



# **Report on Data on Research Ethics Committees in Seven Countries Outside Europe**

## **Final Report**

### **Introduction**

In October 2009, the European Forum for Good Clinical Practice (EFGCP), Ethics Working Party (EWP), produced a report for the UK National Research Ethics Service (NRES) based on its own report entitled *The Procedure for the Ethical Review of Protocols for Clinical Research Projects in the European Union*. The original EFGCP report provided answers to 35 questions, arranged country-by-country, from 26 countries. These were the 24 of the 25 member states that comprised the European Union at the time, plus Norway and Switzerland, but not Luxembourg which operated in the same way as Belgium. The report has been updated on the EFGCP website ([www.efgcp.eu](http://www.efgcp.eu)) on an annual basis, now expanded to cover 31 countries, with two additional questions referring to research involving children and four additional questions relating to the conduct of research ethics committee meetings.

The October document produced for NRES reformatted several of the questions included in the updated EFGCP report on a question-by-question basis and then went on to cover other aspects of some representational national ethical review processes, but did not extend beyond Europe. Again at the behest of NRES, the exercise has been extended further to cover Australia, Brazil, Canada, China, India, Japan and the USA.

The same questions which featured in the October 2009 report are addressed:

- 1 How are research ethics committee members appointed?
- 2 How many research ethics committees are there that are recognised for the review of clinical trials with investigational medicinal products (CTIMPs) for multi-site and single-site trials?
- 3 Do RECs reviewing CTIMP applications also review other projects or do different RECs review projects that are not CTIMPs?
- 4 How many members serve on a research ethics committee?
- 5 How many members constitute a quorum?
- 6 What backgrounds and/or qualifications of members are actively sought?
- 7 How do RECs obtain specialist expertise?
- 8 What training requirements are there for members of RECs?

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

- 9 What training facilities are provided or are available for members of RECs?
- 10 How do RECs assess the progress and outcome of research projects that they have approved?
- 11 Do RECs invite or allow a) applicants or b) observers to attend committee meetings? Are the minutes of an REC made public?
- 12 Is there any scope for Chairman's actions in between meetings? Do RECs ever use subcommittees for anything?

Inevitably, short of professionally editing the various responses received from the contacts EFGCP has established in these seven countries, the length and style of the answers to these questions, country-by-country, vary considerably. Nevertheless, the information they contain enables the review process for which NRES is responsible in England (reflected through UKECA in the United Kingdom as a whole) to be compared with the equivalent process in each of these seven countries, confirming what has already been shown in Europe that the UK REC process is robust and fit for purpose.

1. How are research ethics committee members appointed?
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### **Australia**

Human Research Ethics Committees (HRECs) are established by organisations which are responsible for adequately resourcing them and ensuring that they operate in accordance with the National Statement on Ethical Conduct in Human Research (2007). The Statement is jointly produced by the National Health and Medical Research Council, the Australian Research Council and the Australian Vice-Chancellors' Committee.

It is available in pdf format at

<http://www.nhmrc.gov.au/files/nhmrc/file/publications/synopses/e72-jul09.pdf>.

Hence, the primary responsibility for monitoring the activities of an HREC rests with the organisation(s) that established it. HRECs are required to report their compliance to the National Statement on an annual basis [NS 5.7].

HRECs are usually established by organisations (public, not-for-profit or private) that conduct research involving humans. Universities and hospitals are the most common of these organisations. Not all organisations that conduct research, however, have their own HREC. Some organisations and individual researchers use the services of HRECs within other organisations. Not all HRECs are established by organisations that conduct research. Some organisations have established an HREC to provide the service of ethical review to researchers who do not have an HREC at their own organisation. However, most of them are similar to the United States model of Institutional Review Boards.

### **Brazil**

The structure for the ethical review of research projects involving human subjects was first in October 1996 when Brazil officially adopted guidelines on human experimentation (Resolution CNS-196/96). This led to the establishment in 2000 of the National Commission for Research Ethics (CONEP). This Commission is responsible for accrediting committees for research ethics (CEPs) which are established by universities, academic institutions and medical organizations, in most cases concerned with research in the fields of medicine, dentistry, nursing, psychology and other health sciences.

CONEP itself is a multidisciplinary committee composed of professionals from areas including health, multiple area researchers, bioethics specialists, jurists and others. It is responsible for making rules for research involving human beings in Brazil, acting as a network for the CEPs (the equivalent of IRBs or research ethics committees) where research is being conducted. CONEP is also responsible for the establishment of CEPs, their approval and registration, continuously monitoring their activities. CONEP also advises many governmental areas regarding any ethical issue related to human research.

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

According to the Brazilian government Resolution 370 of 2008 the working conditions for CEPs comprise:

1. The location and hours of operation of the CEP must be defined so that researchers and people who are the subject of research may contact the CEP.
2. There must be a dedicated office with appropriate physical space and facilities in order to maintain the security of confidential documents.
3. Minutes must be approved.
4. Institutions must have an archive facility to maintain related documentation for at least 5 years.
5. The meetings of the CEP must happen at least once a month.
6. The administration of the CEP must be assigned to a unique and designated officer.
7. Internet access equipment must be provided for the exclusive use of the CEP.
8. Exclusive furniture, telephone and facsimile facilities, and all necessary office materials must be provided for the CEP.

### **Canada**

In Canada there is neither national Research Ethics Board (REB) accreditation nor central governance in place. Although there is strong recommendation to institute such a system, it does not appear imminent. As a primary responsibility, REB members are the gatekeepers charged with determining whether to approve the conduct of each clinical trial in Canada. The responsibility for protection of research participants rests at the local REB level. Many REBs in Canada are maintained as volunteer-service committees often with a high membership turnover rate. There is neither formal REB training nor a mandated continuing education process in Canada. At the same time, there is an expectation of REB accountability for ensuring patient safety and protection.

