

Helsinki Statement from an Independent Stakeholders' Group to Expand the Impact of the 2024 Revision of the WMA Declaration of Helsinki

This statement was discussed (by e-mails and two times web meetings on Oct 15 and 19-20 connecting from Helsinki with global participants) and agreed among the authors/signatories and published online in October 18; and was updated in Oct 21 with clarifications reflecting the 2024 Declaration of Helsinki adopted by the World Medical Association in October 19, 2024. Additional signatories were accepted until November 30.

Background information: Kurihara C, Matsuyama K, Baroutsou V. World Medical Association's Declaration of Helsinki, 2024 revision: Celebrating the 60th anniversary, at Helsinki. Clin Eval. 52(3); Other related articles:

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

- Contact: chieko.kurihara@nifty.ne.jp
- Citation for the Helsinki Statement:
 - Helsinki Statement an ad hoc group of stakeholders. Helsinki Statement from an Independent Stakeholders' Group to Expand the Impact of the 2024 Revision of the WMA Declaration of Helsinki. Clin Eval. 52(3):
http://cont.o.oo7.jp/52pop/HelsinkiStatement_18Oct24_final.pdf
 - Shorter way of citation:
Helsinki Statement Stakeholders. Helsinki Statement 2024. Clin Eval. 52(3):
http://cont.o.oo7.jp/52pop/HelsinkiStatement_18Oct24_final.pdf
- Copyright: This statement can be freely used, disseminated, reproduced including publication by original or translated (for which authors cannot take responsibility of accuracy) language.

We would like to congratulate the World Medical Association (WMA) on the 60th anniversary of the Declaration of Helsinki (DoH) since its first adoption in 1964.

Significant revisions to the 2024 DoH include but are not limited to the items listed below. We urge all those engaged in research involving humans to carefully consider the newly agreed ethical principles, particularly pointed below, in every research and research review settings for the implementation of and adherence to it:

1. Throughout the Declaration, the words “research subjects” are replaced with “research participants”.
2. Although the recommendations are directed to physicians, their scope should be also applied to non-physicians, research teams and organizations. (§2^{*1})
3. In recognition of “various structural inequalities” in research, considerations on benefits, risks, and burdens must be reinforced. (§6)
4. Meaningful engagement with participants and their communities is fundamental and should be required at all stages of the research. (§6)
5. The principles of the Declaration must also be upheld during public health crises. (§8)
6. The contextual and dynamic nature of vulnerability must be recognized and it is important to emphasise that the exclusion of vulnerable can exacerbate their disparities. Therefore, their inclusion in research aiming at their benefit must be promoted, with adequate protection. (§19, 20)
7. The functions of research ethics committees have been strengthened. And the

¹ The numbers with § mean the numbers of paragraphs in the 2024 DoH: <https://www.wma.net/policies-post/wma-declaration-of-helsinki/>

committee must be familiar with the local context and involve at least one member of the general public. (§23)

8. The preferences and values of incapable research participants shall be considered during the process of deciding to participate in research. (§28, 29)
9. Data or specimens from research shall be handled in accordance with the “Declaration of Taipei” on Health Databases and Biobanks. (§32)
10. Clinical use of unproven intervention must never be undertaken to circumvent the protection set forth in the DoH, and must be the object of research to evaluate safety and efficacy. (§37)

However, we express our concern that the items below were rejected following discussions during the revision process. We very much hope that these ethical principles will be agreed by relevant stakeholders, their institutions or organizations and jurisdictions, and implemented in research and research review settings, and consequently reflected in future revisions of the DoH:

1. All texts must be written in plain language that is understandable to research participants.
2. The “social value” of research has already been incorporated into policy in several jurisdictions and guidelines. Although it was included in the first public consultation version, it was deleted in the approved 2024 DoH. It goes together with the notion that the purpose of research “*never takes precedence over the rights and interests of individual participants*”. Thus, social value must be reinforced in order to implement relevant research and also to ensure that benefits are shared through co-creation with community.
3. The use of placebo in clinical trials can only be acceptable when there is no proven effective and safe comparator. This was stated in the 2000 DoH², in accordance with DoH’s fundamental principle that the purpose of research “*never takes precedence over the rights and interests of individual participants*”. Some of the signers are in favour of the CIOMS 2016 language: that is, placebo “*in exceptional circumstances could be used even when there is an active comparator if delaying or withholding the established effective intervention will result in no more than a minor increase above minimal risk to the participant and risks are minimized, including through the use of effective mitigation procedures*”. However, since the 2008 DoH the accepted level of risk to the participant is even much higher than CIOMS’ and this was kept in 2024³.

