REVIEWING THE ETHICAL REVIEWERS: THE SIDCER/FERCAP EXPERIENCE*

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Despite playing a key role in a clinical trial, the ethics committee (EC) is an entity over which sponsor auditors have no jurisdiction. Auditors may gain an insight into the ECs' processes by indirectly examining and reviewing their documentation in the trial master file, including membership details, approval letters, correspondence pertaining to the study and sometimes their standard operating procedures (SOPs). They may also schedule an interview with the Chairman or any member of an EC to discuss and exchange better practices. With this limitation to the audit, what is beyond the documentation (and a short interview during an investigator audit), is a complete unknown for the sponsor and their auditors.

Ethical Review Evaluations

There is growing national and international interest in ensuring that ethical review processes achieve the highest standards with regard to protecting individuals and communities. The assurance of research subject protection requires that ethical review standards are established and these along with the performance of the EC, are evaluated.

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With this in mind, the *Special Programme for Research and Training in Tropical Diseases* (TDR) of the *World Health Organization* (WHO) published two guidelines. The first was the *Operational Guidelines for Ethics Committees that Review Biomedical Research* (WHO/TDR, 2000), which aimed to facilitate, support, and ensure that the quality of the ethical review of biomedical research is maintained worldwide. This was followed by *Surveying and Evaluating Ethical Review Practices* (WHO/TDR, 2002), which contributed to an international framework for surveying and evaluating ethical review practices. This guideline suggests a cooperative and educative model and is less concerned with the "enforcement" of standards and more with "learning" from the review of EC practices.

Under the WHO, the *Strategic Initiative for Developing Capacity in Ethical Review* (SIDCER) was formulated as a network of independently established regional fora for ECs, in five regions of the world (WHO/TDR, 2005). These are:

- *Forum for Ethics Committees in the Confederation of Independent States* (FECCIS)
- *Foro Latino Americano de Comites de Etica en Investigacion en Salud [Latin American Forum of Ethics Committees in Health Research]* (FLACEIS)
- *Pan-African Bioethics Initiative* (PABIN)
- *Forum for Institutional Review Boards [IRBs]/Ethics Review Boards [ERBs] in Canada and the United States* (FOCUS)
- *Forum for Ethical Review Committees in the Asian and Western Pacific Region* (FERCAP)

SIDCER has established a framework for surveying and evaluating ethical review practices through a recognition (or accreditation) program. Since 2004, SIDCER/FERCAP has conducted a series of training seminars in Asia for potential surveyors (who are mostly EC members in their respective countries) to carry out the recognition survey, as well as training for EC members in general. Surveys, the methods of which are similar to an industry audit, have been carried out since 2005 with those interested in the *SIDCER Recognition Program*.

The SIDCER Survey

The objectives of the survey are to facilitate and assist ECs toward achieving quality and transparency in ethical review, and to provide feedback on the practices and performances of the EC based on the SIDCER standards in the following areas:

- Structure and composition of the EC
- Adherence to policies and regulations
- Completeness of its review procedures
- Adoption of post-review procedures
- Documentation and archiving

There are numerous benefits to participating in the survey program (Box 1). Before starting this process, an EC requesting a survey must fill-in a self-assessment checklist to assess whether they will later be evaluated. For every survey, a survey team is identified. This team consists of two trained and qualified independent surveyors not originating from the country being surveyed, one local surveyor, and several in-country trainee-surveyors who also act as translators, if required. The survey team members are bound by a confidentiality agreement, signed prior to the survey. They must also declare any conflict of interest (COI) and agree to follow the SIDCER SOPs for surveying and evaluating ethical review practices.

Box 1: *Benefits of Participating in a SIDCER Survey*

- Assurance to the public that the EC protects research subjects from harm and exploitation and preserves their rights
- Validation of compliance with established international standards (for example, WHO, ICH-GCP) which require the ethical and scientific review of research
- An objective evaluation of good practices by independent external surveyors
- The opportunity to learn from the experiences of other countries
- Upgrading the quality of ethical review globally
- The recognition of respectable ECs for the protection of human subjects

Program Activities

A survey plan is presented at the opening meeting. This comprises a three-day activity program, which includes a tour of the EC office, interviews with members and staff, a review of documents and files, and the observation of a full EC board meeting. A final meeting is held at the end to summarize and discuss the survey's findings.

