EUFEMED-Healixia Conference,
May 21-23, 2025. Mechelen, Belgium.

VolREthics
Protecting and empowering
healthy volunteers

Which populations should be included in phase 1 clinical trials?

Ethical perspective

François Bompart, MD, on behalf of the VolREthics initiative

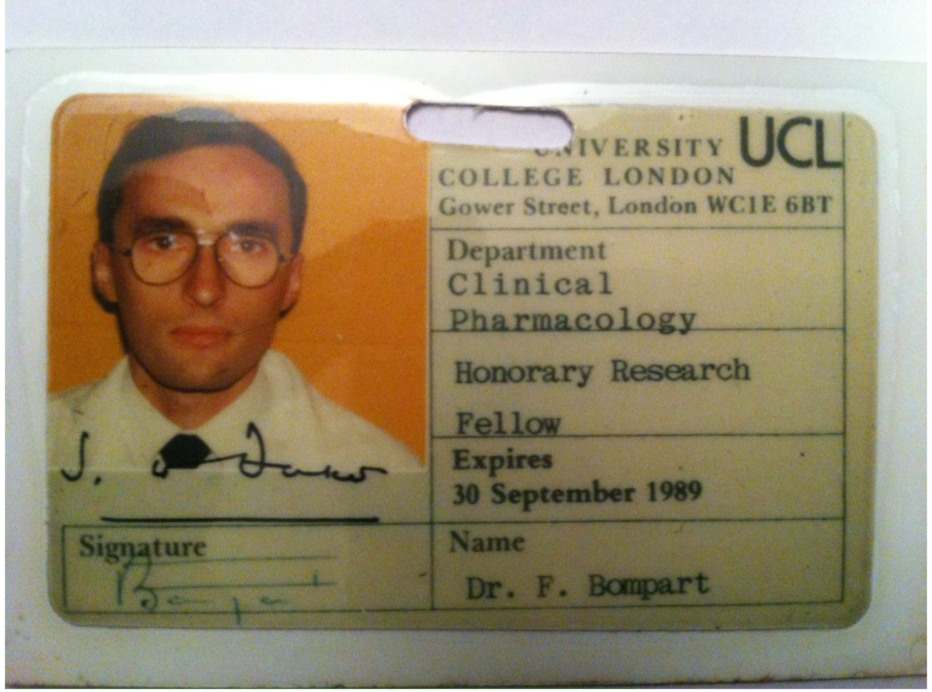
Disclaimer / Background experience

Disclaimer

Former Sanofi employee.
Since 2018, no direct or indirect link with for-profit organizations

Clinical studies with healthy volunteers

- Early 1980s: junior investigator / healthy volunteer
- Late 1980s: investigator
- 1990s-2021: study sponsor



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The VolREthics initiative
(Volunteers in Research and Ethics)

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UNESCO
Organisation des Nations Unies pour l'éducation, la science et la culture
sous le patronage de la Commission nationale française pour l'UNESCO

DNDi
Drugs for Neglected Diseases *initiative*

EDCTP

anrs
MALADIES INFECTIEUSES ÉMERGENTES Inserm

CNCP CONFÉRENCES NATIONALE DES COMITÉS DE PROTECTION DES PERSONNES

ccne
COMITÉ CONSULTATIF NATIONAL D'ÉTHIQUE
POUR LES SCIENCES DE LA VIE ET DE LA SANTÉ

IReSP
Institut pour la Recherche en Santé Publique

THE CONVERSATION

CIOMS

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VolREthics initial objectives (2022)

- 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

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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, KLE Academy of Higher Education & Research (**India**)
- François Hirsch, Inserm (**France**)
- Nandini Kumar, Forum for Ethics Review Committees in India, FERCI (**India**)
- Shadreck Mwale, University of West London (**UK**)
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- Doris Schroeder, University of Central Lancashire (**UK**)
- Esperança Sevene, Eduardo Mondlane University (**Mozambique**)
- Craig Tipple, Drugs for Neglected Disease initiative (**Switzerland**)

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

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

VolREthics definition of « healthy volunteers »

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.

How are healthy volunteers protected among “research participants” ?

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Declaration of Helsinki, CIOMS and GCP guidelines

- **Good Clinical Practice**, ICH guidelines reference E6. *“trial participants”*

- **Council for International Organizations of Medical Sciences (CIOMS)** International ethical guidelines for health-related research involving humans (2016). *“human beings”, “research participants”, “human subjects”*

- **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).

BUT: all focus on **patients** involved in research. Healthy volunteers’ specific protection needs not addressed

Very few countries have specific laws and regulations for healthy volunteers

National registries to ensure respect of wash-out periods between trials:

1. **France 1988,** Volontaires Recherche Médicale (VRB)
2. **UK 2013,** The Over-volunteering Prevention System (TOPS)
3. **Malaysia 2021,** National Healthy Research Volunteer Register (NHRVR)
4. **Morocco** work in progress

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Why are healthy volunteers a blind spot in biomedical research ethics ?

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Little attention paid to healthy volunteers

Unlike patients, healthy volunteers are not organized to get their voices heard

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

Lack of data on the realities of healthy volunteers' involvement in research

Current system meets the needs of most 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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Why does this matter ?

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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

Why does this matter?

- **Globally, many healthy volunteers belong to economically disadvantaged groups**

- **Countries differ widely in available protection** (risk of over participation, insurance, sites accreditation, etc.)

