The Helsinki Declaration 2024:
Advancing bioethics and human rights

Collaborating with WMA and the IFAPP's perspective

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Co-organized by: The Brazilian Society of Bioethics (SBB); International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP)

No conflicts of interest to declare for this presentation

Currently, as President of the International Federation of Associations of Pharmaceutical Medicine (IFAPP) and member of the Executive Committee of CIOMS, I collaborate with non-profit scientific organisations (e.g. PharmaTrain Federation), universities in postgraduate programmes (National and Kapodistrian University of Athens - NKUA, Democritus University of Thrace, Hellenic Open University-EAP, ACG-Deree), patient associations and international organisations to implement initiatives of excellence in clinical research with patient participation according to modern bioethical frameworks as an alumni of the Stavros Niarchos Bioethics Academy.

- I am also a member of the IFAPP Ethics Working Group
- The presentation is authorised by the IFAPP Exec Board , it expresses personal opinions mainly, except in cases with explicit references to IFAPP

Welcome Message

- I extend my **warmest greetings and my deepest gratitude for your presence**, which will enrich our perspectives and discourse.
- I would like to **express my gratitude to the organising committee** and especially to my colleagues in the IFAPP Ethics Working Group, Prof. Chieko Kurihara and Prof. Kotone Matsuyama, our distinguished **speakers and each and every participant**.
- **This webinar is not just an academic or theoretical exercise; it is a call to action**.
- As we delve into the issues of the ongoing revision of the Declaration of Helsinki, **your views and questions may have transformative potential for human life and bioethics.**
- Your input and our discussions can influence actionable change in medical research for the benefit of research participants.
- Without further ado, I wish you a **stimulating dialogue and mutual inspiration**."

Personal expectations regarding the ongoing revision of the DoH

- I expect the new version to be **clearer and stronger to protect human participants** around the world, so that **benefits and risks** are shared **equitably**, especially among **vulnerable patients** and those in **low- and middle-income countries**.
- I also expect **modern ethical challenges** related to new technologies , AI, genetic tools ,and Covid-19 experiences are addressed

WMA Declaration of Helsinki revision process to be recognised for

- **Transparency and public involvement**
  - Designed to be highly transparent and inclusive with multiple public comment periods and regional meetings
- **Global collaboration**
  - Involved various international stakeholders in different parts of the world to ensure a comprehensive global update

Recent publications on DoH revision spark Debate

Viewpoint | Integrating Clinical Trials and Practice

June 20, 2024

Protecting Participants Is Not the Top Priority in Clinical Research

Jerry Menikoff, MD, JD[1]

» Author Affiliations

JAMA. 2024;332(3):195-196. doi:10.1001/jama.2024.7677

The Declaration of Helsinki,[1] adopted 60 years ago by the World Medical Association, is widely viewed as "the 'cornerstone' document pertaining to medical research ethics."[2] Yet it endorses a core premise that is wildly inconsistent with the long-accepted understanding of the ethics of research with human participants. Its endorsement of that premise has real consequences that are harmful to the ability to conduct research ethically. It is long overdue for that position to change. And there is now a particular opportunity to make that change: the World Medical Association is currently engaged in a procedure to revise the declaration.

August 20,2024

The Royal Society of Medicine

Commentary

Journal of the Royal Society of Medicine; 0(0) 1–7
DOI: 10.1177/01410768241261758

60th anniversary of the Declaration of Helsinki: ethical challenges in the 10th amendment

Fernando Hellmann[1], Emmanuelle Marceau[2] and Rosemarie de La Cruz[3]

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The Declaration of Helsinki (DoH), issued by the World Medical Association (WMA), remains an essential ethical framework for research involving human participants worldwide. Established in 1964, the DoH has been significantly revised, with nine previous amendments, demonstrating its commitment to adaptability and its ongoing relevance in guiding ethical research practices amid a changing global landscape, such as a global pandemic.[1]

In anticipation of the DoH's Diamond Jubilee challenges that the ongoing DoH review will need to address. These challenges are stimulated by the impact of global health emergencies and inequalities and unprecedented rapid technological advances, including the rise of digital technology, artificial intelligence and molecular breakthroughs such as CRISPR. These developments are driving considerable changes in research designs and require a comprehensive reassessment of ethical frameworks to address these evolving dynamics effectively.

