

Unit 5: Declaration of Helsinki

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5.1 History

The **Declaration of Helsinki** is the World Medical Association's statement of ethical principles for medical research involving human subjects, and it is the document the whole of Unit 3 leans on. The **World Medical Association (WMA)** was founded in 1947, in the shadow of the medical crimes tried at Nuremberg, and charged itself with the ethics of the profession internationally. The Nuremberg Code of 1947 had set absolute rules but was widely treated by ordinary researchers as a code for barbarians rather than for themselves; the WMA's answer was a code written by physicians for the research physicians actually did, adopted at its **18th General Assembly in Helsinki, Finland, in June 1964**. It has been revised by later assemblies, among them Tokyo (1975), Venice (1983), Hong Kong (1989), Somerset West (1996), Edinburgh (2000), Seoul (2008) and Fortaleza (2013), with notes of clarification added in 2002 and 2004, and a further revision was adopted at Helsinki in 2024, sixty years after the original. Each revision tracks a new pressure: the 1975 revision introduced independent committee review, now universal; later revisions fought over placebo use and post trial access, the subjects of sections 5.4 and 5.5.

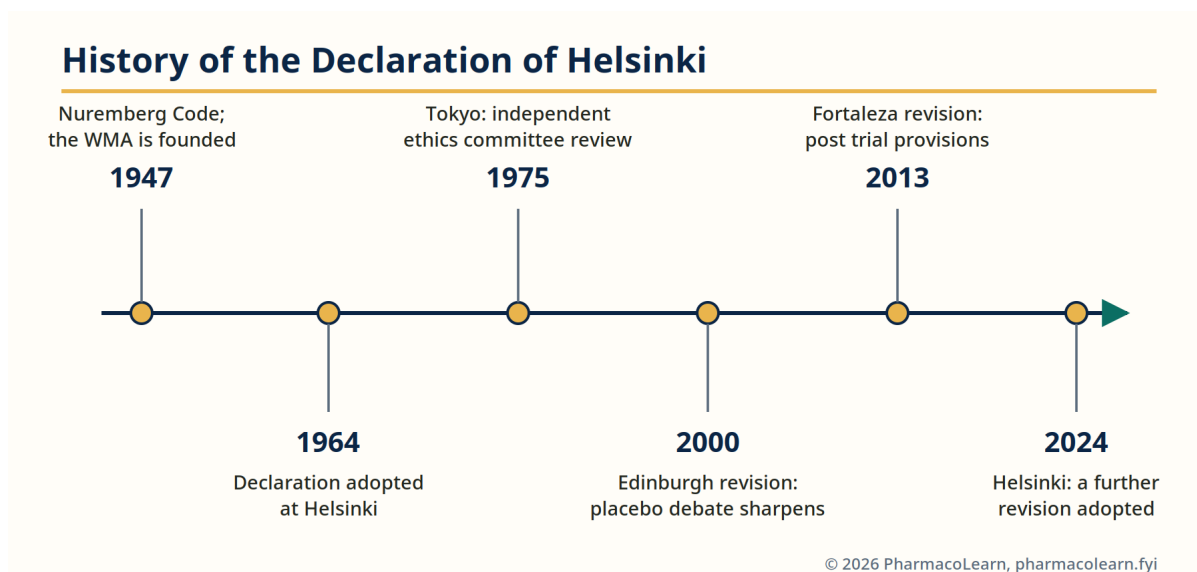


Figure: The Declaration and its revisions. The document is deliberately kept alive: each generation of the profession re argues it against the research of its own time.

5.2 Introduction: what the Declaration is

The Declaration is a **statement of ethical principles**, addressed primarily to physicians, with the World Medical Association encouraging all others who conduct or participate in medical research, students and pharmacologists included, to adopt the same principles. It binds through professional conscience and through adoption: regulators, ethics committees, universities and journal editors require compliance, so that in practice no legitimate research proceeds outside it. Its scope is medical research involving human subjects **and** research on identifiable human material and data, which brings biobanks and record based research inside the frame. Two structural features matter for study. First, the Declaration states the physician's dual duty in its foundation: the health and rights of the patient or subject come first, a duty the Geneva oath tradition carries and research may never invert. Second, it divides its operative principles into

two sets, exactly as the syllabus divides this unit: the **basic principles for all medical research** (the next three sections) and **additional principles for medical research combined with medical care** (section 5.6), because the patient who is also a subject needs protections a healthy volunteer does not.

