Journal of
Pharmaceutical and BioTech Industry

MDPI

Opinion

Frameworks for Ethical Conduct in Clinical Trials and Health Research in Africa

Lembit Rägo * and Jacqueline Sawyer

Council for International Organizations of Medical Sciences, Case Postale 2100, 1211 Geneva 2, Switzerland; sawyer.jacqueline@gmail.com
* Correspondence: ragol@cioms.ch; Tel.: +41-22-791-6497

Abstract

Current estimates suggest that Africa contains about 14% of the world's population and accounts for 20% of the global burden of disease. Yet, it accounts for a mere 3% of clinical trials globally. The time is ripe—even overdue—for determining how best to direct future health research efforts. In response, a call has been heard for a continent-wide Africa-centric research ethics framework to redirect health research in Africa, as well as address the health research ethics malpractices that have violated the rights, dignity and well-being of participating African communities. Nevertheless, we should remain aware of what already exists and what continues to be of value. Creating parallel frameworks risks fragmentation of research, increased costs in having to meet differing requirements and delayed access of patients to new treatments. Existing international consensus documents which have evolved and been fine-tuned over time, offer guidance for ensuring ethical instigation and management of health research. The Declaration of Helsinki enunciates clear principles for ensuring the ethical conduct of clinical research, while CIOMS' 2016 International Ethical Guidelines for Health-related Research involving Humans offer guidance for implementing these principles. It is failure to apply existing ethical principles and guidance—and not any perceived inadequacy of those principles—that has resulted in sub-optimal protection of African research participants.

Keywords: Africa; health research ethics; clinical trials; consensus principles and guidance

Academic Editor: Bozena B. Michniak-Kohn

Received: 16 June 2025
Revised: 24 July 2025
Accepted: 6 August 2025
Published: 8 August 2025

Citation: Rägo, L.; Sawyer, J. Frameworks for Ethical Conduct in Clinical Trials and Health Research in Africa. *J. Pharm. BioTech Ind.* **2025**, 2, 13. https://doi.org/10.3390/jpbi2030013

Current estimates suggest that Africa contains about 14% of the world's population, and accounts for 20% of the global burden of disease. Yet a mere 3% of clinical trials globally are conducted in this region [1–3]. For Fallah et al., representing the Africa Centers for Disease Control and Prevention, "This situation in part stems from the poor research ethics framework and failure of international research principles to protect African research participants optimally" [4]. In parallel, The Lancet advocates for "Redefining implementation science for global health decolonisation" [5]. Adding further complexity to this picture is the need, as underscored by Ntobeko Ntusi, President and CEO of the South African Medical Research Council, to consider how best countries can respond to recent cuts in development aid funding for health [6].

The time is ripe—even overdue—for determining how best to direct future health research efforts. That said, we should remain aware of what already exists and what continues to be of value. Fallah et al. argue that a continent-wide Africa-centric research ethics framework is urgently needed. They refer to Africa's low health literacy levels that impede understanding and granting of informed consent, the vulnerability of its already

disadvantaged groups, and research ethics malpractices that violated the rights, dignity and well-being of participating African communities. They suggest that Africa's complex and diverse cultural and socioeconomic settings necessitate a new ethics framework, one that promotes application of African values and virtues [4]. But if clinical trials—one of the most costly and intensive types of medical research—had to be conducted under the auspices of more than one ethical framework, the implications for pharma and patients could be significant. Repeating trials across different jurisdictions to meet differing requirements would demand increased investment from pharma. Some companies may decide not to conduct clinical trials in all jurisdictions, meaning that some patients may not be able to access the products concerned. Moroever, the results of such clinical trials may not be directly comparable, potentially hindering or fragmenting research.