IFAPP Pharmaceutical Medicine

International Federation of Associations of Pharmaceutical Physicians & Pharmaceutical Medicine

Purpose-driven organisation

- **Ethical, innovative and scientific leadership**

Value proposition :Benefits for members

- **New : Fellowships for**
  - **Young ,Mid Career ,Senior Professionals**
  - **Collaborative culture**
  - **Inclusive, open, transparent, interdisciplinary,**
- **Strategic partnerships with leading international organisations**
- **Scientific societies, academia and regulatory authorities, WMA, CIOMS, PharmaTrain, ECPM, FPM, .**

Deliverables

EMPOWER MEMBERS

Ethics & Competencies

Career & professional development

Communication Community

PROFESSIONAL STANDARDS

On current and future perspectives

Consultations with Stakeholders

Publications

Public consultations

OPEN DIALOGUE

IFAPP TODAY Journal

IFAPP LinkedIn

IFAPP Website

IFAPP Webinars

IFAPP ICPM 2025

IFAPP Ethics Journey

What the IFAPP does for ethics

What IFAPP has contributed to the ongoing DoH revision

What the IFAPP will continue to do

IFAPP Ethical Perspective

Internal Aspects

- Code of Conduct ,a Constitutional requisite
- Ethics Framework for members

External Aspects

- Public Consultations (WHO,WMA, CIOMS, ICH, EMA ,Voire Ethics for Healthy Volunteers)
- Peer Review Publications
- Webinars on Ethics

Ethics Framework for members by IFAPP EWG 3rd edition proposed under discussion

Physician's Code of Conduct
1st edition April 2003
Ethics WG:
Becker, chairperson (Australia), Barrett, co-chairperson (UK), De Botha (S Africa), Brun (Sweden), Cairds (Germany), Chan (Ireland), Carlesi (Italy), Collia (Argentina), Jafary (Pakistan), Nahler (Austria), Jekunen (Finland), Halleux (Belgium), Buehrmann (Germany) Dunton (USA)

Framework for Multidisciplinary team
2nd edition, March 2018
Ethics WG:
Kerpel-Fronius, chairperson (Hungary), Becker, co-chairperson (Australia), Barrett (UK), Brun (Sweden), Carlesi (Italy), Chan (Ireland), Collia (Argentina), Dubois (Belgium), Kleist (Switzerland), Koski (USA), Kurihara (Japan), Filipe Laranjeira (Portugal), Schenk (Germany) Silva (USA).

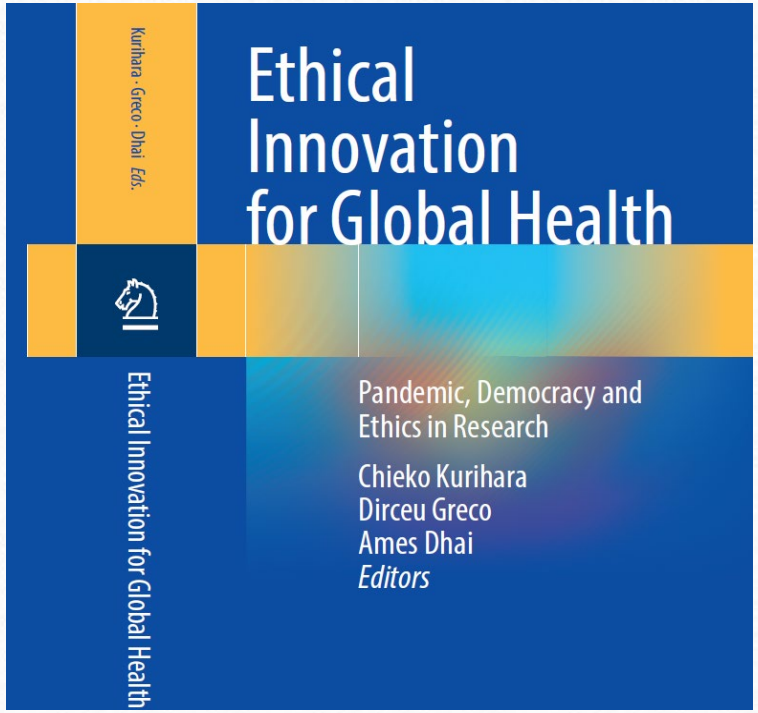
Update of IFAPP Ethics Framework More involvement of patient and public
(support proposal)
Ethics WG:
Matsuyama, chairperson (Japan)
(Not yet team's consensus)
A topic of Intensive discussions on the DoH

