POLICY STATEMENT ON ETHICAL CONSIDERATIONS INVOLVED IN RESEARCH ON HUMAN SUBJECTS

INDIAN COUNCIL OF MEDICAL RESEARCH
New Delhi 110 016
February 1980

POLICY STATEMENT ON ETHICAL CONSIDERATIONS INVOLVED IN RESEARCH ON HUMAN SUBJECTS

INDIAN COUNCIL OF MEDICAL RESEARCH
NEW DELHI

FEBRUARY 1980

INTRODUCTION

There is at the moment considerable medical research being carried out on human subjects at different centres throughout the country. It is expected that the number of clinical investigations undertaken on volunteers and patients would increase in the coming years due to a number of reasons. It is being increasingly felt by scientists, clinical investigators and national health authorities that the resources of the country should be utilized for carrying out research that would be relevant to large numbers of persons living in rural areas in order to develop appropriate health measures for such persons. This would result in an increase in the epidemiological and sociological oriented research involving large numbers of individuals. Further, there is growing awareness in the scientific community that results on experimental models are not always predictive of what would eventually occur in the human and that a few well controlled investigations on a limited number of human subjects for a relatively short duration would yield much more relevant information than a large number of animal experiments carried out for a longer period of time. This awareness and the fact that in certain areas of research there are no animal models at all would lead also to increasing number of human subjects being involved in clinical research. Finally, research on clinical evaluation of remedies used in indigenous systems of medicine and on plants reputed to possess therapeutic properties is also increasing. This factor together with the continuing need for clinically evaluating new drugs developed in national laboratories and institutions and in pharmaceutical houses both in India and abroad would again require clinical trials to be carried out on human subjects throughout the country.

In addition to the increased quantum of medical research being undertaken on human subjects, the scope of clinical investigation has also undergone a change in the last decade. The type of experimental procedures that a patient is submitted to has become more complex and varied as the complexities of medical research have increased.

It is clearly understood that it is essential to carry out research on human subjects if progress is to be maintained and better medical and therapeutic modalities discovered for the benefit of man. It is equally clear that such research on human subjects and patients is associated with some degree of risk to the individual patients or volunteers. The Indian Council of Medical Research (ICMR) feels that in view of the increasing research being carried out on human subjects and the ever widening complexities of medical research, guidelines for experimentation on human subjects in the country are required to make certain, as far as possible:

- that the rights and welfare of human subjects on whom experiments are carried out are adequately protected;
- that the risks to an individual are outweighed by potential benefits to him or to society or by the importance of the knowledge to be gained;

- that informed consent is obtained from the individual by methods that are appropriate and adequate;

- that the clinical investigation on human subjects is carried out by an investigator who has the requisite background and competence to carry out such research; and
- that the investigator has a framework for obtaining advice, support and assistance from his peers before embarking on a particular clinical research programme.

It is hoped that these guidelines formulated by the Central Ethics Committee of the Council would assist investigators involved in clinical research to plan their clinical research in accordance with the principles enunciated in the World Medical Association Declaration of Helsinki (1964) as modified by the 29th World Medical Assembly at Tokyo in 1975 and the Nuremberg Code which has clearly laid down the ten principles to be kept in mind when conducting research on humans. It is expected that the guidelines would protect volunteers and patients participating in clinical research from being exposed to unjustified hazards and risks during their involvement in the research project. These would also protect clinical investigators and researchers by enabling them to obtain support from their peers for the research they intend to carry out.

INSTITUTIONAL ETHICAL COMMITTEES

The Council feels that clinical research on normal volunteers or on patients, whether for therapeutic, non-therapeutic or diagnostic purposes, should be undertaken only after an ethical committee of the concerned institute or college has gone thoroughly into the proposed research, assessed carefully the balance between the possible benefit to the patient/volunteer or to society and the potential risk to the individual participating in the trial and on the basis of such an assessment has approved the project from an ethical point of view.

The Council would, therefore, urge all medical colleges and research centres involved in clinical research to form ethical committees if they do not already have a functioning ethical committee at the moment. The ethical committee should consist of experienced clinicians who have been carrying out clinical research and clinical evaluation in the past, should have on it an expert on drugs and one or two non-medical persons who could provide guidance to the committee in the matter of ethics and law. Wherever possible, a lawyer or a judge should be a member of the institute ethical committee. It is suggested that the ethical committee be kept fairly small (5-7 members) but that appropriate expertise available at the centre, in the region or the country be consulted wherever necessary. The ethical committee at any institute or college should not hesitate to have on it members from other institutes, if there is need for such a step.

The ethical committee should meet at least once every three months and review all proposals for clinical research proposed by investigators in the Institute. The Committee should assess all such proposals and only after approval by the committee should the research be initiated by the investigator and his co-investigators.

