



# ETHICAL CHALLENGES IN RECRUITMENT FOR PHASE 1 TRIALS

Dr Yves DONAZZOLO, MD, MSc

#### **EUROFINS OPTIMED**

1, rue des Essarts 38610 GIERES FRANCE





#### The VolREthics initiative



- VolREthics = Volunteers in Research and Ethics
- A French Inserm initiative set up in 2022 on ethical issues related to the participation of healthy volunteers in biomedical research all over the world
- This initiative is now supported by numerous international partners incl. UNESCO
- EUFEMED participation in VolREthics initiative: mission to promote the interest of early clinical development, develop standards and guidance documents...





# **History of Ethical perception of clinical trials**

Often new legal requirements follow accidents or dramatic events

- 1937: Elixir sulfanilamide case leading to the « Food, Drug & Cosmetic Act »
   (1938): animal testing and FDA authorization required before marketing a new drug
- Code of Nuremberg 1947-1949 : voluntary consent of participants, protection of subjects, qualification of staff...
- 1960's: Thalidomide case: preclinical research and pharmacovigilance





## **History of Ethical perception of clinical trials**

- 1932 1972: Tuskegee Syphilis Experiment: 600 African American men enrolled without free informed consent and without treatment even after 1943 to follow the natural history of syphilis
- 1979: Belmont Report (USA):
  - respect for persons, informed consent
  - benefit: maximazing benefits for the project, minimazing risks for the participant
  - justice considerations
  - foundation of the Office for Human Research Protection





## In summary:

Are the essential principles still guaranteed all over the world to protect the rights and well-being of healthy volunteers and to ensure that the knowledge gained from clinical research is reliable and beneficial to society?





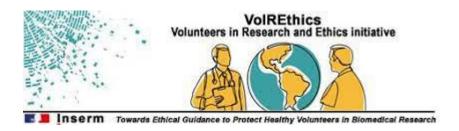
## A new perception of risks

- Absence of risk is an illusion
- Acceptance of an intrinsic element of uncertainty : « Level of uncertainty »
- Adaptation of the rules to mitigate the risk (guideline EMA 2017-2018)





#### The VolREthics initiative



- Healthy volunteers should be recognized as a specific "vulnerable group that should receive specifically considered protection" all over the world
- To lead the sharing and discussion of practices at international level, so that each country can decide on the best way to protect its healthy volunteers
- To issue recommendations to ensure respect for the rights, wellbeing, and safety of healthy volunteers in biomedical research.

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





### **SEVERAL REGIONAL MEETINGS:** some findings

- Economic and educational vulnerability of participants
- Undue inducement : a situation of significant vulnerability creates the conditions for potential coercion and exploitation
- Food as compensation
- Healthcare access as a motivation
- Sometimes need for
  - acts of legislation
  - independent ECs
  - national guidelines for fair compensation
  - conditions for confinement/well-being
  - Ensure protocols align with ethical standards
  - Higher education/training for research teams





## **SEVERAL REGIONAL MEETINGS:** some findings

- Disproportionate number of minoritized participants in phase 1 or Bioequivalence Trials
- Mostly lower income, low education
- Many with a history of incarceration
- Many are immigrants without work permits
- Participants are punished for withdrawing consent
- Completion bonuses





#### **RISKS OF BEING EXPLOITED**

- Permitted means of recruitment of volunteers;
- Inability to freely decide to participate : economic vulnerability, literacy level, pressure from family, peers, lack of access to healthcare...;
- Insufficient or excessive financial compensation;
- Insufficient information on risks and benefits;
- Insufficient attention to well-being during the study;
- Insufficient information on right to withdraw





#### **RISKS OF BEING HARMED**

- Inability of IRBs and CA to assess quality of research, justification to involve HV, assessment of risks;
- Concealed participation in multiple projects;
- Legal standards for study personnel and study sites to ensure safety and well-being of participants;
- Insufficient insurance coverage;
- Risk of ethical dumping





# **SEVERAL REGIONAL MEETINGS:** Key points

- Healthy volunteers definition
- Volunteers motivations
- Registries to prevent over-volunteering
- Ways to Respect, Reduce, Refine and Replace healthy volunteers





#### CONCLUSION





- Geographical differences to be kept in mind
- Prevention of risk to be exploited
- Prevention of risk to be harmed
- May lead to a consensus to ensure respect for the rights, well-being, and safety of healthy volunteers in biomedical research.