FERCAP 2024 Conference – November 24-27, 2024, Kathmandu, Nepal

Healthy volunteers in biomedical research deserve specific protection

François Bompart, MD on behalf of the VolREthics initiative

The VolREthics initiative
(Volunteers in Research and Ethics)

VolREthics initial objectives

- To document the ethical and scientific issues related with healthy volunteers around the world

- To build a repository of new insights and policy recommendations to safeguard the rights, well-being and safety of healthy volunteers globally

International Steering Committee

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Members

- Elisabeth Allen, University of Cape Town (South Africa)
- CK Chew, Institute for Clinical Research (Malaysia)
- Yves Donazzolo, Eurofins (France)
- Jill Fisher, University of North Carolina (USA)
- Benjamin Johnson, Nature Medicine (UK)
- Carleigh Krubiner, Wellcome Trust (UK)
- Sucheta B Kurundkar, Ministry of Science & Technology (India)
- François Hirsch, Inserm (France)
- Nandini Kumar, FERCI (India)
- Shadreck Mwale, University of West London (UK)
- Lorenzo Montrasio, Italian Antidiscrimination Office (Italy)
- Lembit Rägo, CIOMS (Switzerland)
- Doris Schroeder, University of Central Lancashire (UK)
- Esperança Sevene Eduardo Mondlane University (Mozambique)

Observers: Council Of Europe (Laurence Lwoff), ERCEA(Filipa Ferraz-de-Oliveira), EUREC (Dirk Lanzerath), European Commission (Lisa Diependaele), EDCTP (Montserrat Blasquez), UNESCO (Dafna Feinholz), WHO (Katherine Littler).

Secretary : François Bompart, Inserm Ethics Committee (France) & Drugs for Neglected Disease initiative (Switzerland)

VolREthics key meetings

- **First plenary meeting :** February 15-16, 2022, Virtual & UNESCO, Paris, France

- **Regional virtual meetings**
  - **Africa:** May 24, 2022
  - **Asia:** September 23, 2022
  - **North America:** October 19, 2022
  - **Latin America:** December 12, 2022
  - **Europe:** January 27, 2023

- **Second plenary meeting :** April 24-25, 2023, in-person, European Commission premises, Brussels, Belgium
- **Third plenary meeting:** April 18-19, 2024, in-person, Académie Nationale de Médecine, Paris, France

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Key ethical issues related with healthy volunteers

Declaration of Helsinki, CIOMS and GCP guidelines

Focus on patients, no specific provisions for healthy volunteers

- **Good Clinical Practice**, ICH guidelines reference E6

- **Council for International Organizations of Medical Sciences (CIOMS)** International ethical guidelines for health-related research involving humans (2016).

- **Declaration of Helsinki** World Medical Association's Declaration of Helsinki.

Revised 2024 version states, for the first time since 1964, that **its provisions apply to all research participants "whether patients or healthy volunteers"** (paragraph 2).

However, no guidance on specific provisions for healthy volunteers provided in other paragraphs.

Clinicaltrials.gov database (January 2022)

At least 13,000 interventional studies (drugs, devices, or biologics) include the « healthy volunteer » key word

Of which approximately 85% are not « First-in-Man » Phase I studies but mostly pharmacokinetic studies

Roughly

- 50% in the Americas
- 20% in Europe
- 15% in Asia
- 8% in Africa and Middle-East

Limitations of this work

- Limitations of databases in terms of data accuracy, consistency, completeness, duplication, etc
- Databases not designed to be used for research purposes e.g. to give combined information on numbers of patients, volunteers, etc.

VolREthics focuses on specific « healthy volunteers » (1)

We focus on **interventional clinical trials with medicinal products where there is no potential direct health benefit for the individuals involved**, because these studies expose healthy volunteers to the highest risks of

- **Being harmed**
- **Being exploited** through repeat participation to “commercial trials”
- **Having their well-being affected** by strict study conditions.

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VolREthics focuses on specific « healthy volunteers » (2)

We exclude from our scope studies where the risks to healthy volunteers are less pronounced, e.g.

- Interventional studies in which participants can reasonably hope for health benefits, such as preventive vaccine clinical trials

- Non-interventional studies, human and social sciences studies, etc.

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Heathy volunteers vs. patients

- They are healthy : no expectation of direct health benefit, different benefit/risk balance from patients

- 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

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Towards Ethical Guidance to Protect Healthy Volunteers in Biomedical Research

The Global Ethics Charter for the Protection of Healthy Volunteers in Clinical Trials

June, 2024

RÉPUBLIQUE FRANÇAISE
Liberté
Égalité
Fraternité

Inserm
La science pour la santé
From science to health

Ethics Charter – Structure

- **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*

- **Articles : the healthy volunteers' 15 rights in clinical trials**
  - Part 1: Laying the foundation to protect healthy volunteers
  - Part 2: Protecting healthy volunteers from harm
  - Part 3: Protecting healthy volunteers from exploitation

- **Conclusion**

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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.

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The Charter is available in several languages

September 2024

- English
- French
- Portuguese
- Spanish
- Italian

Soon to come : Bengali, Chinese, Hindi, Arabic

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Why is so little attention paid to healthy volunteers ?

- Because, unlike patients, healthy volunteers are **not organized to get their voices heard**

- Because **few severe accidents** are reported (Northwick Park (UK) 2006 : 6 volunteers developed severe multi-organ failures. Biotrial (France) 2016: 1 death, 5 irreversible brain damages and mental handicaps)

- Because **we lack data** on the realities of healthy volunteers' involvement in research

- Because **the current system meets the needs of many stakeholders**
  - Healthy volunteers (payments)
  - Contract Research Organisations (profitable business)
  - Pharmaceutical companies (data needed for science and for registration of pharmaceuticals)
  - Regulatory agencies (data needed for registration of pharmaceuticals)

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Conclusion: the role of ERCs

Most healthy volunteers who participate to research are socio-financially vulnerable. Ethics Research Committees play a critical role to protect them from

- Being harmed. Administering a pharmaceutical compound, even a well-known one, to a healthy person always carries some level of risk
- Being exploited when in situations of vulnerability
- Being affected in their well-being

A few countries, notably Malaysia in the region, lead the way for better protection of healthy volunteers

For more information

https://www.inserm.fr/en/ethics/volrethics/

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