The review of documents and procedures is a tedious and time-consuming exercise. Completing this task in the allotted timeframe is challenging, largely due to the volume of documents to review and the cross-referencing and consistency checks required. A review and evaluation are performed on the following:

- Applicable national laws and regulations for the EC
- All EC SOPs
- Membership files (for example, an individual's *curriculum vitae*, terms of reference, letter of appointment, initial and continuous training records –- including evidence of GCP training)
- Protocol files (a representative sample of protocols reviewed by the EC in the past three years)
- EC documents for reviewing serious adverse event (SAE) reports
- Board meeting agendas and minutes
- Communication records with, for example, applicants, regulatory authorities or the authority under which the EC is established

Observation of a full board meeting, where protocols are addressed and discussed, is carried out to evaluate group dynamics, the management of COI, and the actual adherence to written SOPs –- Are the EC's decision-making procedures in line with their SOPs? Do they follow the "write what you do and do what you write" approach? The surveyors are also required to observe the effectiveness and quality of the review process. Stemming from these surveys, common problems have been identified and consequently recommendations were made (Box 2).

After implementing acceptable corrective action, recognition will be granted to an EC for a maximum period of three years. A recognized EC will be required to produce annual reports for review and monitoring by the SIDCER committee. This should include all relevant activities of the EC in the past year, any amendments to the SOPs and guidelines, and/or new SOPs introduced. Up until the end of 2010, 73 ECs in Asia, including Bhutan, China, India, Indonesia, Philippines, South Korea, Sri Lanka, Taiwan, and Thailand had been surveyed and recognition awarded (FERCAP, 2010) (Box 3).

Box 2: *Common Recommendations to Ethics Committess Following a SIDCER Survey*

EC Structure and Composition

- Improve gender representation (research has impact on the health of both men and women)
- Initiate early and on-going training
- Empower lay persons to raise relevant issues
- Train medical members to assess risks and vulnerability
- Address COI in board membership

EC SOPs

- Address gaps between SOPs and practice
- Improve consistency and completeness of SOPs
- Availability of forms and checklists
- Completeness of review process
- Improve risk assessment processes
- Provide better protection to vulnerable subjects
- Improve the evaluation of investigator team qualifications
- Provide complete patient information sheets
- Check that informed consent form contents reflect the relevant patient information

Board Meetings

- Meet quorum and COI requirements
- Produce complete meeting agendas and minutes, and standardize these
- Organize comments and the flow of discussion
- Summarize issues for board decision
- Consider both scientific and ethical issues
- Improve member preparation for board discussion

Post-Review

- Identify investigator post-review responsibilities in an approval letter
- Suggest appropriate action for SAE reports
- Define investigator responsibilities following study termination
- Submit and follow-up both progress reports and end-of-study reports
- Use a database to monitor approved protocols
- Take appropriate action to address patient queries and complaints

EC Office and Archiving

- Ensure privacy and confidentiality protection
- Provide appropriate facilities for EC functions
- Compile complete protocol files that trace its history
- Ensure availability and completeness of files
- Check separation of active and completed protocols with proper coding and recording

Box 3: *Asian Recognized Ethics Committees*

Bhutan

- Research Ethics Board of Health (REBH), Ministry of Health (MOH) - Bhutan [Thimphu | 2010]

