**Declaration of Helsinki**

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This article is about the document on the ethics of human medical experimentation. For other uses, see Helsinki Declaration (disambiguation).

The Declaration of Helsinki (DoH, Finnish: Helsingin julistus, Swedish: Helsingfors­ deklarationen) is a set of ethical principles regarding human experimentation created in 1964 by the World Medical Association (WMA) for the medical community.It is widely regarded as the definitive document on the ethics of human research.

**Principles**

The Declaration is morally binding on physicians, and this obligation supersedes any national or local laws or regulations if it sets a higher standard for the protection of humans than those laws or regulations. Investigators must still comply with local laws, but they will be held to a higher standard.

**Basic concepts**

The fundamental principle is respect for the individual (Article 8), his or her right to self-determination, and the right to make informed decisions (Articles 20, 21, and 22) regarding initial and ongoing research participation. While there is always a need for research (Article 6), the participant's welfare must always take precedence over the interests of science and society (Articles 5 and 9), and ethical considerations must always take precedence over laws and regulations (Article 9).

The increased vulnerability of individuals and organisations necessitates heightened vigilance (Article 8). When the research participant is incompetent, physically or mentally incapable of giving consent, or a minor (Articles 23, 24), surrogate consent by an individual acting in the participant's best interest should be considered (Article 25), although the participant's consent should still be obtained if at all possible.

**Operational fundamentals**

Research should be based on a thorough comprehension of the scientific background (Article 11), a careful evaluation of risks and benefits (Articles 16 and 17), and a reasonable likelihood that the population being studied will benefit (Article 19). In addition, it should be conducted by investigators who have received appropriate training (Article 15) and who adhere to approved protocols (Article 15), and it should be reviewed by an independent ethical review committee (Article 13). Article 14 of the Declaration requires that the protocol address ethical concerns and indicate that it complies with the Declaration. Article 17 stipulates that studies should be terminated if available data indicates that the initial considerations are no longer met. Article 16 requires that information regarding the investigation be made available to the public. Article 27 stipulates that ethical principles extend to the publication of results and consideration of potential conflicts of interest. Under certain conditions, a placebo or no treatment group may be utilised (Article 29). However, experimental investigations must always be compared to the best methodologies. The interests of the participant after the study is concluded should be considered as part of the overall ethical assessment (Article 30). This includes ensuring that the participant has access to the most effective treatment. Article 32 stipulates that unproven methods should be tested whenever practicable in the context of research where there is a reasonable belief of potential benefit.

**History**

The Declaration was initially enacted in June 1964 in Helsinki, Finland, and has since undergone seven revisions (the most recent at the General Assembly in October 2013) and two clarifications, growing from 11 paragraphs in 1964 to 37 paragraphs in 2013. [5] The Declaration is a significant document in the history of research ethics because it represents the first significant endeavour by the medical community to regulate research itself and serves as the foundation for the majority of subsequent documents.

**Initial version (1975)**

The 1975 revision nearly doubled the original's length. It plainly stated that "concern for the subject's interests must always take precedence over those of science and society." [6] It also introduced the concept of supervision by a 'independent committee' (Article I.2), which evolved into a system of Institutional Review Boards (IRBs) in the United States and research ethics committees or ethical review boards in other countries. [7] In the United States, IRB regulations went into effect in 1981 and are now codified in the Common Rule.

**Second through Fourth Revisions, 1975-2000**

Between 1975 and 2000, subsequent revisions were relatively minor, so the 1975 version effectively governed research for a quarter century of relative stability.

**Third and Second Revisions (1983 and 1989)**

The second revision (1983) included obtaining minors' consent whenever practicable. The third revision (1989) addressed the structure and function of the independent committee in greater detail. Since CIOMS and the World Health Organisation (WHO) also developed their International Ethical Guidelines for Biomedical Research Involving Human Subjects in 1993, the Declaration was no longer the only universal guide.

**Fourth update (1996)**

1994 saw the publication of AIDS Clinical Trials Group (ACTG) Study 076 of 100 on Zidovudine and HIV transmission from mother to child. Zidovudine became the de facto standard of care after a placebo-controlled study demonstrated a nearly 70% reduction in the risk of HIV transmission. The subsequent initiation of further placebo-controlled trials conducted in developing countries and funded by the United States Centres for Disease Control or National Institutes of Health sparked significant concern when it was discovered that patients in US trials had virtually unrestricted access to the drug, whereas those in developing countries did not.