Credit for the slide to Prof Chieko Kurihara

IFAPP : Ethics Working Group (EWG)

EWG regular activities

- Monthly meetings
- Peer-reviewed papers
- IFAPP TODAY Journal articles
- WMA & IFAPP meetings
- Collaborative projects –Book : Ethical Innovation for Global Health
- Contribution to CIOMS – e.g., Research Governance



October 2017

MEMORANDUM OF UNDERSTANDING
BETWEEN
THE WORLD MEDICAL ASSOCIATION (WMA)
AND
THE INTERNATIONAL FEDERATION OF
ASSOCIATIONS OF PHARMACEUTICAL PHYSICIANS (IFAPP)

The purpose of this Memorandum of Understanding (MOU) is to facilitate and stimulate contacts and co-operation between the World Medical Association, hereinafter referred to as „WMA" and the International Federation of Associations of Pharmaceutical Physicians hereinafter referred to as „IFAPP", on all projects of common concern that could be launched in the future.

Considering that the mission of the WMA, as a neutral and independent global federation of National Medical Associations representing physicians worldwide, is to act on behalf of patients and physicians. Considering that the WMA endeavours to achieve the highest possible standards of medical care, ethics, education and health-related human rights for all people.

Collaboration with WMA

- ◆ Sessions with WMA at IFAPP meetings
  - ◆ ICPM 2022 Athens Greece-WMA session hosted
  - ◆ IFAPP Regional Meeting in Amsterdam June 2023-WMA speakers hosted
- ◆ Sessions with IFAPP at WMA meetings
  - ◆IFAPP invited at WMA Asian regional meeting in Tel-Aviv in 2022
  - ◆ IFAPP at Copenhagen regional WMA meeting September 2023
  - ◆IFAPP at Washington WMA regional meeting August 2024
  - IFAPP at the Helsinki WMA GA, October 2024

WMA (Drs Resneck, Kloiber, Tsai, Berggreen Høj) at IFAPP ICPM 2022

Future revision of the Declaration of Helsinki: Dialogue with WMA in Athens. *IFAPP TODAY.* 2022; Nov/Dec (29) : 5-8. https://ifapp.org/static/uploads/2022/11/IFAPP-TODAY-29-2022.pdf

Next Revision of the Declaration of Helsinki: Meetings of the WMA and IFAPP. *IFAPP TODAY.* 2023; May (34):8-12. https://ifapp.org/static/uploads/2023/05/IFAPP-TODAY-34-2023.pdf

Discussion in Amsterdam on Data-driven Research and the WMA Declaration of Helsinki. *IFAPP TODAY.* 2023; Sept (37):5-9. https://ifapp.org/static/uploads/2023/09/IFAPP-TODAY-SEPTEMBER-2023-37.pdf

Invited to WMA Regional meeting in Copenhagen

EMERGING CLINICAL TRIAL DESIGNS
DR VARVARA(BARBARA)BAROUTSOU
IFAPP PRESIDENT

The experiences and challenges with new and emerging trial designs from the perspective of physicians working in and with the pharmaceutical industry.

Credit for the slide to Prof Chieko Kurihara

Exploring New and Emerging Trial Designs Considering the Revision of the Declaration of Helsinki

IFAPP is a member of the international network of the World Medical Association (WMA), and I was truly honoured to be invited as a speaker to the Regional Meeting in Europe on the Revision of the Declaration of Helsinki (DoH), which took place on September 21 and 22, 2023, at the Laegeforeningen, Danish Medical Association, in Copenhagen.

1.IFAPP TODAY Nov-Dec 2023 No 39, 15-17
https://ifapp.org/journal/ifapp-today-november-december-2023-number-39/1
2.IFAPP TODAY Sep 2023 No 37, 5-8.
Discussion in Amsterdam on Data-driven Research and the WMA Declaration of Helsinki.
https://ifapp.org/static/uploads/2023/09/IFAPP-TODAY-SEPTEMBER-2023-37.pdf
3. IFAPP TODAY Nov/Dec 2022 No. 29, 5-7.
Future Revision of the Declaration of Helsinki: Dialogue with the WMA in Athens.
https://ifapp.org/static/uploads/2022/11/IFAPP-TODAY-29-2022.pdf
4. IFAPP TODAY Jan 2022; No. 20, 3-7.
IFAPP Recommendations for the Revision of the Declaration of Helsinki, Version 2013
https://ifapp.org/static/uploads/2022/01/IFAPP-TODAY-20-2022.pdf
5. IFAPP TODAY Jul/Aug 2021; No. 16, 4-7.
Kurihara C. Webinar on COVID-19 and Bioethics: Pandemic and Research Ethics: Democracy, Placebo, and Post-Trial Access.
https://ifapp.org/static/uploads/2021/07/IFAPP-TODAY-16-2021.pdf
6. Front. Pharmacol., 29 October 2020, Sec. Drug Outcomes Research and Policies

