Table 2 Chronology of International Ethics Guidelines for Biomedical Research

Year	Document	Issuing authority
1947	Nuremberg code	
1948	Universal declaration of human rights	United Nations General Assembly
1964	Declaration of Helsinki (1)	WMA
1966	International covenant on civil and political rights	United Nations General Assembly
1975	Declaration of Helsinki (1st revision—Tokyo)	WMA
1983	Declaration of Helsinki (2nd revision—Venice)	WMA
1989	Declaration of Helsinki (3rd revision—Hong Kong)	WMA
1989	Convention on the rights of children	United Nations General Assembly
1991	International guidelines for ethical review of epidemiological studies	CIOMS/WHO
1993	International ethical guidelines for biomedical research involving human subjects	CIOMS/WHO
1995	Guidelines for good clinical practice for trials on pharmaceutical products	WHO
1996	Declaration of Helsinki (4th revision—South Africa)	WMA
1996*	ICH Guidance on Good Clinical Practice	ICH/Committee for Proprietary Medical Products for the Pharmaceutical Industry
2000	Declaration of Helsinki (5th revision—Scotland)	WMA
2000	Ethical considerations in HIV preventive vaccine research	UNAIDS
2000	Operational guidelines for ethics committees that review biomedical research	WHO
2002	Declaration of Helsinki (note of clarification on paragraph 29)	WMA
2002	Surveying and evaluating ethical review practices	WHO
2002[a]	International ethical guidelines for biomedical research involving human subjects	CIOMS/WHO
2004	Declaration of Helsinki (note of clarification on paragraph 30)	WMA
2007[a]	Ethical Considerations in Biomedical HIV Prevention Trials	UNAIDS
2008[a]	Declaration of Helsinki (6th revision—Seoul)	WMA

[a]The four most-quoted guidelines for the conduct of biomedical research with human subjects in developing countries include the following:

- The Declaration of Helsinki, in its last revision contains a terse articulation of 32 principles to guide the conduct of research.
- The Guidance on Good Clinical Practice of the ICH of 1996 provides unified technical standards for clinical trials, so data generated in one country would be mutually acceptable by regulatory authorities the United States, Japan, and the European Union.
- The International Ethical Guidelines for Biomedical Research Involving Human Subjects of CIOMS/WHO 2002 are a lengthy and detailed commentary on the *Declaration of Helsinki* with a special emphasis on research conducted in developing countries. It is intended to help WHO country members to develop their own national ethical policies for clinical research, guiding them how to adapt international ethical principles to their local realities, and to establish adequate procedures for the ethical review of research protocols of studies with human subjects participation. These guidelines contain 23 major recommendations.
- Ethical Considerations in Biomedical HIV Prevention Trials of the UNAIDS of 2007, which were created to help the conduct of this type of research as a response to the current controversies. This document contains 19 guidance points and is unique in its focus on international HIV prevention research.

Abbreviations: WMA, World Medical Association; CIOMS, Council for International Organizations of Medical Sciences; WHO, World Health Organization; ICH, International Conference on Harmonisation; UNAIDS, Joint United Nations Programme on HIV/AIDS.

in one country would be mutually acceptable by regulatory authorities the United States, Japan, and the European Union (14). In 2000, Joint United Nations Programme on HIV/AIDS (UNAIDS) published *Ethical Considerations in HIV Preventive Vaccine Research* to provide guidance to HIV vaccine researchers. This document, renamed *Ethical Considerations in Biomedical HIV Prevention Trials*, was substantially revised in 2007 (15).

Clearly, researchers conducting vaccine trials in developing countries face a complex web of international regulations (Table 1). What guidance can be distilled for researchers?

The most relevant international documents to vaccine researchers are the WMA *Declaration of Helsinki*, CIOMS *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, ICH *Guideline for Good Clinical Practice*, and the UNAIDS *Ethical Considerations in Biomedical HIV Prevention Trials* (Table 2). As we shall discuss below, each of the documents contains controversial provisions. The documents also possess important elements in common. As each document is guided by the same moral principles, it is not surprising that there is considerable convergence among these documents. All the documents require that proposals to conduct clinical research be submitted to an independent committee to ensure ethical acceptability (WMA 15; CIOMS 2; ICH 2.6; UNAIDS 4). Informed consent must be obtained from study participants (WMA 24; CIOMS 4; ICH 2.9; UNAIDS 16). If a potential research subject is incapable of providing consent, then the consent to study participation must be sought from the subject's legally authorized representative (WMA 28; CIOMS 4; ICH 4.8.5; UNAIDS 10). The potential benefits and harms of study participation must be carefully evaluated (WMA 18; CIOMS 8; ICH 2.2; UNAIDS 11, 12). Finally, vulnerable populations in research are entitled to special protection (WMA 9; CIOMS 13; ICH 3.1.1; UNAIDS 8).

While this general guidance is of use to all researchers, those conducting vaccine trials in the international setting require more specific guidance, especially on issues of current controversy. The following guidance is based on provisions in one or more of the relevant international guidelines as interpreted through the lens of grounding moral principles.

CURRENT CONTROVERSIES

1. Is there one international standard for informed consent?

   The obligation to obtain informed consent from research participants is well established. Precisely how informed consent is sought may reasonably differ from one context to another. The principle of respect for persons