**Declaration of Helsinki**

**Pradyumn Tiwari\*1, Vinod Sahu, Shivang Sharma, Nem Kumar Jain**

**School of Pharmacy, ITM University Gwalior**

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) was created in 1964 by the World Medical Association (WMA) as a set of moral principles for the conduct of human research.It is typically seen as the determining criterion in whether using human subjects as research subjects is morally acceptable.

**Principles**

According to them, all domestic, local, and international laws and rules should be superseded if the Declaration establishes a higher standard for the preservation of humanity. Investigators must adhere to local rules even though they will be held to a higher standard.

**Basic concepts**

The guiding principles (Articles 8, 20, 21, and 22) are respect for the individual, his or her right to self-determination, and their competence to make an educated decision regarding their initial and ongoing research involvement. Even though research is always required (see Article 6), the participants' welfare must always come first (see Articles 5 and 9), and ethical considerations must always take precedence over legal and regulatory requirements.

The increased vulnerability of persons and organizations calls for a higher level of awareness (Article 8). If at all possible, you should still get the participant's permission. Where a participant is illiterate, incapable of granting agreement owing to a physical or mental handicap, or a minor, another person acting in the participant's best interest may consent on the participant's behalf (Articles 23, 24).

**Operational fundamentals**

The scientific foundation for research should be thoroughly understood (Article 11), risks and benefits should be carefully weighed (Articles 16 and 17), and there should be a good chance that the people being examined would 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). The protocol must make it clear that it complies with Article 14 of the Declaration in addition to discussing ethical issues. If the evidence at hand suggests that the initial conditions are no longer met, studies shall be terminated in accordance with Article 17. The public must have access to information about the investigation, per Article 16. According to Article 27, ethical standards must be followed while disclosing results and taking into account potential conflicts of interest. A placebo or control group may be used in particular circumstances (Article 29). To compare the most effective strategies to experimental study, though, is a necessary. The participant's interests following the study's conclusion 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. Unproven approaches shall, if it is practical, be investigated in the context of research when there is a reasonable expectation that they may be useful.

**History**

In June 1964, Helsinki, Finland, approved the Declaration's initial draft. Two clarifications, seven updates, and a lengthening—from 11 paragraphs in 1964 to 37 paragraphs in 2013—have been made since then. The most recent change was made in the General Assembly in October 2013. The Declaration is a crucial document in the history of research ethics because it laid the groundwork for the majority of later declarations and because it was the medical community's first significant attempt to govern research.

**Initial version (1975)**

A categorical statement was made to the effect that "concern for the subject's interests must always take precedence over those of science and society." Additionally, it introduced the concept of oversight by an "independent committee" (Article I.2), which prepared the way for the development of Institutional Review Boards (IRBs) in the US and research ethics committees or ethical review boards in other countries. The IRB guidelines that were implemented in the US in 1981 are now part of the Common Rule.

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

The 1975 edition generally served as the benchmark for research over a quarter-century under very stable conditions because just a few minor changes were made between 1975 and 2000.

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

The second modification (1983), where feasible, included obtaining minors' consent. In the third iteration (1989), greater detail was provided regarding the composition and function of the independent committee. The 1993 publication of the International Ethical Guidelines for Biomedical Research Involving Human Subjects by CIOMS and the World Health Organization (WHO) meant that the Declaration was no longer the only international standard.

**Fourth update (1996)**

Zidovudine with HIV Transmission from Mother to Child: AIDS Clinical Trials Group (ACTG) Study 076 of 100 was published in 1994. After a placebo-controlled research revealed a nearly 70% decrease in the frequency of HIV transmission, zidovudine became the de facto standard of care. When it was discovered that patients in US studies had nearly unrestricted access to the medicine but those in developing countries did not, serious questions were raised. This encouraged the US Centers for Disease Control or National Institutes of Health to sponsor more placebo-controlled trials in poorer countries.

**Fifth update (2000)**

After the fourth revision in 1996, there was an almost immediate surge in calls for a more fundamental revision of the declaration. The 2000 update required monitoring to make sure that scientific research on humans conforms to ethical standards. The landmark report on HIV clinical trials by Lurie and Wolfe, published in 1997, highlighted a number of significant issues. There were claims that the studies taking place in developing nations were unethical, and it was found that the decisions taken to alter the research design in Thailand and Africa differed significantly. As a result, the placebo controversy brought up concerns about the level of treatment in underdeveloped nations and the idea that "human subjects in any part of the world should be protected by an irreducible set of ethical standards." The American Medical Association suggested a change in November of that year, and when the updated version (17.C/Rev1/99) was published, it sparked a lot of discussion and prompted a number of symposia and conferences.

