The 2024 Declaration of Helsinki:
Taking Forward Bioethics and Human Rights
Co-organized by: The Brazilian Society of Bioethics;
International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP);
August 5 and 26. 2023

Participation in **WMA meeting in Washington DC**: Taking forward **bioethics and human rights**, maximizing the **impact of the NEW DoH**

Chieko Kurihara

Specially-appointed Professor, Kanagawa Dental University

No conflict of interest related to this presentation.

1. Meeting with Dr. Peter Lurie
2. WMA's meeting
3. Discussion at my session*:
   Maximizing the impact of the DoH;
   Taking forward bioethics and human rights
4. Actions for future, meet at Helsinki

*My participation was representing IFAPP and presentation was authorized by IFAPP but it was my personal opinion

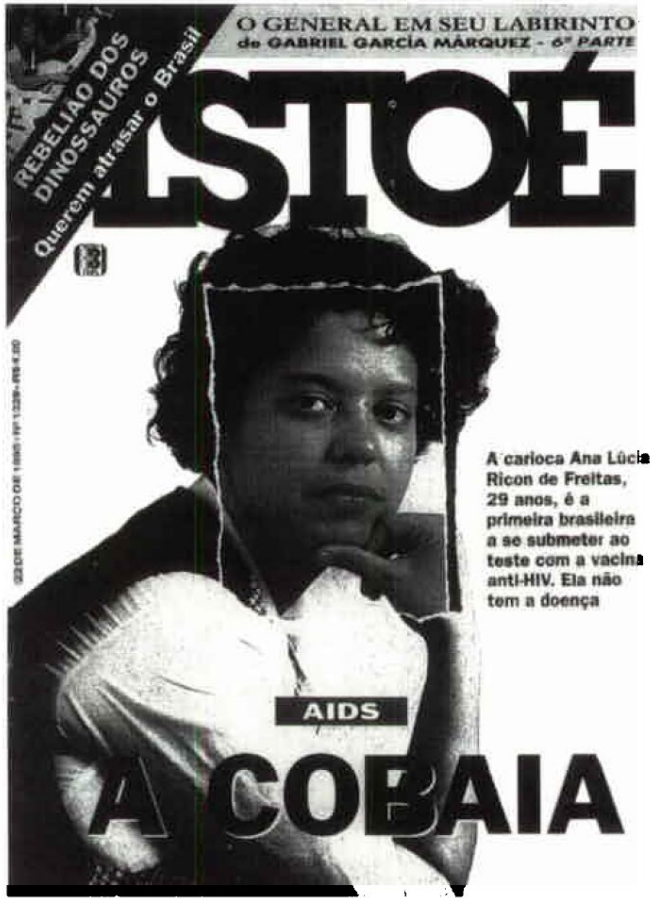
Meeting with Dr. Peter Lurie
August 14, 2024
The Westin Washington DC City Center
(Venue of the WMA meeting)

Discussion at a restaurant in front of the Brazilian Embassy and an open park
To be published with proceedings of our webinar

Brazil: The ebbs and flows of AIDS vaccine trials

An interview with Dirceu Greco

- 1991 WHO **Vaccine development** program ir Brazil, Thai, Uganda, Rwanda
- 1995 Phase 1/2 trial in Brazil with **Dirceu Greco as PI** (Minas Gerais Univ)
- Good example of **community engagement** to improve the protocol, while negative image of mass media "human experimentation"
- Photo of study volunteer with altruism but criticized by the magazine "guinea pig"



"The guinea pig"
(human experimentation)

IAVI Report: A Newsletter on International AIDS Vaccine Research. 1999; 4(4):10-1.