The process of REB member appointment varies broadly. The members are appointed in a number of ways, depending mostly on who is “hosting” the REB. If it is a hospital it may be the VP of research, for example, or the head of the Medical Advisory Committee. In the university setting it may be the Governing Council.

Canada’s national research guidance document, The 1998 *Tri-council Policy Statement (TCPS) Ethical Conduct for Research Involving Humans*<sup>i</sup>, guides research that is undertaken in any institution that receives funding from any of the three federal funding councils, the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada (NSERC), or the Social Sciences and Humanities Research Council of Canada (SSHRC). If, for example any institution is found to be non-compliant they may lose their funding for all nationally funded research, not only the clinical research activities.

This document is very well written and serves as tremendous guidance for Canadians involved in research; however, it is not legislation. The TCPS was 10 years old therefore the second draft is in its final stages (Heather Sampson was one of the writing/editing team for the new version in 2008). The following is taken from the current TCPS:

*B1. Authority of the REB*

Article 1.2

*The institution in which research involving human subjects is carried out shall mandate the REB to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects that is conducted within, or by members of, the institution, using the considerations set forth in this Policy as the minimum standard.*

*The authority of the REB should be delegated through the institution's normal process of governance. In defining the REB's mandate and authority, the institution must make clear the jurisdiction of the REB and its relationship to other relevant bodies or authorities. Institutions must ensure that REBs have the appropriate financial and administrative independence to fulfil their primary duties.*

*Institutions must respect the authority delegated to the REB. The institution may not override negative REB decisions reached on grounds of ethics without a formal appeal mechanism as set out below. Institutions may refuse to allow certain research within its jurisdiction, even though the REB has found it ethically acceptable.*

*Each institution is accountable for the research carried out in its own jurisdiction or under its auspices. An institution can authorize its REB(s) to accept the review of other REBs constituted under the Tri-Council Policy Statement if it so wishes. This might involve specific agreements between institutions for sharing the work.*

**China**

The State Food and Drug Administration takes responsibility at national level. However, each provincial and municipal health authority supervises and administers the local research ethics committees, some of which are based on institutions.

Members of institutional research ethics committees should be chosen from fields such as biomedicine and management, ethics, law, sociology, etc. after opinions have been sought widely by the organizations and institutions that are to have such research ethics committees. Each research ethics committee should have a chairperson and vice chairperson, who are elected by members of the committee and who can be re-elected.

**India**

Currently Research Ethics Committees are not required to be registered with any authority.

The Schedule Y is proposed to be amended – with the introduction of Schedule Y3 wherein Research Ethics Committees in the country will have to be registered with the office of the Drug Controller General of India.

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

Additionally, the Biomedical Research Authority will be set up under the proposed Bill on Biomedical Research on Human Participants (Promotion and Regulation) which would require that all IECs register with this Authority. It will also evaluate and monitor functioning of the IECs, and develop mechanisms for enforcing accountability and transparency by the institutions

**Japan**

Japanese GCP mandates that a research ethics committee must be established by every institution where clinical trials are conducted, unless that institution is too small to operate its own REC in which case the head of that institution can designate a REC established by another institution. Supervision and management of each REC is a responsibility of the head of each institution.

Once a chairman of an REC is appointed by the institution, that chairman appoints the other members (see 6 below).

**USA**

The US Food and Drugs Administration (FDA) is responsible for requiring institutional review boards (IRBs) to review clinical trials for investigational medicinal products. The Office of Human Research Protections (OHRP) requires that all US Federal funded human research be reviewed by an IRB. The OHRP registers IRBs for both the FDA and the OHRP. Registration is not accreditation.

2. How many research ethics committees are there that are recognised for the review of clinical trials with investigational medicinal products (CTIMPs) for multi-site and single-site trials?

**Australia**

There are about 220 HRECs in institutions and organisations across Australia.

**Brazil**

The number of CEPs registered at CONEP by March 2010 is 601.

Considering that CEPs usually have 10 reported members, there are up to 6,000 people involved in the research ethical review process.

Up to 17,000 research projects are submitted to the process each year with up to 40 volunteers in each one, what means up to 680,000 people protected.

**Canada**

The answer to this question is that we simply do not know how many REBs there are in Canada. The best information that we have is the following link that is self-reporting and not particularly reliable: [http://www.ncehr-cnerh.org/english/reb\\_e.php](http://www.ncehr-cnerh.org/english/reb_e.php).

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

In Quebec there is mandatory REB registration to the FRSQ (provincial research funding body) in addition to annual reporting that suggests over 100 institutional REBs exist; however, this does not include private REBs who may voluntarily register.

**China**

There are more than 300 RECs in China, but the accurate number is unknown.

**India**

It is not known how many RECs there are in India, but this will become known when REC registration is made compulsory.

**Japan**

The total number of RECs is not listed, but it is estimated that there are about 120.

**USA**

There are more than 6,100 IRB registered with the OHRP. Approximately 25% of these are from outside of U.S., but the exact number of IRBs is not known as some IRBs are not registered.

3. Do RECs reviewing CTIMP applications also review other projects or do different RECs review projects that are not CTIMPs?

**Australia**

HRECs play a central role in the Australian system of ethical oversight of research involving humans. HRECs review all research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

**Brazil**

The CEP-CONEP system is responsible for assessing and monitoring of all research involving human subjects, defining research as any kind of study, individually or collectively, in which human subjects are involved, directly or indirectly, in part or in full, including the handling of information or materials.

**Canada**

There are a variety of research ethics review boards and committee functions; for example at the Hospital for Sick Children (equivalent to Great Ormond Street) they review all manner of trials and studies whether they are social studies research or biomedical research. Other examples of REBs and Review Boards include those geared to specific types of research, such as oncology or HIV REBs, Social Science, Humanities and Education REBs. Some of the university REBs review only the social

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

sciences as they do not host medical schools. There is no significant reportable difference between hospital and university REBs.