China

- Shanghai Changhai Hospital Ethics Committee, Second Military Medical University (SMMU) [Shanghai | 2007, 2010]
- Affiliated Hospital of Nanjing University of Traditional Chinese Medicine Institutional Review Board [Nanjing, Jiangsu | 2007, 2010]
- Huashan Hospital Institutional Review Board (HIRB), Fudan University [Shanghai | 2008]
- Ethics Committee of the First Affiliated Hospital, Nanjing Medical University, Jiangsu Province Hospital [Nanjing, Juangsu | 2009]
- Southwest Hospital Institutional Review Board [Chongqing | 2010]
- Ethics Committee of Xi Yuan Hospital of China Academy of Chinese Medical Sciences [Beijing | 2010]
- Ethics Committee of Guangdong Provincial Hospital of Traditional Chinese Medicine [Guangzhou | 2010]

- Beijing Tiantan Hospital Institutional Review Board, Capital Medical University [Beijing | 2010]
- Ethics Committee of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine [Tianjin | 2010]
- Shanghai Cancer Center Institutional Review Board (SCCIRB), Fudan University [Shanghai | 2010]

India

- Tata Memorial Centre Human Ethics Committee (TMC-HEC) [Mumbai | 2009]
- Ethics Committee for Research on Human Subjects (ECRHS) of SETH G.S. Medical College and King Edward Memorial (KEM) Hospital Institutional Review Board [Mumbai | 2009]

Indonesia

- National Institutes of Health Research and Development (NIHRD) Ethics Committee [Jakarta | 2009]

Philippines

- University of the Philippines Manila (UPM) National Institutes of Health (NIH) Ethics Review Board [Manila | 2007, 2010]
- Research Institute for Tropical Medicine (RITM) Institutional Review Board, Department of Health (DOH) - Philippines [Muntinlupa, Metro Manila | 2007, 2010]
- University of the Philippines Manila (UPM) College of Medicine (CM) Research Implementation and Development Office (RIDO) Ethics Review Board [Manila | 2007, 2010]
- University of the Philippines Manila (UPM) Philippine General Hospital (PGH) Ethics Review Board [Manila | 2010]

South Korea

- Seoul National University Hospital (SNUH) Institutional Review Board [Seoul | 2006, 2009]
- Asan Medical Centre Institutional Review Board [Seoul | 2006, 2009]
- Kangnam St. Mary's Hospital (KSMH) Institutional Review Board [Seoul | 2007]
- Chonnam National University Hospital Institutional Review Board [Kwangju | 2007, 2010]
- Inje University Busan Paik Hospital (IJUBPH) Institutional Review Board [Busan | 2007, 2010]
- Hallym University Sacred Heart Hospital Institutional Review Board [Kyunggi-do | 2008]

- Daegu Catholic University Medical Center (DCUMC) Institutional Review Board [Daegu | 2008]
- Kyung Hee University Hospital (KHUH) Institutional Review Board [Seoul | 2008]
- Ajou University Hospital Institutional Review Board [Gyeonggi-do | 2008]
- Inha University Hospital Institutional Review Board [Seoul | 2009]
- Kangbuk Samsung Hospital Institutional Review Board [Seoul | 2009]
- Chungnam National University Hospital Institutional Review Board (CNUH-IRB) [Daejeon | 2009]
- International Vaccine Institute (IVI) Institutional Review Board [Seoul | 2009]
- Keimyung University Dongsan Hospital Institutional Review Board [Daegu | 2010]
- Kyungpook National University Hospital Institutional Review Board [Daegu | 2010]
- Yeungnam University Medical Center Institutional Review Board [Daegu | 2010]
- Kangdong Sacred Heart Hospital Institutional Review Board [Seoul | 2010]
- National Cancer Center Hospital Institutional Review Board [Seoul | 2010]
- CHA Bundang Medical Center Institutional Review Board, CHA University [Gyeonggi-do | 2010]
- Busan Dong-A University Hospital Institutional Review Board [Busan | 2010]
- Anam Hospital Institutional Review Board, Korea University Medical Center [Seoul | 2010]

Sri Lanka

- Ethics Review Committee, Faculty of Medicine, University of Colombo [Colombo | 2009]

Taiwan

- Joint Institutional Review Board (JIRB) [Taipei | 2005, 2008]
- Changhua Christian Hospital Institutional Review Board [Changhua | 2005, 2010]
- National Taiwan University Hospital Research Ethics Committee (NTUH REC) [Taipei | 2006, 2009]