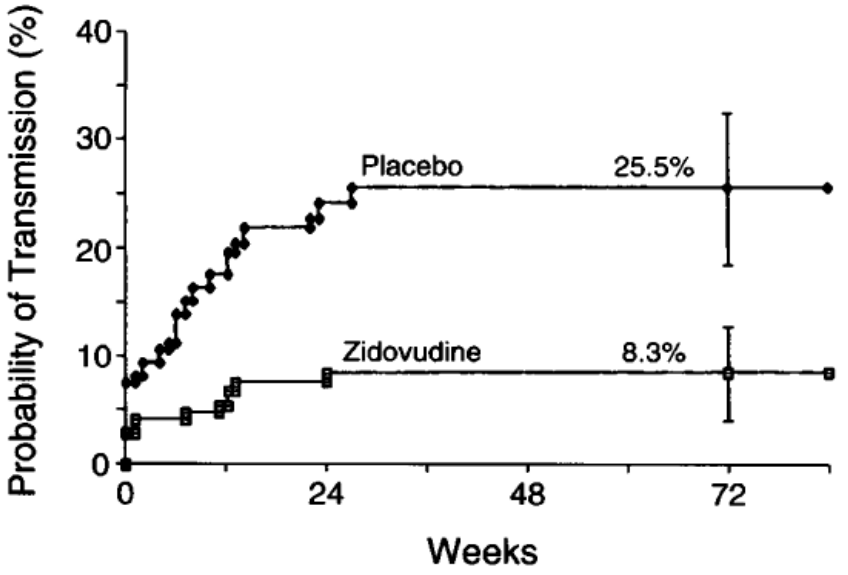
Establishment of Best-Proven Intervention to prevent HIV perinatal transmission

The New England
Journal of Medicine

Volume 331 NOVEMBER 3, 1994 Number 18

REDUCTION OF MATERNAL–INFANT TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 WITH ZIDOVUDINE TREATMENT

EDWARD M. CONNOR, M.D., RHODA S. SPERLING, M.D., RICHARD GELBER, PH.D., PAVEL KISELEV, PH.D., GWENDOLYN SCOTT, M.D., MARY JO O'SULLIVAN, M.D., RUSSELL VANDYKE, M.D., MOHAMMED BEY, M.D., WILLIAM SHEARER, M.D., PH.D., ROBERT L. JACOBSON, M.D., ELEANOR JIMENEZ, M.D., EDWARD O'NEILL, M.D., BRIGITTE BAZIN, M.D., JEAN-FRANÇOIS DELFRAISSY, M.D., MARY CULNANE, M.S., ROBERT COOMBS, M.D., PH.D., MARY ELKINS, M.S., JACK MOYE, M.D., PAMELA STRATTON, M.D., AND JAMES BALSLEY, M.D., PH.D., FOR THE PEDIATRIC AIDS CLINICAL TRIALS GROUP PROTOCOL 076 STUDY GROUP*



Placebo	183	84	42	37
Zidovudine	180	105	51	43

Figure 1. Kaplan–Meier Plots of the Probability of HIV Transmission, According to Treatment Group.

The estimated percentages of infants infected at 72 weeks are shown with 95 percent confidence intervals. The numbers of infants at risk at 24, 48, and 72 weeks are shown below the figure.

- 67.5%RRR → Number Need to Treat: 5.8

- Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Eng J Med 1994; 331: 1173-80.
- Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. N Engl J Med 1996; 335: 1621-9.

The New England Journal of Medicine

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Volume 337(12) 18 September 1997 pp 853-856

Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries

[Sounding Board]

Lurie, Peter; Wolfe, Sidney M.

Public Citizen's Health Research Group; Washington, DC 20009

Outline

- **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. PMID: 9295246.
- **Lurie P, Greco DB**. US exceptionalism comes to research ethics. **Lancet. 2005** Mar 26-Apr 1;365(9465):1117-9.

THE LANCET

This journal Journals Publish Clinical Global health Multimedia Events A

COMMENT | VOLUME 365, ISSUE 9465, P1117-1119, MARCH 26, 2005

Download Full Issue

US exceptionalism comes to research ethics

Peter Lurie • Dirceu B Greco

Published: March 26, 2005 • DOI: https://doi.org/10.1016/S0140-6736(05)71856-0

Rapid response to:

World Medical Association delays decision on Helsinki declaration

BMJ 2003 ; 327 doi: https://doi.org/10.1136/bmj.327.7416.642-e (Published 18 September 2003)
Cite this as: *BMJ* 2003;327:642

Rapid Response:

Crisis of the Declaration of Helsinki becoming a Guidance for industries

25 September 2003
Chieko Kurihara
editorial staff, Rinsho Hyoka (Clinical Evaluation)
Tadahiro Mitsuishi, Jiro Nudeshima.