**China**

Generally, RECs not only review CTIMPs but also review other projects, such as organ transplantations and reproduction technology, etc.

**India**

Research ethics committees are allowed to review studies that are not clinical trials, but they are not required to do so.

**Japan**

Most universities usually operate two RECs. The one which reviews CTIMPs is called “Chiken-Shinsa-Iinkai”, Chiken means Clinical trial, Shinsa means Review and Iinkai means Committee in Japanese. The other REC reviews other research projects involving human subjects. Both types of REC may operate with sub-committees.

**USA**

Yes, some IRBs review for both. They are registered with the OHRP (the Office for Human Research Protection).

4. How many members serve on an REC?
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**Australia**

The minimum membership of an HREC is eight. As far as possible there should be equal numbers of men and women and at least one third of the members should be from outside the institution for which the HREC is reviewing research.

The minimum membership is

- a chairperson, with suitable experience, whose other responsibilities will not impair the HREC’s capacity to carry out its obligations under the National Statement;
- at least two lay people, one man and one woman, who have no affiliation with the institution and do not currently engage in medical, scientific or legal work;
- at least one person with knowledge of, and current experience in, the professional care, counselling or treatment of people; for example, a nurse or allied health professional;
- at least one person who performs a pastoral care in a community; for example, an Aboriginal elder, a minister of religion;
- at least one lawyer, where possible one who is not engaged to advise the institution; and
- at least two people with current research experience that is relevant to research proposals to be considered at the meetings they attend. These two members

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

may be selected, according to need, from an established pool of inducted members with relevant expertise.

No maximum number is specified, but institutions are encouraged to establish a pool of inducted members in each category.

**Brazil**

A CEP must be established by a college party with a number not less than 7 reported members. A CEP must comprise professionals from areas such as health, exact sciences, social sciences and human sciences including, as an example, jurists, theologians, sociologists, philosophers, bioethicists and, at least, a member of society, representing the institution. This can vary depending on the particular CEP aspects and characteristics and the kind of research to be developed. It will have responsibility for assessing the ethical aspects of a project, across all disciplines. Not more than half its members may belong to the same professional category including both genders. It may call on ad hoc consultants either belonging to the institution, or independent, so as to provide appropriate technical information.

**Canada**

Following TCPS guidelines the following quoted material is applicable:

Article 1.3

The REB shall consist of at least five members, including both men and women, of whom:

- a. At least two members have broad expertise in the methods or in the areas of research that are covered by the REB;
- b. At least one member is knowledgeable in ethics;
- c. For biomedical research, at least one member is knowledgeable in the relevant law; this is advisable but not mandatory for other areas of research; and
- d. At least one member has no affiliation with the institution, but is recruited from the community served by the institution.

These basic membership requirements are designed to ensure the expertise, multidisciplinary and independence essential to competent research ethics review by REBs. The concept of independence implies that members of the REB under Article 1.3(a-c) should contain a majority of those whose main responsibilities are in research or teaching. The institution may need to exceed these minimum requirements in order to ensure an adequate and thorough review. The Agencies consider it essential that effective community representation be maintained. Thus, as the size of an REB increases beyond the minimum of five members, the number of community representatives should also increase.

The majority of members of an REB should have both the training and the expertise to make sound judgements on the ethics of research proposals involving human subjects. The terms of REB appointments should be arranged to balance the need to

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

maintain continuity with the need to ensure diversity of opinion and the opportunity to spread knowledge and experience gained from REB membership throughout the institution and community.

Because the REB should reflect the ethical values of this Policy in the context of the society within which it operates, its membership should be broad enough to reflect that society. The members of the REB therefore play different but complementary roles. Article 1.3(a) indicates that general expertise in the relevant sciences or research disciplines is essential. Article 1.3(b) requires a member knowledgeable in ethics, so as to alert the REB to potential ethics issues and options.

The role of the member knowledgeable in the applicable law is to alert REBs to legal issues and their implications, not to provide formal legal opinions nor to serve as legal counsel for the REB. An understanding of relevant legal issues and contexts is advisable for all REBs, although for non-biomedical research such insights may be sought from someone who sits on the REB only for specific research projects. The institution's legal counsel should not be a member of the REB.

The community member requirement of Article 1.3(d) is essential to help broaden the perspective and value base of the REB beyond the institution, and thus advance dialogue with, and accountability to, local communities.

REBs should husband their resources and expertise prudently. For example, in the event that the REB is reviewing a project that requires particular community or research subject representation, or a project that requires specific expertise not available from its regular members, the REB Chair should nominate appropriate *ad hoc* members for the duration of the review. Should this occur regularly, the membership of the REB should be modified.

Institutions should consider the nomination of substitute REB members so that Boards are not paralysed by illness or other unforeseen eventualities. The use of substitute members should not, however, alter the membership structure as outlined in Article 1.3

### **China**

No less than five people, with a gender balance.

### **India**

According to 'Ethical guidelines for biomedical research on human participants' by the Indian Council of Medical Research (ICMR) 2006 and Schedule Y, membership should be between seven and twelve.

### **Japan**

Japanese regulations, based on GCP principles, require a minimum of five members.

## **USA**

The minimum is 5 with expertise, plus non-scientist and non-affiliated members. This means that there are usually around 11 – 15 members. Many institutions have multiple IRBs.

5. How many members constitute a quorum?
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## **Australia**

The word ‘quorum’ is not used. Instead, members from the pool mentioned under question 4 may attend meetings as needed to meet minimum HREC requirements (that is, eight), and may also be available to provide expertise for the research under review.