- Chang Gung Memorial Hospital (CGMH) Institutional Review Board [Taoyuan | 2006, 2009]
- Taipei Veterans General Hospital (VGHTPE) Institutional Review Board [Taipei | 2006, 2010]
- Tri-Service General Hospital Institutional Review Board (TSGHIRB), National Defense Medical Center [Taipei | 2006, 2009]
- Chi-Mei Medical Center Institutional Review Board of Human Study Committee [Tainan | 2007, 2010]
- National Cheng Kung University Hospital (NCKUH) Human Experiment and Ethics Committee [Tainan | 2007, 2010]
- Kaohsiung Medical University, Chung-Ho Memorial Hospital Institutional Review Board [Kaohsiung | 2007, 2010]
- Taichung Veterans General Hospital (TCVGH) Institutional Review Board [Taichung | 2007, 2010]
- Chung Shan Medical University Hospital Institutional Review Board [Taichung | 2007, 2010]
- Taipei Medical University Municipal Wanfang Hospital Institutional Review Board [Taipei | 2008]
- Cathay General Hospital Institutional Review Board [Taipei | 2008]
- Buddhist Tzu Chi General Hospital - Hualien Institutional Review Board [Hualien | 2008]
- Kaohsiung Veterans General Hospital Institutional Review Board [Kaohsiung | 2008]
- Mackay Memorial Hospital Institutional Review Board [Taipei | 2008]
- China Medical University Hospital Institutional Review Board [Taichung | 2009]
- Human Subject Research Ethics Committee/Institutional Review Board-Academia Sinica (HSREC/IRB-AS) [Taipei | 2009]
- Shin Kong Wu Ho-Su Memorial Hospital (SKH) Institutional Review Board [Taipei | 2009]
- Buddhist Tzu Chi General Hospital - Taipei Institutional Review Board [Taipei | 2009]
- Taipei Medical University-Joint Institutional Review Board (TMU-JIRB) [Taipei | 2010]
- Far Eastern Memorial Hospital Research Ethics Review Committee [Taipei | 2010]

Thailand

- Royal Thai Army Medical Department Institutional Review Board [Bangkok | 2005, 2009]
- Faculty of Medicine, Chulalongkorn University Institutional Review Board [Bangkok | 2006, 2009]
- Department for Development of Traditional and Alternative Medicine (DTAM), Traditional and Alternative Ethics Committee (TAMEC), Ministry of Public Health (MOPH) - Thailand [Nonthaburi | 2007, 2010]
- Joint Research Ethics Committees (JREC) [Bangkok | 2008]
- Ethics Committee of the Faculty of Tropical Medicine, Mahidol University [Bangkok | 2008]
- Faculty of Medicine Research Ethics Committee, Chiang Mai University [Chiang Mai | 2008]
- Research Institute for Health Sciences (RIHES) Human Experimentation Committee, Chiang Mai University [Chiang Mai | 2008]
- The Ethical Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University (ERCCU) [Bangkok | 2008]
- Khon Kaen University Ethics Committee for Human Research (KKU EC) [Khon Kaen | 2008]
- Siriraj Institutional Review Board (SIRB), Faculty of Medicine, Siriraj Hospital, Mahidol University [Bangkok | 2009]
- Faculty of Medicine (Number 1 Human Ethics Committee), Thammasat University [Rangsit | 2010]

Conclusion

When conducted in an open and honest manner, the recognition survey can identify an EC's strengths and areas requiring improvement. Independent external surveyors provide an objective evaluation of good practice and validate their compliance with international guidelines. The survey has the ability to recognize a competent EC, which can adequately protect human subjects, and it improves the perceived quality of ethical review globally.

The *SIDCER Recognition Program* started in Asia through FERCAP has provided recognition to 73 ECs in the region, with growing interest from others both in Asia and worldwide. This accreditation provides sponsors with the confidence that ethical review of research proposals is carried out according to established guidelines and practices and performance of the EC meet international standards.

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