² 2000 DoH (Rescind, archived version): <https://www.wma.net/wp-content/uploads/2018/07/DoH-Oct2000.pdf>

³ 2024 DoH in §33, placebo can be used, even if there is proven intervention, when the participant “*will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention*”.

4. At the end of the trial, research participants who still need interventions that have been shown to be safe and effective must have access to them ensured by the sponsor(s). The 2024 DoH is a lot weaker than the 2000 in relation to participant right. This is because instead of ensuring access it just says “it must be arranged” (§ 34)⁴. In addition, to tackle health disparities, scientific sound, and ethical strategies are needed to ensure access in public health system in the host community, and most importantly, for all in need globally.
5. The timely dissemination of research results and technology transfer of the products of research involving humans must be recognised as public goods, so that transparency is ensured and everyone can have fair and equitable access to the research results and benefits⁵.

In closing:

The 2000 DoH presented the highest protection to research participants in terms of placebo use and post-trial access. As the DoH has long been a driving force and respected document for ethics in human research, WMA should aim for the ideal of the highest ethical standards being applied.

We will collaborate to strengthen research ethics principles with the equal participation of all relevant stakeholders, including civil society, and in relation to the 2024 DoH, we present the current proposal aimed at maximizing the ethical impact of the DoH on research practice, research review process and in the protection of participants globally.

Authors* and signatories:

(**): Corresponding author)

On behalf of the Helsinki Statement an ad hoc group of stakeholders:

Individual authors/signatories, from September 25 to November 30, 2024

(Alphabetical order.; Some are duplicated in institutional signatory below.)

Heba Abdelkafy, Egypt; Heba ali ali, Egypt; Adriana Ribeiro Alves, Chile - Brasil; Beatrice Amugune; KENYA; Zaida Arteta, Uruguay; Reinaldo Ayer, Brazil; Geraldo P. Balaccua, Philippines; Varvara Baroutsou**, Greece; Sander Becker, Australia; Rosemarie Bernabe,

⁴ Compared to 2013 version to state “...**should** make provisions for post-trial access...”, the text in 2024 was strengthened to “...*post-trial provisions* **must** be arranged...” but weakened compared to 2000 version to state “...*should be assured of access*,,,” , In addition, in the 2024 DoH, exception must be explicitly approved by a research ethics committee. Such excuse is not relevant to high-level ethical principle, however, in practice strengthened responsibility of REC must be recognised.

⁵ Regarding the research results, new texts for avoiding research misconduct (§ 21) and research waste (§ 12) suggest improvement, however, considering that “social value” was once proposed and then deleted, and insufficient transparency and benefit sharing measures in result disclosure policy, this topic was not included in 10 celebrated items.

