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The Global Ethics Charter for the protection of healthy volunteers in clinical trials

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The Ethics Charter is a tool to be used for

- Advocacy on specificities of healthy volunteers' ethical and scientific issues
- Debate within countries/regions on most adapted protection tools
- Prospective work on other categories of healthy people involved in research

Healthy volunteers differ from Patients in research

- They are healthy : no expectation of direct health benefit, different benefit/risk balance from patients
 - First-in-man studies designed to detect side-effects
 - Administering a pharmaceutical compound, even a well-known one, to a healthy person always carries some level of risk
- They receive financial compensation : risk being exploited when in situations of vulnerability
- Studies are run under very constrained conditions that may impinge on their well-being

The Global Ethics Charter – Process

- 4Q2023: review of position papers' recommendations on selected topics
- December 14-15, 2023: Working group's co-chairs meeting, Paris
- February 28, 2024: Draft Ethics Charter issued
- February 28 – March 30, 2024: Public consultation (English, French, Spanish)
- “Pre-final” Draft Ethics Charter discussed during April 18-19, 2024, plenary meeting, Paris
- Final version issued June 2024



Ethics Charter – Structure

- **Healthy volunteers’ 15 rights in clinical trials**
- **Preamble**
 - *Definition of “healthy volunteers”*
 - *Why is specific protection of healthy volunteers needed among “human research participants”*
 - *Contribution to existing ethical guidelines*
 - *Objectives, target audiences*
- **15 Articles**
 - Part 1: Laying the foundation to protect healthy volunteers
 - Part 2: Protecting healthy volunteers from harm
 - Part 3: Protecting healthy volunteers from exploitation
- **Conclusion**

Healthy volunteers' 15 rights in clinical trials

To be protected from the risks of harm and exploitation, healthy volunteers are entitled to:

1. Laws and regulations that specifically protect them as research participants,
2. Assurance that their participation in research is ethical and scientifically necessary,
3. Adequate representation throughout the research process,
4. Transparency about clinical trials in which they are involved,
5. Adequate research ethics oversight,
6. Adequate trial site and investigator oversight,
7. Protection from physical harm,
8. Adequate attention paid to their well-being,
9. Adequate protection from potential long-term harm,
10. Protection from the risks of over-volunteering,
11. Recruitment through fair and respectful practices,
12. Relevant study information to provide genuine informed consent,
13. Fair financial compensation for their participation,
14. Post-trial compensation for research-related injury,
15. Adequate processes for confidential reporting of concerns.

Laying the Foundation to Protect Healthy Volunteers

Articles:

1. Laws and regulations to protect healthy volunteers
2. Assurance that healthy volunteers' participation in research is ethical and scientifically necessary
3. Healthy volunteers' representatives
4. Clinical trial transparency



Article 1.

Laws and regulations to protect healthy volunteers.

In line with international ethics standards and with the principles outlined in this Charter, countries should ensure that their laws, regulations, and guidelines that protect research participants include specific provisions for healthy volunteers.

These provisions should effectively mitigate the risks of harm and exploitation while fostering healthy volunteers' autonomy to participate in clinical research.

Furthermore, laws should include measures to prevent and sanction misconduct.



Article 2.

Assurance that healthy volunteers' participation in research is ethical & scientifically necessary.

Countries should put in place measures to ensure that healthy volunteers' involvement in clinical research is always ethical and scientifically necessary.

To this end, stakeholders should join efforts to develop and use innovative methods to **reduce** the number of healthy volunteers involved, **refine** the methodologies to avoid unnecessary burdens, and **replace** healthy volunteer studies with alternative methods, when possible.

Article 3.

Adequate representation of healthy volunteers throughout the research process.

Countries should encourage the formation of groups representing healthy volunteers' interests in the development of laws, regulations, and guidelines designed to safeguard the interests of healthy volunteers throughout the clinical trial process.