IFAPP recommended topics for the revision of Declaration of Helsinki version 2013

1. Connection of Declaration of Helsinki (DoH) & Declaration of Taipei (DoT)
2. Ethical approval & consent for secondary use of data
3. Incidental findings
4. Registration of "data sharing plan" and study results in public databases
5. Shared responsibility
6. Patient & Public involvement plan
7. Diversity of membership & qualified experience of Research Ethics Committees (REC)
8. Terminology aspects of human subjects & humans, participants, etc.
9. Medical research for common nomenclature between organisations
10. Placebo use wording & alignment of wording CIOMS & WMA (paragraph 33 DoH)
11. Vulnerable population
12. Post-trial access

What about the proposed draft of 2024 DoH?

Highest Standard? (deontology, human rights)

Minimum Requirement? (utilitarian pragmatism)

Credit for the slide to Prof Chieko Kurihara

Peer review IFAPP EWG members(2&3) and affiliated members (1)publications on DoH

frontiers **Under final review (1)**

Vulnerability, social value and the equitable sharing of benefits from research: beyond the placebo and access debates

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Keywords: vulnerability, social value, post-trial access, global health, Declaration of Helsinki

(2)

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Check for updates

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Declaration of Helsinki: ethical norm in pursuit of common global goals

Chieko Kurihara[1,2]*, Sandor Kerpel-Fronius[2,7], Sander Becker[2,4], Anthony Chan[2,5], Yasmin Nagaty[2,6], Shehla Naseem[2,7], Johanna Schenk[2,8], Kotone Matsuyama[2,9] and Varvara Baroutsou[2]

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The World Medical Association's Declaration of Helsinki is in the process of being revised. The following amendments are recommended to be incorporated in pursuit of the common goal of promoting health for all. 1. Data-driven research that facilitates broad informed consent and dynamic consent, assuring participant's rights, and the sharing of individual participant data (IPD) and research results to promote open science and generate social value. 2. Risk minimisation in a placebo-controlled study and post-trial access to the best-proven interventions for all who need them. 3. A future-oriented research framework for co-creation with all the relevant stakeholders.

KEYWORDS
Declaration of Helsinki, data-driven research, placebo, post-trial access, stakeholder involvement, health for all

1 Introduction

The Declaration of Helsinki (DoH) of the World Medical Association (WMA) (1), first adopted in 1964, is the world's most widely recognised ethical principle for medical research involving humans. The WMA began the process of revising the DoH in April 2022, from the last version dated 2013. Research involving humans is a core activity in the development of medicines. For this reason, the authors have discussed the ideal function of the ethical norm of research involving humans, considering our global experience of the COVID-19 pandemic and other disasters, including war situations. The DoH is a fundamental ethical norm, not guidance for specific changing situations. However, as described below, the drastic changes in both global society and the scientific environment over the past decade have posed an acute challenge to this fundamental norm.

(3)

frontiers in Pharmacology

PERSPECTIVE
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Linking the Declarations of Helsinki and of Taipei: Critical Challenges of Future-Oriented Research Ethics

Chieko Kurihara[1], Varvara Baroutsou[2], Sander Becker[3], Johan Brun[4], Brigitte Franke-Bray[5], Roberto Carlesi[6], Anthony Chan[7], Luis Francisco Collia[8], Peter Kleist[9], Luis Filipe Laranjeira[10], Kotone Matsuyama[11], Shehla Naseem[12], Johanna Schenk[13], Honorio Silva[14] and Sandor Kerpel-Fronius[15] on behalf of Working Group on Ethics of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine*

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Expansion of data-driven research in the 21st century has posed challenges in the evolution of the international agreed framework of research ethics. The World Medical Association (WMA)'s Declaration of Helsinki (DoH) has provided ethical principles for medical research involving humans since 1964, with the last update in 2013. To complement the DoH, WMA issued the Declaration of Taipei (DoT) in 2016 to provide additional principles for health databases and biobanks. However, the ethical principles for secondary use of data or material obtained in research remain unclear. With such a perspective, the Working Group on Ethics (WGE) of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP) suggests a closer scientific linkage in the DoH to the DoT focusing specifically on areas that will facilitate data-driven research, and to further strengthen the protection of research participants.

