



KINGDOM OF CAMBODIA

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MINISTRY OF HEALTH

**ETHICAL GUIDELINES
FOR
HEALTH RESEARCH
INVOLVING HUMAN SUBJECTS**

January 2001

ETHICAL GUIDELINES FOR HEALTH RESEARCH INVOLVING HUMAN SUBJECTS

All health research involving human subjects shall conduct in accordance with *three* basic **ethical principles**, namely:

1. **Beneficence**, which requires that good should result, harm should avoid or that benefits should justify the expected risk or harm;
2. **Respect for rights**. Including the free choice of the subject and protection of those of diminished autonomy; and
3. **Justice** which requires an equal distribution of burden and benefits.

PART I.

ETHICAL REVIEW OF EXPERIMENTAL and CLINICAL STUDIES

Proposals for clinical and experimental studies should respond to the following ethical criteria related to informed consents of subjects, selection of research subjects, confidentiality of data and compensation for accidental injury.

A-INFORMED CONSENT OF SUBJECTS

Article 1: Individual informed consent

For all experimental and clinical research involving human subjects, the investigator must obtain the informed consent of the prospective subjects or, in the case of an individual who is not capable of giving informed consent, the proxy consent of a properly authorised representative. Informed consent should not be sought or obtained by the use of financial or other material good benefit as result of consent obtained.

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Article 2: Essential information for prospective research subjects

Before requesting an individual's consent to participate in research, the investigator must provide the individual with the following information, in language that he or she is capable of understanding:

- that each individual is invited to participate as a subject in research, and the aims and methods of the research;
- the expected duration of the subject's participation;
- the benefits that might reasonably be expected to result to the subject or to others as an outcome of the research;
- any foreseeable risks or discomfort to the subject, associated with participation in the research;
- any alternative procedures or courses of treatment that might be as advantageous to the subject as the procedure or treatment being tested;
- the extent to which confidentiality of records in which the subject is identified will be maintained;
- the extent of the investigator's responsibility, if any, to provide medical services to the subject
- that therapy will be provided free of charge for specified types of research-related injury and its complications;
- whether the subject or the subject's family or dependants will be compensated for disability or death resulting from such injury; and
- that the individual is free to refuse to participate and will be free to withdraw from the research at **any time** without penalty or loss of benefits to which he or she would otherwise be entitled.

Article 3: Obligations of investigators regarding informed consent

The investigator has a duty to:

- communicate to the prospective subject all the information necessary for adequately informed consent;
- give the prospective subject full opportunity and encouragement to ask questions;
- exclude the possibility of unjustified deception, undue influence and intimidation;
- seek consent only after the prospective subject has adequate knowledge of the relevant facts and of the consequences of participation, and has had sufficient opportunity to consider whether to participate;
- always obtain from each prospective subject a signed form as evidence of informed consent; and
- renew the informed consent of each subject if there are material changes in the conditions or procedures of the research.

Article 4: Inducement to participate

Subjects participated in clinical research may be paid for inconvenience and time spent. All subjects should be reimbursed for expenses incurred, in connection with their participation in research; they may also receive free medical services. However, the payments should not be so large or the medical services so extensive as to induce

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prospective subjects to consent to participate in the research against their better judgement ("undue inducement"). All payments, reimbursements and medical services to be provided to research subjects should be approved by an ethical review committee.

Article 5: Research involving children

Before undertaking research involving children, the investigator must ensure that children will not be involved in research that might equally well be carried out with adults. When children are judged to be indispensable for research on diseases of childhood and conditions to which children are particularly susceptible, the consent of a parent or other legal guardian, after a full explanation of the aims of the experiment and of possible hazards, discomfort or inconvenience, is always necessary.

Article 6: Research involving persons with mental or behavioural disorders

The mentally ill and the mentally defective persons should never be the subjects of research that might equally well be carried out on adults who are in full possession of their mental faculties. They are, however, the only subjects available for research on the origin and treatment of mental disease or disability. The agreement of the immediate family - whether spouse, parent, adult offspring or sibling - should be sought.

Article 7: Research involving prisoners

For prisoners the same conditions as for any other person and as described in PART I, Article 2 apply. Their agreement to participate in any research should be given, before any activity can take place. Research on prisoners with serious illness or at risk of serious illness should be denied.

B-SELECTION OF RESEARCH SUBJECTS

Article 8: Equitable distribution of burdens and benefits

Individuals or communities to be invited to be subjects of research should be selected in such a way that the burdens and benefits of the research will be equitably distributed. Special justification is required for inviting vulnerable individuals and, if they are selected, the means of protecting their rights and welfare must be particularly strictly applied. Gender equality must be respected.

Article 9: Selection of pregnant or nursing (breastfeeding) women as research subjects

Pregnant or nursing women should not be subjects of any clinical trials except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable subjects.