My argument in WMA meeting:
Current terminology "no increase of serious or irreversible harm" is from Guidance for Industry (ICH-E10 guideline) NOT for Ethical Principles
NOT understandable for patient and public

https://www.bmj.com/rapid-response/2011/10/30/crisis-declaration-helsinki-becoming-guidance-industries

Webinar to discuss placebo, access during COVID-19 pandemic, June 2021

http://cont.o.oo7.jp/49sup38/49sup38contents_e.html

Proceedings

Clin Eval 2021; Vol. 49, Sup 38.
http://cont.o.oo7.jp/49sup38/49sup38contents_e.html

Kurihara C. Webinar COVID-19 and Bioethics - Pandemic and Research Ethics: Democracy, Placebo and Post-Trial Access. *IFAPP TODAY*. 2021; Jul/Aug (16): 4-7.

What is the acceptable risk of placebo-controlled trial when there is a proven intervention??

…**Discrepancy** between **DoH** and **CIOMS**

Who is accountable?

DoH

No increase of risk of serious or irreversible harm

Acceptable, up to reasonable person

Continuing pain, burden, but not “serious” (regulatory definition: hospital admission), and not irreversible

Not acceptable

CIOMS

Minor increase above minimal risk

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North American Regional Meeting on the Declaration of Helsinki, held by AMA and WMA

Day 1 (Aug 15. 2024)

- Opening remarks from AMA President; FDA Commissioner
- Overview of the revision by the AMA WG chair for the DoH
- Vulnerability, community engagement global justice
- Data research and privacy
- Public health emergency and compassionate use
- Scientific and social value
- Research Ethics Committee

Day 2 (Aug 16, 2024)

- US government：FDA, OHRP, NIH, CDC
- Maximizing impact: communications, advocacy and implementation

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Maximizing impact: Communications, advocacy and implementation

MODERATOR

Lujain Alqodmani, MD, president, World Medical Association

SPEAKERS

Otmar Kloiber, MD, secretary-general, World Medical Association

Hans Van Delden, professor, University Medical Center

Lara Bloom, board member, International Alliance of Patient Organizations

Chieko Kurihara, BA, ethics working group, International Federation of Associations of Pharmaceutical Physicians

Continuing discussions on the revision of the DoH with various stakeholders

◆Publications since DoH 1975 Tokyo Revision sometimes inviting WMA, FDA..

