World Medical Association Declaration of Helsinki

Ethical Principles for Medical Research on Human Subjects

Adopted by the 18th World Medical Assembly, Helsinki, June 1964 and amended by the 29th World Medical Assembly, Tokyo, October 1975, the 35th World Medical Assembly, Venice, October 1983, 41st World Medical Assembly, Hong Kong, September 1989, the 48th World Medical Assembly, Somerset West (South Africa), October 1996, and the 52nd World Medical Assembly, Edinburgh, October 2000.

A. INTRODUCTION

1. The Helsinki Declaration, developed by the World Medical Association, constitutes a declaration of ethical principles whose objective is to provide recommendations to physicians and other participants in medical research carried out on human subjects. This also includes medical research carried out on data of human character or non-anonymous biological samples.

2. The mission of the physician is to promote and safeguard the health of the people. He or she excercises this right to the to the best of his or her knowledge and conscience.

3. The Geneva International Ethical Code of the World Medical Association binds the physician with the words, "The health of my patient will be my first priority," and the International Code of Medical Ethics declares that, "the physician must act only in the interest of the patient when providing medical care which may have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is founded on research which ultimately may have to resort to experimentation involving human subjects.

5. In medical research on human subjects, the interests of science and of society must never infringe upon the well-being of the human subject.

6. The primary objective of medical research on human subjects must be the improvement of diagnostic, therapeutic and preventative methods, as well as the understanding of the causes and mechanisms of illnesses. The diagnostic, therapeutic and preventative methods, even the most proven, must continuously be tested through research for their effectiveness, efficiency, and their accessibility.

7. In current medical research as in medical practice, implementation of most of the diagnostic, therapeutic and preventative methods, are exposed to both risks and constraints.

8. Medical research is subject to ethical standards that aim to guarantee respect for all human beings and to protect health and rights. Certain subject categories are more vulnerable than others and call for special protection. The special needs of subjects that are at an economic and medical disadvantage must be recognised. Special attention must be brought to those who cannot give or refuse consent for themselves, to those that are susceptible to give their consent under duress, to those who will not personally benefit from research, and to those for whom the research runs alongside medical care.

9. The Researcher must be aware of the ethical, legal and regulatory requirements for research on human subjects in their own country, as well as any additional international requirements which may be applicable. No national ethical, legal or regulatory requirement must be allowed to reduce or eliminate the protective measures for human subjects declared by this Declaration.

B. FUNDAMENTAL PRINCIPLES APPLICABLE TO ALL FORMS OF MEDICAL RESEARCH

10. In medical research, the duty of the physician is to protect the life, health, dignity and privacy of the human subject.

11. Medical research carried out on human subjects must conform to scientific principles which are generally recognised. It must be founded on thorough knowledge of

scientific literature and other sources of pertinent information as well as on appropriate laboratory experimentation, and where appropriate, through animal experimentation.

12. Necessary precautions must be carried out with any research that may effect the environment and the well-being of animals utilised during research must be respected.

13. The design and performance of each phase of experimentation on human subjects must be clearly defined in an experimental protocol. This protocol must be submitted for examination, commentary, opinion and, if the case arises, for approval to an ethical review committee joined together for this sole purpose. This committee must be independent of the sponsor, the investigator or of all other forms of undue influence. It must conform to the existing laws of the country where the research is being carried out. The committee has the right to follow the process of the research project. The investigator must provide the committee with all information on the progress of the study, particularly of any undesirable or grave events during the course of the research. The researcher must equally communicate to the committee, for review information relative to funding, sponsors, all institutional affiliations, eventual conflicts of interest as well as incentives for persons to take part in any research.

14. The protocol of the research must contain a statement on the ethical implications of the research. It must specify that the enunciated principles in this Declaration are respected.

15. The studies on the human subject must be carried out by scientifically qualified persons, and under the supervision of a competent physician. The responsibility regarding the subject must always be incumbent upon a qualified medical person and not upon the subject, even if the subject has given consent.

16. All research must be preceded by a careful assessment of the possible risks and constraints on the one hand, and on the other the foreseeable benefits for the subject or others. This does not hinder the participation volunteers to the

medical research. The outline of all parts of the research must be accessible to others.

17. A physician must not undertake a research project unless they believe to have properly taken into consideration all the possible risks and that these risks can be controlled in an acceptable manner. Physicians should cease any investigation if there is sign of risk on the subject or if there is conclusive proof of positive and beneficial results.

18. A study cannot be carried out unless the importance of the objective outweighs the constraints and risks run by the subject. It is particularly the case when concerning a volunteer.

19. Medical research involving humans are not legitimate unless the societies to which the human subjects belong can eventually benefit from the results of the research.