Where there is less than full attendance of the minimum membership at a meeting, the Chairperson should be satisfied, before a decision is reached, that the views of those absent who belong to the minimum membership have been received and understood.

## **Brazil**

50% + 1

## **Canada**

This is an institutional or REB-centric decision once the original 5 member expertise per Article 1.3 of the TCPS stipulation is met.

## **China**

This varies; however, for the majority of RECs, a quorum is 50% + 1; for others it is two-thirds of the total membership.

## **India**

A minimum of five persons is required to form a quorum.

## **Japan**

This is determined solely by the institution appointing the research ethics committee.

## **USA**

Half of the total members plus one.

6. What backgrounds and/or qualifications of members are actively sought?

**Australia**

As specified under question 4 above:

The minimum membership is

- a chairperson, with suitable experience, whose other responsibilities will not impair the HREC's capacity to carry out its obligations under the National Statement;
- at least two lay people, one man and one woman, who have no affiliation with the institution and do not currently engage in medical, scientific or legal work;
- at least one person with knowledge of, and current experience in, the professional care, counselling or treatment of people; for example, a nurse or allied health professional;
- at least one person who performs a pastoral care in a community; for example, an Aboriginal elder, a minister of religion;
- at least one lawyer, where possible one who is not engaged to advise the institution; and
- at least two people with current research experience that is relevant to research proposals to be considered at the meetings they attend. These two members may be selected, according to need, from an established pool of inducted members with relevant expertise.

**Brazil**

The composition of each CEP must be set at the discretion of the institution. Half the CEP participants must have expertise on research and elected by their companions. The CEP coordinator is chosen by their reported members during their very first meeting.

**Canada**

Please see Article 1.3 of the TCPS above as this is the best information we have for what is required. Some REBs may choose to also request members with additional expertise such as a pharmacy representative and/or a biostatistician. The "community member" is not well defined in the TCPS and is often interpreted by each REB to suit their own community.

**China**

Research ethics committees include specialists in biomedicine, management, ethics, law, sociology, statistics, and many other disciplines. There is no strict structure.

**India**

A pharmacologist, a lawyer, a social worker, a lay person and clinicians relevant to the type of study being reviewed.

## **Japan**

Japanese GCP requirements specify that an REC shall have the ability to complete adequate review of research activities from both the scientific and the ethical point of view. Each REC shall include at least one person whose profession is *outside* that of those associated with the conduct of clinical trials such as medicine, dentistry or pharmacology, and each REC shall include a person or persons who does or do not have a conflict of interest with the institution.

Additionally, membership includes clinicians experienced in research, lawyers, ethicist(s), from within and without the institution, plus outside citizen(s). These lay persons include science writers and news reporters and although they are difficult to recruit women are particularly welcomed.

## **USA**

- Community members to reflect local culture & value
- Non-scientist to represent subjects
- Medical & scientific expertise
- Gender & ethnics diversifications

7. How do RECs obtain specialist expertise?
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## **Australia**

The institution should ensure that the HREC has access to the expertise necessary to enable it to address the ethical issues arising from the categories of research it is likely to consider. This may necessitate going outside the HREC membership.

## **Brazil**

About 85% of research ethics committees in Brazil are linked to knowledge and research institutions and hospitals uniformly distributed throughout the country. The local institutional committee has, however, experts belonging to almost all health and human science areas.

## **Canada**

There is no single defined method or recommendation for assessing the need for or obtaining REB review expertise. The Chair will seek internal/external expertise at his/her discretion.

## **China**

RECs can appoint or invite an independent consultant according to the project to be reviewed.

### **India**

When required, subject experts are invited to offer their views, but there are as yet no guidelines on when or of this should be done.

### **Japan**

There are networks of specialists who can be called upon by an REC when it requires one in a particular field not already represented on the committee. Some committees appoint subcommittees to obtain opinions from specialists.

### **USA**

There is an *ad hoc* agreement to co-opt a committee member who is a consultant with special expertise when one is needed.

8. What are the training requirements for members of RECs?
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### **Australia**

The institution that establishes an HREC is responsible for ensuring that:

- members have relevant experience and/or expertise; and
- members undertake appropriate induction, which could include mentoring by a current HREC member, and continuing education.

The National Statement on Ethical Conduct in Human Research specifies that each member of an HREC should:

- become familiar with the National Statement, and consult other guidelines relevant to the review of specific research proposals;
- prepare for and attend scheduled meetings of the committee or, if unavailable, provide opinions on the ethical acceptability of research proposals before meetings, subject to institutional policies on absences; and
- attend continuing education or training programmes in research ethics at least every three years.

### **Brazil**

CEPs are responsible for developing capability mechanisms for their appointed members. Besides that, CONEP provides regional and national meetings in order to empower and standardize the functioning of the system CEP-CONEP.

### **Canada**

Neither training nor annual education is mandated, it is REB-centric. The TCPS requires training but does not define it. A recent article is appended from the Canadian Research Ethics governance network grant of which Heather Sampson is a co-investigator and lead author that addresses the issue of REB member education.

### **China**

In general, before members are appointed, they should have special training on bioethics; thereafter they should attend annual training courses.

### **India**

There are no formal requirements yet, but REC members are encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training organized by constituted body, so that they become aware of their role and responsibilities.

For drug trial review it is recognised that REC members should be trained in the principles of Good Clinical Practice. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms.

### **Japan**

There are no official requirements for training. The training of members is solely up to each institution.

### **USA**

There is a requirement that all IRB members should be trained in ethical principles, in FDA and other relevant federal regulations and in IRB written policies, and standard operating procedures (SOPs). Members should also be aware of international guidelines.

9. What training facilities are provided or are available for members of RECs?
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### **Australia**

A number of commercial organisations, such as the Queensland Clinical Trials Network (which claims to be Australia's first and only registered Training Organisation to tailor a unit for HREC members), provide training facilities for REC members, but there are none provided by the National Health and Medical Research Council.