臨床評価

Clinical Evaluation Vol. 49, Suppl XXXVIII 2021

IFAPP Pharmaceutical Medicine

MoU with WMA, 2017

◆Monthly meetings

◆Peer-reviewed papers

◆IFAPP TODAY

◆ Sessions inviting WMA at IFAPP meetings

Research ethics microcosm

◆Webinar on placebo, access during COVID-19 pandemic Inviting WMA

Group of patient & public

◆Monthly meetings

◆A publication in Springer book

◆Chapters from Global South Asia, WMA, CIOMS, DNDi, IFAPP, Patient group

JAPhMed

The Japanese Association of Pharmaceutical Medicine

◆Monthly meetings

◆Asian regional meeting on July 27

Brazilian Society of Bioethics

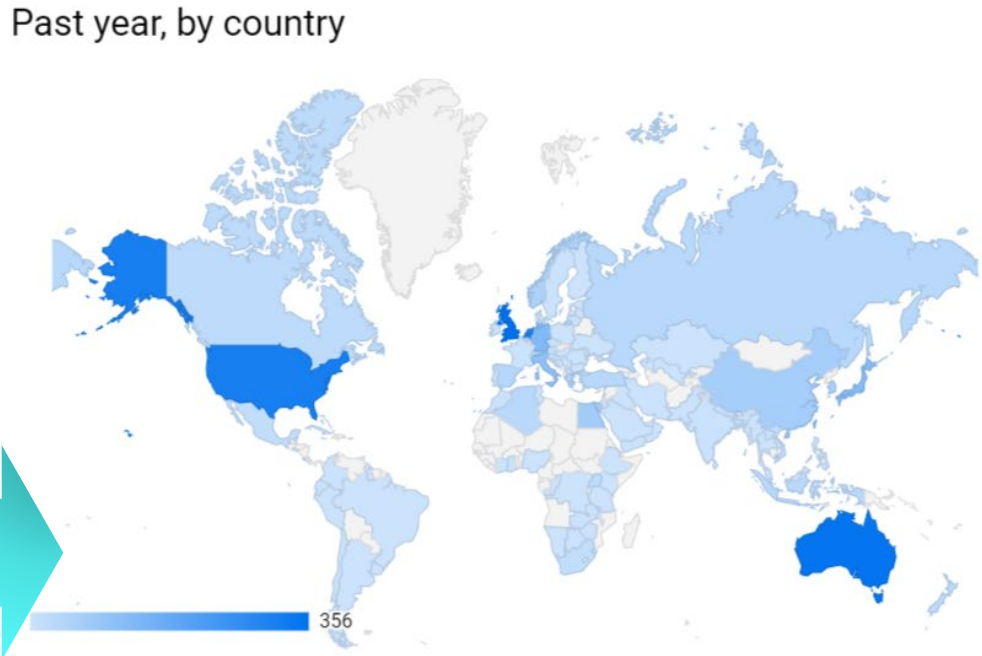
IFAPP

Japan Association for Bioethics

◆Webinar, Aug 5, 26

Graphic Recording: Kanna Yoshikawa

Next collaboration of Springer book authors



	Country	Downloads
1.	United Kingdom	356
2.	Australia	348
3.	United States	316
4.	Netherlands	301
5.	Germany	129
6.	Japan	119
7.	Taiwan	116
8.	Italy	104
9.	Hong Kong	87
10.	Egypt	72

1 - 10 / 109

2,700 downloads in 109 countries worldwide, during 8 months form publication (as of Jul 26)

NEXT: Publication
(Tentative title)
The 2024 revision of the Declaration of Helsinki: A commitment to the highest ethical standards

What is the value of the NEW DoH?

Highest Ethical Principle? (deontology, human rights)

Minimum Requirements? (utilitarian pragmatism)

- Kurihara C, Greco D, Dhai A, Saio T, Tsubaki H. Ethics of placebo-controlled trials: historical analysis including experiences during the COVID-19 pandemic.
- Kurihara C, Greco D, Dhai A. Post-trial access: historical analysis considering the experience of COVID-19 pandemic.
Ethical innovation for global health: pandemic, democracy and ethics in research. Springer; 2023.
Ethics
- Webinar: The 2024 Declaration of Helsinki: Taking Forward Bioethics and Human Rights: Video Recording (Aug 5 and 26)
https://youtu.be/W4fA9iaEOg0?si=RrbdbRFcoz7-mzQ1

Table 1 Key concepts missing in the new DoH (1)

Protection items	DoH	CIOMS*1	Patient group	IFAPP*2	GL Japan	GCP (R3)	Brazil	
Social value	–	◎	◎	○	◎	–		
Community Engagement/Patient Public Involvement	△incomprehensible	◎	◎	◎	–	◎		
Benefit Sharing	–	◎	◎	○	–	–		
Avoid **Discrimination/Stigmatization** (risk to target group)	–	◎	◎	–	○	–		
Consider **Future Generations/Sustainability**	△	–	◎	–	–	–		
Inclusiveness of the **vulnerable**	–	◎	○	◎	–	–		
Right to know/not to know the result (including incidental findings up to the status of information)	– (△)	◎	◎	◎	◎	–		
Broad informed consent/dynamic consent	–	◎*1	◎	◎	○	–		
Fairness of REC/Patient Public Involvement (democracy)	–	◎	◎	◎	○	○		

*1: “Dynamic consent” is not in health research guidelines but in Report XI for patient engagement.
*2: Not official opinions of IFAPP, but of some members of IFAPP.

◎Strongly argued ○medium △weak or not explicit

My proposal

1. **Missing items in the Table 1 should be filled;**
   - consistency with CIOMS, e.g. inclusiveness of the vulnerable
2. **Placebo-controlled trial: risk should be minimized;**
   - consistency with CIOMS

"No increase of risk of ~~serious or irreversible~~ harm"

3. **Post-trial access should be assured to:**
   - ➢ **Study participants**
   - ➢ **Trial host community**
   - ➢ **Those most in need worldwide**

NOT necessary for **Ethical Guidelines**

"~~Exceptional case must be approved by ethics committee~~"

See references in the last slides.

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3. Discussion at my session:
   Maximizing the impact of the DoH;
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4. Actions for future, meet at Helsinki

Actions for the future

- Continuing expression of objections and clarifying missing items in respectful matter would be important for the improvement of the impact of the New DoH.
- Continuing collaboration with the WMA to fill the missing items and caring for contested opinions would contribute to **better protections of research participants**. It would be achieved by:
    - Publications of books, papers;
    - Webinars; In-person meetings;
    - Actual research practice, ethics committee reviews, etc.
- Let's start preparation for the **next 10 years**!

