

THE CURRENT SITUATION REGARDING THE ESTABLISHMENT OF NATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH IN THAILAND AND ITS NEIGHBORING COUNTRIES

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Abstract. This study discusses the establishment of ethical guidelines for ethical review for biomedical research performed in Thailand, and to some extent, in neighboring countries. There are differences, from country to country, at national and institutional levels regarding guidelines for ethical review committees. Only a handbook issued by Mahidol University describes guidelines for human genetic research and on research dealing with reproductive technology. Both these areas require special consideration to avoid violating human dignity, rights, and confidentiality. This indicates that further efforts should be made to establish research guidelines and/or principles dealing with the human genome.

INTRODUCTION

Biomedical research on human subjects should be carried out giving highest priority to human rights and dignity. Since the Second World War, however, there has been a realization that science (possesses) a danger, tempting medical doctors and researchers to gain new knowledge and develop new technology at the expense of humanity in the name of research.

Beginning with the pronouncement of the Nuremberg Code (1947) and the Declaration of Helsinki (1964), various efforts have been made to avoid violations against human dignity and rights in the world. Based on a wide range of consultations and discussions, through seminars and workshops, representatives from various international organizations, the Operational Guidelines for Ethics Committees That Review Biomedical Research was proposed by the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS) in the year of 2000 (WHO, 2000).

With regard to research on the human genome, the Universal Declaration on the Human

Genome and Human Rights was adopted by the General Conference of the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1997, followed by endorsement in the General Assembly of the United Nations in 1998. Research on the human genome may result in discovery of the etiology of many diseases, and the development of new strategies for diagnosis, treatment and prevention of diseases. At the same time it may cause serious ethical issues regarding the manipulation of human life resulting in a violation of human dignity and rights. In Japan, for example, the Fundamental Principles of Research on the Human Genome were established to avoid misuse of new knowledge and technology and for human benefit and well being. This was established by the Council for Science and Technology (Bioethics Committee, 2000).

One of the important principles described here and also included in the above-mentioned guidelines is 'informed consent'. Since there would be no advancement of science itself without the understanding and acceptance of society, the significance and benefits of the research, together with details including the research process, demerits, rights of withdrawal and being informed or not informed, should be explained to people in simple terms, if they are going to participate. Understanding of the human genome

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may differ between people in developing countries and those in industrialized countries where plenty of information regarding the human genome is available. Special attention should be given to obtain informed consent from people in developing countries where they may be involved in research on the human genome, including genome epidemiology.

The aim of the present study was to analyze the current situation regarding the establishment of ethical guidelines for biomedical research, including research on the human genome, in Thailand and its neighboring countries.

MATERIALS AND METHODS

Copies of ethical guidelines related to biomedical research were obtained from Cambodia, Myanmar and Thailand during the three-year study period, Japanese fiscal years 2002 to 2004. In Cambodia, through the courtesy of Dr Reiko Tsuyuoka, WHO, we obtained copies of the Ethical Guidelines for Health Research Involving Human Subjects (Ministry of Health, Cambodia, 2002) and Standard Operating Procedures (National Ethics Committee for Health Research, 2002), both of which were issued in December 2002. In Myanmar, a copy of a document entitled Ethical Review Committee of the Department of Medical Research (Lower Myanmar) (Ethical Review Committee, Myanmar, 2002) was obtained. In Thailand, we were able to obtain operational guidelines for submission of a research proposal to be reviewed by the Ethical Review Committee of the Ministry of Public Health (Ethical Review Committee for Research in Human Subjects, 2002) or of faculties (Faculty of Medicine and Faculty of Tropical Medicine) of the Mahidol University (Ethics Committee of Human Experimentation, 1998; Ethical Review Committee, Faculty of Medicine at Siriraj Hospital, Thailand, 2002). A Handbook for the Research in Human Experimentation was also available from Mahidol University (Committee on Human Rights Related to Human Experimentation, 2002). In addition, a copy of a research proposal (Coleman *et al*, 2000) involving patients with malaria was provided to us through the courtesy of Dr Jetsumon Prachumsri, Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, as a typical example for

submission of a research proposal which follows operational guidelines under the Ministry of Public Health. We carried out comparative studies on these documents, especially in regard to terms of their structure and contents, the composition of the ethics committee, description of research on the human genome, and the procedure to obtain informed consent from research participants.