Keywords: research ethics, data science, medicines development, privacy protection, data sharing, Declaration of Helsinki, Declaration of Taipei

1 INTRODUCTION

Expanding interests in data-driven clinical science in the 21st century have posed some critical challenges in the recent evolution of research ethics. The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) has endorsed renovation (ICH GCP Renovation, 2017) to facilitate utilization of reliable real-world data (RWD) for regulatory decision. This expands the usability of data derived from ordinary medical practice and research, as well as from health databases and biobanks. The World Medical Association (WMA) has since clarified some principles for these types of research but we believe it requires further clarity.

The WMA had established its paramount deontology of physicians to prioritize health and interests of a patient, as described in the Declaration of Geneva (WMA Declaration of Geneva, 1948) and the International Code of Medical Ethics (WMA ICoME, 1949), both issued in its second and third years

WMA DoH recommended amendments in our publications of previous slide

Ethical Norm in pursuit of common goals

- Proposals
  - **Data driven research broad consent and dynamic consent** ,assuring participants; rights and the sharing of IPD and results to promote **open science and social value**
  - **Risk minimisation in placebo-controlled trials and post trial access in best proven intervention**
  - A future oriented research framework for **co creation with stakeholders**

TYPE Policy Brief

PUBLISHED 02 April 2024
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Linking the Declarations of Helsinki and of Taipei

- Proposals
  - To complement the DoH, WMA issued the Declaration of Taipei (DoT) in 2016 to provide additional principles for **health databases and biobanks.**
  - the ethical principles **for secondary use of data** or material obtained in research remain unclear.
  - **IFAPP suggests a closer scientific linkage in the DoH to the DoT focusing specifically on areas that will facilitate data-driven research, and to further strengthen the protection of research participants.**

Front. Pharmacol., 29 October 2020
Sec. Drugs Outcomes Research and Policies
Volume 11 - 2020 | https://doi.org/10.3389/fphar.2020.579714

Vulnerability , social value and the equitable sharing of research benefits: beyond the placebo and access debates our proposal –submitted to Frontiers

Under final review

frontiers

Vulnerability, social value and the equitable sharing of benefits from research: beyond the placebo and access debates

Chieko Kurihara[1, 2*], Dirceu Greco[3], Ames Dhai[4], Kotone Matsuyama[2, 5], Varvara Baroutsou[2,6]

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Keywords: vulnerability, social value, post-trial access, global health, Declaration of Helsinki

Abstract

The vulnerability of research participants is a critical topic for the 2024 revision of the Declaration of Helsinki, with the proposal to include "social value" . However, this proposal has been withdrawn and the relationship between the two concepts has not been clarified. This paper attempts to clarify: 1. the recent reform for the ethical inclusion of vulnerable study participants to promote diversity; 2. the social value, prerequisite for everyone, especially for those who are vulnerable and the most in need; 3. the requirement for promoting the inclusion of vulnerable participants, in particular the review of the norms for placebo-controlled trials and post-trial access; 4. finally, the direction of research ethics reform to achieve social value and equitable global health.

1.the recent reform for the ethical inclusion of **vulnerable study participants to promote diversity;**

2. the **social value, prerequisite for everyone**, especially for those who are **vulnerable and the most in need**;

3. the requirement for promoting the inclusion of vulnerable participants, in particular the review of the norms **for placebo-controlled trials and post-trial access;**

4. finally, the direction of research **ethics reform to achieve social value and equitable global health.**

Alternatives to using **Placebos in Clinical Trials in the current era**

https://www.fda.gov/media/138004/download
https://www.bmj.com/content/381/bmj-2022-072108
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-design-and-conduct-externally-controlled-trials-drug-and-biological-products

CTs: Clinical Trials

Active comparator : existing standard/best proven

Alternative studies designs to minimize placebo use :

Adaptive trials	Historic controls, synthetic controls,	Non inferiority trials	Add on trials (standard treatment vs standard treatment + new drug	Crossover trials

DoH declares :Placebo should not be used ,if it is withholding effective treatment from participants.

