

1. Introduction: the 2024 revision of the Declaration of Helsinki

1.1 Significance of the 2024 revision of the DoH

The World Medical Association's (WMA) 10th Amendment to the Declaration of Helsinki (DoH)¹ was adopted on 19 October 2024, marking the 60th anniversary of its first adoption in Helsinki, Finland, in 1964. The 2024 WMA General Assembly (GA) was held in Helsinki. This revision was reported in the WMA press release² and a series of articles in *JAMA*^{3,4,5,6,7,8,9} on the day of adoption, and soon after in *Science*¹⁰, *Nature Medicine*¹¹, and *BMJ*¹².

The authors attended in the GA and the commemorative ceremonies as the members of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP), an international organisation under the Memorandum of Understanding (MoU) with the WMA for collaboration. In this report, we outline the two-and-a-half-year process of the revision, as well as the GA, and the main contents of the amendment, including interviews with experts.

A more concise report was previously published in *IFAPP TODAY*¹³.

The major changes in the 2024 amendment were the replacement of the term “research subject” with “research participant” viewing them as partners of “co-creation” and requiring “meaningful engagement” of participants and their communities in all stages of the research. While recognising structural inequities in research, the concept of protecting vulnerable people, who have been likely to be excluded from research, has been shifted to promoting their inclusion on the premise to providing

¹ WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants. 2024. <https://www.wma.net/policies-post/wma-declaration-of-helsinki/>

² World Medical Association. Revised Declaration of Helsinki adopted by the global medical community, strengthening ethical standards in clinical research involving humans. 21st October 2024. <https://www.wma.net/news-post/revised-declaration-of-helsinki-adopted-by-the-global-medical-community-strengthening-ethical-standards-in-clinical-research-involving-humans/>

³ Bibbins-Domingo K, Brubaker L, Curfman G. The 2024 Revision to the Declaration of Helsinki: Modern Ethics for Medical Research. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22530. Epub ahead of print. PMID: 39425945.

⁴ Resneck JS Jr. Revisions to the Declaration of Helsinki on Its 60th Anniversary: A Modernized Set of Ethical Principles to Promote and Ensure Respect for Participants in a Rapidly Innovating Medical Research Ecosystem. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.21902. Epub ahead of print. PMID: 39425954.

⁵ Shaw JA. The Revised Declaration of Helsinki-Considerations for the Future of Artificial Intelligence in Health and Medical Research. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22074. Epub ahead of print. PMID: 39425951.

⁶ Bloom L. Revisiting the Declaration of Helsinki-A Patient-Centered Perspective. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22077. Epub ahead of print. PMID: 39425946.

⁷ Reis AA, Upshur R, Moodley K. Future-Proofing Research Ethics-Key Revisions of the Declaration of Helsinki 2024. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22254. Epub ahead of print. PMID: 39425950.

⁸ Saenz C, Carracedo S. The Revision of the Declaration of Helsinki Viewed From the Americas-Paving the Way to Better Research. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22270. Epub ahead of print. PMID: 39425947.

⁹ Bierer BE. Declaration of Helsinki-Revisions for the 21st Century. *JAMA*. 2024 Oct 19. doi: 10.1001/jama.2024.22281. Epub ahead of print. PMID: 39425949.

¹⁰ O'Grady C. Cornerstone medical ethics guidelines get a major update. *Science*. 2024 Nov;386(6721):473-474. doi: 10.1126/science.adu2384. Epub 2024 Oct 31.

¹¹ Declaration of Helsinki embraces health equity. *Nat Med*. 2024 Dec 2. doi: 10.1038/s41591-024-03433-5. Epub ahead of print. PMID: 39623088.

¹² Sheather J. Declaration of Helsinki puts global justice up front. *BMJ*. 2024 Nov 1;387:q2405. doi: 10.1136/bmj.q2405. PMID: 39486836.