### **Brazil**

Continuous activities are expected to be provided for appointed CEP members to improve their knowledge of research ethics.

### **Canada**

There are no training facilities per se for REB members. There is an annual Canadian Association of Research Ethics Boards (CAREB) <http://www.careb-accer.org/>

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

meeting plus a National Council on Ethical Human Research (NCEHR) <http://www.ncehr-cnerh.org/english/home.php> meeting. The attendees pay for travel and attendance. These expenses may be borne by the attendees or the REB/host institution. Attendance at these meetings is entirely voluntary.

This lack of training facilities in the national landscape/on a national level may be explained by the fact that there is no central healthcare funding and therefore no central research ethics board funding. There is provincial healthcare funding that is provided each year by the federal government; research ethics presently does not appear on that agenda.

Recently, however, there are examples of newly formed central review boards in places, such as Newfoundland, designed to respond to problems of research oversight in the past.

### **China**

The Ethics Committee of the Ministry of Health and the Ethics Committees at the provincial and municipal levels organize training programmes for the members of research ethics committees, locally.

### **India**

There are no formal requirements yet, but REC members are encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by its own members or regular training organized by constituted body, so that they become aware of their role and responsibilities.

For drug trial review it is recognised that REC members should be trained in the principles of Good Clinical Practice. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms.

### **Japan**

There are no official courses provided, but institutions may provide their own. Additionally, e-courses are available, produced by a number of different institutions.

### **USA**

The OHRP provides education and regular workshops. Some universities have their own training curricula. Many universities subscribe to the Collaborative Institutional Training Initiative (CITI) web training modules.

10. How do RECs assess the progress and outcome of research projects that they have approved?

### **Australia**

Those granted ethical approval for a research project are required to submit regular safety reports, an annual report and a final report. The actual monitoring of the implementation of this requirement is not specified.

### **Brazil**

According to Resolution 196/96, research protocols are followed up annually. However, the periods the research protocols are followed up may be more frequent, and reports are required every six months for CTIMPs. Annual reports are required for projects involving vaccines or new diagnostic tests or when the research refers to clinical trials on drugs licensed in Brazil but for different conditions than those for which the drug is licensed.

### **Canada**

This is also a varied and REB-centric function. It can range from asking for an annual clinical research project accrual and adverse event update on the annual REB renewal form to an insitutional research quality assurance committee oversight that includes asking patient/participants for their reaction to being asked to take part in research.

On an ad hoc basis, a four stage practical approach to effect monitoring clinical research in Canada has been formulated:

- 1) continuing (annual) review;
- 2) monitoring of the consent process;
- 3) monitoring for adherence to protocol; and
- 4) monitoring of data integrity.

The authors recommended four monitoring categories that seemed straightforward and the authors were confident in 1995 that as REBs fulfilled the then prevalent Medical Research Council responsibilities that clinical research monitoring would become commonplace with patient-participant safety as the final objective. At the beginning of 2010, there is no formal clinical trial monitoring in place in Canada.

The Review Procedures for Ongoing Research in Canada appear as Annex II to this report.

### **China**

There will be progress reports and annual reports for the research projects that have previously been submitted to the RECs for approval. This is a requirement, but how it is achieved is not specified.

## **India**

### **Periodic Review**

The ongoing research may be reviewed at regular intervals of six months to one year as may be specified in the SOP of the ethics committee.

### **Continuing Review**

REC has the responsibility to continue reviewing approved projects for continuation, new information, adverse event monitoring, follow-up and later after completion if need be.

### **Monitoring**

Actual site visits can be made especially in the event of reporting of adverse events or violations of human rights. Additionally, periodic status reports must be asked for at appropriate intervals based on the safety concerns and this should be specified in the SOP of the EC. SAE reports from the site as well as other sites are reviewed by EC and appropriate action taken when required. In case the IEC desires so, reports of monitoring done by the sponsor and the recommendations of the DSMB may also be sought.

## **Japan**

They rely on annual reports.

## **USA**

All projects are required to submit an annual continuing review, and there is a requirement that adverse events should be reported and that the report of the data safety monitoring board (DSMB) should be submitted, if there is such a DSMB.

11. Do RECs invite or allow a) applicants or b) observers to attend committee meetings? Are the minutes of an REC meeting made public?

## **Australia**

An HREC may invite researcher(s), and researchers may request, to be present for discussion of their proposed research. Observers are not permitted.

The minutes of HREC meetings are confidential and are not made public. However, the nature of research projects reviewed in general terms is set out in the Annual Report of an HREC.

**EFGCP Report on  
Data on Research Ethics Committees in Seven Countries outside Europe**

**Brazil**

The meetings of all CEPs are held in secret. In some cases meetings are open to include specialist advisors related to dilemmas that might arise concerning the ethics of some clinical or experimental research projects. Applicants are not invited.

The minutes of CEP meetings are not made available to the public.

**Canada**

This decision is locally driven; within one institution the practices may vary. At the University Health Network in Toronto there are three REBs; two do not invite the applicants to REB meetings and one insists on their attendance.

There is no mandatory public reporting of minutes. Depending on the institution, the REB may report to the Medical Advisory Committee or to the Governing Council. Private REBs do not have a reporting structure. Some REBs report to the institutional Vice President of Research.

REB minutes are not made public; however if they are reported to a Medical Advisory Committee (MAC) in a hospital setting, the MAC versions of the minutes may be made public, on demand though it should be noted that this is unusual.

There are similarities between the US IRB structure and the Canadian REB model; however each Canadian institution can decide on its own internal reporting mechanism. There is the potential for conflict of interest between the REB and their decision making process and the institutional “host” as has been experienced in the USA.

