.

However, while respect for persons emphasizes self-determination, autonomy and individual choice, it should not be taken to exclude respect for those whose capacities for self-determination and the exercise of personal choice are compromised or absent (often termed vulnerable participants or groups). A person in this situation should still be treated with the respect due to persons as described above. This may involve protecting or promoting their remaining capacity for autonomy, respecting prior expressions of self-determination, and protecting the person against exploitation, discomfort and harm.

As an example of what groups may be considered vulnerable, for research undertaken in Australia, the ethics framework outlined above would be expected to apply to research involving, *inter alia*:

- Women who are pregnant and the human fetus;
- People who may be involved in illegal activities;
- People highly dependent on medical care;
- People with a cognitive impairment, an intellectual disability, or a mental illness;
- People in dependent or unequal relationships;
- Children and young people;
- Aboriginal and Torres Strait Islander People (First Nations groups); and
- People in other countries.[19]

In review of research applications involving vulnerable groups there is often a strong emphasis on the issue of informed consent; on the provision of sufficient information to potential participants, on lack of coercion and on the consent process. However consideration should also be given to populations that may not fall in to the above categories, who are mentally and physically capable of giving consent, but who may also be considered vulnerable. For religious, cultural, or economic reasons, for example, consent may be given which is not truly autonomous. If an elder gives consent for research to be carried out in their community how free are community members to then individually decline participation? When the only access to medical help is via involvement in a research study, again, how autonomous is such consent? Issues such as these should be considered in ethical review and may impact site selection of research projects.

[19] *National Statement on Ethical Conduct in Human Research*. Canberra, National Health and Medical Research Council, 2007 (http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e72.pdf, accessed 29 May 2012).

Case Study 8: Protections for Aboriginal and Torres Straight Islanders in Australia

In Australia a separate document has been produced specifically for those researchers conducting health research with Aboriginal and Torres Strait Islander (ATSI) groups - *Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research*.[1]This document was created following submissions by ATSI communities, as well as researchers and health organization working with these communities, that separate guidance was required, supplementary to the National Statement covering all Australians. From its inception to finalization the document was a joint effort with ATSI groups, and was based on their experiences, values and world views.

The guidelines are based on six (6) values:

1. Spirit and Integrity - an overarching value that binds all others into a coherent whole.
2. Reciprocity - inclusion and recognition of partners' contributions. Researchers demonstrate a benefit for the community which contributes to its cohesion and survival. Communities have the right to define the benefits according to their own values and priorities.
3. Respect - acknowledgment of the right of people to have different values, norms and aspirations. Respect for, and understanding of, the consequences of research for the community.
4. Equality - research should seek to advance the elimination of inequalities. All partners in the research process should be treated equally; all benefits of the research should be distributed equally.
5. Survival and Protection - of communities and the collective identity, recognizing the importance of the personal and collective bond within ATSI communities.
6. Responsibility - research proposals must take into account aspects of responsibility including doing no harm and accountability. As an example this may include issues of transparency in the exchange of ideas, negotiations regarding methodology, dissemination of results, potential outcomes and benefits.

[1] *Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health*. National Health and Medical Research Council, 2003 (www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e52.pdf, accessed 25 June 2012).

VI. Points for discussion at the Global Summit

The scope and range of research involving humans has changed enormously since the formulation of the *Nuremberg Code*. Funding sources have moved from government bodies to commercial companies, from millions of dollars to a multibillion dollar industry. Single site research is giving way to multicentre studies. The challenge for NECs is to ensure that their RECs remain relevant to their stakeholders; the governments and other bodies who sponsor research, to those that conduct research and to the public who are potential participants in research and the ultimate consumers of research.

The following points are raised for discussion, in an effort to ensure the relevance, and accountability, of RECs:

- Registration, accreditation and monitoring of RECs
- Cooperation or collaboration between REC, including harmonization of protocols and procedures of RECs
- Multisite research— single ethical approval, application of relevant norms or laws across national boundaries. Can the legal term “equivalent protection” be used in these cases?
- How to introduce the concept of accountability in the REC's work?
- Working with vulnerable groups— how to define vulnerable persons, should there be a standard definition?
- What are the risks involved in carrying out collaborative research in places/countries with weak or nonexistent enforcement of their laws, endemic institutional corruption, and governance problems in general?
- According to the final report on the Questionnaires, 86% of RECs are charging fees, does this create a “conflict of interest,” if so, what can be done? Who should pay the REC members? Researchers, the institution where they work, the government, no one?
- Minimal educational and training standards for REC members. Who will provide it? Who will pay for it?

Annex.

