Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

Clin Eval 52 (3) 2025

Report

World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki*

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Abstract

The 10th amendment of the World Medical Association (WMA)'s Declaration of Helsinki (DoH) was adopted on October 19, 2024, during the General Assembly (GA) in Helsinki, Finland. The authors participated in the GA as the members of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP). This report outlines the revision process and discussions during the GA, based on interviews with key experts.

It also introduces "Helsinki Statement" we issued on October 18 independently from both the WMA and IFAPP collaborating with global stakeholders, for expanding the impact of the new DoH, including tackling with the remaining challenges, in order to improve the practice of research conduct and research review, aiming at achievement of equitable global health.

Key words

the Declaration of Helsinki, community engagement, vulnerability, co-creation, the Declaration of Taipei

＊This article includes summaries of interviews with participants in the General Assembly (GA) of the World Medical Association (WMA), held from 16 to 19, October, 2024, in Helsinki, Finland. Each summary of interview was reviewed by each interviewee. Photos were mainly taken by the authors and photos provided by the WMA are with the note "Photo: ©WMA". Authors (interviewers) participated in the GA of the WMA as members of IFAPP but this article is written independently from the IFAPP. "Preprint" of this article was published online between December 10 to 24, 2024, and replaced with the final version published online in early 2025, at the journal website: *Clin Eval*. 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

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 release[2] 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 twoand-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

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[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 biobanks[14] 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 Copenhagen[15], and Kurihara at the last regional meeting in Washington DC[16]. 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).

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[14] The World Medical Association. The Declaration of Taipei on ethical considerations regard- ing 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, Collia 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, Dhai 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 DoH[21] since 2020, the publication of a Springer book[22], 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, Dhai A, editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023. p.243-69.

[22] Kurihara C, Greco D, Dhai 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

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
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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:	
	・No "additional risks of **serious or irreversible** harm"	・No additional risks of harm (motion to delete "serious or irreversible")
	Similar position: ・ICH-E10[24]; ・DoH 2002～2013; ・CIOMS 2002	Similar position: ・DoH 1996; 2000; ・CIOMS 2016[25]※2; ・IFAPP members' paper ※3; ・Helsinki Statement[26]
Para 34	・Post-trial **provisions** must be **arranged**; ・Exception must be approved by a research ethics committee	・Post-trial **access** provisions must be **guaranteed**; ・Text for exception should be deleted
	Similar position: ・DoH 2004～2013	Similar position: DoH 2000; IFAPP members' paper※3 Helsinki Statement[26]

※1 Slightly modified from the Table in our paper published in IFAPP TODAY[13];
※2 Acceptable risk of placebo if proven intervention exist in the CIOMS 2016 guidelines[25] 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 2000[27].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/

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2. Interviews with key experts

2.1 Dr. Lujain Alqodmani, the Immediate Past President of the World Medical Association (2023-2024)

Interview: Chieko Kurihara, Kotone Matsuyama, Varvara Baroutsou

① Message from the President for peace, health and human rights

Dr. Lujain Alqodmani who served as the President of the World Medical Association (WMA) for the term 2023 to 2024 accepted our interview just before the adoption of the Declaration of Helsinki (DoH) at the General Assembly (GA) plenary session on October 19. Her last speech as the President at the Council session on October 18 was truly impressive[28]. She started her speech from the episode when she was in the United Nation and her husband was caring her daughter Yasmin, who also played an important role at the GA in Helsinki to give us message that the world leader can accomplish her simultaneous pursuit of responsibility as a mother.

In her final message as the WMA President, she called for peace for the sake of health, for the sake of rights, for the dignity of all people, and for the enjoyment of equal capacity-building opportunities. Let us work together to call for peace and to identify the key determinants of health, to set priorities, to reflect the voices of those who cannot speak, and to ensure that medical research contributes to improving health not only through individual research participation, but also to the realization of equitable global health, including realization of women's rights around the world.

Dr. Lujain Alqodmani's last speech as the President of the WMA, at the Council session on October 18, 2024. Photo: ©WMA

Before the formal ceremonial dinner, talk between Presidents of the WMA and IFAPP, with WMA President's daughter, Yasmin.

Interview with Dr. Lujain Alqodmani, just before the adoption of the revised DoH on October 19.

②DoH as a symbol of global collaboration

She stated that the Declaration of Helsinki is a symbol of our determination to act together, a symbol of shared commitment and unity toward the highest ethical standards, discussed and agreed among the stakeholders from a number of regions including conflict-affected countries. She was very much proud and honorable with the achievement through the exciting process of extensive discussions in regional meetings. The workgroup achieved a marvelous job. The inputs and the reflections of the diversity of the WMA is fantastic and it was valuable to integrate the expertise and feedback received from partners, including IFAPP. Adoption at the GA is just a starting point. The next step is

[28] Lujain Alqodmani. Valedictory speech by the WMA President, Dr. Lujain Alqodmani Helsinki, Finland, 18 October, 2024. *World Medical Journal.* 2004; 70(4): 4-5.
https://www.wma.net/wp-content/uploads/2024/12/WMJ_2024_04.pdf#page=26

implementation, dissemination, communication. This was also the key topic of the last session of the last regional meeting in Washington, DC, where Dr. Alqodmani was a moderator and Kurihara was a panelist.

The DoH is not a document only for physicians but it is a document for all healthcare professionals or researchers and for patients, so we have great collaboration now with alliance of patient organizations. We wish to explain to the patients what are their rights.

③Tackle with the inhuman situations

During our interview, Dr. Alqodmani also spoke about the need to tackle with the inhuman situations taking place in the world. Since she was inaugurated as the President of the WMA October 2023, throughout her presidency, there has been immense danger in health care all over the world. We are now seeing devastative situations of tremendous attacks against the healthcare facilities and other complex situations of violating humanitarian laws. In Ukraine, unfortunately, in Sudan, in Gaza, and now in Lebanon.

And not just during conflicts, but also in many other disaster situations. There are heartbreaking, tragic incidents are emerging that the doctors face, although they have to be assured safe working environments. Like the incident of the rape and killing of Indian junior doctor that happened in India and many doctors are now taking streets, demanding for a safe working environment.