RESULTS

Cambodia

Beneficence, respects for rights, and justice were clearly defined as three ethical principles required for all health research involving human subjects in the Ethical Guidelines for Health Research Involving Human Subjects issued by the Ministry of Health, Cambodia (Ministry of Health, 2002). According to Standard Operating Procedures (SOP) also issued by the Cambodian Ministry of Health, the National Ethics Committee for Health Research (NECHR) has been described as 'the only entrance for all research proposals to be reviewed' and setting up of Institutional Review Boards will be considered 'later on' (National Ethics Committee for Health Research, 2002). Therefore, all proposals need to be reviewed at the national level. The Ethical Guidelines consist of three parts: the first and second parts describe essential points for the ethical review of experimental and clinical studies, and those for review of observational epidemiological studies, respectively, both including ethical criteria related to informed consent. The third part describes ethical review procedures, in which the Ethical Review Committee is described so as to include ten to twelve experts of epidemiology, sociology, law, statistics, clinical medicine, microbiology, and pharmacy. Experts from the WHO and other organizations concerned may be invited to the committee in the role of technical advisors. In addition to these members, the NECHR is described to have a Chairperson (Director General for Health), a Deputy Chairperson and a secretary. The SOP covers details of necessary documentation, procedures, elements of review, and forms for application and informed consent. The review fee will be as much as the equivalent of US\$100. The requirement of obtaining informed consent

from the prospective subjects (in the case of an individual who is not capable of giving informed consent, proxy consent from a properly authorized representative) is clearly described with a list of essential information for prospective subjects in the first part of the Ethical Guidelines for Health Research, but not in the SOD, although the latter includes an example of the consent form as one of the attached documents. There is no discussion of research related to the human genome.

Myanmar

The document obtained from Myanmar also describes the role of the Ethics Committee and its composition, and review procedures for research proposals with some details, in order that the Committee may contribute to 'safeguarding the dignity, rights, safety, and well being of all actual or potential research participants' (Ethical Review Committee, Myanmar, 2002). However, the document seems to be at the institutional level rather than the national level, because the document describes about the Institutional Ethical Committee (IEC): and the Committee consists of seven members, six of whom are selected from the Department of Medical Research. the document states that 'the chairperson of the committees should preferably be from outside the Institution to maintain the independence of the Committee'. Thus, the composition of the Committee is different from that of the Cambodian NECHR. Another difference between the ethics committees of both the countries is that the IEC in Myanmar reviews proposals for research involving laboratory animals. With regard to informed consent, the Myanmar document describes in detail the process of obtaining informed consent, although a sample of the consent form is not included.

Thailand

The Handbook for Research in Human Experimentation was issued in 2002 by the Committee on Human Rights Related to Human Experimentation at Mahidol University, although the Committee itself was formed in 1982 (Committee on Human Rights Related to Human Experimentation, 2002). This document gives a definition of and the principles of human experimentation, a list of 15 points for ethical consideration and consideration for special care groups.

According to the definition, human experimentation includes research on biomedical materials from humans, such as excreta used for the diagnosis of parasitic infections. The document also refers to the WHO's Operational Guidelines (WHO, 2000) especially related to the elements of ethical review. Special attention is given to experimentation using new medicine and good clinical practice. What is unique in this document is the detailed description of human genetic research and on research dealing with reproductive technology, both of which require special consideration, because of the risk of violating human dignity, rights, and confidentiality. The Handbook also pays attention to genetic research in families and relatives besides the participants, gene manipulation, banking of genetic materials, and commercial use of genetic data. To obtain informed consent from participants, the document states that the process should consist of information, understanding, and a willingness of the participants, details of which are well explained, followed by recommendations and an example of an informed consent form. In its Annex, the document includes 1) Recommendations for Human Research by the National Research Committee, 2) extracts from some parts of the regulations of the Medical Council on maintaining ethics in the medical profession (issued in 2001), 3) Code of Conduct for Researchers, 4) Declaration of Helsinki, 5) The Phases of Clinical Trials for Vaccines and Drugs, 6) Standard Operating Procedure for Clinical Investigators, and 7) Responsibilities of the Investigator, *ie* extracts from WHO Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products.

In addition to this Handbook, the various faculties of Mahidol University seem to hold their own respective guidelines for the submission of research proposals related to human subjects. Thus, we obtained one document from the Faculty of Medicine at Siriraj Hospital (Ethical Review Committee, 2002) and another one from the Faculty of Tropical Medicine (Ethics Committee of Human Experimentation, 1998). The former document was issued in January 2002 as a revision of the first edition that was issued in October 2001. The later document of the Faculty of Tropical Medicine was issued in February 1998, thus being rather simple, although essen-

tial ethical criteria for biomedical research are included. The former gives comprehensive but practical instructions for submission of research proposals and provides criteria to be approved by the Ethical Review Committee. However, the document has no discussion of research on the human genome in the chapter dealing with research projects required to be submitted for approval, whereas details are described concerning clinical trials of drugs in the text and the format for research proposals is attached as a documentary example. In addition, a detailed description of ethical considerations, an illustration of the information sheet to be distributed to participants and an example of an informed consent form are available in the annex. An executive summary and a checklist to receive ethical approval are also provided for the Ethical Review Committee as attached documents.