Ideally, these groups should include past & present healthy volunteers, but other options could be considered to ensure their representation is sustainable over time. Interactions between associations representing healthy volunteers should be facilitated to combat disparities in standards within and across countries, particularly those that could lead to the misuse of populations in lower-income and -resource settings.

Clinical trial sites and other stakeholders (e.g., sponsors, ethics review boards) should engage with these representatives to improve the design and conduct of trials with healthy volunteers.



Article 4.

Transparency about clinical trials in which healthy volunteers are involved.

As is required for later-phase trials, all data, including those from early Phase I trials that involve healthy volunteers, should be made available to the public through existing databases, such as clinicaltrials.gov, the WHO International Clinical Trials Registry Platform, EudraCT (European Union Drug Regulating Authorities Clinical Trials Database), and CTRI (Clinical Trials Registry – India).

There is also a need for more public access to data about the number and types of trials involving healthy volunteers globally to enable more research in this field.

Part 2

Protecting Healthy Volunteers from Harm

Articles:

5. Research ethics oversight
6. Site and Investigator oversight
7. Protection from physical harm
8. Attention to participant well-being
9. Monitoring of potential long-term harms
10. Preventing over-volunteering



Article 5.

Adequate research ethics oversight.

In addition to following existing guidelines and ethical standards, scientific and ethics review boards involved in assessing healthy volunteer trials should possess the necessary expertise, training, and resources to thoroughly assess & integrity of such trials.

Board members should understand the risks specific to healthy volunteer trials and how to minimise them.

Members should include at least one representative of healthy volunteers' interests who has the requisite knowledge and experience to protect them from harm, ideally from first-hand experience as a healthy volunteer.

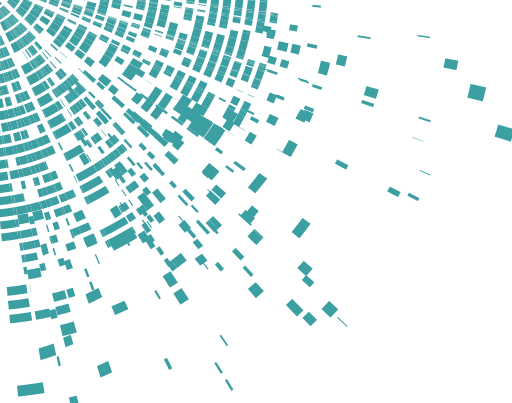


Article 6.

Adequate trial Site and Investigator oversight.

Countries should establish oversight mechanisms to ensure that sites conducting clinical trials are adequately equipped and staffed with appropriately trained and qualified personnel who will uphold the quality and integrity of the research and safeguard the well-being of healthy volunteers.

Oversight should include mandatory inspections of research facilities and review of staff credentials.



Article 7.

Protection from physical harm.

Risks to healthy volunteers should be minimised through the design of the clinical trials, which should adhere to the latest guidelines on the safe administration of experimental medicinal products and include only medical procedures that are scientifically necessary to address the research questions.

The safety of volunteers should be ensured by continuous monitoring for the emergence of adverse events, with access to acute medical care provided throughout the trial.



Article 8.

Adequate attention paid to healthy volunteer well-being.

It is imperative to prioritise healthy volunteers' well-being during clinical trials. Clinical trial facilities should have sufficient space and be designed to prioritize the safety and well-being of participants.

Whenever strict trial conditions are warranted by the study, justification should be given, reviewed, and approved by an ethics review board.

To mitigate participants' feelings of isolation, trial sites should provide access to communication technologies, as well as other amenities or activities to enhance well-being during confinement.

Additionally, sites should train their staff members to treat healthy volunteers respectfully and to minimise risks of psychological and other non-physical harm and to address such harms promptly whenever they occur.



Article 9.

Adequate protection from potential long-term harm.

Should any adverse event occur, healthy volunteers must be monitored until either they have returned to their baseline level of health or long-term or permanent changes to their health are acknowledged with an appropriate care plan in place.

Regulators and sponsors should implement a system for post-trial, long-term monitoring of adverse events and health care for healthy volunteers. This system should ensure all adverse events that occurred during the trial have been recorded and resolved within the stipulated period and appropriate medical care provided.