**China**

Research ethics committees often invite applicants to attend committee meetings as they can describe their applications. If necessary, RECs are permitted to invite observers.

The minutes of REC meetings are not made available to the public.

**India**

If deemed necessary, RECs invite or allow applicants or observers to attend meetings.

The minutes of REC meetings are not made available to the public.

**Japan**

It is up to each institution to decide how its research ethics committee (“Chiken-Shinsa-Inkai”) conducts its business. Some RECs invite applicants to attend and respond to committee meetings and sometimes certain appointed members of the committee judge whether it is desirable to invite applicants, depending on the importance/graveness of the research.

The minutes of REC meetings **are** made available to the public.

### **USA**

Applicants, but not other observers, are allowed to be present for the presentation and consideration of their protocols and to answer questions. They must be absent when the decision or vote is taken. The minutes of an REC meeting are not made public.

12. Is there any scope for Chairman's actions in between meetings? Do RECs ever use subcommittees for anything?

### **Australia**

There is little scope for the Chairperson to do anything without the involvement of the minimum membership of the committee (see question 5 above). Sub-committees are not used.

### **Brazil**

The CEPs coordinators develop an extremely complex activity and must act in the dilemmas and, in special, those opposite ones. They have the responsibility in conducting the meetings by stimulating the team mutual cooperation and lead the result to the plenary sitting meetings for approval.

They have to provide the research protocols to be sent to the reported members in rotation, assure the terms fulfilments and sign CEP opinions on behalf of the college.

It is a responsibility of the CEPs coordinators to provide the continuous members knowledge development or assign someone else to do this task. Subcommittees are allowed to analyze specific documents or projects as far as the final decision belongs to the college established.

### **Canada**

Yes to both questions: the REB Chairman can exercise authority within the REB mandate and remit between meetings. There are subcommittees struck for a variety of review purposes; usually for situations such as "tissue committee" work, student reviews and other activities.

### **China**

Chairmen are permitted to take action in between meetings, but it is not routine. Based on the work load, the RECs will set up subcommittees, such as subcommittees for reproductive health, organ transplantation, and clinical research for medical devices, etc.

## **India**

Yes to both questions: depending on the SOPs of the Committee, the Chairman may be consulted in case of applications for an expedited review, serious adverse event reports, etc.

RECs may create subcommittees – particularly for evaluating serious adverse events.

## **Japan**

Chairman's action may be taken for fast-track reviews, but sub-committees are only used to obtain opinions from specialists, not to make provisional decisions.

## **USA**

The Chairman or his/her designee can conduct an expedited review, and sub-committees are used to assess adverse events or to conduct an expedited review. All decisions must be on the agenda of the next meeting of the full committee for consideration or approval.

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*EFGCP - July 2010*

## **Annex I**

### **CHINA**

#### **Regulations on Ethical Reviews of Biomedical Research Involving Humans**

##### **Chapter 1: General Principles**

###### **Article 1**

In accordance with the "Regulations on Medical Practitioners of the People's Republic of China" and the "Regulations on Management of Medical Institutions", these "Regulations on Ethical Review of Biomedical Research Involving Humans" are promulgated to regulate biomedical research involving humans and practices of related technologies to protect human life and health, and human dignity, and to respect and protect the rights of the research subjects.

## **Article 2**

All ethical review work on biomedical research involving humans should abide by these “Regulations”.

## **Article 3**

Activities referred to in these “Regulations” of biomedical research involving humans and related technologies include the following:

1. Research activities about the physical and pathological phenomena of a human body, using modern methods of physics, chemistry and biology, as well as research activities for disease diagnosis, treatment and prevention;
2. Activities of trial use on human bodies of medical and health technologies and products as biomedical research results. Not included in the review scope of these “Regulations” are clinical practices that have been used for more than two years before the “Regulations” comes into effect, or, the technologies that have already been approved by health authorities before these “Regulations” comes into effect.

## **Article 4**

Reviews on ethics should comply with national laws and regulations, as well as life ethical principles commonly recognized, and reviews on ethics shall be carried out independently and objectively in a fair and transparent manner.

## **Chapter 2: Ethics Committee**

### **Article 5**

The Ministry of Health of China has its Medical Ethics Committee. Provincial health authorities have their steering consulting organizations of ethics reviews under their administration. Committees set up by the Ministry of Health and provincial health authorities are expert consulting organizations for medical ethics that consider important ethical issues and provide suggestions for policy-making and when necessary organize ethical reviews of important research projects; and that guide and monitor ethical reviews conducted by ethics committees in their administrative areas. A “Constitution” of the ethics expert committee set up by the Ministry of Health and provincial health authorities is to be made separately.

### **Article 6**

Institutions that conduct biomedical research involving humans and application of related technologies, including medical and health institutions, scientific and research institutes, disease prevention and control institutions and women and child health care institutions, should establish their institutional ethics committees. Major responsibilities of the institutional ethics committees include the review and monitor of ethics for biomedical research and application of related technologies carried out by their own institutions or by organizations affiliated to their own institutions. Institutional ethics committees should also conduct reviews on ethics as requested and entrusted by social sectors and shall run training programs on ethics.

### **Article 7**

Members of the institutional ethics committees should be chosen from fields such as biomedicine and management, ethics, law, sociology, etc. after opinions are sought widely by the organizations and institutions that are to have such ethics committees. Each ethics committee should consist of no less than five people, with a gender balance. In areas where minority ethnic groups live, minority ethnic people should be considered to serve as committee members.

### **Article 8**

The term of each ethics committee member should be five years and can be reappointed. Each ethics committee should have a chairperson and several vice chairpersons, who are elected by members of the ethics committee and who can be re-elected. The organization or institution that sets up the ethics committee should give financial compensations for the members of the ethics committee based on the work they carry out.