**Fifth update (2000)**

Almost immediately after the fourth revision in 1996, pressure mounted for a more fundamental approach to revising the declaration. The 2000 revision would require monitoring of scientific research on human subjects to assure compliance with ethical standards. In 1997, Lurie and Wolfe published their seminal paper on HIV clinical trials, bringing to light a number of fundamental issues. These included claims that the ongoing trials in developing nations were unethical and the identification of a fundamental disparity between the decisions to alter the study design in Thailand and Africa. In turn, the issue of placebo use raised questions regarding the standard of care in developing countries and whether, as Marcia Angell wrote in 1988, "human subjects in any part of the world should be protected by an irreducible set of ethical standards" In November of that year, the American Medical Association proposed a revision, and the following year, a proposed revision (17.C/Rev1/99) was circulated, sparking considerable debate and culminating in a number of symposia and conferences.

**Sixth update (2008)**

In May 2007, the sixth revision cycle commenced. This was a call for submissions that concluded in August of 2007. The terms of reference were revised minimally in comparison to 2000. In November 2007, a draught revision was issued for public comment until February 2008, which resulted in a March 2008 workshop in Helsinki.In May, the remarks were incorporated into a second draught.The comments were compiled in August 2008 following workshops conducted in Cairo and Sao Paulo. The Working Group then drafted a final text for consideration by the Ethics Committee and ultimate approval by the General Assembly on October 18.In comparison to previous election cycles, the public discourse was moderate and generally favourable. Numerous sources, some of which have been published, such as Feminist Approaches to Bioethics, provided input.Other organisations include CIOMS and the United States government.

**Seventh update (2013)**

The most recent version of Helsinki (2013) reflected the controversy surrounding the standard of care that arose from the trials of vertical transmission. The revised declaration of 2013 also emphasises the need to disseminate research results, including negative and inconclusive studies, and stipulates that research-related injuries must be treated and compensated.In addition, the revised version is thought to be more applicable to settings with limited resources, as it addresses the need to assure access to a proven-effective intervention.

**Timeline (WMA meetings)**

* 1964: Original version. 18th Meeting, Helsinki
* 1975: First revision. 29th Meeting, Tokyo
* 1983: Second revision. 35th Meeting, Venice
* 1989: Third revision. 41st Meeting, Hong Kong
* 1996: Fourth revision. 48th Meeting, Somerset West (South Africa)
* 2000: Fifth revision. 52nd Meeting, Edinburgh
* 2002: First clarification, Washington
* 2004: Second clarification, Tokyo
* 2008: Sixth revision, 59th Meeting, Seoul
* 2013: Seventh revision, 64th Meeting, Fortaleza

**Introduction**

Declaration of Helsinki, published by the World Medical Association (WMA) to advise the protection of human participants in medical research. The Declaration of Helsinki was endorsed by the 18th General Assembly of the WMA in Helsinki in 1964. Although not devoid of controversy, it has served as the benchmark for the ethics of medical research.

The impact of the declaration is extensive. Although it is not a legally binding document, it has been incorporated into the laws that govern medical research in countries around the world and has served as a foundation for the creation of other international guidelines. As the declaration expanded and became more prescriptive, it became more controversial, prompting some organisations to modify or forsake its standards.

**Fundamental principles for medical research**

In medical research, it is the physician's responsibility to safeguard the subject's life, health, privacy, and dignity. Medical research involving human subjects must adhere to generally accepted scientific principles, be based on a comprehensive understanding of the scientific literature and other pertinent sources of information, and be supported by adequate laboratory and, when necessary, animal experimentation. Research that may have an effect on the environment must be conducted with caution, and the welfare of animals used in research must be respected.

In an experimental protocol, the design and execution of each experiment involving human subjects should be specified in detail. This protocol should be submitted to a specially appointed ethical review committee for consideration, comment, guidance, and if necessary, approval. This committee must be independent of the investigator, the sponsor, and any other form of undue influence. This independent committee must adhere to the laws and regulations of the nation in which the research experiment is conducted. The committee is permitted to observe ongoing trials. The researcher is obligated to provide the committee with monitoring data, particularly concerning any severe adverse events. The researcher must also submit for review information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, and subject incentives. The research protocol must always include a statement of the relevant ethical considerations and signify compliance with the principles outlined in this Declaration.