④Doctors' moral duty for SDGs

There is our moral duty. Despite the fact that we are nearing the end of 2024 and only five years away from fulfilling "sustainable development goals" (SDGs), including the universal health coverage. We are still left behind. We are still lacking a very strong political power. Commitment from our government to really prioritize health is needed. The health of the people and the rights of the professionals that provide health care must be at the top of their political agenda.

⑤Support for the realization of women's rights

Dr. Alqodmani is the fifth woman President of the WMA, representing the Kuwait Medical Association. In Kuwait, women have the right to vote, to be members of the parliament. There have been women who are ministers of health, directors of hospitals, CEOs and other privileged positions at organizations. But never had a woman who has been the president of the Kuwait Medical Association. There's still so much work to be done to ensure to create the right support structure and the leadership avenue for women. Structures to support vulnerable people including women would be necessary, considering each situation. Maternity leave for women residents is one month. The doctors have to go back to work, leaving her child behind. There are many other challenges, but great progress has been seen compared to some other countries.

⑥As a Global Leader

She is engaged in medical service as an emergency physician in Kuwait, holding vital roles such as the co-chair of the WMA Environment Caucus and International Relations Director at Kuwait Meical Association, also having influential positions at Women in Global Health and the International Federation of Medical Students' Association, where she represented the Eastern Mediterranean Region.

The duties of the WMA President were handed over to the incoming President at the GA on October 19. Interviewers expressed our hope that IFAPP will continue to collaborate with the Past President by creating opportunities to learn from her marvelous rich experience.

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2.2 Dr. Jack Resneck, American Medical Association, Chair of the Workgroup for the revision of the DoH

Summarized from the Dr. Jack Resneck's presentations in Helsinki, considering some conversations, by Kurihara C, Matsuyama K, Baroutsou V.

①Overview of the revision

Dr. Jack Resneck, American Medical Association, who chaired the Workgroup was highly appraised during the meetings for his excellent management of the regional meetings held in various locations and the day-and-night conversations through e-mails and web meetings.

Dr. Resneck introduced various challenges raised during the regional meetings, focusing on topics to respond the changes in the society and medicine, e.g., the development of artificial intelligence (AI) and privacy protection (Tel Aviv), controversial placebo-controlled trials (Sao Paulo) and post-trial access (Vatican), emerging clinical trial designs (Copenhagen), the public health crisis (Tokyo), research in low-resource settings. The final meeting in Washington, DC, encompassed all these topics and remaining challenges and strategies for implementation of the revised DoH.

The paramount importance of the revision was the change of the term "subject" to "participant" with the promotion of meaningful community engagement regarding community members as partners of co-creation, ensuring sharing of benefits from research (Para. 6). The revision also highlighted collaborative responsibilities of non-physicians in teams and organizations (Para. 7).

Right: Conversation to celebrate the achievement, just after the adoption of the DoH at the Plenary Session of the General Assembly October 19, to the Workgroup Chair from IFAPP President.

Left: Presentation by Dr. Jack Resneck, Workgroup Chair on the successful revision of the DoH at the General Assembly October 19, 2024. Photo: ©WMA.

②Justic principle and medical ethics

Discussions of research in low-resource settings, particularly in view of global justice, included the need to recognize structural inequalities in research in risks and benefits assessment (Para. 6), and that the purpose of research is to advance individual and public health (Para. 7) maintaining the core principle that these purposes never take precedence over the rights of individual research participants (Para. 7) and that the benefit from research should be shared equally in the community.

③Protection of the vulnerable

The protection of vulnerable people was discussed at three regional meetings, with the principle of viewing vulnerability as dynamic, which had been traditionally considered fixed, and promoting their participation in research in an equitable and inclusive manner (Para. 19, 20), including women, children, and marginalised people. Whereas reforming the previous idea regarding exclusion to be the default, reflecting the regretful history, a protective sentence was also retained (last sentence in Para. 20).

④Research integrity, ethics review, and the Taipei Declaration

It is also important to note that the "research waste" should be avoided (Para. 21) and "research misconduct" must be prevented (Para. 12), ensuring scientific integrity. Research ethics committee's function was strengthened with the familiarity with local context and inclusion of a member of the general public (Para. 23). The reference to the Taipei Declaration and the statement of principles for handling large amounts of data and samples (Para. 32) are also in line with today's rapid development of AI research.

⑤Placebo use and post-trial access

The use of placebos when there is a proven intervention (Para. 33) was discussed with the Latin American community at the meeting in São Paulo involving stakeholders including CONFEMEL (Confederación Médica Latinoamericana y del Caribe, the association of medical organizations from Ibero-America and Caribe, it represents around 500,000 doctors grouped in associations). The revised texts in the motions from Uruguay Medical Association were discussed in Workgroup but through discussions reached to the final proposal. Post-trial access was strengthened by changing the term "should" to "must" with regard to making arrangement for access prior to starting clinical trials (Para. 34).

⑥Informed consent and unproven treatment

When obtaining consent from a representative for incapable person, this person's preferences and values should be respected (Para. 28, 29). Regarding the clinical use of unproven treatments, emphasis was made that this should not be a way to circumvent the protection of the participant set in the DoH (Para. 37).

During the GA, Dr. Resneck repeatedly expressed his gratitude to the members of the workgroup for accomplishing the hard task to achieve these substantial revisions.

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2.3 Dr. Mvuyisi Mzukwa, Chairperson, South African Medical Association

Interview: Kurihara C

①Community engagement and vulnerability

Dr. Mvuyisi Mzukwa, Chairperson of the South African Medical Association (SAMA), regards the 2024 revision as an important milestone. The WMA's regional meetings were held in various regions and two times of public consultations were provided, that are inclusive and fair process, where a variety of views have been presented. The regional meeting in Johannesburg, South Africa, emphasized the importance of community engagement which leads to benefit sharing in the community; the new text in paragraph 6 on community engagement was mainly based on the proposal from the SAMA and extensive discussion in Johannesburg. This was presented by Dr. Edward Ngwenya during the meeting in Johannesburg.

Regarding the direction to promote research participation of vulnerable groups, it is important to respect the dignity of communities and participants, considering contextual and dynamic vulnerability. This was also important focus at the Johannesburg meeting. The process was inclusive way to listen to African voices. Promotion of engagement must be with strengthening protection.