Skierka and Michels *BMC Medical Ethics* (2018) 19:24
https://doi.org/10.1186/s12910-018-0262-9

BMC Medical Ethics

RESEARCH ARTICLE Open Access

Ethical principles and placebo-controlled trials – interpretation and implementation of the Declaration of Helsinki's placebo paragraph in medical research

Antonia-Sophie Skierka[1*] and Karin B. Michels[2,3,4*]

Abstract

Background: In October 2013, the Declaration of Helsinki was revised a seventh time in its 50 year history. While it is the most widely accepted set of ethical principles for the protection of patients participating in medical research, the Declaration of Helsinki has also been subject of constant controversy. In particular, its paragraph on the use of placebo controls in clinical trials divides the research community into active-control and placebo orthodox proponents, both continuously demanding revisions of the Declaration of Helsinki in favour of their position. The goal of the present project is to compare the mainly theoretical controversy with regulatory implementation.

Methods: We distributed a questionnaire to national drug regulatory authorities from different countries to collect information on the authorities' respective approaches to interpretation and implementation of the Declarations' placebo paragraph in the conduct of medical research.

Results: Our findings suggest that the majority of drug regulatory authorities have established a practice of a middle ground, allowing placebo controls in some instances. Various interpretations of "serious harm" and "methodological reasons" are proposed as well as safeguards to avoid abuse of the option to use placebo-controls.

Conclusion: Leaving the placebo paragraph open to various interpretation is a result of the Declaration of Helsinki's character as a guidance document. With the current version controversy will continue. The Declaration should be continued to be strengthened to enforce the appreciation of conducting medical research with the highest ethical standard.

Keywords: Placebo, Declaration of Helsinki, World medical association

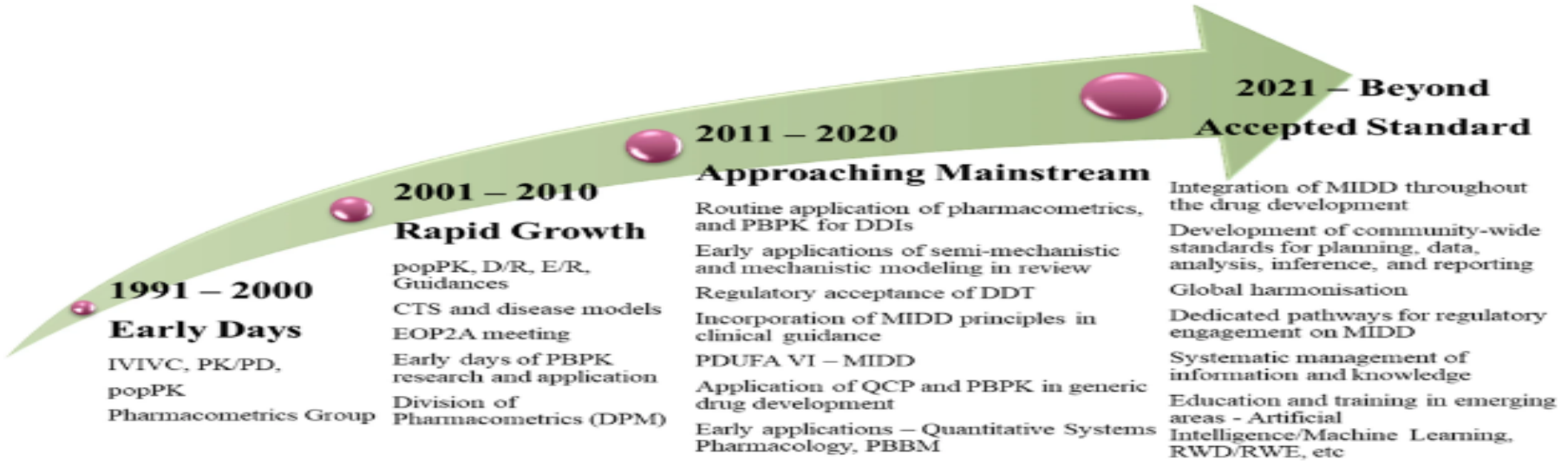
Study on the topic of placebo : International Regulatory Authorities view.

