ETHICS COMMITTEES AND EXTERNALLY-SPONSORED RESEARCH IN IRAN

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ABSTRACT

Globally, there have been considerable debates on the ethical conduct and review of collaborative international researches. One of the great challenges is to conduct clinical trials in developing countries as Externally-Sponsored Researches (ESR).

This descriptive survey has reviewed the status of this type of researches in Iran during 2002 to 2003. This study was carried out in 44 universities of medical sciences and 32 research centers. The questionnaires containing closed and open-ended questions were sent to their Ethics Review Committees (ECs). After collection of data and coding, they were analyzed by means of SPSS software version 11.5.

Forty one universities and 25 research centers have been responded but only 35 ECs retrieved the questionnaire. According to the collected data, 26 and 54 studies have been carried out as a collaborative research or externally-sponsored researches in Iran in 2002 and 2003, respectively. Although more than half of ECs' members have received necessary preliminary educations but there were professional educational courses in only 25% of ECs. About 17% of ESR projects have not been examined in ECs, although they have been evaluated in the Scientific Research Council. Only one of the evaluated ESR proposals has been rejected and the rest have been approved and conducted. Socio-cultural issues and religious beliefs, scientific validity, and national priorities were the most important factors for proposals evaluation.

The ethical issues concerning international collaboration for clinical research in developing countries are complex. We should enhance educational programs for researchers and establish appropriate regulatory guidelines at national and international levels.

Keywords: Collaborative international research, Externally-sponsored research, Ethics committee, Research ethics, Developing countries, Iran

INTRODUCTION

Externally-Sponsored Researches (ESRs) are researches which are funded by sponsor agencies of countries with relatively high economic development, and conducted in countries that are relatively less developed. These researches give rise to many important ethical challenges. The reported unethical conducts of some multinational pharmaceutical companies in conducting clinical trials in developing countries have been highlighted recently (1). For instance, an increasing number of clinical trials of HIV vaccines are now being conducted or planned in developing countries(2). Appreciation of concerns regarding research in developing countries requires some knowledge of the growing global disparities in wealth and health, and of the life style and world view of potential research subjects (3). There is a marked disparity between the burden of disease in developing countries and the proportion of medical research that is devoted to the diseases of the developing world (4). The 10/90 disequilibrium is a term coined to describe the situation where only 10% of global research funds are going to diseases which comprise 90% of the global burden (5-7). Furthermore, in a situation of general poverty combined with a high burden of disease, there is no way to prevent victims or potential victims of a deadly epidemic such as HIV/AIDS from being unduly induced by any type of research participation proposal that holds out the possibility of any type of treatment (8). It is clear that in developing countries the major incentive to participating in research may be access to otherwise unavailable health care. This is acceptable if the potential benefits of the research to the subjects and their community outweigh the potential harms in the long term as well as in the short term. Collaborative research should also

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include the enhancement of local capacity for grappling with these ethical problems in ways that allow the quest for universalism to include all who have something to contribute to collective understanding and to the reasoning processes (3).

One of the obstacles to research in developing countries is the complex process of ethical approval for studies, particularly those funded by institutions and industrial sponsors in developed countries (4). There are three key levels of assessment: the proposal's relevance to priorities within host countries, the scientific validity of the research, and its ethical acceptability (9). The role of reviewing committee for reseach ethics is critical to contribute to safeguarding the safety and dignity of research participants. According to great emphasis on ethics that has been expressed by the medical and religious professions in the Islamic Republic of Iran in recent years, compilation of a strategic plan for medical ethics activities carried out in 2002 by the Research and Technology Deputy of Ministry of Health and Medical Education (10). National and Regional Ethical Committees (ECs) in universities and research centres were established nationwide. Currently, these ECs supervice of medical researches and protection of human subjects. This research is designed to evaluate the current approach of ECs for ESRs in the medical universities and research centers, reviews the status of externally sponsored research projects in Iran within 2002 to 2003, discusses current problems and suggests potential solutions. This paper also briefly presents some results about the current status of the ECs in Iran.

METHODS

Also, the survey has evaluated the functions and compositions of ethics committees regarding Externally-Sponsored Research (ESR). It must be mentioned that the survey has been designed as a multinational collaborative project entitled "*Ethics Review on Externally-Sponsored Research in developing countries*", to collect data from several countries including Iran, Japan (11), Philippines, Pakistan, and India. However, our manuscript encompasses the results of this study in Iran.

The project started in June of 2003. In this investigation, the targets were vice-chancellor of research and technology of medical universities (44 public universities) and research centers affiliated to public universities (those that have a special ratified budgetary line). The questionnaires (including open and close-ended questions) were distributed by mail. Firstly, we carried out a pilot-study in 6 centers. After brief revision, the main study was started. It took about six months that we collected most responses. After coding the questionnaire, data entry and analyses were done by SPSS software version 11.5. Because some answers were not valid, we excluded these questions in analyses.

RESULTS

Our project conducted nationwide survey on current status of ECS Supported by the government seeking number and ethical status of ESR projects within 2002 and 2003 in the country. Forty one universities and 25 research centers have been responded which totally 35 respondents have been retrieved the questionnaires. The rest have been sent an explanatory letter. The total response rate was about 80%. Table 1 lists the characteristics of responses.