The principle of convergence, whereby different parties agree to apply the same rules and regulations even though the contexts may differ, offers an alternative and tested approach. Thus, internationally agreed and harmonized standards for medical product regulation contribute significantly to global public health [7]. Of note is that African regulators are increasingly involved in developing these standards, within the environments of both the World Health Organization (WHO) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Thus, medicines regulators in Egypt, Madagascar, Senegal, South Africa, Tanzania, Tunisia, Uganda, Zambia and Zimbabwe, as well as the African Medicines Regulatory Harmonisation Initiative, all contributed to the Fifty-eighth report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations [8]. This Committee oversees the maintenance of The International Pharmacopoeia and provides guidance for use by relevant WHO programmes and regulatory authorities in Member States, to ensure that medicines meet unified standards of quality, safety and efficacy. With respect to ICH, the Egyptian Drug Authority is now a member, while Algeria's National Agency for Pharmaceutical Products, Nigeria's National Agency for Food and Drug Administration and Control, the South African Health Products Regulatory Agency and Tunisia's Directorate for Pharmacy and Medicine have observer status, as do the East African Community and the South African Development Community [9].

Moreover, it is surely failure to apply existing ethical principles and guidance—and not any perceived inadequacy of those principles—that has resulted in sub-optimal protection of African research participants. Such failure is in part explained by lack of capacity. Results of a study published in 2021 indicated that although 18 out of 35 African countries had legislation to regulate the conduct of health research, some legislation was either grossly outdated or too limiting in scope, and that some countries had multiple laws. In 12 countries, health research legislation was absent [10]. A 2017 study covering Egypt, Kenya, South Africa and Zimbabwe points to systemic flaws that thwart the ethical conduct of clinical trials, including the lack of human and financial resources of the bodies charged with overseeing clinical trials, the involvement of multiple bodies in oversight and approval of trials, and conflict of interest whereby, for example, medical doctors are paid substantial sums to recruit trial participants [11].

Existing international consensus documents, which have evolved and been fine-tuned over time, offer considerable guidance for ensuring ethical management of health research, no matter where it is situated. Foremost among these is the Declaration of Helsinki (DoH). Fully aware that "medical research takes place in the context of various structural inequities", it enunciates clear principles aimed at safeguarding the health, well-being and rights of research participants [12], while the 2016 International Ethical Guidelines (IEG) for Health-related Research involving Humans of the Council for International Organizations of Medical Sciences (CIOMS) offer clear guidance for implementing these

principles [13]. Indeed, the IEG were "the first to refer to vulnerability as a (secondary) principle incorporated in the principle of respect for persons" [14]. They define how the relationship between global south and global north researchers should be: "one of equal partners whose common aim is to develop a long-term collaboration through South-South and North-South cooperation that sustains site research capacity". They also offer advice on how to "safeguard against power differences."

So, although calls to "decolonize" global health are increasingly heard [15–17], as well as demands that implementation science [IS] promote equity and take context fully into account, "equity" and "context" have long been enshrined in the DoH and IEG.

The IEG are actively promoted and implemented. For example, the Pan American Health Organization (PAHO) refers extensively to them—presenting them as a standard—in their own guidance and tools for ensuring that health research is ethical research [18,19]. A bibliometric analysis concluded that the IEG (2016) have had "significant impact in health and medical science literature", and "served as a foundation for health-related research around the world in the areas of ethics, informed consent, and research ethics and the linkage of these topics to under-represented populations in such research" [20].

Would it be inappropriate to promote application of the IEG in Africa too? Is it the case that ethical research values of the African and Latin American regions differ? We think not. The problems that Fallah et al. highlight (low health literacy levels that impede understanding and granting of informed consent, vulnerability of already disadvantaged groups, research ethics malpractices) are common in low-resource settings [4]. Accordingly, CIOMS' Clinical Research in Resource-limited Settings clearly describes the challenges that can undermine health research in low- and middle-income countries (LMIC) and how these can be overcome [21].

Likewise, guidance on optimizing IS for global health, and examples of good implementation research (IR) as applied in LMIC, can be found [22], together with overviews of where IS and IR fall short, and the necessary corrective action [23]. With respect to patient involvement in clinical research, CIOMS and the European Patients' Academy on Therapeutic Innovation (EUPATI) have described in depth the efforts and investment needed to engage meaningfully with participating patient communities, so that a quality informed consent process, improved trial designs, adjusted to trial participants' health and social needs (and therefore fewer drop outs) can be assured [24,25].