### **Article 9**

Responsibilities of the institutional ethics committee will be to review research protocols to maintain and protect the dignity and rights of the research subjects; to guarantee that any research project will not in any way put the research subjects in any risk; at the same time, to supervise and monitor the research projects that have been approved, and to cope with any complaints and incidents concerning research subjects.

### **Article 10**

Institutional ethics committees have the following powers:

1. To require from the researchers proof of informed consent, or, as requested by the researchers, to approve the exemption of the requirement procedure for an informed consent;

2. To require the researchers to modify their research protocols;
3. To require the researchers to suspend or terminate their research activities;
4. To decide to approve, not to approve, or approve only after protocols are modified.

### **Article 11**

Ethics committee members should keep all ethically reviewed research projects confidential.

### **Article 12**

Ethics committees should make their own decisions without any outside interferences; and review results should be timely made available or public.

### **Article 13**

Ethics committees should be under the supervision and administration of their administrative regional and health authorities.

## **Chapter 3: Review Procedures**

### **Article 14**

Review principles for biomedical researches involving humans are:

1. To keep strictly to the informed consent procedure to respect and protect the rights of the potential research subjects so that they can make independent decisions to accept or reject the test, and never to cheat, allure, coerce the potential research subjects to agree, and to allow them to withdraw at any stage of a test;
2. The safety, health and rights of the research subjects should be considered first before scientific and social interests are considered so as to benefit, to the greatest extent possible, the research subjects and to avoid any possible injuries or damages to them;
3. To alleviate or exempt financial burdens resulting from the benefits research subjects receive from a test;
4. To respect and protect the privacy of the research subjects, to timely inform them of the storage and security measures concerning their personal data, and never to release those data to a third party not relevant or any media;
5. To ensure that the research subjects receive free medical treatment and compensations for any possible injuries caused by a test;
6. To give special protection to those research subjects (vulnerable groups) who have lost or lack capability to protect their own rights,

including children, pregnant women, mentally-retarded persons, mental patients, prisoners, and economically and educationally disadvantaged people.

### **Article 15**

Research projects should submit the following materials to the ethics committees for ethical reviews:

1. The Application Form for Ethical Review;
2. The Application Protocol for Results of Research or Related Technologies;
3. A written informed consent of the potential research subject.

### **Article 16**

Research project applicants must first obtain informed consent out of his or her own free will in writing from the potential research subject. If a written form is not obtainable, an oral informed consent must be first obtained, together with a written proof indicating that such an oral one is obtained. For those potential research subjects who are not able or not possible to make their own decisions, informed consent in writing must be obtained from their guardians or surrogates.

### **Article 17**

In the process of obtaining informed consent, the applicants must provide the potential research subjects with comprehensive and understandable information relevant for the test, and the wording in the letter of informed consent should be easy to understand and can be in local language in minority ethical areas that is understood by the potential research subjects, and the potential research subjects should be allowed time long enough to consider whether or not to accept to be research subjects.

### **Article 18**

When the practical procedure or a condition of a research project changes, another informed consent must be obtained, and a new application for ethical reviews must be submitted.

### **Article 19**

Ethics committees should not accept any research project ethical review applications that are against national laws and regulations. If there is any interest conflict between an ethics committee and an applied project, the ethics committee concerned should actively refuse to get involved. If in any

way refusal to get involved is not possible, the conflict of interest should be made clear to the applicants.

## **Article 20**

Ethics committees should review the following:

1. Qualifications, competence and experience of the researchers meet the requirements for the research project;
2. The Research Protocol is of a scientific nature and complies with ethical principles;
3. Whether or not the balance between the risks and the benefits the research subjects may get is appropriate;
4. Whether or not the information provided to the potential research subjects (or their family members, guardians, and lawful surrogates) is comprehensive and understandable, and whether or not the methods used to obtain informed consent are appropriate;
5. Whether or not measures are taken to protect the confidentiality of the data of the research subjects;
6. Whether or not the standards for selection and rejection of the potential research subjects are appropriate and justified;
7. Whether or not the rights which the research subjects should enjoy have been made clear to them, including the right to withdraw from the test without a reason and without reprisal;
8. Whether or not the research subjects will get appropriate financial compensations, and if and when they are injured or die in the test, whether or not the medical treatment and financial compensation are appropriate;
9. Whether or not there are designated personnel in the research team who are responsible for dealing with matters related to the informed consent and the safety of the research subjects;
10. Whether or not protective measures are taken for possible risks in a test for the tested persons;
11. Whether or not there is a conflict of interest between the researchers and the research subjects.

## **Article 21**

Ethics committees should make decisions to approve, not approve or reconsider a review application after modifications are made. Decisions made by ethics committees must be agreed to by two-thirds of the ethics committee members. Reasons must be given why a specific decision is made. When the probability of an injury or discomfort for a research subject is no higher than that in one's daily life or regular treatment (namely, projects with risks lower than the minimum risk level), the research project can be ethically reviewed by the committee chairperson, or by one or several committee members designated by the committee chairperson.

### **Article 22**

When a research project approved by the ethics committee needs to be changed while being carried out, this must be reported to the ethics committee for approval. Any grave negative responses from the research subjects or negative incidents during the application of an approved research project must be reported to the ethics committee.

### **Article 23**

Without the approval of the ethics committee, no applied research projects should be conducted.

## **Chapter 4: Supervision and Management**

### **Article 24**

The supervision and management of the ethical review of biomedical research involving humans should be included in the scientific and research work scope of health authorities at all levels. The supervision and management work should include the following:

1. Whether or not an ethics committee is established as required in an institution that carries out biomedical research involving humans;
2. Whether or not the institutional ethics committee conducts ethical reviews in accordance with the ethical review principles;
3. Whether or not the ethical review contents and procedures meet the requirements;
4. Whether or not there is a dispute over the implementation of the reviewed results.