5.3 Basic principles for all medical research: foundations

The basic principles open with the **scientific foundation**: research must rest on generally accepted scientific principles, on adequate laboratory and animal work (where Unit 4's facility rules earn their place in an ethics unit) and on a thorough knowledge of the literature; a badly designed study is unethical in itself, because it exposes subjects to risk for knowledge it cannot produce. The **protocol** must be written, must state the ethical considerations involved, and must be submitted before the study begins to a **research ethics committee** for consideration, comment, guidance and approval; the committee must be independent of the researcher and sponsor and entitled to monitor the study as it runs. Research may be conducted only by **appropriately trained and qualified** individuals, under the supervision of a competent clinician where medical care is involved. **Risk discipline** runs through the set: risks must be assessed before the study and managed during it, research may proceed only where the importance of the objective outweighs the inherent risks and burdens, and it must stop where risks are found to outweigh benefits or where conclusive results are reached. The welfare clause stands over all of it: the duty to protect the life, health, dignity, integrity, self determination, privacy and confidentiality of subjects takes precedence over every other interest in the study.

5.4 Basic principles: consent, vulnerability and protection

The consent principles of the Declaration are the fullest statement of the doctrine of section 3.7. Participation must be **voluntary and informed**: each potential subject must be told the aims, methods, funding, conflicts of interest, expected benefits, risks, discomforts, the right to refuse or withdraw without reprisal, and all other relevant aspects, and consent, preferably written, taken only after the subject has understood. Where the subject cannot consent (a child, an unconscious or mentally incapable patient), consent is sought from the legally authorised representative, the subject's own assent is sought where he can give any, and his dissent is respected; research on those who cannot consent is permitted only for their condition, at minimal risk and burden beyond narrow exceptions, and only where it cannot be done in persons able to consent. **Vulnerable groups and individuals** receive specially considered protection, and research with them must respond to their health needs and be likely to benefit them. Privacy and confidentiality of subjects' information must be protected (section 3.8). Identifiable samples and data carry their own consent principle, with a committee governed exception for cases where consent is impossible or impracticable. Physicians must not take part in research that does not conform to these principles, and editors must not publish it: the Declaration arms its principles with the publication gate.

5.5 Basic principles: placebo, post trial duties and reporting

Three principles of the basic set are examined constantly and so are stated separately. **Placebo**: where a proven intervention exists, a new intervention is tested against it; placebo or no treatment controls are acceptable only where no proven intervention exists, or where compelling and scientifically sound methodological reasons require placebo **and** the patients receiving it face no additional risk of serious or irreversible harm; extreme care is required to avoid abuse of the option. **Post trial access**: in advance of the trial, sponsors, researchers and host country authorities must make provisions for post trial access, for all participants who still need it, to interventions identified as beneficial in the trial; the provision is disclosed during consent. Participants are also entitled, at the study's conclusion, to be informed of its outcome and to share in its benefits. **Registration and publication**: every research study involving human subjects must be registered in a publicly accessible database before the first subject is recruited, and researchers have a

duty to make results publicly available, negative and inconclusive as well as positive, with reports that are complete and accurate; authorship and funding are disclosed. These three, taken together, are the Declaration's answer to the abuses of selective knowledge: trials hidden, results buried and subjects used and abandoned.

5.6 Additional principles for medical research combined with medical care

When research is combined with medical care, the same physician owes the patient two loyalties, and the additional principles police the join. A physician may combine research with care **only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value** and there is good reason to believe participation will not adversely affect the patients' health. The patient's refusal to participate, or withdrawal, **must never adversely affect the patient physician relationship** or the care he receives. Where medical research is combined with care, the patient must be fully informed which aspects of his care are related to the research, and the therapeutic misconception, the patient's natural belief that everything done to him is chosen for his personal benefit, must be actively countered in the consent conversation. If a patient is under the care of one physician and enrolled by another, the roles must be clear. The principles close with a rule of restitution and candour for the combined setting: patients who are harmed as a result of participation are entitled to treatment and compensation, and unproven interventions used in the care of an individual patient, where proven ones do not exist or have failed, are permissible only with expert advice, informed consent, and a duty to record and share the experience so that improvisation hardens, where it can, into knowledge.

5.7 The Declaration among the ethics codes

Instrument	Year and source	Character	Distinctive note
Nuremberg Code	1947, war crimes tribunal judgement	Absolute rules for permissible experiments	Voluntary consent stated without exception; no provision for those who cannot consent
Declaration of Helsinki	1964, World Medical Association, revised since	Ethical principles for medical research	Committee review, proxy consent under safeguards, placebo and post trial rules, research combined with care
Belmont Report	1979, United States national commission	Principles for federally funded research	Respect for persons, beneficence, justice: the American statement of the four values of Unit 3
CIOMS Guidelines	1982 onwards, Council for International Organizations of Medical Sciences with WHO	Detailed international ethical guidelines	Applies Helsinki principles to settings and topics in depth, including low resource settings
ICMR National Ethical Guidelines	2017 edition, Indian Council of Medical Research	India's national framework	The operative guidelines for Indian ethics committees, with the NDCT Rules 2019 for drug trials

Read together, the codes are one tradition at different working depths. Helsinki is the one a pharmacy student must be able to expound: its history, its two sets of principles, and its three most examined doctrines, committee review, informed consent with protection for those who cannot give it, and the placebo and post trial rules. With it, the subject closes where it began: Unit 1's machinery makes research true, Unit 2's tests make its conclusions measured, and Units 3 to 5 make it right.