- **Reputational risks for all stakeholders**

We need an even global playing field for studies involving healthy volunteers

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

June, 2024

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60 ans Inserm
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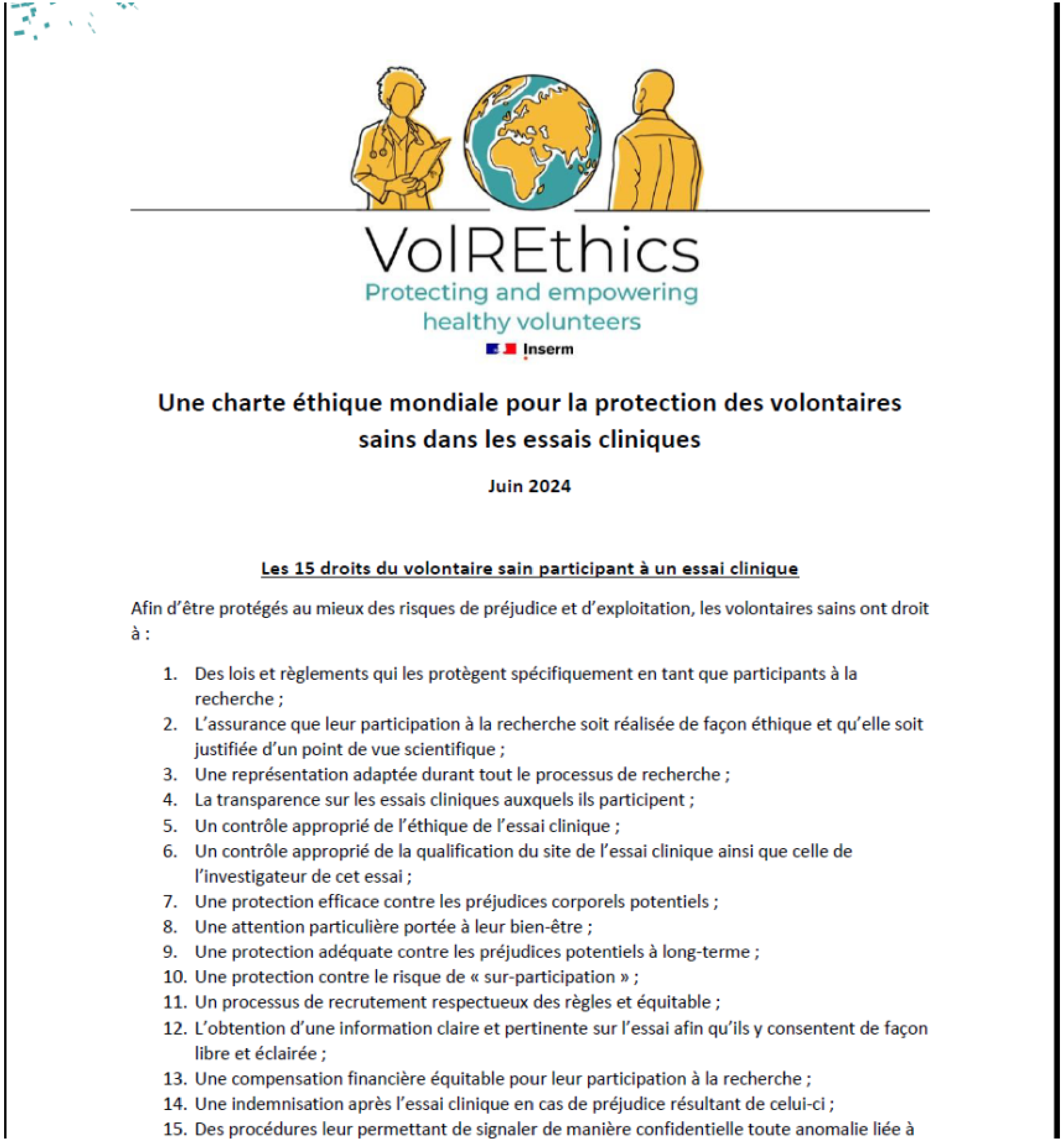

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Une charte éthique mondiale pour la protection des volontaires sains dans les essais cliniques

Juin 2024

Les 15 droits du volontaire sain participant à un essai clinique

Afin d'être protégés au mieux des risques de préjudice et d'exploitation, les volontaires sains ont droit à :

1. Des lois et règlements qui les protègent spécifiquement en tant que participants à la recherche ;
2. L'assurance que leur participation à la recherche soit réalisée de façon éthique et qu'elle soit justifiée d'un point de vue scientifique ;
3. Une représentation adaptée durant tout le processus de recherche ;
4. La transparence sur les essais cliniques auxquels ils participent ;
5. Un contrôle approprié de l'éthique de l'essai clinique ;
6. Un contrôle approprié de la qualification du site de l'essai clinique ainsi que celle de l'investigateur de cet essai ;
7. Une protection efficace contre les préjudices corporels potentiels ;
8. Une attention particulière portée à leur bien-être ;
9. Une protection adéquate contre les préjudices potentiels à long-terme ;
10. Une protection contre le risque de « sur-participation » ;
11. Un processus de recrutement respectueux des règles et équitable ;
12. L'obtention d'une information claire et pertinente sur l'essai afin qu'ils y consentent de façon libre et éclairée ;
13. Une compensation financière équitable pour leur participation à la recherche ;
14. Une indemnisation après l'essai clinique en cas de préjudice résultant de celui-ci ;
15. Des procédures leur permettant de signaler de manière confidentielle toute anomalie liée à

Available in

- Arabic
- English
- Chinese
- French
- Hindi
- Italian
- Malay
- Portuguese
- Spanish

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 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

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VolREthics Association

Work in progress, under French “1901 law”

Cross-membership with EUFEMED

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

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