This is not to say that further refinement is not called for. The pace of health research continues to accelerate, generating new issues which may outpace existing consensus statements. The use of AI in preparation of clinical trials is a case in point [26]. Indeed, many research ethics committees are probably not well enough informed about AI's weaker points use and therefore not able to evaluate, for example, whether AI negatively influenced a trial design or selection of inclusion or exclusion criteria [27].

But we need not develop new ethical or other frameworks repeatedly. Rather, existing consensus statements and guidelines for health research must evolve. (Hence the latest version of the DoH is the 10th version.) In the meantime, what is needed is rigorous adherence—on the part of all those involved in health research—to the principles of current versions of the DoH and IEG. Sponsors, including pharma, can help ensure this. In addition, many organizations including CIOMS, continue to provide online and in person training to help improve medical research ethics knowledge and expertise, and their application in real-life and research settings, as well as identify upcoming issues for which international deliberation will be required to determine equitable and workable approaches for managing them [28,29].

Author Contributions: Conceptualization, J.S. and L.R.; writing—original draft preparation, J.S.; writing—review and editing, L.R.; supervision, L.R. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: No new data were created for the purposes of this article.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. WHO Regional Office for Africa. Atlas of African Health Statistics 2022: Health Situation Analysis of the WHO African Region. Brazzaville, WHO Regional Office for Africa. 2022. Available online: https://aho.afro.who.int/atlas-download/af (accessed on 4 May 2025).
2. Niohuru, I. Healthcare and Disease Burden in Africa: The Impact of Socioeconomic Factors on Public Health. In *SpringerBriefs in Economics*; Springer: Berlin/Heidelberg, Germany, 2023. [CrossRef]
3. World Health Organization. *Global Action Plan for Clinical Trial Ecosystem Strengthening*; World Health Organization: Geneva, Switzerland, 2025. [CrossRef]
4. Fallah, M.P.; Dereje, N.; Temfack, E.; Tajudeen, R.; Kaseya, J. A call for an Africa-centric health research ethics framework: A way forward for shaping global health research. *Lancet Global Health* **2025**, *13*, e616–e617. [CrossRef] [PubMed]
5. Editorial. Redefining implementation science for global health decolonisation. *Lancet* **2025**, *13*, e599. Available online: https://www.thelancet.com/action/showPdf?pii=S2214-109X%2825%2900116-0 (accessed on 8 May 2025).
6. Ntusi, N. US aid cuts are an opportunity to reimagine global health. *Nat. Med.* **2025**, *31*, 719. [CrossRef] [PubMed]
7. Feng, K.; Miranda, A.V.; Obnial, J.C.; Ebhodaghe, I.D.; Lucero-Prisno, D.E. Drug regulatory harmonization in the Association of Southeast Asian Nations: Is it time for an ASEAN medicines agency? A policy review. *Clin. Epidemiol. Glob. Health* **2024**, *28*, 101649. [CrossRef]
8. *WHO Expert Committee on Specifications for Pharmaceutical Preparations*; Fifty-Eighth Report; WHO Technical Report Series 1060; WHO: Geneva, Switzerland, 2025. Available online: https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf (accessed on 21 July 2025).
9. ICH. Available online: www.ICH.org/page/members-observers (accessed on 19 July 2025).
10. Nabyonga-Orem, J.; Asamani, J.A.; Makanga, M. The state of health research governance in Africa: What do we know and how can we improve? *Health Res. Policy Syst.* **2021**, *19*, 11. [CrossRef] [PubMed]
11. WEMOS Health Unlimited. Clinical Trials in Africa. The Cases of Egypt, Kenya, Zimbabwe and South Africa. 2017. Available online: https://www.wemos.org/wp-content/uploads/2023/04/Clinical-trials-in-Africa_2017.pdf (accessed on 21 July 2025).
12. World Medical Association. Declaration of Helsinki. Most Recent Iteration: December 2024. Available online: https://www.wma.net/policies-post/wma-declaration-of-helsinki/ (accessed on 7 April 2025).
13. CIOMS. *International Ethical Guidelines for Health-Related Research Involving Humans*; CIOMS: Geneva, Switzerland, 2016. [CrossRef]
14. Lindholm, O.; Karjalainen, S.; Launis, V. Chasing 'vulnerability' across six decades of the Declaration of Helsinki. *Monash Bioeth. Rev.* **2025**, *43*, 1–23. [CrossRef] [PubMed]
15. Kwete, X.; Tang, K.; Chen, L.; Ren, R.; Chen, Q.; Wu, Z.; Cai, Y.; Li, H. Decolonizing global health: What should be the target of this movement and where does it lead us? *Glob. Health Res. Policy* **2022**, *7*, 3. [CrossRef] [PubMed]
16. McCoy, D.; Kapilashrami, A.; Kumar, R.; Rhule, E.; Khosla, R. Developing an agenda for the decolonization of global health. *Bull. World Health Organ.* **2023**, *102*, 130–136. [CrossRef] [PubMed]
17. Mehjabeen, D.; Patel, K.; Jindal, R.M. Decolonizing global health: A scoping review. *BMC Health Serv. Res.* **2025**, *25*, 828. [CrossRef] [PubMed]
18. PAHO Infographic, Oversight of Research. Available online: https://www.paho.org/en/documents/infographic-oversight-research (accessed on 4 May 2025).
19. PAHO Tool for the Accreditation of Research Ethics Committees. 2024. Available online: https://iris.paho.org/handle/10665.2/58904 (accessed on 4 May 2025).
20. Haunschild, R.; Kays, J.; Rägo, L.; Kays, M. Bibliometric analysis of publications that cited the CIOMS 2016 "International ethical guidelines for health-related research involving humans". *Heliyon* **2024**, *10*, e36833. Available online: https://www.cell.com/heliyon/fulltext/S2405-8440(24)12864-2?uuid=uuid%3Afd56e78f-a470-45e8-a2be-f1c4b16f723d (accessed on 4 May 2025). [CrossRef] [PubMed]
21. CIOMS. *Clinical Research in Resource-Limited Settings*; A Consensus by a CIOMS Working Group; CIOMS: Geneva, Switzerland, 2021. [CrossRef]