Among respondents, 9 research centers had not set up independent ethics committee at the time of study but some were preparing to set it up. Four of them have replied the completed questionnaires that three centers had ESR projects.

Table 2 represents number and decisions about ESR projects. Among the reviewed proposals, only one proposal has been rejected due to sociocultural reasons. Endocrinology and Metabolism Research Center (EMRC) of Tehran University of Medical Sciences (TUMS), Center for Research and Training in Skin Diseases and Leprosy (CRTSDL) affiliated to TUMS, Digestive Disease Research Center of TUMS, and Pasteur Institute of Iran (IPI) have the most ESRs projects within 2002-2003. According to data, about 17% of ESR projects have not been examined in ECs, although they have been evaluated in the Scientific Research Council.

We asked questions about the items that ECS takes into account while reviewing an ESR project. Whether the research topic is one of the health priorities, its methodology is scientific and reliable, and it is in harmony with cultural and societal believes and do not violate them. As shown in table 3, almost always adaptation of research with socio-cultural faiths has been considered**.**

Status and Function of ECs

The composition of ECs members has been shown in table 4. Number of ECs members is varied between 4 to 13 people with a mean of 7 (± 1.7). Most of the respondents have stated that there is some financial compensation for membership.

There is no limitation for participation of female representatives in ECS but their participation is not mandatory. About 90% the ECs have included religious scholars in their membership. Also, law experts and ethicists have been included in 86% and 57%, respectively. Any of them have lay persons in their composition.

For membership, previous special training is not obligatory but many of ECs provide educational materials for self-training or establish short-term workshops for members. Only in 5 medical

universities and 4 research centers, the members passed special courses about research ethics.
The approval from the National Ethics Committee is not considered a necessary requirement for all ESR projects by the most ECs. Some ECs stated that depending on the case and a local ethics committee they might decide independently in some projects.
In the issue of the subjects' protection in clinical trials, the ECs have pointed out 'International Standards' in 58%, 'Local Standards' in 31.5% and both in 10.5%. However, the extent of minimizing the risks reduction, they have observed 'International Standards' in 74%, 'Local Standards' in 16%, and both in 10%. Informed consent is always obtained and the research participants sign the related documents. Some ECs have special justification sessions for participants.
In risk to benefit assessment, 42% of respondents gave priority to 'the subjects' while only 8.5% gave priority to 'the society'. About 50% of respondents were in agreement with the equivalent priority of the subjects and the society.

DISCUSSION

In the current decades, great efforts are being exerted in medical ethics research worldwide and in Iran. Challenges and ethical dilemmas facing biomedical research in the developing world have been addressed by trying to conform with some of the regulations laid down in the international regulatory texts. Among international ethical guidelines, the Declaration of Helsinki (12) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (13) prepared by Council for International Organisations of Medical Sciences (CIOMS) in collaboration with WHO have emphasized the issue of collaborative research ethics. The guidelines have undergone further revisions. Over the last few years these guidelines have also been complemented by efforts in different countries, such as the consultations of the Nuffield Council for Bioethics in the United Kingdom (14) and the National Bioethics Advisory Commission in the USA (15).The Nuffield Council on Bioethics published its report. Titled: "*The Ethics of Research Related to Health Care in Developing Countries"* on April 24th 2002. The report presents a number of recommendations on key issues in developing world research (9). The Working Party of the Nuffield Council on Bioethics recommends that all countries should establish an effective system for the ethical review of research, which includes the establishment and maintenance of research ethics committees that are independent of government and sponsors of research. Externally sponsored research should be reviewed by an independent committee in the sponsor's country as well as in the country where the research is to be conducted (9). Furthermore, the Working Party recommends that national and international sponsors of research should ensure that adequate provision is made for training of all those professionals involved in research related to healthcare in the ethics of research (9).
In our country, the establishment of the National Committee for Medical Research in 1998 paved the way for the organizing the Regional Committees in medical universities throughout the country (16). These committees undertake the supervision and observation of national and international laws on medical ethics in research (16). The national codes of ethics for biomedical researchers have been prepared by Ministry of Health and Medical Education (MOHME) in 2000. These codes have been an official guideline to deal with ethical issues in researches yet. Likewise, through a proposal entitled "*Compilation of National Guidelines on Medical Research*", the Medical Ethics and Medical History Research Center (MEHRC) have considered updating ethical codes of research.
After compilation of a strategic plan for medical ethics activities, which was carried out in 2002 by the Research and Technology Deputy of MOHME (10), considerable plans and activities carried out in this field. For instance, given the lack of appropriate educational sources for ethics courses in the medical and health care sciences, the book titled "*Health care professional and Ethical Issues*" was authorized in approaching goals of the strategic plan (17). The book entitled "*Ethics in Medical Research*" is also in the course of authoring by MOHME. In addition, bioethics educational courses, such as establishment of MPH course (with medical ethics tendency) were designed and developed by TUMS in current years. On the other hand, periodical workshops on "*medical ethics education*" and "*ethics in biomedical research*" have been conducted during 2002-2006.
Over the past decades we have had experience of working in a partnership model with international organisations and universities. The above mentioned results show that there are some problems such as insufficient experiences and expertises in research ethics and lack of appropriate guidelines for ethical review of ESRs in our country. Although more than half of ECs' members have received necessary introductory education, but there were specific professional educational courses in only 9 (about 25%) of ECs. According to current law, every governmental medical university or research center is required to establish an ethics review committee. As a role, the research centers that do not have independent EC should

obtain approval of the official university for conducting research projects. It must be mentioned that the share of private sectors in research is insignificant in our country.