The deletion of the word "social value" was disappointing, but many objections were understandable. Words can have different meanings depending on the social background.

Dr. Mvuyisi Mzukwa, Chairperson of the SAMA, a member of the Workgroup for the revision of the DoH at GA in Helsinki. On October 18, 2024, during the Council session.

Dr. Edward Ngwenya, a member of the Workgroup for the revision of the DoH, during the regional meeting in Johannesburg, explaining proposals from SAMA for extensive discussions on community engagement and vulnerability. On February 19, 2024, the second day of the meeting. Image captured from video.

②Placebo and post-trial

SAMA has sympathy with the Uruguay's position. As for the difference of the level of the risk of placebo group when there is a proven intervention between CIOMS (*minor increase above minimal risk*) and the DoH (*no increase of serious or irreversible harm*), we support the CIOMS, however, there had been explanations that there is no significant difference between these languages, thus, current wording would be a compromising position.

Provision for post-trial access "must" be arranged, and exception "must" be approved by the Research Ethics Committee. This approval must be based on understanding of the value of the community, the function of which has been strengthened. This strengthened post-trial access requirement needs to be disseminated widely.

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

2.4 Prof. Daniel Fu-Chang Tsai, Taiwan Medical Association; National Taiwan University

Interview: Kurihara C, Matsuyama K, Baroutsou V

①Extensive changes, including the incorporation of the Taipei Declaration

Prof. Daniel Fu-Chang Tsai, Taiwan Medical Association, stated that the 2024 revision is extensive and includes some new concepts. The change from "research subject" to "research participant", the broadening of the scope to include non-physicians, the engagement of organizations and community, and the incorporation of the Taipei Declaration into the DoH are important changes.

②Post-trial provision and inclusion of vulnerable people

Post-trial provision (access) is not always possible and may sometimes be a violation of laws. Physicians' obligation to provide care to patients after completion of the trial needs to be found in a way that is both ethically and legally appropriate and feasible in terms of resources.

Much has been discussed about vulnerable populations. Strengthened protection of vulnerable people has resulted in difficulties in research, which leads to inadequate evidence for better health for these people. We have moved in the direction that they should not be excluded unless there is sufficient reasoning.

Prof. Daniel Fu-Chang Tsai, interviewed by Kotone Matsuyama on cutting-edge research and research review in Taiwan.

Prof. Danel Fu-Chang Tsai, and interviewers: Kurihara, Matsuyama, just after the Council session October 18, 2024. As Prof. Tsai has been long engaged in the WMA's activity, his lecture in 2013 Tokyo meeting and achievement at the time of 2016 Taipei Declaration were previously reported in Clinical Evaluation in 2013 (http://cont.o.oo7.jp/41_2/p337-49eng.pdf) and in 2018 (http://cont.o.oo7.jp/46_1/p135-45.pdf).

③Taipei Declaration and Biobanks in Taiwan

Mentioning the DoT in the DoH will raise awareness about the ethical operation of biobanks and health databases. Taiwan has been struggling with strict legal regulations on biobanks. Now a consortium of biobanks has been established by the government, and researchers can apply through a single window for the use of resources from different biobanks relevant to their study purposes. Coded samples from which personal information is removed are available. Research ethics committee review at the hospitals or research institutes of research using samples from biobank is required, which evaluates not only the appropriateness of the use of the samples but also the scientific values of the research.

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
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④Ethical review system in Taiwan including reviewing advanced technology

In Taiwan, a joint IRB system was established in 1997 but its use has been decreasing. Instead, the Collaborative IRB (CIRB) system was launched in 2013 and has been widely used to enhance review efficiency and quality. This means that one IRB conducts the primary review for multi-center research while other collaborative IRBs will conduct expedited reviews after the primary review is approved. Many institutions in Taiwan have received international accreditations from FERCAP (The Forum for Ethical Review Committees in the Asian and Western Pacific Region, WHO) and/or AAHRPP (Association for the Accreditation of Human Research Protection Programs, an international accreditation provided by a US organization). However, the review quality is standardized and monitored by the domestic accreditation system set up and operated by the Ministry of Health & Welfare of the Taiwan Government under a clear legislative framework. The review of research involving advanced technologies, e.g., regenerative medicine, stem cell therapy, gene therapy, CAR-T cell therapy, etc., is reviewed by accredited IRBs and the Taiwan FDA's review, with relevant expertise in specific scientific details. Concerning the regulation of research and application of regenerative medicine, Taiwan has learned from the experiences of the Japanese model.

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval.* 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

2.5 Dr. Ramin Parsa-Parsi, German Medical Association; Workgroup Chair of the 2013 revision of the DoH

Interview: Kurihara C, Matsuyama K, Baroutsou V

①Most impressive or important changes to the DoH

Since its adoption in 1964, the Declaration of Helsinki (DOH) has been revised several times to make it more comprehensive and to respond to the changing research environment. However, the core set of ethical principles in medical research remain consistent. Hence, most of the changes made in the latest review of the DoH serve to clarify the existing provisions.

One significant development is the fact that the DoH now addresses not only physicians, but all individuals, teams and organisations involved in medical research, because the World Medical Association (WMA) considers the DoH principles fundamental to the respect for and protection of all research participants. Furthermore, by more prominently referring to healthy volunteers in clinical studies, the revised DoH recognises their significant contribution.

Another significant development is the reference to the WMA Declaration of Taipei (DoT) in paragraph 32, which provides guidance on research using health databases, big data and biobanks. This reference will increase the visibility of the DoT. The WMA will therefore have to ensure that this document, adopted in 2016, is updated accordingly.

The most important changes may, however, be the amendments to paragraphs 19 and 20 on the subject of vulnerability. These amendments, which followed long and comprehensive deliberations during three expert meetings, present a new compromise wording that will have significant impact on medical research with groups or individuals in situations of vulnerability.

Left: Dr. Ramin Parsa-Pasi at the venue just after the adoption of the 2024 DoH on October 19, at the Plenary Sesson of the General Assembly.