22. ESSENCE Steering Committee. *Seven Approaches to Investing in Implementation Research in Low- and Middle-Income Countries*; ESSENCE Good Practice Document Series; World Health Organization: Geneva, Switzerland, 2020. Available online: https://tdr.who.int/publications/m/item/2020-09-29-seven-approaches-to-investing-in-implementation-research-in-low-and-middle-income-countries (accessed on 8 June 2025).
23. Geng, E.H.; Nash, D.; Phanuphak, N.; Green, K.; Sunil, S.; Grimsrud, A.; Sohn, A.H.; Mayer, K.H.; Bärnighausen, T.; Bekker, L.-G. The question of *the question*: Impactful implementation science to address the HIV epidemic. *J. Int. AIDS. Soc.* **2022**, *25*, e25898. [CrossRef] [PubMed]
24. CIOMS. *Patient Involvement in the Development, Regulation and Safe Use of Medicines. Report of the CIOMS Working Group XI*; CIOMS: Geneva, Switzerland, 2022. [CrossRef]
25. EUPATI. Available online: www.eupati.eu/our-activities-and-learning-approach/ (accessed on 8 June 2025).
26. Ribeiro, J.; Lopes, H. AI ethics in medical research: The 2024 Declaration of Helsinki. *Lancet* **2024**, *404*, 2048–2049. Available online: https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(24)02376-6.pdf (accessed on 22 July 2025). [CrossRef] [PubMed]
27. Esmaili, A.; Rahmani, A.; Alijanpour, A.; Jayervand, F.; Akhondzardaini, R.; Sharifi, M.H.; Shams, S.E.; Rashvandi, H.; Yeganegi, M.; Shahbazi, A.; et al. Challenges for ethics review committees in regulating medical artificial intelligence research. *Indian J. Surg. Oncol.* **2025**. [CrossRef]
28. CIOMS Online Training Relating to IEG. Available online: https://cioms.ch/online-training/ (accessed on 19 July 2025).
29. Training and Resources in Research Ethics Evaluation (TREE). Available online: https://elearning.trree.org (accessed on 19 July 2025).