The results indicate that the **DoH** is the most accepted ethical guideline on medical research and **seen as a minimum ethical standard** by **international drug regulatory authorities**. The use of the most currently **effective treatment as the comparison** is preferred to **avoid abuse of placebo-controlled trials ambiguous and open to various interpretations.**

Review: Role of Model-Informed Drug Development Approaches in the Lifecycle of Drug Development and Regulatory Decision-Making Review Article -Published: 12 May 2022
Volume 39, pages 1669–1680, (2022)
•Cite this article

Fig. 1

From: Review: Role of Model-Informed Drug Development Approaches in the Lifecycle of Drug Development and Regulatory Decision-Making



Evolution of MIDD at the FDA. A brief summary of key highlights for every decade with future aspirations are provided. Abbreviations: ICIVC – *in vitro–in vivo* correlation; PK/PD – pharmacokinetics/pharmacodynamics; popPK – population pharmacokinetics; D/R – dose–response; E/R – exposure–response; CTS – clinical trial simulations; EOP2A – end of phase 2A; PBPK – physiologically based pharmacokinetics; DDI – drug–drug interactions; DDT – drug development tools; MIDD – model-informed drug development; QCP – quantitative clinical pharmacology; PBBM – physiologically based biopharmaceutics models; RWD/RWE – real world data/real world evidence; RTRT – real time release test; MIE – model-integrated evidence; PDUFA – Prescription Drug User Fee Act.

> Methods Mol Biol. 2024:2716:51-99. doi: 10.1007/978-1-0716-3449-3_4.

In Silico Clinical Trials: Is It Possible?

Simon Arsène [1], Yves Parès [1], Eliott Tixier [1], Solène Granjeon-Noriot [1], Bastien Martin [1], Lara Bruezière [1], Claire Couty [1], Eulalie Courcelles [1], Riad Kahoul [1], Julie Pitrat [1], Natacha Go [1], Claudio Monteiro [1], Julie Kleine-Schultjann [1], Sarah Jemai [1], Emmanuel Pham [1], Jean-Pierre Boissel [1], Alexander Kulesza [2]

Affiliations + expand

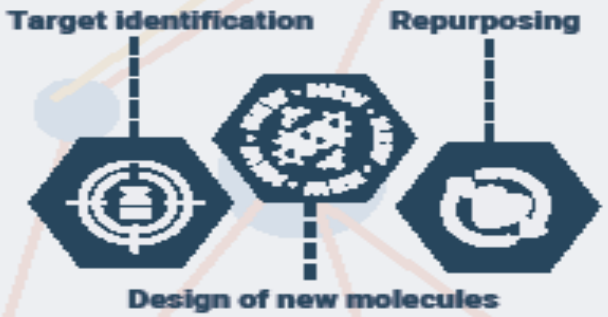
PMID: 37702936 DOI: 10.1007/978-1-0716-3449-3_4

Abstract

Modeling and simulation (M&S), including in silico (clinical) trials, helps accelerate drug research and development and reduce costs and have coined the term "model-informed drug development (MIDD)." Data-driven, inferential approaches are now becoming increasingly complemented by emerging complex physiologically and knowledge-based disease (and drug) models, but differ in setup, bottlenecks, data requirements, and applications (also reminiscent of the different scientific communities they arose from). At the same time, and within the MIDD landscape, regulators and drug developers start to embrace in silico trials as a potential tool to refine, reduce, and ultimately replace

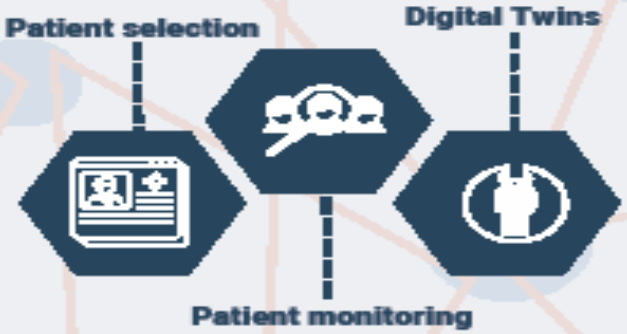
FOUR MAIN USES OF AI IN MEDICINES R&D AND SPECIFIC RISKS

AI IN MEDICINE DISCOVERY



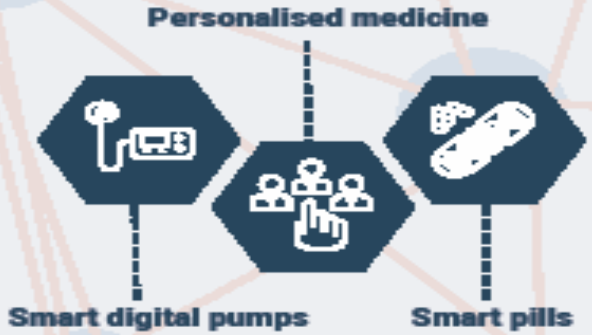
Mostly positive use cases with few specific risks.