Right: Cerebration message for the 60th Anniversary of the DoH, at the event space Töölön Juhlasali where the DoH was first adopted in 1964, offered by the Finnish Medical

Other two messages are from Dr Kati Millimaki, the former WMA President, Finnish Medical Association, well known as one of the "three wise women" who strongly contributed to the 2000 DoH; and Kurihara, IFAPP.
https://ifapp.org/journal/november-december-2024-number-49/

Dr. Parsa-Parsi contributed as the former working group chair of the 2013 revision of the DoH and also chaired the revisions of the other two core documents cited in the DoH: the Declaration of Geneva (2017 revision) and the International Code of Medical Ethics (2022 revision).

②Achievements of Munich Regional Meeting (May 2024)

The German Medical Association (GMA) was very pleased to host one of the topical conferences in Munich as part of the ongoing revision of the WMA's DoH. The GMA teamed up with the WMA, the German National Academy of Sciences (Leopoldina), the American Medical Association, and the State Chamber of Physicians of Bavaria, to organise this meeting. Bioethics experts from around the world attended the meeting and focused their discussion on the aspect of vulnerability in order to contribute to the DoH revision process.

The conference focused on children and adolescents, pregnant people, the elderly, the incarcerated and people with disabilities. Previously, the DoH called for research to first be carried out on non-vulnerable groups; however, the strict application of the principle of subsidiarity could in fact be disadvantageous for the vulnerable groups, as they may, for example, be subject to delayed access to new therapies. The revised DoH now states that the harms of exclusion must be considered and weighed against any harms of inclusion. Of course, the protection for individuals and groups in a situation of vulnerability remains an important priority. The research must still respond to the health needs or priorities of this group. In addition, it must first be ruled out whether the research in question can be carried out on a less vulnerable group, and the group must stand to benefit from the resulting knowledge, practices or interventions.

③Comparing the 2013 and 2024 revisions

Both the 2013 and the 2024 revisions of the DoH represent the culmination of a comprehensive and systematic revision process. The respective international workgroups put great effort into being as inclusive and transparent as possible. The outcome of several expert conferences on different continents contributed to the discussion processes. In addition, stakeholders from around the world had the opportunity to submit their feedback during open public consultation phases. Issues such as the use of placebos in clinical trials with human participants, informed consent and or post-trial provisions were intensely discussed during both phases. The same applied to the discussions around vulnerable groups; however, the most recent revision process had a much stronger focus on this subject. The 2013 version of the DoH first introduced a paragraph on medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories. The 2024 version, on the other, hand expanded on these provisions by referring to the WMA's Declaration of Taipei. This addition reflects the evolution of data-driven research.

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2.6 Prof. Urban Wiesing, German Medical Association; Tuebingen University

Interview: Kurihara C, Matsuyama K

①Stability of ethical principles in the age of AI and post COVID-19

Prof. Urban Wiesing of the German Medical Association stated that a major achievement was the confirmation that we do not need to change the fundamental ethical principles. Confronting the new technologies such as digitalization, AI, and the experience of the COVID-19, do we need new ethical principle? The answer is very simple and clear: No. What we need is to work to apply them to new situations. A new paragraph on public health crises has been added, which states that the DoH principles remain the same. New technologies such as crisper, gene therapy, germline manipulation, etc. are emerging, but what is needed is an adequate risk-benefit assessment, not a change in principles or the addition of new principles. A distinguished research result from Tuebingen University was published in the front page of the Lancet. The emergence of such studies does not require special new legislations.

Prof. Wiesing, interviewed by Kotone Matsuyama on the revision of the DoH and review of cutting-edge research in Germany, Oct 16, 2024.

Prof. Urban Wiesing together with interviewers Kotone Matsuyama and Chieko Kurihara, just after the adoption of the revised DoH at the plenary session of the General Assembly. Prof. Wiesing has been engaged in long process not only this time of revision of the DoH, as well as other core documents of the WMA.

②Reform of principle for the vulnerable and various challenges

Having such premise emphasized, what we consider important is that paragraphs 19 and 20 brought significant change of the concept of vulnerable groups. The importance of promoting research while protecting vulnerable groups was recognized in this revision. Emphasis was placed on avoiding research waste ensuring research conducted with high level of science.

Regarding the use of personal data, the establishment of the European Health Data Space (EHDS) is underway, but even within the framework of the same EU General Data Protection Regulations, it differs greatly among countries, e.g., that of Denmark with liberalism and of Germany with strict regulations.

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2.7 Dr. Otmar Kloiber, Secretary General of the WMA

Interview: Kurihara C, Matsuyama K, Baroutsou V

①Important paradigm change

One important paradigm change in the revision is the replacement of the legal term "research subject" by "research participant". This is more than a matter of courtesy, but recognizes that patients play a key role in co-creation rather than being passive subjects. Patient involvement is required at all stages of research design, implementation, and result dissemination, but care should be taken to avoid manipulation of research data or results. In addition, and as advocated by the South African Medical Association in particular, community engagement in all steps of research is now promoted.

The second paradigm change lies in the aspect of vulnerability. While previously the priority was given to the exclusion of people or groups with vulnerabilities, now the question has to be asked, whether the vulnerability may be a reason to include, especially when an exclusion could aggravate the vulnerability or otherwise harm the group in question.

Dr. Otmar Kloiber, Secretary General of the WMA organizing the Council meeting on October 18, 2024.
Photo: ©WMA

Secretary General discussing with IFAPP President, IFAPP Working group chair and a member just after the completion of all the program of the General Assembly on October 19.
Dr. Kloiber provided many records of lectures and discussions in Clin Eval, mainly interview in Tokyo just before the 2013 revision of the DoH (http://cont.o.oo7.jp/41_2/p351-72eng.pdf), invited lecture and discussion at the Japanese Society of Clinical Pharmacology and Therapeutics in 2019 (http://cont.o.oo7.jp/48_1/48_1contents_e.html), and webinar in 2021 during the COVID-19 pandemic(http://cont.o.oo7.jp/49sup38/49sup38contents_e.html).