Article 10.

Protection from the risks of over-volunteering.

Preventing over-volunteering, i.e. not respecting exclusion (or “washout”) periods between trials, is crucial to protect participants and the integrity of clinical trials.

Countries should develop and maintain mandatory systems across all clinical research settings to prevent over-volunteering.

Consistent with national and international data privacy requirements, these systems should enable individual participant identification to ensure healthy volunteers adhere to the exclusion periods between trials. Wherever possible, these systems should operate across national borders.



Part 3

Protecting Healthy Volunteers from **Exploitation**

Articles:

11. Recruitment practices
12. Informed consent
13. Financial compensation
14. Compensation for research-related injury
15. Reporting and management of participant concerns



Article 11.

Recruitment through fair and respectful practices.

Countries should develop frameworks to ensure that recruitment practices for healthy volunteer trials adhere to the highest ethical standards that prevent excessive emphasis on financial compensation, misleading language, and other forms of undue influence.

It is also essential to prevent either unjustly targeting or excluding disenfranchised populations, including—but not limited to—financially vulnerable individuals, marginalised communities, the unhoused, and migrants.



Article 12.

Relevant study information to provide genuine informed consent.

In addition to following all current guidelines and ethical standards, informed consent materials and processes should be tailored to address the specificities of healthy volunteer trials.

Information about financial compensation should include details about when and how payment will be made, how compensation will be determined if the study is stopped early or the participant exercises their right to withdraw from the research, and any potential economic risks to participants (e.g., income tax consequences or eligibility for social services). Additionally, detailed information about the risks of failing to follow protocol restrictions, such as dietary requirements and rules about frequency of study enrolment, should be provided.



Article 13.

Fair financial compensation for participation.

All compensation of healthy volunteers for trial participation has the potential to compromise trial results by incentivizing the concealment of health conditions and adverse events, as well as over-volunteering to earn more income.

Countries should develop guidelines on compensation to provide fair and equitable compensation across clinical trial sites.

Financial compensation should be reflective of the demands associated with each trial and be approved by ethics review boards. Insufficient compensation for healthy volunteers has the potential to take unfair advantage of lower-income volunteers.

Disbursements should be made fairly during the trial, and when offered, completion bonuses to encourage final outpatient study visits should be modest to avoid compromising volunteers' right to withdraw from the trial at any time without prejudice.



Article 14.

Post-trial compensation for research-related injury

Healthy volunteers should be protected from the risk of increased financial harm if they experience an injury related to the trial. Because healthy volunteers are healthy, it is imperative to provide, at minimum, compensation in the form of medical care for any research-related injuries that may occur.

As with all clinical trials, sponsors and research clinics should have adequate insurance to cover all harms caused by clinical trial participation, from screening through the post-trial period, for injuries related to the clinical trial.

There should be a transparent and easily accessible process for healthy volunteers who are harmed in a clinical trial to claim post-trial care and/or financial compensation. The entities responsible for adjudicating whether an injury is trial-related should be independent and without any conflicts of interest.



Article 15.

Adequate processes for confidential reporting of concerns.

Procedures should be established to allow healthy volunteers to report any concerns to clinical site staff, ethics review boards, or regulatory agencies during and after the clinical trial, without fear of reprisal or loss of entitled financial compensation.

Details on how and where volunteers can report concerns should be clearly outlined in informed consent documents. The volunteers' identity should be confidential unless their identity is essential for resolving the complaint and should only be shared with their permission. Participants should be informed about the outcome of any complaints. Written records should be maintained that document reported issues and the corresponding actions taken.



Conclusion

This Charter aims to support the global recognition of healthy volunteers as a group of human research participants who deserve specific ethical and regulatory protection.

While it focuses on healthy volunteers involved in interventional clinical trials with medicinal products where there is no potential direct health benefit for the individuals involved, we expect that the key principles outlined here may also be relevant to other types of research that involve healthy human research participants.