AI IN CLINICAL TRIALS



Specific risks that relate to informed consent, the quality of evidence and validation of the AI methods used.

AI IN PHARMACEUTICAL PRODUCTS



Specific risks that relate to patient safety, AI liability, discrimination and black-box decision making.

AI IN PHARMACEUTICAL PROMOTION

Fundamentally controversial, leads to higher sales instead of healthier patients.

REGULATORY FRAMEWORK

EU MEDICAL DEVICES REGULATION
Sets out requirements for all medical devices, including AI assisted medical devices.
No specific AI requirements

EU CLINICAL TRIALS REGULATION
Sets out standards for clinical trial conduct and patient participation, including for CTs using AI systems.
No specific AI requirements

EU MEDICINAL PRODUCTS REGULATION
Sets out rules governing development, approval and use of medicines in Europe.
No specific AI requirements

EU ARTIFICIAL INTELLIGENCE ACT
Regulates AI-assisted medical devices, but does not regulate AI used in pharmaceutical R&D.
Few AI systems regulated

EU GENERAL DATA PROTECTION REGULATION
Regulates all uses of data in the EU, including uses by AI systems.
Regulates all data uses

Besides specific risks, Artificial Intelligence always carries general risks relating to bias and discrimination, privacy and cybersecurity.

https://healthai.haiweb.org/ai-in-medicines-research-and-development/

Final Recommendation for DoH revision

- Be our guide of "**highest ethical standards**"
  - DoH to ensure consistency with CIOMS
- **Best-proven intervention in the world must be assured in any comparative** arms and risk should be minimized (as in CIOMS)
  - Ethics committee excuse in post-trial access paragraph should be deleted.
  - **Leaving the placebo paragraph open to various interpretations will continue the controversy**
  - **Post trial access** should be assured in protocol/consent form to:
    - study participants
    - host community
    - those most in need worldwide

We will act on our proposals as a commitment derived from

Fundamental

- Ethical Principles for Biomedical Research
  - **Autonomy**
  - **Beneficence and non-Maleficence**
  - **Justice**

Given that

- **Ethics considerations are important determinants of research study design and execution**

In parallel we will introduce debates **in ELSI** due to rapid scientific developments and emerging technologies in the field of:

- ❖ Gene Editing & CRISPR
- ❖ RWD with genomic information
- ❖ Genetic Privacy & Data Security
- ❖ AI in Research & Development
- ❖ Equity and Access to Genetic Technologies

Thank you for your attention

Questions & Discussion

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Back up slides

Medical Research should be conducted primarily to improve human health.

Ethical principles and placebo-controlled trials – interpretation and implementation
of the Declaration of Helsinki's placebo paragraph in medical research

- Skierka and Michels BMC Medical Ethics (2018) 19:24

Defining "methodological reasons": The Declaration of Helsinki states that "compelling and scientifically sound methodological reasons" may justify the use of placebo in a clinical trial. As pointed out earlier, there are some reasons accepted from both camps for placebo use in clinical trials: if no current proven intervention for the respective condition exists, or if a patient population that is not responding to available treatment [8]. Our survey results suggest (Table 2) that the majority of regulatory authorities interpret the "methodological reasons" in the above mentioned way. Nevertheless, several responses also mirror various other methodologic justifications often quoted by defenders of placebo controls:

- Active controls' lack of assay sensitivity.
- Standard treatment is not always effective.
- Smaller sample sizes are required for superiority trials.

Clinical trials,

- A Methodology Perspective ,Wiley Book , 4rth edition 2024

TABLE 3.3 Principles for Ethical Clinical Trials

Collaborative partnership
Scientific value
Scientific validity
Fairness of subject selection
Favorable risk–benefit
Independent review
Informed consent
Respect for enrolled subjects

Source: Adapted from Emanuel et al. [558].