②Placebo use: difference between DoH and CIOMS

Regarding the difference in wordings of acceptable risk of research participants in placebo arm when there is a proven intervention between CIOMS (minor increase above minimal risk) and the DoH (no increase of risk of serious or irreversible harm), CIOMS people explained that there is no major difference. The DoH's position is that the risks of harm, pain, discomfort or suffering which are not serious or irreversible would be assessed comparing with the value of research by the research ethics committee and then by each research participant, as there are variety of significance and duration of such detriments.

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③Importance of governance structure articulated in the Declaration of Taipei

Referring the Declaration of Taipei (DoT) is another significant change that addresses research using identifiable data or specimen in situations where we cannot obtain explicit consent from individuals. The DoT extends the ideas of protection that have been shaped with the DoH into the world of virtual research, where some of the traditional tools of protection can no longer be applied or may be overburdening the research. The DoT offers substitute measures by and adherence to defined governance, technical security and ethical review. As more and more research will be done with data and specimens, the reference from the DoH to the DoT is necessary.

④Strengthened requirement for the use of unproven intervention in practice

In the strengthened paragraph of "Unproven Interventions in Clinical Practice", the new text "*These interventions must never be undertaken to circumvent the protections for research participants set forth in this Declaration.*" was added to clarify the already existing text "*…it should subsequently be made the object of research designed to evaluate safety and efficacy*". This is in response to the misunderstanding (or the purposeful misinterpretation) that the text of the DoH allows for the serial continuation of clinical practice of unproven intervention that should be conducted as research following all requirements of the DoH. The DoH gives valuable ethical guidelines for all new medical practices and methods, however, the last paragraph focusses on the use of unproven interventions individually and compassionately in practice.

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval.* 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
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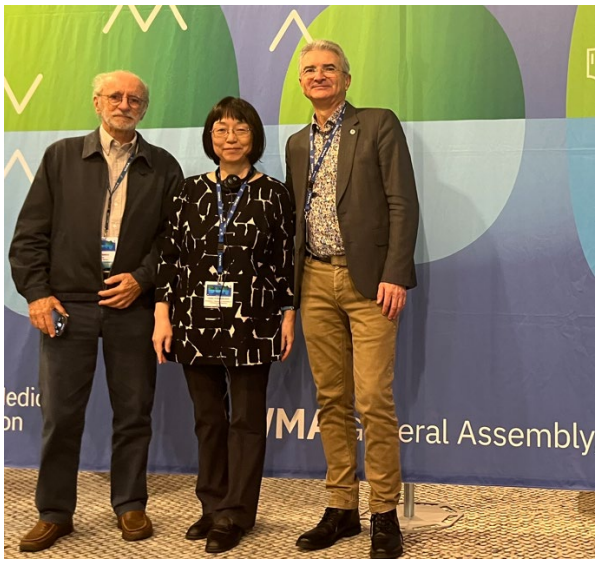
2.8 Prof. Dominique Sprumont, Professor of Health Law, University of Neuchatel, bridging between the CIOMS and the WMA

Interview: Kurihara C, Matsuyama K, Baroutsou V

①As a bridge maker

Prof. Sprumont received his PhD in 1993 on the thesis of protection of research participants in biomedical research with the support of Prof. Jay Katz and Prof. Robert Levine at Yale Law School and Yale Medical School. Returning to Switzerland he started his career as a legal advisor at the Swiss Drug Agency and drafted the 1993 regulation on clinical trials with medicinal products. Being supported by Prof. Levine he committed to the revision of the CIOMS guidelines since the 1993 revision, and subsequently for the 2000 and later revisions of the DoH, and was also involved in the drafting Taipei Declaration adopted in 2016. In all the process, he was acting as a bridge maker between stakeholders. He recently chaired the CIOMS Working Group on Good Governance Practice for Research Institutions. Kotone Matsuyama participated in this WG representing the IFAPP and the corresponding international guidelines were published in November 2023.



Left: Prof. Dominique Sprumont, at the ceremony just after the adoption of the DoH at the plenary session of the General Assembly, on October 19, 2024. He continuously attended the WMA regional meetings as a panelist, an academic adviser to the WMA, as well as bridge maker with CIOMS, as CIOMS Executive Committee member. Photo: ©WMA.

Right: With Prof. Dirceu Greco and an interviewer Chieko Kurihara, who interviewed both professors on each perspective on some controversial topics.

②Community engagement and Ubuntology

The inclusion of community engagement in this revision is a major change. The Belmont Report of the United States influenced the core foundation of the Declaration of Helsinki, but there has been a major shift in the WMA approach from individualism, which primarily respects autonomy, to a more collective one. Especially at the regional conference in Johannesburg, I learned the philosophy of Ubuntology, "We are therefore I am, I am therefore we are." This was introduced in contrast to the Kantian principle of autonomy "I think, therefore I am". This is also in line with the Western concept of "solidarity" and "reciprocity", as well as in the philosophy of Confucianism in Asia, and the Japanese culture to cherish "harmony" among people in spite of their differences and particularities.

③Social value of research and research waste

Another important change is the statement about avoiding "research waste". We learned from COVID-19 that the majority of research conducted during the pandemic was of limited or no social value. It is critical to evaluate the value of research not only from the view of the protection of research participants. Such paternalistic idea to overemphasize protection, which can be defined as "protectionism", is something of the past. Beyond the fact the protection of human participants must be guaranteed in medical research, research involving human participants must also respond to the common interest.

The term "social value" was clearly stated in the CIOMS guidelines as a requirement that does not supersede respect for human rights, and that scientific validity alone is not sufficient. However, if the expression "social value" was once included in the draft revision of the DoH, it was later deleted. The official reason was that some opinions during public consultation considered the concept as vague, but some national medical associations also expressed objection that it reminded too much the idea of communism or socialism. Experiences with the concept of social values vary according to historical and personal experiences and political context. For this reason, the DoH used instead the term "advance individual and public health", which is still consistent with the notion of social value as grounded in the 2016 CIOMS guidelines.

④Placebo debate

I have been involved in the placebo debate for a long time and have learned from it that it is difficult to find agreement between opposing views and that we should be careful not to spend too much time on it not to lose the opportunities to discuss other important topics. We have explained to the Workgroup that there is not a major difference of the wordings for acceptable risk of participants in placebo arm between CIOMS (minor increase above minimal risk) and the DoH (no increase of risk of serious or irreversible harm). The regional meeting in Sao Paulo addressed this issue head-on, but no one presented explicit evidence that the DoH's language has caused ethically problematic placebo-controlled trials being conducted.