Meet at Helsinki!

General Assembly of the WMA in Helsinki
Oct 16-19
To cerebrate 60 years of the DoH: New version

Some of us will have web/in-person meeting

Thank you for your attention!

Hope that you visit these websites to upload continuous discussions.

Patient and public perspectives on the WMA Declaration of Helsinki

http://cont.o.oo7.jp/grareco.html

Graphic Recording: Kanna Yoshikawa

Ethical Innovation for Global Health: Pandemic, Democracy and Ethics in Research

http://cont.o.oo7.jp/sympo/eigh.html

The 2024 Declaration of Helsinki: Taking Forward Bioethics and Human Rights.

August 5 and 26, 2024 Zoom webinar

Co-organized by:
Brazilian Society of Bioethics; IFAPP; et al.
Supported by
Japanese Association for Bioethics

Video-recording and presentations:

http://cont.o.oo7.jp/sympo/eigh.html

Selected References (1)

DoH and DoT

- Kurihara C, Baroutsou V, Becker S, et al. 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
- Kloiber O. Declaration of Helsinki: Challenges and new trends ahead of us. *Clin Eval.* 2020; 48(1): W9-W27.http://cont.o.oo7.jp/48_1/w9-w27.pdf

Placebo and access

- Kurihara C, Greco D, Dhai A, Saio T, Tsubaki H. Ethics of placebo-controlled trials: historical analysis including experiences during the COVID-19 pandemic.
- Kurihara C, Greco D, Dhai A. Post-trial access: historical analysis considering the experience of COVID-19 pandemic.
- Baroutsou V. Medicines development for global health: learning from COVID-19 vaccines R&D.
- *In: Ethical innovation for global health: pandemic, democracy and ethics in research*. Springer; 2023.
- Matsuyama K, Kurihara C, Crawley FP, Kerpel-Fronius S. Utilization of genetic information for medicines development and equitable benefit sharing. Front Genet. 2023 Jun 14;14:1085864. doi: 10.3389/fgene.2023.1085864..
- Greco D. Past, Present, and Future of Ethics of International Health Research: Research as a stepping-stone to Universal Public Health Care Access. Clin Eval. 2020 ; 48(1): 207-31. http://cont.o.oo7.jp/48_1/w29-w53.pdf
- Kloiber O, Greco D, et al. Intenational collaborative research and new trend of research ethics: Follow-up session. Clin Eval. 2020 ; 48(1): 233-65. http://cont.o.oo7.jp/48_1/w55-w87.pdf
- Greco D, Invited lecturer. Kimura R, Special guest. Victoria Perottino M, et al. Ethics of international collaborative research: Perspectives from Brazil: Part 1 Selected notes on Paulo Freire: Part 2 Access, Compulsory license, Case Study. Clin Eval. 2020 ; 48(1): 273-301. http://cont.o.oo7.jp/48_1/w95-w123.pdf

Selected References (2)

Placebo and access

- Kloiber O. Interview. Discussion toward the 50th anniversary of the Declaration of Helsinki: Interview with Dr. Otmar Kloiber, Secretary General, World Medical Association. *Clinical Evaluation*. 2013; 41(2): 351-72.

http://cont.o.oo7.jp/41_2/p351-72eng.pdf

- Temple R. Kurihara C, Interview. Interview with Dr. Robert Temple on drug evaluation policy of FDA: Ethics, science of placebo-control and comparative effectiveness studies. *Clinical Evaluation.* 2014; 42(2): 539-51.

http://cont.o.oo7.jp/42_2/p539-51eng.pdf

- Kurihara C, et al. Rapid response: Crisis of the Declaration of Helsinki becoming a Guidance for industries. Response to *BMJ* 2003; 327 doi: https://doi.org/10.1136/bmj.327.7416.642-e (Published 18 September 2003)

https://www.bmj.com/rapid-response/2011/10/30/crisis-declaration-helsinki-becoming-guidance-industries