According to the results of current study, it seems that some of ESR projects have not been reviewed by the ECs. Currently, in most of the universities and research centers in Iran, "*the Scientific Research Council*" decide whether the proposed research is conforms to the generally accepted scientific principles. In addition to different professions and specialists, there is ordinarily one or more epidemiologist or biostatistician in the Scientific Research Council. All projects are initially sent for scientific approval, and addressing this issue is not considered as an ordinary responsibility of the ECs.

CONCLUSION AND RECOMMENDATION

The recent debate has focused on controversies The recent debate has focused on controversies surrounding internationally sponsored research. Although successful cross-cultural and international collaborations have to overcome many regional and global barriers (18), but there is a necessity to perform research within a framework that is appropriate to the religious, social, medical, and political context of the countries. Ethical and scientific standards should be observed in these researches. Collaborative projects should be reviewed by a comprehensive process. The main ECs' tasks are ethical review of research proposals, education of researchers and the community, and monitoring of research conduct**.** ECs in both the host and the sponsoring country should review and approve the proposals. Acceptable ethical standards should be observed in ESRs by both the host and the sponsoring country.

In our country, the necessary principles and issues which ECs need to consider reviewing should be outlined ESRs. Also, concerning necessity of monitoring and track of the progress of an approved research, ECs should have standard qualified procedures for supervision on investigations on a regular basis. On the other hand, providing supportive approaches for ECs, such as financial and educational support, is a responsibility of national governments. As far as possible, ECs members should have opportunities for required education and training. Training of ECs members could improve process of ethics review and monitoring of these researches, and could enable them to fulfil their tasks effectively.

At international level, research needs to respond to community needs and national priorities, and the development of a national research agenda in developing countries must be firmly grounded in a process of priority setting (19,20). Local capacity could be developed by strengthening models for reviewing the ethics of research. Strengthening local capacity by developing ethics research training programs is an immediate need. The opportunities afforded by the Internet for learning and education in ethics should also be utilized (19).

Ethical principles and research guidelines should try to balance individual rights with the good of the community.

As mentioned before, less than 10% of the world's research resources are earmarked for 90% of the health problems (6,7). Important steps in redressing this imbalance are to promote equity in health research. Therefore, research in developing countries should lead to strength of their research capacity. These researches should be sensitive to cultural differences. Many members of ECs in developed countries have little (if any) experience in the developing world and do not understand local constraints (4). Therefore, collaborative international research should involve approval by IRBs at the sponsoring and developing countries.

ACKNOWLEDGMENT

We would like to thank all of the vice-chancellors of research and technology of medical universities and research centres for sharing with us and sincere cooperation. We also wish to thank the Endocrinology and Metabolism Research Center (EMRC) of Tehran University of Medical Sciences which funded this project.

Table 1. The number and categories of responses.

Categories	Universities no.	Research Centers no.	Total no.
With ESR projects, completed questionnaire	10	9	19
With ESR projects, not completed questionnaire	1	0	1
Without ESR projects	30	11	41
Not completed questionnaire because lack of independent Ethics committee	0	5	5
no response	3	7	10
Total	44	32	76

Table 2. Number and decisions about ESRs.

Number	2002			2003			
	ratified	*rejected*	*total*	*ratified*	*rejected*	*not evaluated in ECs*	*total*
Universities (no = 11)	4	0	4	22	1	8	31
Research centers (no = 9)	22	0	22	22	0	1	23
Total (no = 20)	26	0	26	44	1	9	54

Table 3. The degree of concerns of ECs for reviewing medical researches.

The Points taken Into Account by ECs in Reviewing ESRs	Universities (no.=11)				Research Centers (no.=9)			
	Always	*Sometimes*	*Seldom*	*Never*	*Always*	*Sometimes*	*Seldom*	*Never*
Health priorities of the country	4	5	1	0	4	3	2	0
Scientific reliability of research methodology	5	5	0	0	7	0	2	0
Respecting social and cultural issues	10	0	0	0	9	0	0	0

Table 4 – The composition of ECs.

Composition / Number	*Physician*	*Religious scholar*	*Ethicist*	*Lawyer*	*Epidemiologist*	*Nurse*	*Health care management PhD*	*Vice–chancellor or chancellor*	*Basic sciences*	*Others*
Universities (21)	20	21	15	20	19	2	1	7	5	1
Research centers (14)	13	11	5	10	13	1	0	1	8	1
Total (35)	33	32	20	30	32	3	1	8	13	2

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