The ethical committee should review every proposal for research on human subjects to assess, among other considerations, whether:

- voluntary consent of the individual is being obtained;

- the experiments are so designed that they would yield meaningful results that could not be obtained by other methods;

- the animal experiments carried out support the need for clinical experimentation;

- the experiments would be conducted in a manner to avoid all unnecessary physical and mental suffering and injury;

- the experiments have been planned in a manner so that the degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment;

- proper preparations would be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death;

- safeguards have been taken to see that the experimentation would be conducted only by scientifically qualified persons who possess the requisite competence, experience and qualities to carry out the research;

- it would be made perfectly clear to the subject or patient that he would be at liberty to bring the experiment to an end at any time he desires to do so;

- the scientist in charge of the research project is prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, skill and careful judgement required of him, that a continuation of the experiment is likely to result in injury, disability or death to the experimental subject.

The Council recognizes the fact that it may take time for all the institutes in the country to form ethical committees and for a period of one year the Central Ethical Committee of the Indian Council of Medical Research would undertake to review, on ethical grounds, proposals submitted to the Council, irrespective whether it is submitted for support of the research proposed or not. This would be done with a view to assisting the investigators from the different institutes during the interim period when the institutional ethical committees are being formed at these institutions. The Council would also, if required to, assist these institutes to set up ethical committees and help in their functioning in the early stages.

The Council feels that if the Ethical Committee is to play a useful role and discharge its functions effectively, it must be independent.

SUPPORT OF CLINICAL RESEARCH BY THE COUNCIL

The Council would not consider support for any proposal for research on human subjects unless the research proposal has been approved by the Ethical Committee of the institute concerned. As has already been stated, the Council would take on the responsibility of assessing proposals on ethical considerations for an interim period of one year. The Council would also carry out this evaluation for proposals that may be sought to be sent for support to international agencies such as World Health Organization which does not entertain proposals for research support unless approved by the Ethical Committee of the institute. This assistance by the Council would enable investigators in institutes, which at the moment, do not have institute Ethical Committee to obtain support from these agencies.

IMPLEMENTATION OF ETHICAL COMMITTEE'S GUIDELINES

In addition to its other functions, the Ethical Committee should monitor the implementation of these guidelines and check whether the principles laid down regarding research on human subjects are being followed and whether the recommendations made by the institute Ethical Committee about a particular project are being observed by the investigators in charge of the projects.

The Council would, of course, retain the right of reviewing at any time the ethical procedures being observed in any project being supported by it.

DRUG TRIALS

The Council would like to make it clear that clinical evaluation of any new drug to be used for prophylactic, diagnostic or therapeutic purposes should be carried out, only after approval, as is necessary

under law, has been received from the Drugs Controller of India. The investigator should then formulate the research proposal and submit it to the Ethical Committee of the institute. This guiding principle should be followed irrespective of whether the drug has been developed in this country or abroad or whether clinical trials with the substance or drug have been carried out outside India. Similar principles should be followed for evaluation of new devices or other similar agents.

CLINICAL TRIALS WITH PLANTS AND INDIGENOUS SYSTEMS OF MEDICINE

The Council would suggest that for clinical evaluation of plants being utilized for therapeutic purposes, assessment of treatments being used in the traditional systems of medicine the protocols for such clinical research should again be approved by the Ethical Committee of the institute. There is no need for clearance to be obtained from the Drugs Controller of India for such trials of products already in widespread use in the traditional systems of medicine today in the country.

INFORMED CONSENT

The question of "informed consent" and the best way of obtaining informed consent is one that is difficult and one in which the norms and forms used in other countries are really not fully relevant to the conditions prevailing in this country. Although the procedure of obtaining the signatures of the person giving his/her consent cannot be dispensed with, at the same time, it must be emphasized that in the context of the conditions prevailing in the country, mere signatures would not ensure the requirements of informed consent. The Council can only lay down the broad guiding principles that form the basis for obtaining informed consent and then leave it to individual ethical review committees to develop their own procedures. These principles are that the proposed participants in a clinical research programme should be made aware, by a person not in a position to influence the patient such as the treating physician but for example, by a social worker, of the fact that a new drug or procedure is being evaluated. The patient for a new clinical trial should be informed briefly of the potential possible benefits of the new treatment as against the existing and the possible side-effects or hazards of the new treatment when compared to the existing treatment. If it is a randomized double blind trial, the patient should be told that he would be given either the old treatment or the new. He then should be informed in clear terms that if he wished to withdraw at any time from the trial, he could do so and then asked whether, in the circumstances explained to him, he would like to participate in the trial. The question of any payments to cover his/her expenses in taking part in the trial should be discussed after his/her agreement to participate in the trial and not suggested at a time when it could be used as an inducement to him to join in the trial.