Norway; Laís Souza Bonilha, Brazil; Elda Bussinguer, Brazil; Shereen Cox, Jamaica; Francis P. Crawley*, Belgium; Luis Manuel López Dávila, Guatemala; Ames Dhai, South Africa; Nilza Maria Diniz*, Brazil; Samah Mohamed Elaidy, Egypt; Cláudio França, Brazil; Gabriel Frassetto, Brazil; Yoshikazu Funabashi, Japan; Amany Gad, Egypt; Samuel Goldenberg, Brazil; Dirceu Greco**, Brazil; Fernando Hellman, Brazil; Hiroshi Nakahata, Japan; Shehla Naseem, Pakistan; Namita Ghimire, Nepal; Yumi Ikehara, Japan; Keiko Inoue*, Japan; Hiroto Kai*, Japan; Yuki Kai, Japan; Sarai Keestra*, Netherland; Noriko Kishi*, Japan; Yu Komura*, Japan; Akemi Kuge*, Japan; Shija kevin kuhumba, Tanzania; Chieko Kurihara**, Japan; Daniela Paciel López, Uruguay; Gladness Henna A. Martinez, Philippines; Joy Amethyst A. Martinez, Philippines; Gerson Zafalon Martins, Brazil; Kotone Matsuyama**, Japan; José Minarrieta, Uruguay; Ayano Miyake, Japan; Toshie Murakami*, Japan; Toshinori Murayama, Yasmin Nagaty, Egypt; Shinobu Nakashima, Japan; Yuki Nishiyama, Japan; Mercedes Okumura, Brazil; Hakan S. Orer, Turkey; Maria Victoria Perottino, Brazil; Susana van der Ploeg, Brazil; Young-Joon Ryu Republic of Korea (South Korea); Takeo Saio**, Japan; Yoshiko Saito*, Japan; Kimie Sakurai, Japan; Azza Saleh, Egypt; Delia Sanchez*, Uruguay; Jennifer Braathen Salgueiro, Brasil; Patricio Santillan-Doherty, Mexico; Pablo de Castro Santos, Brazil; Midori Senoo, Japan; Amr Shebaita, Egypt; Dra. Liliana Virginia Siede, Argentina; Hany Sleem*, Egypt; Eman Sobh, Egypt; Lenka Sochorova, Czech Republic; Jan Helge Solbakk, Norway; Kaori Suzuki, Japan; Katsura Suzuki*, Japan; Hiroko Takahashi, Japan; Kazuma Tamaru, Japan; Unai Tupinambás, Brazil; Eiko Uchida*, Japan; Claude Vergesès, Panama; Susana M. Vidal*, Argentina; Taeko Wada, Japan; Hisanori Wakamatsu, Japan; Konomi Wakasa, Japan; Nobutaka Yagi, Japan; Sachie Yoshida, Japan, Diego Carlos Zanella, Brazil

An institutional signatory, Oct 25, Francis P. Crawley*, representing Good Clinical Practice Alliance - Europe (GCPA) & Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), Belgium

An institutional signatory, Oct 25, represented by Hany Sleem*, the designated coordinator of the Egyptian Network of Research Ethics Committees (ENREC), Egypt, on behalf of its members:

Amany M. Gad; Maha Abdelkawy; Marzoka Abd Elaziz Gadallah; Alaa Ismail; Nievin Ahmed Mahran; Naglaa Ahmed Galal; Nermine elmaraghy; Eman Sobh; Shimaa A. Al-Touny; Mohamed Emad Eldin Abdelghaffar; Ghada A.kazamel; Shaymaa M.Nagi; Ahmed ziada; Osama Fekry Al Balah; Osama Azmy; Mona Essa; Mohamed Mostafa Ali Balbola; Abir A. Elfiky; Awatef ELSayed Ahmed; Mervat I Fawzy; Hala F Zaki; Ahmed Hamdy Moustafa Hussein; Safaa Elnaggar; Ahmed Yousef; Amani Waheed; Amin Abdel Baki; Amr Mamdouh Kamel Shebaita; Manal Mohamed Anwar; Eldarir S E; Olfat Elsayed Hassanein; Enas kassem; Amr Gibaly; Maisa Nour El Din Mohamed Shawky; Mariam A. AbuShady;

Tarek Abulezz; Hany Sleen; Nevien Ahmed Samy; Hassnaa Othman Mohammed; Diao Marzouk Hany Lotfy; and El Mokadem Naglaa

A Signatory as members of a group, Nov 7, Bioethics Working Group, Japanese Institute for Public Engagement (Ji4pe), Japan

Chieko Kurihara**, Yoshiko Saito*, Hiroto Kai*, Yoshikazu Funabashi, Keiko Inoue*, Noriko Kishi*, Akemi Kuge*, Toshie Murakami*, Midori Senoo*, Katsura Suzuki*, Hiroko Takahashi, Eiko Uchida, Konomi Wakasa, Kyoko Imamura*