Report on the analysis of RECs questionnaires

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This report refers to the analysis of questionnaires provided by National Ethics Committees (NEC) regarding Research Ethics Committees (RECs), as of February 2012. These questionnaires have been prepared by the Working Group of NECs on Research Ethics, established in preparation for the 9th Global Summit of National Ethics Committees, to be held in Tunisia in September 2012. The aim of this survey is to provide data for a Background Paper focusing on ethical issues related to RECs and clinical trial registration to be published on the website of the Global Summit in June 2012. The questions relate to the systems for ethics review of research (e.g. RECs accreditation, handling complaints and conflicts of interest.) In January 2012, the questionnaire was sent to NECs of 86 countries listed in the WHO database (ONEC). As of mid-April, 22 % of the surveyed countries provided answers. The 19 countries include: Burkina Faso, Nigeria, Uganda, Jamaica, Mexico, India, Nepal, Belgium, Denmark, Finland, Italy, Lithuania, Luxemburg, Russia, Lebanon, Sudan, Tunisia, Indonesia and Philippines.

To get a more representative overview for each region, additional data was gathered from reports made by the European Forum for Good Clinical Practices (EFGCP)[20],[21] and by the US Presidential Commission for the Study of Bioethical Issues[22]. The additional countries included from these reports are: Argentina, Bolivia, Brazil, Canada, Chile, Columbia, USA, Austria, France, The Netherlands, Switzerland, Turkey, UK, Australia, China and Japan.

Complete responses of each country and additional information that could not be summarized in this report can be found in the tables attached. This refers, in particular, to the list of norms governing ethics review of research, the description of the system for accreditation of RECs and the agencies at the national level responsible for oversight of health research; the procedure for the establishment of RECs, REC registration.

1. System for ethics review of research

a. Norms governing ethics review of research (binding and non-binding) and their enforcement

The situation about the existence of norms governing ethics review of research (binding and non-binding) and their enforcement is very heterogeneous among countries and regions.

[20] EFGCP, *Report on Data on Research Ethics Committees in Seven Countries Outside Europe*, July 2010

[21] EFGCP, *The EFGCP Report on The Procedure for the Ethical Review of Protocols for Clinical Research Projects in Europe,* April 2011

[22] US Presidential Commission for the Study of Bioethical Issues, International Research Panel, *Research across borders*, September 2011

Sub Saharan African countries surveyed (Burkina Faso, Nigeria and Uganda) indicate that they have laws governing ethics review of research and that they are being enforced.

Most of the Latin American countries analysed (Argentina, Bolivia, Chile, Columbia, Jamaica and Mexico) do not have specific laws, but provisions, which are not always being enforced. In particular, in most of these countries, there is no punishment for violating these norms and there is no mechanism to monitor and control the current regulations.

In the countries from the South East Asia (India, Indonesia and Nepal), guidelines and specific laws--where they exist—seems to be enforced. One of these countries underlines the fact that registration of RECs is important for the enforcement of norms governing ethics review of research, especially when the countries have no laws, but only provisions.

The European countries (Belgium, Denmark, Finland, Italy, Lithuania, Luxemburg, Russia, Switzerland and the United Kingdom) have laws which are being enforced.

In the Eastern Mediterranean Region (Lebanon and Tunisia), one country indicates having binding norms which are being enforced, while the other has no binding regulations.

Philippines indicates that their norms (non-binding and binding, where available) are being enforced.

Most of these norms were passed during the last 15 years.

b. RECs certification/accreditation, national agency responsible for oversight and their role in oversight

RECs are rarely certified / accredited. The situation in WHO regions is the following:

- In the AFRO region, two of the three surveyed countries (Burkina Faso, Nigeria and Uganda), have a system in place for registration/accreditation of RECs. All these countries have an established agency responsible for oversight of health research which plays a role in the oversight of RECs.

In two of the three AMRO countries analysed (Brazil, Jamaica and Mexico) there is no system for certification/accreditation of RECs in place.

- In the two SEARO countries surveyed (Nepal and India), one of the respondent countries has a well established agency which plays a role in monitoring.
- 70 % of EURO countries analysed (Belgium, Denmark, Finland, France, Italy, Lithuania, Luxemburg, The Netherlands, Russia, Switzerland and UK) do not have a system for certification/accreditation of RECs. About half of these countries have an agency, the majority of which play a role in monitoring and oversight of health research and protection of human subjects.
- The accreditation practices in EMRO and in WPRO are unclear. In EMRO, the three countries analysed (Lebanon, Sudan and Tunisia) indicate they have an established agency, which plays a role in oversight. For WPRO, half of the

countries analysed indicate they have an established agency, which aids in oversight.

Where a system exists, one of the common criteria for accreditation includes the functionality of the structure and membership of the REC.

2. REC establishment

Almost 80 % of the respondents have stated that their RECs have common standards operating procedures and policies.