C- CONFIDENTIALITY OF DATA

Article 10: Safeguarding confidentiality

The investigator must establish secured safeguards of the confidentiality of research data. Subjects should be told of the limits to the investigators' ability to safeguard confidentiality and of the anticipated consequences of breaches of confidentiality.

D- COMPENSATION OF RESEARCH SUBJECTS FOR ACCIDENTAL INJURY

Article 11: Right of subjects to compensation

Research subjects who suffer physical injury as a direct or indirect (e.g. traffic accidents on the way to research investigation) result of their participation are entitled to such financial or other assistance as would compensate them equitably temporary or permanent impairment or disability. In the case of death, their dependants are entitled to material compensation. The right to compensation may not be waived.

E- STUDY DATA AND RESULTS

Article 12: Study reports and data

Any research carried out in the Kingdom of Cambodia, whether locally or externally sponsored or administered, should have a copy of the research report deposited at the National Institute of Public Health and their data belonging to the nationals.

Article 13: Release of study results

Study results should be publicised without any interference from sponsoring or administrative authorities.

PART II-

**ETHICAL REVIEW OF
OBSERVATIONAL EPIDEMIOLOGICAL STUDIES**

Proposals for observational epidemiological research should comply with the following ethical criteria with regards to issues of informed consent, maximising benefit, minimising harm, confidentiality and conflict of interest.

A- INFORMED CONSENT

Article 1: Individual informed consent

When individuals are to be subject of observational epidemiological studies, their informed consent will be usually sought. Consent is informed when it is given by a person who understands the purpose and nature of the study, what participation in the study requires the person to do and to risk, and what benefits are intended to result from the study.

For several types of observational epidemiological research individual informed consent is either impracticable or inadvisable. In such cases the ethical review committee should determine whether it is ethically acceptable to proceed without individual informed consent and whether the investigator's plans to protect the safety and respect the privacy of research subjects and to maintain the confidentiality of the data are adequate.

Article 2: Community agreement

When it is not possible or too time consuming to request informed consent from every individual to be studied, the agreement of a representative of a community or group may be sought. However, the refusal of individuals to participate in a study has to be respected.

Article 3: Selective disclosure of information

For certain epidemiological studies no-disclosure is permitted even essential, so as to not influence the spontaneous conduct under investigation, and to avoid obtaining responses that the respondent might give in order to please the questioner. An ethical review committee may permit disclosure of only selected information when this course is justified.

B-MAXIMISING BENEFITS

Article 4: Communication of study results

Research findings and advice to communities should be communicated to the communities and to the health authorities, by whatever suitable means available.

Article 5: Health care for the community

The undertaking of an epidemiological project may create the expectation in the community concerned that it will be provided with health care, at least while the research workers are present. Such an expectation should not be frustrated, and, where people need health care, arrangement should be made to have them treated or they should be referred to a local health service that can provide the needed care.

Article 6: Training local health personnel

While studies are in progress, the opportunity should be taken to train local health workers in skills and techniques that can be used to improve health services (such as ability to monitor disease or mortality rates).

C-MINIMISING HARMS

Article 7: Causing harm and doing wrong

Investigators planning studies should avoid the risk of causing harm, in the sense of bringing disadvantage, and of doing wrong, in the sense of transgressing values.

Article 8: Preventing harm to groups

Epidemiological studies may inadvertently expose groups as well as individuals to harm, such as economic loss, stigmatisation, blame, or withdrawal of services. Investigators who find sensitive information that may put a group at risk of adverse criticism or treatment should be discreet in communicating and explaining their findings.

D-CONFIDENTIALITY

Article 9: Confidentiality

Investigators should make arrangement for protecting the confidentiality of data relating to individuals or groups, which if disclosed to third parties, may cause harm or distress. This could be done by, for example, omitting information that might lead to the identification of individual subjects, or limiting access to the data, or by other means.

E-CONFLICT OF INTEREST

Article 10: Identification of conflict of interest

Investigators should have no undisclosed conflict of interest with their study collaborators, sponsors, or subjects. Investigators should disclose to the ethical committee any potential conflict of interest. Conflict can arise when a commercial or other sponsor may wish to use study results to promote a product or service, or when it may not be politically convenient to disclose findings.

Article 11: Scientific objectivity and advocacy

Honesty and impartiality are essential in designing and conducting studies, and presenting and interpreting findings. Data should not be withheld, misinterpreted or manipulated. Investigators may discover health hazards that demand correction, and become advocates to protect and restore health. In this event, their advocacy must be seen to rely on objective, scientific data.

F-STUDY DATA AND RESULTS

Article 12: Study reports and data

Any research carried out in the Kingdom of Cambodia, whether locally or externally sponsored or administered, should have a copy of the research report deposited at the National Institute of Public Health and their data belonging to the nationals.