In theory, the Uruguay Medical Association's argument is supported. The DoH has taken a pragmatic stance in its choice of words, which is a political science to maintain a highly influential document on the legislations worldwide and research ethics principles globally. Such topics raising conflicting views should be considered a practical decision by research ethics committees and regulatory authorities in each community, case by case basis. Art. 33 par. 2 of the DoH can not be clearer about this: "Extreme care must be taken to avoid abuse of this option." In case of doubt, the use of placebo should be avoided.

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2.9 Prof. Dirceu Greco, Professor Emeritus, Infectious Diseases and Bioethics, Federal University of Minas Gerais, Brazil; Member of 2016 revision of the CIOMS Guidelines, WMA Associate member

Interview: Kurihara C, Matsuyama K, Baroutsou V

①Placebo-controlled trials and post-trial access

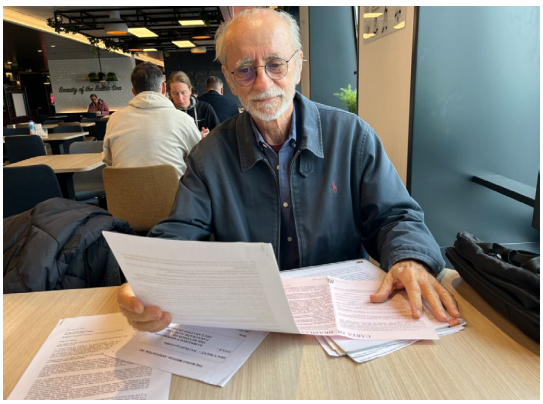
Prof. Dirceu Greco, a member of the CIOMS 2016 Working Group, initially gave a brief history of the DoH: The 1964 DoH was a proposal aimed at doctors for ethical regulation in research. The 2000 version set the highest ethical standards, but notes of clarification were added in 2002 and 2004 for the paragraphs of placebo-controlled trials and post-trial access, respectively, and these notes were included in the main text in 2008. Then these texts were slightly modified in 2013 and 2024. The changes included meant a regression in ethical standards.

The controversy over placebo-controlled trials and the right to post-trial access dates back to 1994, when methods for preventing mother-to-child transmission of HIV/AIDS were already scientifically established. In the implementation of 15 ethically questionable clinical trials in developing countries, with the aim of evaluating the efficacy of less expensive regimens, placebo was used in the control group. These clinical trials were vehemently criticized by Peter Lurie and Sydney Wolf in their paper[29], and an editorial by Marcia Angel[30] supported Lurie and Wolf, both published in the *NEJM* in 1997. These publications gave rise to fierce debates and this was reflected in WMA and in the revision of the DoH.

In the 2000 GA in Edinburgh the approved version maintained the 1996 principles, which were based on principles already clarified in 1975, to allow a placebo control only when there was no proven treatment. And also, the principle of guaranteeing access to products that have shown to be safe and effective for the participants who still need them after the completion of the trial was included for the first time in the 2000 version.

At the ceremony just after the adoption of the DoH, October 19, 2024. From the right, Prof. Dirceu Greco, Baroutsou, Kurihara.

Prof. Greco and Chieko Kurihara, at the place of the hotel Scandic Grand Helsinki, where the second web meeting to agree on the Helsinki Statement, midnight of October 20, 2024. Photo was taken later. Baroutsou and Matsuyama also participated at the venue of Helsinki.



Prof. Greco explaining brief history shortly after the 2000 revision of the DoH, showing related documents.

[29] Lurie P, Wolfe SM. Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. *N Engl J Med.* 1997 Sep 18;337(12):853-6. doi: 10.1056/NEJM199709183371212.
[30] Angell M. The ethics of clinical research in the third world. *N Engl J Med.* 1997; 337: 847–9.

②The history leading to the 2016 edition of the CIOMS guidelines

Shortly after the adoption of this revision in October 2000, questions were raised, mainly by the US FDA and the pharmaceutical industry, arguing that the principles of placebo and post-trial access would not respond to the needs of science and, according to them, would make it difficult to implement many clinical trials. Then in March 2001 a conference was held in Pretoria, South Africa, by the WMA and relevant stakeholders, where the pros and cons of these paragraphs were debated[31]. Prof. Greco was one of the speakers, with the participation of well-known researchers and ethicists. Subsequently, a small subgroup was created by the WMA to discuss these paragraphs and as a result, clarification notes were issued, in 2002 for placebo and in 2004 for post-trial access, which reversed the 2000 principles. In the subgroup that discussed the 2004 note Dirceu Greco and Otmar Kloiber (who at the time represented the German Medical Association) were included. The minutes of the public consultation show that Chieko Kurihara and Ruth Macklin defended the same position as Dirceu Greco, which is the right to post-trial access. Macklin later joined with Greco in advocating for the protection and promotion of human rights in the Working Group for the 2016 CIOMS ethical guidelines.

The 2002 CIOMS guidelines adopted language similar to the current DoH regarding acceptable risk for placebo-controlled trials when there is a proven intervention (without increase of risk of serious or irreversible harm), but in the 2016 revision, this was substantially changed to "*minor increase above minimal risk*". There was a lot of discussion among the working group participants. Prof. Greco with Prof. Macklin advocated for this change. In fact, Prof. Greco's original position was that even "minor increase above minimal risk" is not acceptable, i.e., placebo-controlled trials are not acceptable when there is a proven intervention. This is also the basic stance of Latin American countries.

③Responses of Brazil and Latin American countries

Brazil brought the 2000 DoH principles into a national legislation in 2008[32]. This was decided shortly before the 2008 revision of the DoH, which incorporated the 2002 and 2004 notes of clarification into the main text. Other Latin American countries build consensus on a position similar to that of Brazil, in the form of statements by CONFEMEL (Confederación Médica Latinoamericana y del Caribe), an association of medical organizations in Ibero-America and the Caribbean, which represents around 500,000 doctors grouped in national associations) [33] and in international declarations from the federation of research institutions. For this reason, placebo-controlled trials, when there is a proven intervention, cannot be conducted in Brazil or Uruguay.