¹³ Kurihara C, Matsuyama K, Baroutsou V. Collaboration with the WMA and Key Contribution to the 2024 Revision of the Declaration of Helsinki. *IFAPP TODAY*. 2024; Nov/Dec (49): 8-12. <https://ifapp.org/wp-content/uploads/2024/11/IFAPP-TODAY-49-NovDec-2024.pdf>

adequate safeguards and sharing the benefit of research. Linking with the Declaration of Taipei (DoT) on health databases and biobanks¹⁴ is expected to have a major impact on research practice.

On the other hand, the remaining challenges include the issues of placebo-controlled trials and post-trial access.

The authors have been involved in this revision process as members of the Ethics Working Group of the IFAPP, and also from an independent academic perspective, apart from IFAPP. It has taken a variety of forms, including official submissions of opinions, meetings and publications, collaborating with experts and groups of patients and the public, with the aim that the improved principles will reflect the perspectives of the most vulnerable research participants. The content of each paper or lecture or presentation does not represent the consensus of the IFAPP. We are still engaged in some projects in the form of discussion meetings and publications to implement the new DoH, into actual research and research review practices.

This report outlines a brief process of revision and future perspectives.

1.2 WMA Regional Meetings and Participation of the IFAPP

The official start of the revision process by the WMA was in April 2022; prior to this, IFAPP submitted an opinion in 2019 to clarify the points requiring revisions, in accordance with the MoU with the WMA, and in response to the WMA's request. Subsequently, the authors have stimulated international discussions in various forms of collaboration with, but independently of the WMA. Baroutsou was invited to speak at the WMA's regional meeting in Copenhagen¹⁵, and Kurihara at the last regional meeting in Washington DC¹⁶. Most of the WMA regional meetings were streamed live, and some of the recordings are still available (Table 1). Thus, Kurihara was able to attend all of the meetings, either in person or remotely.

IFAPP members held numerous web meetings with WMA speakers, published three peer-reviewed papers^{17 18 19} in international journals, and held discussions with the Japanese Association of Pharmaceutical Medicine (JAPhMed) IFAPP's Japanese member, and published articles in *IFAPP TODAY*, the official journal of IFAPP (see proceedings of lecture by Baroutsou for details)²⁰. During 2024, there were two public consultations (Table 1), where opinions were submitted jointly by members of the IFAPP Ethics Working Group (not an official opinion of IFAPP).

¹⁴ The World Medical Association. The Declaration of Taipei on ethical considerations regarding health databases and biobanks. 2002. Last revised 2016. Available at <https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/>

¹⁵ Baroutsou V. Exploring New and Emerging Trial Designs Considering the Revision of the Declaration of Helsinki. *IFAPP TODAY*. 2023; Nov/Dec (39): 14-17. <https://ifapp.org/wp-content/uploads/2023/11/IFAPP-TODAY-39-2023.pdf>

¹⁶ Kurihara C. Participation in WMA meeting in Washington DC: Taking forward bioethics and human rights, maximizing the impact of the NEW DoH. *Clin Eval*. 2024; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html

¹⁷ Kurihara C, Baroutsou V, Becker S, Brun J, Franke-Bray B, Carlesi R, Chan A, Colli LF, Kleist P, Laranjeira LF, Matsuyama K, Naseem S, Schenk J, Silva H and Kerpel-Fronius S. Linking the Declarations of Helsinki and of Taipei: Critical Challenges of Future-Oriented Research Ethics. *Front. Pharmacol*. 2020. 11: 579714. doi: 10.3389/fphar.2020.579714

¹⁸ Kurihara C, Kerpel-Fronius S, Becker S, Chan A, Nagaty Y, Naseem S, Schenk J, Matsuyama K, Baroutsou V. Declaration of Helsinki: ethical norm in pursuit of common global goals. *Front Med (Lausanne)*. 2024 Apr 2;11:1360653. doi: 10.3389/fmed.2024.1360653.