If the proposed research is not a trial which would in any way directly benefit the subject or the patient, then the benefit that would accrue to society or to other persons suffering from the disease should be clearly explained to the subject, as also the possible hazards to him, before asking him whether he would like to participate in the trial. Again, he should clearly be informed that he could withdraw from the trial any time he would like to.

CLINICAL RESEARCH ON CHILDREN

Research on children should be carried out only if there is possibility of some direct benefit to the child by taking part in the clinical trial or research project. An experiment on children could be carried out if:

- it is an experiment on the clinical efficacy of a new treatment with the immediate aim of curing the child's

- it is an experiment on an ill child in order to find out more about the condition or disease from which the child is suffering.

A good indication to judge whether an experiment on a child is ethical or not is for the investigator to ask himself the question "Would I do this to my own child?" Voluntary informed consent must be obtained from the parents or guardian of the child before carrying out the research project.

CLINICAL RESEARCH ON MENTALLY DEFICIENT PATIENTS

Clinical research on mentally retarded children or adults is again a very difficult question and has been the subject of much controversy in the past. Research on such persons should, again, be carried out only if:

- the research on a new treatment could cure the patient;

- the clinical research being carried out would add more information about the condition or disease from which the patient is suffering.

Informed voluntary consent needs to be obtained from the guardian/relatives of the patient before any research can be conducted on mentally deficient patients. If the patient has intervals when he is in

possession of all his faculties, then, his consent during such a period should also be obtained before including him as a subject for the proposed research.

CLINICAL RESEARCH ON PRISONERS, MEDICAL STUDENTS & LABORATORY PERSONNEL

Research on prisoners should never be carried out as it is not only difficult to obtain informed voluntary consent from prisoners but inducements offered to the prisoner for taking part in the trial would make it unethical to include such persons as subjects in a research programme. Similar considerations also apply, to a lesser extent, to carrying out clinical research on medical students and laboratory personnel but there may be exceptional occasions when research on such subjects would be perfectly ethical. The Ethical Committee should judge each research programme involving such persons with particular reference to the fact whether the teacher or investigator is in a position to influence the decision of the subject to take part in the research.

FINANCIAL REIMBURSEMENTS TO PARTICIPANTS TAKING PART IN CLINICAL RESEARCH PROJECTS

While it is reasonable to reimburse subjects and patients for taking part in a trial for the loss in time, leave taken and other expenses that they may have incurred such as transportation expenses, expenses on food, if the procedure is a long drawn one, or in employment of a part-time helper to look after the children during absence of a housewife from the house, this reimbursement should not be of such magnitude so as to act as an inducement to the person to join the trial. The Ethical Committee of the institute concerned would be the best judge of what constitutes a reasonable reimbursement in a particular situation as that would depend on several factors such as the time required to be spent in the hospital, the procedure itself and local factors such as existing costs of transportation etc.

PUBLICATION OF PAPERS ON CLINICAL RESEARCH IN THE INDIAN JOURNAL OF MEDICAL RESEARCH

The official publication of the Indian Council of Medical Research - the Indian Journal of Medical Research - would review papers submitted to the journal for publication from an ethical point of view also before approving such papers for publication. It is expected that in due course of time, those papers that have been based on clinical research carried out only after approval of the institute Ethical Committee would be considered for publication in the Indian Journal of Medical Research.

CLINICAL RESEARCH SUPPORTED BY AGENCIES OTHER THAN THE INDIAN COUNCIL OF MEDICAL RESEARCH

These guidelines have been prepared to assist all investigators in the country who are involved in carrying out clinical research on human subjects. It is hoped that other agencies in the country supporting clinical research in India would either incorporate some of these suggestions in their own evaluation of proposals for support of clinical research or adopt the guidelines laid down by the Council. The Council would, from time to time, organize meetings of all agencies supporting clinical research in India in an attempt to make uniform the ethical safeguards that are required of clinical investigators before carrying out research on human subjects.

THE ICMR COMMITTEE TO CONSIDER ETHICAL ASPECTS OF INVESTIGATIONS ON HUMAN SUBJECTS

Mr Justice H.R.Khanna, (Chairman)
S-368, Panchsheel Park
New Delhi 110 017

Dr Ranjit Roy Chaudhury
Dean and Head
Department of Pharmacology
Postgraduate Institute of Medical
Education and Research
Chandigarh 160 012

Dr S.S.Gothoskar
Drugs Controller of India
Directorate General of Health Services
Nirman Bhawan
New Delhi 110 011

Dr S.Padmavati
A-1/116, Safdarjung Enclave
New Delhi 110 016

Prof V.Ramalingaswami
Director-General
Indian Council of Medical Research
New Delhi 110 016

Dr B.Sankaran
Director General of Health Services
Nirman Bhawan
New Delhi 110 011

Dr Badri N.Saxena (Member-Secretary)
Deputy Director General
Indian Council of Medical Research
New Delhi 110 016

Published by the Indian Council of Medical Research, New Delhi 110 029.