WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI
Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53th WMA General Assembly, Washington 2002 (Note of Clarification on paragraph 29 added)
55th WMA General Assembly, Tokyo 2004 (Note of Clarification on Paragraph 30 added)
59th WMA General Assembly, Seoul, October 2008

WMA Declaration of Helsinki Working Group

Draft revised text for public consultation, 15 April – 15 June 2013

Annotated version

		Comments
	Preamble	
1	The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects**,** including research on identifiable human material and data. The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.	Old paragraph 1. No changes.
2	~~Although~~ **Consistent with the mandate of the WMA,** the Declaration is addressed primarily to physicians~~,~~**.** **T**~~t~~he WMA encourages other participants in medical research involving human subjects to adopt these principles.	Old paragraph 2. Clarifies why the Declaration is addressed primarily to physicians.
	General Principles	
3	The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."	Old paragraph 4. No changes.
4	It is the duty of the physician to promote and safeguard the health **and well-being** of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.	Old paragraph 3. Expands the duty of physicians.
5	Medical progress is based on research that ultimately must include studies involving human subjects.	Old paragraph 5 separated into two parts; this is the first part. The second part is in paragraph 13.

6	The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best ~~current~~ **proven** interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.	Old paragraph 7. Change made for terminological consistency with rest of document.
7	Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights.	Old paragraph 9, divided into 2 parts; this is the first part. The second part of old paragraph 9 is now in paragraph 19
8	In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.	Old paragraph 6. There is an acknowledged internal inconsistency in the document but this paragraph is intended to be aspirational.
9	It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.	First sentence is old paragraph 11. Last sentence moved up from the last part of old paragraph 16. First part of old paragraph 16 is now paragraph 12.
10	Physicians ~~should~~ **must** consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.	Old paragraph 10. "Should" changed to "must" to strengthen the wording of the paragraph.
11	Appropriate caution must be exercised in the conduct of medical research that may harm the environment.	Old paragraph 13. No changes.
12	Medical research involving human subjects must be conducted only by individuals with the appropriate scientific **education,** training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.	First part of old paragraph 16 with the addition of "education". Second part of old paragraph 16 is moved to paragraph 9.
13	Populations that are underrepresented in medical research should be provided appropriate access to participation in research.	From old paragraph 5, second sentence. No changes. First part of old paragraph 5 is now the new paragraph 5.
14	The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.	Old paragraph 31. No changes.

15	**Adequate compensation and treatment for subjects who are harmed as a result of participating in the research must be ensured.**	New paragraph. It reflects the obligation to ensure that subjects who are harmed will receive compensation and treatment.
	Risks, Burdens and Benefits	
16	In medical practice and in medical research, most interventions involve risks and burdens. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.	Combines two previous paragraphs (old paragraphs 8 and 21). No changes.
17	Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation. **Measures to minimise the risks must be implemented. The risks must always be monitored by the researcher throughout the trial.**	Old paragraph 18. No changes. Second part is new. Addresses the issue of risk minimization and monitoring during the trial.
18	Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.	Old paragraph 20. No changes.
	Vulnerable Populations	
19	Some research populations are particularly vulnerable and ~~need special protection~~ **have an increased likelihood of incurring additional and greater harm.** These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence. **All vulnerable groups need specifically considered protection.**	Second part of old paragraph 9. First part of old paragraph 9 is now part of paragraph 7.
20	Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community **and the research cannot be carried out in a non-vulnerable population. In addition,** ~~and if there is a reasonable likelihood that~~ this population or community **should** stand~~s~~ to benefit from the **knowledge, practices or interventions that result from the** ~~results of the~~ research. **Consideration should also be given to ensuring that the community receives a fair level of additional benefits.**	Old paragraph 17. Combines fair benefit and reasonable benefits approaches. Captures several important principles with respect to vulnerable populations.

	Scientific Requirements and Research Protocols	
21	Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.	Old paragraph 12. No changes.
22	The design and performance of each research study involving human subjects must be clearly described in a research protocol. **The research protocol should discuss and justify the chosen study design.** The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and **information regarding** provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol ~~should~~ **must** describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study ~~or access to other appropriate care or benefits~~.	Old paragraph 14. Editorial clarification Clarifies obligation to include this information in the study protocol.
	Research Ethics Committees	
23	The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must **be transparent in its functioning, must** be independent of the researcher, the sponsor and any other undue influence **and must be duly qualified**. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee. **At the end of the study, the investigators must submit a final report to the committee containing a summary of the study's findings and conclusions.**	Old paragraph 15. Adds the issue of transparency of REC's. The issue of qualification of the REC and its members is now addressed, recommended by several commentators. Clarifies what should occur at the end of the study.
	Privacy and Confidentiality	
24	Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.	Old paragraph 23. No changes.

	Informed Consent	
25	Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees.	Old paragraph 22. No changes.
26	In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, **post-trial access** and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.	Old paragraph 24.
27	When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.	Old paragraph 26. No changes.
28	For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden.	Old paragraph 27. No changes.
29	When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.	Old paragraph 28. No changes.
30	Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized	Old paragraph 29. No changes.

	representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.	
31	The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.	Old paragraph 34. No changes.
32	For medical research using identifiable human material or data, **such as research on material or data contained in biobanks or similar repositories,** physicians must normally seek consent for ~~the~~ **its** ~~collection,~~ analysis, storage and/or reuse. There may be **exceptional** situations where consent would be impossible or **impracticable** ~~impractical~~ to obtain for such research ~~or would pose a threat to the validity of the research~~. In such situations the research may be done only after consideration and approval of a research ethics committee.	Old paragraph 25.
	Use of Placebo	
33	The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best ~~current~~ proven intervention**(s)**, except in the following circumstances: The use of placebo~~,~~ or no ~~treatment~~**intervention** is acceptable in studies where no ~~current~~ proven intervention exists; or Where for compelling and scientifically sound methodological reasons the use of **any intervention less effective than the best proven one,** placebo **or no treatment** is necessary to determine the efficacy or safety of an intervention and the patients who receive **any intervention less effective than the best proven one,** placebo or no treatment will not be subject to ~~any~~ **additional** risk**s** of serious or irreversible harm **as a result of not receiving the best proven intervention**. Extreme care must be taken to avoid abuse of this option.	Old paragraph 32.
	Post-Trial Access	
34	**In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the study. This information should also be**	Old paragraph 33. Clarifies and strengthens post-trial access issue.

	disclosed to participants during the informed consent process. All study participants should be informed about the outcome of the study. ~~At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.~~	

	Trial Registration and Publication of Results	
35	Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.	Old paragraph 19. No changes.
36	**Researchers,** ~~A~~**a**uthors, **sponsors,** editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.	Old paragraph 30. Adds researchers and sponsors to those who have ethical obligations.
	Unproven Interventions	
37	In the treatment of a**n individual** patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. ~~Where possible, t~~**T**his intervention should **subsequently** be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.	Old paragraph 35. Intended to clarify the intent of this paragraph. Strengthens requirement to make the intervention the object of subsequent research.

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