Frequently Asked Questions

Q: Randomization and blinding both fight bias. Why does a good study need both? They fight different biases at different points. Randomization works at allocation: it stops selection bias and balances known and unknown confounders between groups before treatment starts. Blinding works during the study: it stops the expectations of subjects and assessors from distorting treatment, measurement and reporting. A randomized but unblinded trial can still be bent by an assessor who knows the groups; a blinded but unrandomized study starts with unequal groups that blinding cannot repair.

Q: A study reports $P = 0.06$ and describes the drug as almost effective. What is wrong with that? At the conventional alpha of 0.05 the result is not statistically significant, and the data do not justify rejecting the null hypothesis. $P = 0.06$ is weak evidence against the null, not a near miss grade of effectiveness; the honest statements are the size of the observed effect with its confidence interval, and that a larger study would be needed to resolve it. Note the symmetry: $P = 0.04$ is not proof either, only the conventional threshold crossed.

Q: When should a researcher choose a non parametric test instead of a t test? When the parametric assumptions are not defensible: the data are ordinal (scores, grades), the distribution is strongly skewed, outliers dominate the values, or the samples are very small with no basis for assuming normality. The rank tests then compare distributions honestly at some cost in power. If the data are interval scale, roughly normal and the variances are comparable, the t test is the more powerful and the correct choice.

Q: Why do paired designs, the paired t test and the crossover, manage with fewer subjects? Because they remove between subject variation from the error term. In a parallel design the treatment difference must be seen through the full spread of differences between different people; in a paired design each subject is compared with himself, and only the much smaller variation of within person change remains as noise. The price is the design's conditions: stable conditions, reversible effects and adequate washout.

Q: Which belongs in a results table, the standard deviation or the standard error? The standard deviation, because it describes the data: how widely the observations themselves spread. The standard error describes the precision of the estimated mean, and quoting SE where SD is expected makes the data look deceptively tight. SE has its proper place in stating confidence intervals for estimates; the two must always be named, never interchanged silently.

Q: A competent patient refuses a treatment his doctors believe would save his life. Which principle governs? Autonomy. Beneficence and non maleficence argue for treatment, but a competent, informed refusal is decisive in modern medical ethics and law. The team's duties are to ensure the refusal is truly informed and uncoerced, to document it, to offer every acceptable alternative, and to continue all other care without penalty. The answer reverses only where capacity is absent, when surrogates decide on the best interests standard.

Q: Why is the planned sample size inflated for expected dropouts, instead of simply recruiting replacements as subjects leave? Because the inflation is calculated before the study, from the dropout rate the setting is known to produce, keeping the study's power as designed. Replacing leavers ad hoc breaks the recruitment frame (replacements are recruited later, often differently, and in a trial they cannot restore the original randomization balance). Dropouts also bias if their reasons relate to treatment, which is why analysis by intention to treat and honest reporting of dropout numbers matter as much as the head count.

Q: What does the ethics committee actually examine before approving a protocol? The scientific soundness and social value of the question (a study that cannot answer its question is unethical exposure), the risk benefit balance, the fairness of subject selection, the consent process and documents, protections

for vulnerable subjects, privacy and confidentiality arrangements, compensation and treatment provisions for research related harm, and the qualifications of the team. Approval is prospective and continuing: amendments, safety reports and progress reports return to the same committee.

Q: Who approves an animal experiment in an Indian institution, the IAEC or CPCSEA? Both, at different levels. The institution must be registered with CPCSEA, and its Institutional Animal Ethics Committee, which includes a CPCSEA nominee, approves experiments on small laboratory animals after reviewing necessity, numbers, pain relief and competence. Proposals involving large animals go beyond the institution to CPCSEA itself for approval. No approval, no experiment; the approval number follows the work into its records and publications.

Q: What does the Declaration of Helsinki cover that the Nuremberg Code did not? Research combined with medical care, and the machinery of ordinary ethical research. Nuremberg stated absolute conditions for experiments, above all voluntary consent without exception, which left no lawful room for research on children or unconscious patients. Helsinki, written by physicians for ongoing practice, added independent committee review, consent through legally authorised representatives under strict safeguards, the placebo and post trial rules, and a whole set of additional principles for the patient who is also a research subject.

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