Article 13: Release of study results

Study results should be publicised without any interference from sponsoring or administrative authorities. ឧប

PART III

ETHICAL REVIEW PROCEDURES

The purpose of ethical review is to consider the features of a proposed study in the light of ethical principles, so as to ensure that investigators have anticipated and satisfactorily resolved possible ethical objections, and to assess their responses to ethical issues raised by the study.

Article 1: Requirement of ethical review

Sponsors and investigators are requested to submit their proposals to ethical review. This applies to all sources of proposals- academic, governmental, health-care, commercial and others, except regular surveys required for monitoring and evaluation purpose. This also applies for externally sponsored studies, which in addition should provide training of health personnel to carry out similar study projects independently. For project monitoring and evaluation or population Census, general agreement following government guidelines should be part of project agreements.

An exception is justified when epidemiologists must investigate outbreaks of acute communicable diseases. Nevertheless, in such circumstances the investigators should respect the rights of individuals, namely freedom, privacy, and confidentiality.

Article 2: Information to be provided by investigators

The investigator must submit a detailed protocol comprising:

- a clear statement of the objectives, having regards at the present state of knowledge, and a justification for undertaking the investigation in human subject;
- a precise description of all proposed procedures and interventions, including intended dosage of drugs and planned duration of treatment;
- a statistical plan indicating the number of subjects to be involved;
- the criteria for terminating the study; and
- the criteria for determining admission and withdrawal of individual subjects, including full details of the procedure for obtaining informed consent.

Also, the protocol should:

- include information to establish the safety of each procedure and intervention, and of any drug, vaccine or device to be tested, including the results of relevant laboratory and animal research;
- specify the presumed benefits to subjects, and the possible risks of proposed procedures;
- indicate the means and documents proposed to be used for eliciting informed consent, or, when such consent cannot be requested, state what approved alternative means of

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obtaining agreement will be used, and how it is proposed to protect rights and assure the welfare of subjects;
-provide evidence that the investigator is properly qualified and experienced, or, when necessary, work under a competent supervisor, and that the investigator has access to adequate facilities for the safe and efficient conduct of the research; and
-describe the proposed means of protecting confidentiality during the processing and publication of study results.

Article 3: Ethical Review Committee

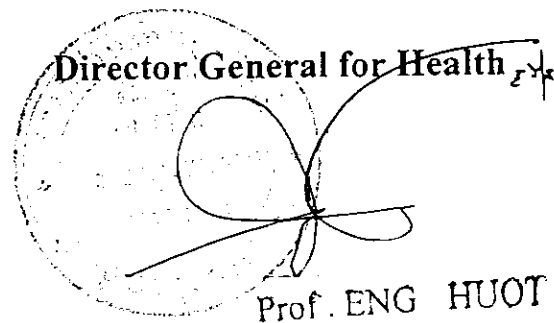
A national ethical review committee should be constituted to review study protocols from scientific and ethical standpoints.

- ◆ Quality of research proposals should be assessed for scientific soundness.
- ◆ The relevance of any study should be measured against expenditure, energy and investment of time and resources, risks and expected outcome.
- ◆ Unnecessary studies should be avoided. The committee should always analyse, if a similar study has not yet been done in Cambodia. Expected results should be sufficiently relevant for any supplementary knowledge or strategy development.

The committee should establish working rules- regarding for instance, frequency of meetings, a quorum of members, decision-making procedures, and review of decisions.

The membership of the national review committee should include Epidemiologist(s), Sociologist(s), Lawyer(s), Statistician(s), Clinician(s), Microbiologist(s), Pharmacist(s). They should be appointed by the minister of health based on their competencies and integrity, and could be drawn from the Ministry of Health relevant departments and institutes. Expert from WHO and other organisation concerned should be part of the committee in the quality of technical advisors.

Phnom-Penh... January 2001


Director General for Health
Prof. ENG HUOT

Annex I:

An **experimental study** is a study in which the investigator intentionally alters one or more factors under controlled conditions to study the effects of doing so. Experimental studies involving human subjects include (field and clinical) trials, which are done to test a preventive or therapeutic regimen or diagnostic procedure.

"Clinical research" is the term used for any study if one or more of its components is diagnostic, prophylactic or therapeutic in nature and is applied to human subject. This includes also the administration of placebos, the performance of laboratory tests, and any means used for the purposes of both curative and preventive medical care.

Annex II:

Observational epidemiological research includes cross-sectional studies (surveys), case-control studies, and cohort studies. These types of study carry minimal risk to study subjects. They involve no intervention other than asking questions, carrying out medical examinations and, sometimes, laboratory tests or x-ray examinations. The informed consent of subjects is normally required, although there are some exceptions - for example, very large cohort studies conducted exclusively by examining medical records. ✂