Revising the Declaration of Helsinki

The Declaration of Helsinki is undergoing its seventh revision. Reaction to the first draft, out for public consultation until June 15, has been polarised. Kelly Morris investigates.

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For more on the **Helsinki Declaration revision** see **Perspectives** *Lancet* 2013; **381:** 1532–33

Since the DJeclaration of Helsinki was originally published in 1964 by the World Medical Association (WMA), its primary purpose has been to set international ethical principles for research involving human participants. With the document now undergoing its seventh revision, a core aim of the working party is to preserve the unique character and status of the document. However, critics argue that the WMA has missed a golden opportunity to overhaul the declaration.

In the first draft, out for public consultation until June 15, some major changes include the need for compensation for study participants who are inadvertently harmed, and attempts to further clarify the role of placebos, post-study arrangements, and research involving identifiable human material. Although the WMA was congratulated for the inclusiveness and transparency of its workshop process, the declaration has not undergone radical change. Major revision could occur after the public consultation; if not, the final draft, due out in October, will be published in 2014 with some arguing for further revision.

"Based on the feedback received during the course of the revision process, it was agreed that this revision should represent an evolution rather than a revolution", working-group chair Ramin Parsa-Parsi, from the German Medical Association, tells *The Lancet*. The declaration is distinguished from other international guidance, as the only one "developed democratically by physicians for physicians", he points out. "As a document of ethical principles, rather than a rule book for researchers, its uniqueness lies in its comprehensive yet readable character. Its international reputation as the ethical standard for research involving human beings is reflected in the fact that many countries already use the Declaration of Helsinki as their official guidance for researchers, and some have also implemented it into their regulations or laws."

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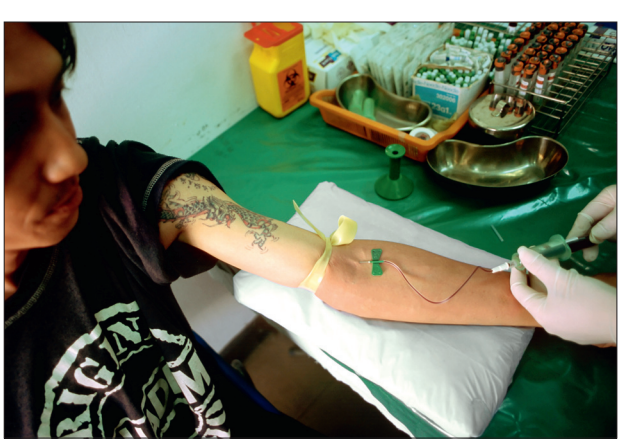
Warwick Anderson, chief executive officer of Australia's National Health and Medical Research Council, is very supportive of both the declaration and the consultative process being undertaken by the WMA. "If the declaration didn't exist, it would have to be invented, as we need a basic set of values", says Anderson. "In a sense, it does take a backseat in Australia, as we follow our own National Statement but we welcome the new revision", he adds. He will be asking the Australian Health Ethics Committee to reflect on the revision and feedback, "and to modify our own guidance where that's needed". Australia's original National Statement drew expressly on the declaration, and, explains Don Chalmers, dean of the Law School, University of Tasmania, the current statement was ratified in the knowledge of its close regard for the declaration. In other cases, the declaration has been abandoned as guidance—eg, by the US Food and Drug Administration and the US National Institutes of Health—in favour of federal and other international guidance. In Europe, pressure is on to change the proposed new Clinical Trials Regulation, which is in early draft stage, as it includes minimal reference to the declaration, little statement on ethical principles, and removes the need for member state ethical approval to be done by ethics committees.

Chalmers believes that the core pillars of research ethics outlined in the Nuremberg Code—notably fully informed and freely given consent, scientific merit, and independent assessment—remain vital in today's world, alongside recognition of the need for international health equity. Two relevant paragraphs that have seen several iterations yet remain controversial are use of placebos and post-trial access.