¹⁹ Kurihara C, Greco D, Dhali A, Matsuyama K, Baroutsou V. Vulnerability, social value and the equitable sharing of benefits from research: beyond the placebo and access debates. *Front. Med*. 2024; 11:1432267. doi: 10.3389/fmed.2024.1432267

²⁰ Baroutsou V. Collaboration with the WMA and the IFAPP's perspective. *Clin Eval*. 2024; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html

Other activities independent of IFAPP included monthly web meetings with a patient and public group to discuss the DoH²¹ since 2020, the publication of a Springer book²², and numerous meetings and proceedings publications in the Japanese journal *Clinical Evaluation*²³.

Table 1 WMA Regional Meetings, General Assembly, where IFAPP members participated

<https://www.wma.net/what-we-do/events/>

Year, month, date Meeting venue	Topics URL: materials are available	Participants from the IFAPP
2022 December 9-11 Tel-Aviv, Israel	General Data-driven research	Chieko Kurihara, EWG of the IFAPP, in-person participation
2023 February 24, 25 Sao Paulo, Brazil	Placebo-controlled trial	Chieko Kurihara, EWG of the IFAPP, in-person participation
2023 September 21, 22 Copenhagen, Denmark	Emerging trial design	Varvara Baroutsou, President of the IFAPP, invited as a speaker, in-person participation
2023 November 30, December 1 Tokyo, Japan	Disaster settings	Chieko Kurihara, EWG of the IFAPP, in-person participation
2024 January 13 – February 7 Public Consultation (phase 1)		
2024 January 18, 19 Vatican City State	Resource-poor settings Vulnerable population; post-trial access https://www.wma.net/events-post/wma-conference-on-the-revision-of-the-declaration-of-helsinki-research-in-resource-poor-settings/	Chieko Kurihara, EWG of the IFAPP, online observation
2024 February 18, 19 Johannesburg, South Africa	Vulnerability https://www.wma.net/events-post/wma-regional-meeting-in-africa-on-the-revision-of-the-declaration-of-helsinki/	Chieko Kurihara, EWG of the IFAPP, online observation
2024 May 14, 15 Munich, Germany	Research with vulnerable people https://www.wma.net/events-post/research-with-vulnerable-people-a-targeted-interdisciplinary-discussion-within-the-scope-of-the-wma-declaration-of-helsinki-revision/	Chieko Kurihara, EWG of the IFAPP, online observation
2024 June 3 – 24 Public Consultation (phase 2)		
2024 August 15, 16 Washington DC, United States	General Maximizing impact of the DoH: communications, advocacy and implementation	Chieko Kurihara, EWG of the IFAPP, invited as a speaker, in-person participation
2024 October 16-19 General Assembly Helsinki, Finland	Adoption of the 2024 revision of the DoH	Varvara Baroutsou, Chieko Kurihara, and Kotone Matsuyama, IFAPP, in-person participation

²¹ Kurihara C, Inoue K, Kai H, Suzuki K, Saeki H, Funabashi Y, Kishi N, Kuge A, Murakami T, Saito Y, Uchida E, Tsutsumi N, Imamura K. Our “WMA Declaration of Helsinki”: opinions and proposals from patient and public for research ethics. In: Kurihara C, Greco D, Dhali A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023. p.243-69.

²² Kurihara C, Greco D, Dhali A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023.

²³ *Clin Eval*. 2024; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html

1.3 Overview of the WMA General Assembly in Helsinki

The WMA GA in Helsinki was held from Wednesday 16 October, to Saturday 19 October, 2024. In the Medical Ethics Committee on the 16th, the Uruguay Medical Association submitted motions against paragraph 33 on the use of placebo and paragraph 34 on post-trial access (Table 2). Although a small number of medical associations expressed their support, the German Medical Association and the Dutch Medical Association stated that the original proposal should be retained so as not to inhibit necessary research. Uruguayan proposal was put to a vote and lost. The original proposed draft was then approved by the Medical Ethics Committee. During the subsequent opportunities for discussions at the Council and GA sessions, no further views were expressed.