Future-oriented framework

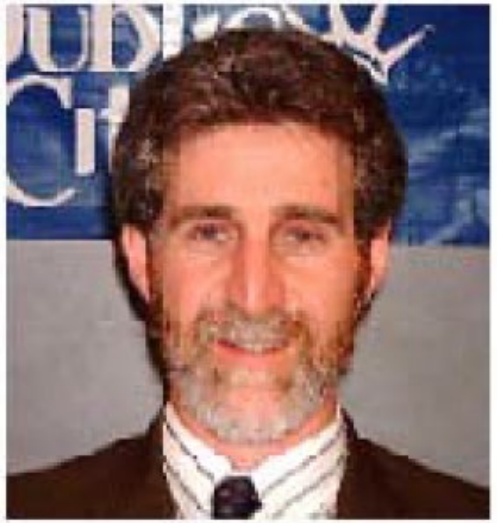
- Kurihara C, Kerpel-Fronius S, Becker S, Chan A, Nagaty Y, Naseem S, Schenk J, Matsuyama K, Baroutsou V. Declaration of Helsinki: ethical norm in pursuit of common global goals. Front Med (Lausanne). 2024 Apr 2;11:1360653. doi: 10.3389/fmed.2024.1360653.
- Kurihara C, Inoue K, Kai H, et al. Our "WMA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

- Back up

Pros and Cons

Robert J Levine

Supported placebo-controlled trials in developing countries when there is established interventions in developed countries, being engaged in AMA, WMA, CIOMS 2002, other important documents including the Belmont Report



Peter Lurie

Supported 2000 revision of the DoH

Criticized another placebo-controlled trial in Latin America which cannot be performed in US or Europe.

Stephan W Lagakos

Statistician engaged in 1 active-controlled trial of HIV perinatal transmission, differently from other 15 placebo-controlled trials

Levine RJ, Lurie P, Lagakos SW. Kurihara C, Interview. Clin Eval. 2001;28(3):409-22.
http://cont.o.oo7.jp/28_3/p409-22/report.html

Table 1 Established key concepts missing in the proposed draft (2)

Protection items	**DoH**	**CIOMS** *1	**Patient group**	**IFAPP** *2	**GL Japan**	**GCP** (R3)	**Brazil**	
Best proven/risk minimization in comparative arms	–	◎	◎	◎	–	–		
Post-trial **access** for participant (informed consent **form**), **community** (for those most in need **globally**)	△	○	◎	◎	△	–		
Publication ethics (research integrity) items	DoH	CIOMS	Patient group	IFAPP	GL Japan	GCP (R3)		
Open Access (to result published in journal)*3	△	–	◎	–	–	–		
Result publication in public database	△	◎	○	◎	◎	◎		
Individual participant data (IPD) sharing (Open Science)	–	◎	○	◎	△ *5	–		
Clinical use of unproven intervention*4	**DoH**	**CIOMS**	**Patient group**	**IFAPP**	**GL Japan**	**GCP** (R3)		
Data accumulation	–	–	○	△	–	–		
Safety/efficacy monitoring	–	–	○	△	–	–		

*3: Open Access (to full rext) is coming to be mandated for public-funded studies in US, EU, Japan but not yet included in human research guidelines.
*4: Points missing in the DoH comparing with WHO-MEURI were discussed in patient and public group.
*5: Not in ethical research guidelines for non-interventional studies/surgical study etc. but in Clinical Research Act and GCP for clinical trial of medicinal products in Japan.

◎Strongly argued ○medium △weak or not explicit

Current revision: main changes

● **Improvement**

(New)

- **Community engagement**
- **DoH should be adhered in public health emergency**
- Contextual vulnerability and inclusiveness (still remaining text of obstacle)
- Scientific misconduct, research waste
- e-consent (no detail, but raise considerations)
- **Taipei Declaration for secondary use of data/material from research**

(Strengthened)

- REC: reviews at **sponsoring** & **host** country
- Scientific rigor
- Post-trial access (small improvement with big excuse: “exceptional case must be approved by REC”)

Current revision: main changes

- **Disappointing**

- **Social value**, once included but deleted
- **Placebo** (when there is proven intervention): no meaningful change, lacking accountability: **Discrepancy with CIOMS**

- **Main remaining issues to be "highest standard"**

- **Post-trial access** for trial **host community**, those **most in need** globally
- **Right to know/not to know** individual research results
- "**Broad informed consent**" and "**dynamic consent**" (defined in CIOMS)
- **Trial result publication** in public database
- **Open access**, **open science**