**Sixth update (2008)**

In May 2007, the sixth revision cycle was launched. This call for entries expired in August 2007. The terms of reference had slight change in comparison to 2000. A workshop was held in Helsinki in March 2008 as a result of the publishing of a draft revision in November 2007 for public comment until February 2008.In May, the suggestions were included in a second draft.The comments were compiled in August 2008 after workshops in Cairo and Sao Paulo. The Working Group then produced a final draft, which would be examined by the Ethics Committee before being accepted by the General Assembly on October 18.This election season, in contrast to previous ones, was very quiet and generally favorable. Numerous sources, some of which were published, such as Feminist Approaches to Bioethics, contributed.Other organizations include CIOMS and the US government.

**Seventh update (2013)**

The most recent version of Helsinki (2013) reflects the dispute about the standard of treatment that emerged as a result of the vertical transmission investigations. The revised declaration from 2013 highlights the need of publicizing research findings, especially those from negative and inconclusive studies, and it requires that injuries experienced during study participation be treated and compensated.Additionally, the revised version is thought to be more appropriate for settings with limited resources since it addresses the need to give access to a proven-effective intervention.

**Timeline (WMA meetings)**

* 34th Meeting, Venice, 35th Meeting, Helsinki, 18th Meeting, 1975,
* 29th Meeting, Tokyo, 1983, and second revision
* 48th Meeting, Somerset West (South Africa), Third Revision,
* 1989 Fifth revision, 2000.
* 41st Meeting, Hong Kong; 1996: Fourth 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**

The Declaration of Helsinki, which provides guidelines for the protection of human research subjects, was released by the World Medical Association (WMA). The Helsinki Declaration was adopted at the WMA's 18th General Assembly in Helsinki in 1964. It has functioned as the industry benchmark for medical research ethics, notwithstanding considerable disagreement.

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.

**Reference-**

1. World Medical Association (2013). "Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects". JAMA. 310 (20): 2191–2194.
2. WMA Press Release: WMA revises the Declaration of Helsinki. 9 October 2000 Archived 27 September 2006 at the Wayback Machine
3. Snežana, Bošnjak (2001). "The declaration of Helsinki: The cornerstone of research ethics". Archive of Oncology. 9 (3): 179–84.
4. 4. Tyebkhan, G (2003). "Declaration of Helsinki: the ethical cornerstone of human clinical research". Indian Journal of Dermatology, Venereology and Leprology. 69 (3): 245–7. PMID 17642902.
5. Ethical Principles for Medical Research. The JAMA Network. Retrieved 26 July 2015.
6. World Health Organization 2001 Bulletin of the World Health Organization, 2001, 79 (4) 373 to 374.
7. Health, Center for Drug Evaluation and Research,Center for Biologics Evaluation and Research,Center for Devices and Radiological (2019-04-20). "Search for FDA Guidance Documents - Acceptance of Foreign Clinical Studies". www.fda.gov.
8. Angell M (October 1988). "Ethical imperialism? Ethics in international collaborative clinical research". The New England Journal of Medicine. 319 (16): 1081–3.
9. Sprumont D, Girardin S, Lemmens T. The Declaration of Helsinki and the law: an international and comparative analysis. In: Frewer A, Schmidt U, eds. History and theory of human experimentation: the Declaration of Helsinki and modern medical ethics. Stuttgart: Franz Steiner Verlag, 2007
10. Human D, Fluss S. The World Medical Association's Declaration of Helsinki: historical and contemporary perspectives. 5th draft. 2001. www.wma.net/e/ethicsunit/pdf/draft\_historical\_contemporary\_perspectives.pdf.
11. Angell M. Ethical imperialism? Ethics in international collaborative clinical research. N Engl J Med 1988. 319:1081-3.
12. World Medical Association. 1983. Declaration of Helsinki, 2nd (Venice) amendment.
13. World Medical Association. 1989. Declaration of Helsinki, 3rd (Hong Kong) amendment.
14. World Medical Association. 1996. Declaration of Helsinki, 4th (Somerset West) amendment.
15. Temple R Impact of the Declaration of Helsinki on Medical Research from a Regulatory Perspective. 2003. Address to the Scientific Session, World Medical Association General Assembly, September, Helsinki.
16. Neda N Impact of the Declaration of Helsinki on Medical Research in the Developing World. Address to Scientific Meeting, World Medical Association Annual Assembly, September 2003, Helsinki