Table 2 DoH 2024 and motions from Uruguay on placebo and access^{*1}

	DoH 2024	Motions from the Uruguay Medical Association
Para 33	If proven intervention exists, placebo-controlled trials can be acceptable if:	
	<ul style="list-style-type: none"> • No “additional risks of serious or irreversible harm” 	<ul style="list-style-type: none"> • No additional risks of harm (motion to delete “serious or irreversible”)
	Similar position: <ul style="list-style-type: none"> • ICH-E10²⁴; • DoH 2002~2013; • CIOMS 2002 	Similar position: <ul style="list-style-type: none"> • DoH 1996; 2000; • CIOMS 2016^{25*}2; • IFAPP members’ paper ^{*3}; • Helsinki Statement²⁶
Para 34	<ul style="list-style-type: none"> • Post-trial provisions must be arranged; • Exception must be approved by a research ethics committee 	<ul style="list-style-type: none"> • Post-trial access provisions must be guaranteed; • Text for exception should be deleted
	Similar position: <ul style="list-style-type: none"> • DoH 2004~2013 	Similar position: <ul style="list-style-type: none"> DoH 2000; IFAPP members’ paper^{*3} Helsinki Statement²⁶

^{*1} Slightly modified from the Table in our paper published in IFAPP TODAY¹³;

^{*2} Acceptable risk of placebo if proven intervention exist in the CIOMS 2016 guidelines²⁵ is “minor increase above minimal risk”;

^{*3} This does not mean that it is a consensus of IFAPP or’ IFAPP’s Ethics Working Group



Discussions on the revision of the 2024 DoH at the Medical Ethics Committee, Oct 16, 2024, at the General Assembly venue, Scandic Marina Congress Center, Helsinki, Finland.

²⁴ ICH harmonised tripartite guideline: choice of control group and related issues in clinical trials E10. 2000.

²⁵ Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans. 2016. <https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/>

²⁶ Helsinki Statement Stakeholders. Helsinki Statement 2024. *Clin Eval*. 52(3):

http://cont.o.oo7.jp/52pop/HelsinkiStatement_18Oct24_final.pdf

English, Japanese, Arabic versions are available at the website below; other translations are welcomed.

http://cont.o.oo7.jp/52pop/52pop_contents_e.html

During these meetings, Dr. Jack Resneck, of the American Medical Association, who chaired the workgroup, gave a comprehensive explanation of how the revisions responded to changes in the society and medicine. The President of the WMA, the President of the Finnish Medical Association who hosted this GA, and others expressed their appreciation for the excellence of the revision. The following section 2 will present the views of key experts who supported the final version and those who disagreed, based on interviews with them, their comments at formal meetings, and free discussions. All positions included here had the permission of the commentators.

1.4 Remaining challenges: Uruguay Medical Association's position and Helsinki Statement

The website of the Uruguayan Medical Association published on 16 October that Latin America and Southwest Europe (Spain, Portugal, France, and Italy) consider paragraphs 33 and 34 to be a regression from the highest ethical principles set forth in 2000²⁷. The authors of this report held two web meetings on 15 and 20 October between Helsinki and the rest of the world and issued the "Helsinki Statement"²⁶ on 18 October which was notified to the WMA. This was not an IFAPP's initiative but was organised by the authors in cooperation with external experts. The statement congratulated the 10 improvements in this revision. It also expressed the desire to collaborate for the implementation of this revision and to address the remaining challenges including the issues of placebo and access, in both research conduct and research review, with the aim of strengthening the protection of research participants while ensuring scientific integrity of research. The Statement was endorsed by many particularly in the Global South and Asia, which are briefly presented at the end of this report.

²⁷ Sindicato Médico del Uruguay. SMU propone cambios en la Declaración de Helsinki. miércoles 16 de octubre de 2024. <https://www.smu.org.uy/el-smu-en-la-asamblea-de-la-asociacion-medica-mundial-propone-cambios-en-la-declaracion-de-helsinki/>