Nevertheless, says Steven Joffe, a physician-bioethicist at the global health and social medicine department at Harvard Medical School, Boston, MA, USA, these paragraphs are examples of "where the process of repeated revisions has created confusion, internal inconsistency, and weakened the moral standing of the document". An ongoing question is whether the new term "best proven intervention", as the ideal comparator in a trial, means the best proven anywhere in the world or the best proven locally? This critical



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A research volunteer takes part in an AIDS vaccine trial, Bangkok, Thailand

distinction is left ambiguous in the draft revision, he points out, because, with the former interpretation, the principle can conflict with the need for research to be responsive to pressing local questions.

With regard to post-trial access, the draft now reads: "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." Moreover, in disadvantaged and vulnerable populations: "Consideration should also be given to ensuring that the community receives a fair level of additional benefits." Practical concerns over these statements include what to do in the delay between closure of a trial and analysis of the findings, what constitutes an additional benefit, who pays the bill, and whether such arrangements are a disincentive to researchers.

"The issue of post-trial access needs more ongoing discussion and thought", Anderson notes, especially in relation to international collaboration in clinical trials. "A key question is who is responsible for what? We need to get this right, by thinking about who can reasonably be held responsible and how to exert those responsibilities between sponsors of trials, individual researchers, governments, and health systems." Joffe questions the underlying ethical judgments in these statements: "It's important to address beforehand the arrangements surrounding closure of a trial. But if research is responsive and welcomed by a community, and consent for participation is truly informed and given freely, what is the ethical basis for further moral obligations?"

One welcome addition is paragraph 15: "Adequate compensation and treatment for subjects who are harmed as a result of participating in the research must be ensured." The concern again is implementation. "The challenge is figuring out when an injury is a direct consequence of the research", says Joffe, who is pessimistic about adoption of compensation schemes by the US Government, even though experience so far suggests that existing systems are low cost with relatively few claims.

The consideration of vulnerable groups in research remains confused, say critics, and requires separation between: disadvantaged populations; vulnerability due to diminished decisional capacity or undue influence by the recruiting researchers; and vulnerability to risks of increased harms by nature of the population under study.

No specific changes were felt warranted to cover genomic data and its sharing, but Anderson states: "there is almost a need for an additional level of ethics surrounding data." Issues range from protection of privacy of family members where genomic data is involved, to the counterbalancing issues of open access to ensure that at least publicly funded research data can be shared between researchers, via international consortia, and with the public.

One major topic of discussion during the workshop process was biobanks, which are essential tools for charting a course from genomic research to important health-care benefits, including personalised medicine, explains Chalmers. Although the necessity of consent for collection of identifiable human material has been removed in the current revision, it falls short of major changes—eg, to consider broad consent and waiver of consent, which are already occurring in practice. Chalmers hopes at least that "the modest revision to consent for specimen analysis in the latest version foreshadows more detailed consideration of the unique ethical and cross-border issues surrounding biobanks in the next update".

However, the working group counters that the suggested wording is "as comprehensive, up-to-date, and appropriate as it can be in the context of a document of ethical principles", and, says Parsa-Parsi, "this includes the wording pertaining to biobanks".

At a fundamental level, many critics believe the declaration is flawed by failing to aim its guidance at all involved in research, and to distinguish research, which inherently involves risk, from patient care and the duty of physicians. The latter issue is encapsulated in paragraph 8: "In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests", but this statement conflicts with other paragraphs in the document and with other guidance. Much research could even be construed as conflicting with this principle, and instead, the public good of the scientific objective is considered to outweigh risks for participants. For example, in studies of novel cancer therapeutics, additional biopsies to study the histological effects of an agent are a potential risk that confers no benefit to participants, although such biopsies are widely considered permissible and some patients consent for humanitarian reasons.

The WMA acknowledges this core internal inconsistency but Parsa-Parsi states that "this paragraph has always been one of the core principles of the document and is of undisputed importance. It was purposefully left in as it was considered important to preserve the aspirational character of the document". Joffe concurs that the preamble should remind all researchers of their responsibilities and the harm caused when research has been done without attention to ethical principles. However, he proposes, "the declaration would benefit from stating a basic set of ethical principles outlining the thought processes that researchers, sponsors, and decision makers need to go through, while acknowledging that there must be room for judgment".

Kelly Morris