20. The research subjects who lend themselves to medical research must be volunteers informed on the modalities of their participation in the research project.

21. The rights of the research subject's integrity must always be respected. Every precaution must be taken to respect the privacy of the subject, the confidentiality of the data concerning the subject, and to limit the repercussions of the study on his or her physical and psychological being.

22. In any study, the person lending themselves to the research must be properly informed of the objectives, methods, funding, eventual conflicts of interest, affiliations of the Investigator Researcher to one or any institutions, of the benefits sought out as well as the potential risks of the study and the constraints that may result on the human subject. The subject must be informed that he or she has the right to no longer participate to the study and that they are free to withdraw their consent without fear or prejudice. After having been assured of the subject's comprehension on the information given, the physician must obtain a free and clear written consent from the subject. When consent cannot be obtained in written form, the procedure for

consent must be formally explicit and include the presence of witnesses.

23. When the research investigator seeks informed consent from an individual for a research project, they must be particularly careful if the research subject is a dependant or is exposed to give his consent under duress. It is therefore suggested that the consent be solicited by a physician well-informed on the study but not taking part and not concerned by the relationship between the subject and the researcher.

24. When the research subject is legally incompetent, physically or mentally incapable to give their consent, or when dealing with a minor, the investigator researcher must obtain the clear consent of the legal representative in accordance with the current applicable law. These subjects cannot be included in a study unless the research is vital to the betterment of the health of the population to which they belong, and cannot be carried out on persons apt to give consent.

25. When a subject deemed legally incompetent as in the case of a minor is however in the right to express their agreement to the participation of the study, the investigator must obtain an agreement accompanied by a legal representative.

26. Research on persons from whom it is impossible to obtain clear consent, even in the form of proxy or advance consent, must not be carried out unless the physical or mental condition that hinders the consent is a required characteristic of the subject to be included in the study. The specific reasons to include these subjects in a study despite their incapacity to give their consent must be stated in the protocol that will be submitted to the committee for examination and approval. The protocol must equally specify that the consent of the subject or of the subject's legal representative for the study must be obtained as soon as possible.

27. Both authors and publishers of scientific journals have ethical obligations. In publication of the results of a study,

the investigators must strive to maintain the accuracy of the results. Negative results as well as positive ones must be published or rendered accessible. Funding, affiliation to one or more institutions and eventual conflicts of interest must be stated in the publications. Reports of a study that do not conform to the stated principles in the declaration must not be accepted for publication.

C. ADDITIONAL PRINCIPALS FOR MEDICAL RESEARCH DURING MEDICAL CARE

28. The physician cannot carry out medical research while a subject is in medical care unless the research is justified by a possible diagnostic, therapeutic or preventative interest. When research is associated with medical care, the patient having lent himself to research must benefit from the additional protection standards.

29. The benefits, risks, constraints and effectiveness of a new method must be tested by comparison with the best diagnostic, therapeutic and preventative methods being used. This does not exclude the use of placebo or the intervention in studies for which there are no diagnostic, therapeutic and preventative methods being tested.

30. All patients having participated in a medical study must be assured that they will benefit from the best diagnostic, therapeutic and preventative methods.

31. The physician must provide the patient with complete information on the aspects of the care which is linked to particular dispositions of the research protocol. The refusal of a patient to participate in a study must not in any case interfere with the existing relationship between the physician and the patient.

32. When during the treatment of a patient, the established preventative, diagnostic, or therapeutic methods show themselves to be inexistent or insufficiently effective, the physician, with the clear consent of the patient, must be able to use new or unproven methods if the physician feels that these other methods might lead to saving the patient’s life, re-establish health or reduce the suffering of the patient.

These measures must, whenever possible, be made the object of research designed to evaluate their security and their efficiency. All new information must be recorded and where appropriate, published. Other appropriate recommendations stated in the present declaration are applicable.

NOTE OF CLARIFICATION CONCERNING PARAGRAPH 29.

The WMA reaffirms that paragraph 29 of the Declaration of Helsinki (October 2000) is the object of various interpretations and possible misunderstandings. The WMA reaffirms that tests placebo witnesses must be used with great precaution and in a general way, when there is no tested treatment. Furthermore, even if a tested treatment exists, placebo witnessed testing can be ethically acceptable in the following conditions:

- when, for imperious and scientifically sound methodological reasons there exists no other means to allow to determine efficiency or the safety of diagnostic, therapeutic and preventative methods ; or

- when a diagnostic, therapeutic and preventative method is tested for a minor condition and participation in the testing does not expose the subject to other important risks.

All the provisions stated in the Declaration of Helsinki must be adhered to, in particular, the need for ethical and scientific review.