An institutional signatory, Nov 30, represented by Nobutaka Yagi, on behalf of YORIAI Lab, Japan, with members who agreed to be listed:

Masumi Hoshiyama, Takayoshi Inoue, Kotone Matsuyama**, Ayano Miyake, Nao Moriyama, Yuki Nishiyama, Kimie Sakurai, Keisuke Shimizu, Takeshi Shukunobe, Hiromi Todoroki

An institutional signatory, Dec 16, represented by Namita Ghimire, on behalf of Ethical Review Board of the Nepal Health Research Council (NHRC), Nepal

List of References

- 1) 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
<https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2024.1432267/full>
- 2) 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.
<https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2024.1360653/full>
- 3) Kurihara C, Greco D, Dhali A., editors. *Ethical innovation for global health: pandemic, democracy and ethics in research*: Springer; 2023.
<https://link.springer.com/book/10.1007/978-981-99-6163-4>
- 4) 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
- 5) Clinical Evaluation. Vol. 52 Preprint Online Publication on Oct 10, 2024.
Special Issue: The 60th-year Anniversary of the WMA Declaration of Helsinki
http://cont.o.oo7.jp/52pop/52pop_contents_e.html
 - The 2024 Declaration of Helsinki: Taking Forward Bioethics and Human Rights.

<http://cont.o.oo7.jp/sympo/igh.html>

- Interview with Dr. Peter Lurie on the ethical controversies of placebo-controlled trials.
http://cont.o.oo7.jp/52pop/Preprint_Interview_Lurie.pdf
 - 6) Kurihara C, Saito Y, Kai H, et al. Patient Public Declaration of Research Ethics (1st edition): Research ethics of the people, by the people, for the people – Expanding the impact of the 2024 revision of the Declaration of Helsinki. *Clinical Evaluation*. 2024; 52. Preprint Online Publication on Oct 10, 2024.
http://cont.o.oo7.jp/52pop/Preprint_Patient%20Public%20Declaration.pdf
 - 7) Saio T. Noblesse oblige of the WMA in peril: Saving its honor at the Diamond Anniversary. *Clinical Evaluation*. 2024; 52. Preprint Online Publication on Oct 10, 2024.
http://cont.o.oo7.jp/52pop/Preprint_Noblis%20Oblige.pdf
 - 8) Clinical Evaluation. Patient and public perspectives on the WMA Declaration of Helsinki
<http://cont.o.oo7.jp/grareco.html>
 - 9) COVID-19 and bioethics Part 3: Pandemic and research ethics – Democracy, placebo and post-trial access. *Clinical Evaluation*. Vol.49, Suppl XXXVIII 2021
http://cont.o.oo7.jp/49sup38/49sup38contents_e.html
 - 10) 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/>
- (Added after the announcement of this Statement)
- 11) 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/>
 - 12) 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/>
 - 13) Sindicato Médico del Uruguay. World Medical Association Submission of a Motion to Amend (on Paragraph 33, submitted to) 227th Council Session and General Assembly, Helsinki 2024, October 2024. 8/10/2024.
 - 14) Sindicato Médico del Uruguay. World Medical Association Submission of a Motion to Amend (on Paragraph 34, submitted to) 227th Council Session and General Assembly, Helsinki 2024, October 2024. 10/10/2024.
 - 15) World Medical Association. Proposed revision of WMA Declaration of Helsinki. MEC 227/DoH/Oct2024.
 - 16) 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/>

(Adopted 2024 DoH, related papers published from JAMA as below, and other information are available.)

[Editor's Note]

- 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.

[View point]

- 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.
 - 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.
 - 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.
 - 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.
 - 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.
 - 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.
- 17) [News] 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.
- 18) [Editorial] Declaration of Helsinki embraces health equity. Nat Med. 2024 Dec 2. doi: 10.1038/s41591-024-03433-5. Epub ahead of print. PMID: 39623088.
- 19) Sheather J. Declaration of Helsinki puts global justice up front. BMJ. 2024 Nov 1; 387: q2405. doi: 10.1136/bmj.q2405. PMID: 39486836.
- 20) 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>