Medical research involving human participants should only be conducted by scientifically qualified researchers under the supervision of a clinically competent physician. Even if the subject has granted consent, the responsibility for the human subject must always rest with a medically qualified individual and never with the subject of the research. Every medical research endeavour involving human subjects should be preceded by a thorough evaluation of risks, burdens, and anticipated benefits to the subject and others. This does not preclude healthy volunteers from participating in medical research. All study designs should be publicly accessible. Physicians should not engage in research involving human subjects unless they are confident that the associated risks have been adequately appraised and can be managed satisfactorily. If the risks are found to outweigh the prospective benefits or if there is conclusive evidence of positive and beneficial results, physicians should cease their investigation.

Human subjects should only be used in medical research when the importance of the objective transcends the inherent risks and burdens to the subject. This is especially essential when healthy volunteers serve as human subjects. Medical research is only justified if there is a reasonable probability that the populations in which the research is conducted will benefit from its outcomes. The subjects must be willing and knowledgeable participants in the study. Always uphold the right of research subjects to maintain their integrity. Every precaution must be taken to protect the subject's privacy, maintain the confidentiality of patient information, and minimise the impact of the study on the subject's physical and mental integrity and personality.

 In any research involving human subjects, each prospective subject must be adequately informed of the research's objectives, methods, funding sources, any potential conflicts of interest, the researcher's institutional affiliations, the anticipated benefits and potential risks of the study, and any discomfort that may be involved. The subject should be informed that he or she has the right to decline participation in the study or withdraw consent to participate at any time without fear of retaliation. The physician should then obtain the subject's freely given informed consent, preferably in writing, after ensuring that the subject has comprehended the information. If consent cannot be obtained in writing, it must be documented formally and witnessed. When obtaining informed assent for the research project, the physician should be especially cautious if the subject is dependent on the physician or may be coerced into consenting. In such a situation, the informed consent should be obtained by a physician who is well-informed, not involved in the investigation, and entirely independent of this relationship.

In accordance with applicable law, the researcher must obtain informed consent from the legally authorised representative of a research subject who is legally incompetent, physically or mentally incapable of giving consent, or a legally incompetent minor. These groups should not be included in research unless the research is necessary to promote the health of the population they represent and cannot be conducted on legally competent individuals instead. When a subject deemed legally incompetent, such as a minor child, is able to consent to research participation decisions, the researcher must seek the subject's consent in addition to that of the legally authorised representative.

Research on individuals from whom consent cannot be obtained, including proxy or advance consent, should only be conducted if the physical or mental condition that precludes obtaining informed consent is an essential characteristic of the research population. The specific reasons for involving research subjects with a condition that prevents them from providing informed assent must be included in the experimental protocol for the review committee's consideration and approval. The protocol should stipulate that consent to continue participating in the study must be obtained as soon as feasible from the individual or a legally authorised surrogate.

 Authors and publishers both have ethical responsibilities. In the publication of research results, the investigators must maintain the veracity of the results. Both positive and negative results should be published or otherwise made accessible to the public. Publication should disclose funding sources, institutional affiliations, and any potential conflicts of interest. Reports of experimentation that do not comply with the principles outlined in this Declaration should not be published.

**Additional principles for medical research and care combined**

The physician may combine medical research with medical care only if the research's prospective prophylactic, diagnostic, or therapeutic value justifies the combination. When medical research and medical care are combined, additional standards are applied to protect the research subjects.

The benefits, risks, burdens, and efficacy of a new method should be compared to those of the most effective preventative, diagnostic, and therapeutic methods currently available. This does not preclude the use of placebo or no treatment in studies in the absence of a proved preventative, diagnostic, or therapeutic method. At the conclusion of the research, every patient who participated in the study must have access to the most effective proven preventative, diagnostic, and therapeutic methods identified by the study. The physician must inform the patient of all aspects of care that are associated with the research. The refusal of a patient to participate in a study must never compromise the relationship between patient and physician.

In the treatment of a patient, where proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, the physician, with the patient's informed consent, must be able to use unproven or new prophylactic, diagnostic, and therapeutic methods if, in the physician's opinion, they offer the possibility of saving life, restoring health, or alleviating suffering. When feasible, these measures should be the subject of research to determine their safety and effectiveness. In every instance, new information should be recorded and, when applicable, made public. The remaining pertinent guidelines of this Declaration must be implemented.

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