Where, then, do these placebo-controlled trials go in the world? If such trials, as some today claim, are no longer carried out anywhere, this is another reason for the WMA to return to the terms of the 2000 version, which is also consistent with its core principle that states that the purpose of the research never precedes the right of participant.

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[31] Pérez, A.C., Smith, R.N. The revised *Declaration of Helsinki*: interpreting and implementing ethical principles in biomedical research. *International Journal of Pharmaceutical Medicine. 2001; 15:* 131-43. https://doi.org/10.2165/00124363-200106000-00006

[32] Brazilian Research Ethics Commission Resolution 466/2012, which succeeded Resolution 404/2008.

[33] CONFEMEL. Intervención de la Dra. Zaida Arteta en la Asamblea General de la AMM. 16 octubre, 2024. https://www.confemel.com/intervencion-de-la-dra-zaida-arteta-en-la-asamblea-general-de-la-amm/

④Double standard

In fact, there were still cases of placebo-controlled trials in Vietnam even after effective vaccines against COVID-19 were developed, and other similar cases were reported[34]. Prof. Greco's position is that, especially to avoid exploitative studies carried out by big pharmaceutical companies, such as placebo-controlled trials in less-regulated, resource-limited countries when proven interventions exist, the DoH principles should return to the 2000 version.

In the current DoH the risks that may result from assignment to the placebo arm, which is much greater than in the 2016 CIOMS guidelines, i.e. prolonged pain and suffering, which is not serious or irreversible, can be left to the assessment of the research ethics committee or the individual participant.

But who would participate in a placebo-controlled trial that could increase the risk of long-lasting pain and suffering when an effective treatment exists?

They would be those who cannot access effective interventions without entering a clinical trial, particularly those who cannot adequate insurance coverage in the United States or those in areas without access to treatments that have been shown to be effective.

The WMA's position would be contrary to the "double standard". However, removing barriers to conducting placebo-controlled trials where there is a proven intervention characterizes a double standard, meaning that what is stated in the DoH (best proven) is different from what is stated in another item (no additional risks of serious or irreversible harm) actually allowing local standard.

The WMA's position is clear: "best proven" does NOT mean "best-proven intervention available in the region". Rather, WMA's position is "best proven intervention in the world". This was clearly sated by Dr. Jack Resneck, during the regional meeting of WMA in Sao Paulo, and also by Dr. Otmar Kloiber, WMA Secretary General[35].

[34] Kurihara C, Greco D, Dhai 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

[35] Kloiber O, Greco D, Watanabe H, Imamura K, Yamamoto Y, Matsuyama K, Saio T, Kurihara C. International collaborative research and new trends of research ethics: Follow-up session. *Clin Eval.* 2020 ; 48(1): 233-65.

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval*. 2025; 52(3).
http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

2.10 Dr. Jon Snaedal, Icelandic Medical Association, Workgroup chair for the Taipei Declaration in 2016

Interview: Kurihara C, Matsuyama K

The Declaration of Taipei (DoT) is considered to be an extension of the Declaration of Helsinki (DoH) as it addresses secondary use of data or samples obtained in research involving human participants. An interview with Dr. Snaedal at the time of the adoption of the DoT in 2016 was published in Clinical Evaluation, Vol. 46, No. 1[36].

Internal consideration for the revision of the DoT will start this winter, and open discussion is supposed to officially start in the spring of 2025 since the WMA has a policy of reviewing its document every 10 years. Since the DoT has not yet received as much international attention as the DoH, it is important to gather diverse opinions and an open consultation process of revision is likely to be decided at the WMA spring meeting 2025 in Montevideo.

Dr. Jon Snaedal, Icelandic Medical Association, during the Council Session, October 18, 2024, with Kotone Matsuyama.

[36] Snaedal. Interviewed by Kurihara C, Saio T. Interview with Dr. Jon Snaedal, Chair of the World Medical Association Workgroup for the Taipei Declaration; Representative of the Icelandic Medical Association: Health databases, biobank and fundamental human rights. Clin Eval. 2018; 46(1): 165-70.
http://cont.o.oo7.jp/46_1/w15-w20.pdf

2.11 Prof. Kim Ock-joo, Seoul National University, South Korea

Summarised by Kurihara C.

Prof. Kim Ock-joo is a well-known Korean bioethicist, whom Kurihara met many times previously. It was very nice to be able to see her at WMA's regional meeting in Washington DC and then in at General Assembly in Helsinki. At the Washington DC meeting, a speaker representing US Center for Disease Control and Prevention (CDC) argued to deregulate the core principle of the DoH which defines that the purpose of research can "*never take precedence over the rights and interests of individual research participants*" (paragraph 7, previously 8). Then Prof. Kim immediately expressed a strong objection on it. It was impressive that she stated that during educational lecture to her students and researchers she always emphasizes this important principle. This is the same as in Japan.

At the same session in Washington DC, Kurihara also raised question to the representative of the Food and Drug Administration regarding her negative perspective on post-trial access, and also questioned after the completion of the session to representative of Office for Human Research Protection (OHRP) regarding her negative perspective on inclusion of the Declaration of Taipei in the DoH.

Just before this Washington DC meeting, similar argument as CDC representative was stated in *JAMA* by the immediate past Director of the US OHRP[37]. Clear objection was expressed from Japan[38]. This may suggest a difference of level of acceptable "research risk" between utilitarian (higher risk is acceptable for the sake of collective benefit) and deontologist (rights and dignity of an individual is a paramount).

Previous publications collaborating with Prof. Kim, including interview and lecture meetings in Tokyo can be found in this journal, previous issues[39][40][41].

Prof. Kim Ock-joo, during the Council Session, October 18, 2024.

[37] Menikoff J. Protecting Participants Is Not the Top Priority in Clinical Research. *JAMA*. 2024 Jun 20. doi: 10.1001/jama.2024.7677. Epub ahead of print. PMID: 38900422.