The size of REC membership varies from 5 to 28, with an average of 10.

3. REC performance

Full-time staff in RECs' secretariats

About half of the respondent countries have full time staff in their RECs. 20 % of the countries have full time staff only in their NEC. For the respondents who have full time staff, the average is one-three staff members per REC and up to four, for NECs. The staff members include secretaries, lawyers, nurses, social scientists. The remaining RECs have part time staff.

*Average time RECs take to reach a final decision about a research protocol*The average time is 6 weeks, with differences depending on the REC: from 1 week (2 countries) to 3 months

Fees for review of protocols

68 % of the respondent countries have declared that their RECs charge fees.

Records of deliberations

Most of the RECs keep proper records of their deliberations and decisions (minutes or reports), often confidential.

Communication between RECs and National regulatory authorities (NRA)

Often by regular reports, letters or email, or by regular meetings.

Electronic tracking of submissions and reviews of protocols

About 33 % of the respondents have an electronic system to track submissions and reviews of protocols, mostly MS Word, Excel or other ordinary database softwares.

Monitoring of RECs

In about 40 % of the respondent countries, RECs are regularly monitored. There is no monitoring in the analysed countries from AFRO and AMRO. In Europe, 67 % of the RECs are monitored. RECs performance is usually monitored by National Ethics Committees, sometimes by the Ministry of Health.

Monitoring of approved studies by RECs

In 18 % of the respondent countries RECs do not monitor studies after their approval. In almost 30 % of the respondent countries, RECs carry out monitoring but they do not do it in a systematic way. In 41 % of the respondent countries, monitoring is carried out annually, often through progress reports. 25 % of the respondent countries reported that even though there is a general requirement for

annual reports, this is not done in all cases. In 10 % of the responded countries, monitoring is carried out every six months or monthly.

4. REC registration

Registering system

About 40 % of the respondent countries have a system for registering all RECs in their territory. About 38 % lack any system, although almost 35 %, have plans to create a REC registry. 24 % of the respondents, all in EURO, stated that there is no need for registration, as RECs are not formed on a voluntary basis, but rather, are established and regulated by law.

For almost all the countries which have a system for registering or have plans to create it, the REC registry is operated (or will be operated) by the National Ethics Committee. These registries are mostly funded by Governments and Ministries of Health.

5. REC training and networking

About 23 % of the NEC stated that there is a requirement for continuing education of members of RECs, especially respondents from AFRO and WPRO. For many countries that do not have a requirement for continuing education, there are measures encouraging RECs members to undergo regular training, especially in AMRO, SEARO, EURO and WPRO.

For most of the countries (84 %), there is no assessment of the quality and the impact of training and networking activities.

6. Specific procedures

Jurisdiction of RECs

There are diverse jurisdictions for RECS: country (Ministry of Health), regions or districts, research institutions, universities, health-care institutions, either private or public.

Joint review of protocols and acceptance of ethics review from another REC

Almost 70 % of the respondent countries do not carry out any joint review of protocols.

Almost 55 % of the respondent countries have declared that their RECs do not accept ethics review from another REC.

7. Clinical trial registration

Most of the responding countries indicate that clinical trials are required to be registered, usually in their national clinical trial registry (especially for countries from AMRO, EURO and EMRO). Oftentimes, in Africa and to some extent, in Europe clinical trials are registered in regional registries.

In many countries (8/15), especially in EURO, clinical trials are required to be registered when the application is submitted to RECs. In a few cases, mostly in AFRO and in EURO, registration is required after the approval by REC. Many of these countries (almost 65 %), particularly in AFRO and EURO regions, indicate they have a public accessible registry.

Information about ethics review is sometimes disclosed in the clinical trial registry: 54 % of the 13 countries which have answered this question: Burkina Faso, Nigeria, India (name and contact details of REC), Denmark (the final decision is written in the database, but there is not public access), Lithuania, Lebanon and Tunisia.

8. Handling complaints and conflicts of interest

Systemic documenting complaints about RECs decisions

In about half of the respondent countries, there is a system for documenting complaints regarding RECs decisions. None of the surveyed countries from EMRO have any system for documenting complaints. The system varies among countries: the complaints can be part of records kept by the RECs and published in an annual report. In about 40 % of the countries which allow complaints, the complainants can apply to the NEC within 15-31 days from the receipt of the decision.

Conflict of interest

Most surveyed NECs reported having policies on conflicts of interest, particularly in countries in AFRO, AMRO, SEARO and EURO. They usually have such policies both for REC members and for researchers. It should be noted that in some countries the situation is heterogeneous (some RECs have policies, while others do not) and in others, including countries in EURO, there are no specific policies for conflicts of interest, but, nevertheless, there are general measures related to official liability.