Furthermore, we obtained another institutional document issued from the Ministry of Public Health (Ethical Review Committee for Research in Human Subjects, 2002). The document provides instructions for submission of research proposal to be reviewed by the Ethical Review Committee for Research in Human Subjects of the Ministry. According to the document, proposals should be reviewed by at least two advisors (three advisors in the case of studies on AIDS vaccines) prior to being brought to the Ethical Review Committee. The advisors will present a summary of the proposal with detailed ethical considerations and other relevant comments to the Committee, which then reviews the proposal from both ethical and scientific aspects. The document includes examples of information sheets for participants and an informed consent form. In addition, the document also includes Ethical Criteria for the Ethical Review Committee for Research in Human Subjects, the Ministry of Public Health, first written in 1993 and revised in 1995. Thus, the Ministry of Public Health is responsible for reviewing ethical issues in the medical research 1) submitted by the Ministry's personnel or organizations, or 2) conducted in geographical areas under the responsibility of the Ministry, 3) in cases requested by other organizations for ethical review, and 4) cases requiring national authority approval.

Thus, a research proposal involving patients with malaria (Coleman *et al*, 2000), which was

provided to us by the courtesy of AFRIMS, is a typical example that follows the operational guidelines under the Ministry of Public Health (Ethical Review Committee for Research in Human Subjects, 2002). This proposal describes all items and topics in detail required along the guidelines. Since the research needs blood samples from volunteers carrying malaria parasites, the quantity and purpose of the blood collection and usage are described in detail. Furthermore, it is clearly mentioned in the document that no genetic analyses will be done on the blood itself (*ie*, the investigators are not interested in the genetics of the human subject, but only of the malaria parasite). In its Appendix, the document includes the sequence of events and a flow diagram for patients enrolled in the study, a summary of previous data concerning mosquito feeding with malaria patient blood, information letters and consent forms in English and Thai, and blood and blood component donation forms in both languages. From the viewpoint of the ethical review, the protocol is to be submitted to the Thai Ministry of Public Health Ethical Review Board and to the US side of ethical review committee and board related to the use of human subjects.

DISCUSSION

The present study revealed that the establishment of guidelines for ethical review of biomedical research has been performed in Thailand and to some extent in its neighboring countries as well. In Cambodia, the establishment of the guidelines has been accomplished at the national level, but there exist no guidelines at the institutional level. In Myanmar, the guideline seemed to be a mixture of both national and institutional levels. There are some differences from country to country concerning the composition of ethical review committees, and whether or not the review committees should cover animal experimentation in addition to human experimentation.

The importance of obtaining informed consent from research participants has been well recognized by researchers in medical and health fields, whenever research is carried out on human subjects or materials that are obtained from humans. Concerning studies on the human ge-

nome, however, a clear-cut description is rather scant, except in some institutions in Thailand (Committee on Human Rights Related to Human Experimentation, 2002), indicating that further efforts to establish research guidelines and principles dealing with the human genome is necessary in this region, since research on human genome and its outcomes may elicit serious ethical issues and social problems due to the risk of violating the human dignity and rights.

There exist guidelines for ethical reviews on research dealing with the human genome only in the Handbook for Research in Human Experimentation, which has been issued by the Committee on Human Rights Related to Human Experimentation, Mahidol University, Thailand (2002). This is probably due to the fact that research activities are quite high in Thailand, thereby providing opportunities for Thai researchers to be involved in international cooperative research using advanced technology related to the human genome.

To obtain informed consent from research participants, researchers themselves must understand the meanings of genetic information, gene, genome, DNA, polymorphism, etc, related to human genome studies. This is necessary, otherwise people living in developing countries lacking knowledge of the human genome may not be able to understand researchers' explanations. This lack of knowledge can present "special obstacles to obtaining truly informed consent from the population" (WHO Advisory Committee on Health Research, 2002). Research on genome epidemiology, for example, should be carefully designed so that community people can understand its significance and the benefits of the research and so they can make an informed decision on whether to participate. It would be interesting to study whether any difference exists between industrialized and developing countries concerning the understanding of genome research in the community and the researchers.

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