[38] Saio T. Preprint: Noblesse oblige of the WMA in peril: Saving its honor at the Diamond Anniversary. *Clin Eval.* 52(3). http://cont.o.oo7.jp/52pop/Preprint_Noblis%20Oblige.pdf

[39] Kurihara C. Revision of Bioethics and Safety Act in South Korea—Comprehensive system of human research subjects protection and quality assurance of research, comparing with Japan—. *Clin Eval.* 2012; 40(1): 790-90. http://cont.o.oo7.jp/40_1/p79-90eng.pdf

[40] Kurihara C. Human Research Protection Program and IRB review in Seoul National University Hospital—Interview with Prof. Ock-Joo Kim after observation of IRB—. *Clin Eval.* 2013; 41(2):421-30. http://cont.o.oo7.jp/41_2/p421-30eng.pdf

[41] Kurihara C. Trend of research ethics and conflict of interest management in Korea and Taiwan—Common sense in the world but uncommon in Japan—. *Clin Eval.* 2014; 42(2): 591-610. http://cont.o.oo7.jp/42_2/p591-610eng.pdf

Citation: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. *Clin Eval.* 2025; 52(3). http://cont.o.oo7.jp/52pop/52pop_contents_e.html
Preprint Online Publication: Dec 24, 2024; Journal Publication: Feb 25, 2025.

3. Conclusions and future perspectives: the Helsinki Statement

An overview of the 2024 revision of the DoH are outlined above. As noted in section 1.4, the authors published the "Helsinki Statement" [26] one day before the adoption of the DoH. In the first half of the "Helsinki Statement", we praised 10 points which we considered improvements. In the second part of the "Helsinki Statement" we focused on the remaining challenges, including the items on placebo use and post-trial access, in accordance with Uruguay's motions.

The "Helsinki Statement:" is an expression of the consensus of independent stakeholders who aim to expand the impact of the improved elements of the DoH and to work together to strengthen the protection and rights of research participants while ensuring the scientific integrity of research, and to implement the practice of conducting and reviewing research.

Among the signatories, those who have contributed sufficiently and agreed to be authors are "authors" and the others are "signatories." The five people (Chieko Kurihara, Dirceu Greco, Kotone Matsuyama, Takeo Saio and Varvara Baroutsou) who were directly involved in the planning and implementation of the initiative were named as corresponding authors. The names of all individuals and countries have been included in the publication. The call for signatories has been distributed to the registrants of the two web symposia, mentioned above, as well as to international and national mailing lists and other interested parties and groups that the corresponding authors deemed appropriate. IFAPP distributed the information of the web symposia but did not distribute the information of "Helsinki Statement", as this was not an official IFAPP activity. The period to receive endorsements was until 30 November (some agreements were made after this date). Table 3 shows the regional distribution of the signatories.

Table 3 Regional distribution of signatories to the Helsinki Statement

		Individuals	Groups
Africa (global south)	Egypt, individual	9	
	Egypt, in a group	32	1
Asia	Japan, individual	30	
	Japan, in a group	7	2
Latin America (global south)	Brazil	17	
	Uruguay	4	
	Mexico	3	
	Argentina	2	
	Panama	1	
	Chile-Brasil	1	
	Guatemala	1	
	Jamaica*	1	
Africa (global south)	Kenya	1	
	South Africa	1	
	Tanzania*	1	
Austraria	Austraria	1	
Europe	Belgium	1	1
	Greece	1	
	Netherland	1	
	Czech Republic*	1	
	Norway*	2	
Asia	Philippine	3	
	Pakistan	1	
	Nepal, Group	1	1
	Turkey	1	
	South Korea*	1	
		125	5

*=Country added after November 7 (Previous update)

Global South	74	
Asia	44	
Europe	6	
Austraria	1	
	125	Individuals
	5	groups
	24	Countries

Recognising the possible bias in the distribution of information, the fact that many of the signatories were from the Global South and Asia shows the importance of further communication with these supporters, for the implementation of the revised DoH with emphasis on the remaining challenges.

It is particularly noteworthy that on October 25, one week after the 18 October announcement of the "Helsinki Statement", the agreement of 32 individuals belonging to the Egyptian Network of Research Ethics Committees (ENREC) was informed, on the premise that their names could be publicised, and an Arabic translation of the Statement was published on 7 November, 2024[42]. A note in the Arabic translation clarifies that the change from "research subject" to "research participant" did not apply to the Arabic version of the DoH. When asked about the background, the representative of the ENREC provided the following explanation:

> —— Since the literal Arabic translation of the word "subject" (شئ) is typically reserved for inanimate objects, we opt for a more suitable term from the outset. Consequently, we use the word "مشارك", which most accurately captures the essence of the English word "participant". (Published under the permission of the representative of ENREC)

While it is not possible to say much about this point in this report, we believe that there would be essential elements to learn through further communication with the signatories of the "Helsinki Statement". Similarly, the term "research subject" was not appropriate in the Greek language, and the term research participant has long been established in ethical, regulatory, and legislative texts on medical research in Greece. This could be elaborated on the implications and value of the DoH.

The authors of the Helsinki Statement will continue to work together to improve the implementation of the 2024 version of the DoH. To this end, we hope that this report contributes to a common understanding of the context for future collaboration with a wider range of stakeholders.

Conflict of interest

There is no conflict of interest related to publication of this report.

Acknowledgment

There is no direct funding for this report. CK received travel expenses from IFAPP for her in-person participation in WMA's Regional Meeting in Tel Aviv; from the WMA for her in-person participation in WMA's Regional Meeting in Washington D.C. and waiver of registration fee for a journalist from WMA to attend the General Assembly in Helsinki.; MK joined the WMA meeting as a part of a survey of ethical issues related to the use of advanced medical technology and bioresources according to the Japan Agency for Medical Research and Development (AMED) grant (no. 24bm1523009s0801).; VB received travel expenses from IFAPP for her personal attendance at the WMA Regional Meeting in Copenhagen in 2023 and the WMA General Assembly in Helsinki in 2024, and a free registration waiver from WMA for her attendance at the WMA General Assembly in Helsinki in 2024.

The authors deeply appreciate all the collaborators, commentators who contributed to the development of this report.

[42] Together with Japanese and English versions, Arabic version is published in website and printed version of *Clin Eval.* Vol. 52 No. 3. Other language versions are welcomed.
http://cont.o.oo7.jp/52pop/52pop_contents_e.html