### **Article 25**

The Ministry of Health manages in a macro way the ethics committees nationwide, makes and perfects regulations on ethical reviews, researches on and makes relevant policies. Provincial health authorities shoulder the responsibility for the supervision and management of the work of the ethics committees in the provinces.

### **Article 26**

Foreign institutions or individuals that have obtained their national or regional approval to carry out biomedical research involving humans within China should apply to ethics committees set up under these "Regulations" for a review.

### **Article 27**

At the conclusion of a biomedical research project involving humans, the project responsible person must submit a certificate indicating that the research project has undergone ethical reviews by the ethics committee. Before a research paper about a biomedical research project involving humans is published, the author(s) must submit a certificate indicating that the research project has undergone ethical reviews by the ethics committee.

### **Article 28**

Any individual or organization has the right and obligation to report any breach of the regulations or unethical activities.

### **Article 29**

When a breach of the regulations or an unethical activity is found, the institution and health authorities where the research project is carried out has the power to penalize the researchers related, to give them an open criticism, and to abolish their qualifications for rewards; and to suspend the application of the research project according to the seriousness of the misconduct, and transfer the case to courts if it is against national laws.

## **Chapter 5: Supplementary Article**

### **Article 29**

These "Regulations" will come into effect on the day it is announced.

Note:

These "Regulations" were made by the Ministry of Health of China and came into effect on January 11, 2007.

This English version is translated by the Chinese Medical Association.

## **Annex II**

### **CANADA**

#### **Review Procedures for Ongoing Research in Canada**

##### ***Tri-council Policy Statement (TCPS) Ethical Conduct for Research Involving Humans***

###### **Article 1.13**

- a. Ongoing research shall be subject to continuing ethics review. The rigour of the review should be in accordance with a proportionate approach to ethics assessment.
- b. As part of each research proposal submitted for REB review, the researcher shall propose to the REB the continuing review process deemed appropriate for that project.
- c. Normally, continuing review should consist of at least the submission of a succinct annual status report to the REB. The REB shall be promptly notified when the project concludes.

Beyond scrutinizing reports, the REB itself should not normally carry out the continuing ethics review, except in specific cases where the REB believes that it is best suited to intervene. For research posing significant risks, the REB should receive reports on the progress of the research project at intervals to be predetermined. These reports should include an assessment of how closely the researcher and the research team have complied with the ethical safeguards initially proposed.

In accordance with the principle of proportionate review, research that exposes subjects to minimal risk or less requires only a minimal review process. The continuing review of research exceeding the threshold of minimal risk that is referred to in Article 1.13(b), in addition to annual review (Article 1.13(c)) might include:

- Formal review of the process of free and informed consent;
- Establishment of a safety monitoring committee;
- Periodic review by a third party of the documents generated by the study;
- Review of reports of adverse events;
- Review of patients' charts; or
- A random audit of the process of free and informed consent.

Other models of a continuing ethics review may be designed by researchers and REBs to fit particular circumstances.

The process of a continuing ethics review should be understood as a collective responsibility, to be carried out with a common interest in maintaining the highest ethical and scientific standards. Research institutions should strive to educate researchers on the process of a continuing ethics review through workshops, seminars and other educational opportunities.

### ***G. Review of Multicentred Research***

Principles of institutional accountability require each local REB to be responsible for the ethical acceptability of research undertaken within its institution. However, in multicentred research, when several REBs consider the same proposal from the perspectives of their respective institutions, they may reach different conclusions on one or more aspects of the proposed research. To facilitate coordination of ethics review, when submitting a proposal for multicentred research, the researcher may wish to distinguish between core elements of the research—which cannot be altered without invalidating the pooling of data from the participating institutions—and those elements that can be altered to comply with local requirements without invalidating the research project.

REBs may also wish to coordinate their review of multicentred projects, and to communicate any concerns that they may have with other REBs reviewing the same project. The needed communication would be facilitated if the researcher provides information on the institutional REBs that will consider the project.

### ***H. Review of Research in Other Jurisdictions or Countries***

#### **Article 1.14**

Research to be performed outside the jurisdiction or country of the institution that employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher's institution; and (b) by the REB, where such exists, with the legal responsibility and equivalent ethical and procedural safeguards in the country or jurisdiction where the research is to be done.

An institution is responsible for the ethical conduct of research undertaken by its faculty, staff or students regardless of the location where the research is conducted. Thus, review of research by that institution's REB is required in addition to review by any agency having jurisdiction over the site of the research.

Rules pertaining to research abroad should be created and interpreted in the spirit of the Helsinki Accords and subsequent documents that encourage the

free movement of researchers across national boundaries. REBs should, therefore, not veto research about authoritarian or dictatorial countries on the grounds that the regime or its agents have not given approval for the research project or have expressed a dislike of the researchers. They should, however, legitimately concern themselves about the safety of research subjects and indeed of the researchers, and the security of research materials.

University research should be open. It is thus unethical for researchers to engage in covert activities for intelligence, police or military purposes under the guise of university research. REBs must disallow any such research.

Researchers should normally provide copies of publications or other research reports to the institution, normally the host institution, that is best suited to act as a repository and disseminator of the results. This may not be necessary in countries when the results are readily available in print or electronically. However, such reporting is particularly important in countries where Western publications are unavailable or prohibitively expensive. If feasible, and so long as the human rights of the research subjects and the ethical rights set out in this Policy are not compromised, a copy of the field material ought to be provided as well, with due regard to commitments concerning anonymity and confidentiality of research subjects. These latter safeguards are especially important in countries with authoritarian regimes.

Furthermore, researchers should ensure that the benefits of their research are available in the host country. Benefits may, for example, take the form of information-sharing, training for local personnel both in the host country and in Canada, or health care or similar services. However, since researchers are not aid agencies, REBs should not try to force them to undertake aid work.