Inserm

La science pour la santé
From science to health

Ethical implication of the enrollment of human healthy volunteers in biomedical research / outlook for an international workshop

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Inserm Ethics Committee

Inserm

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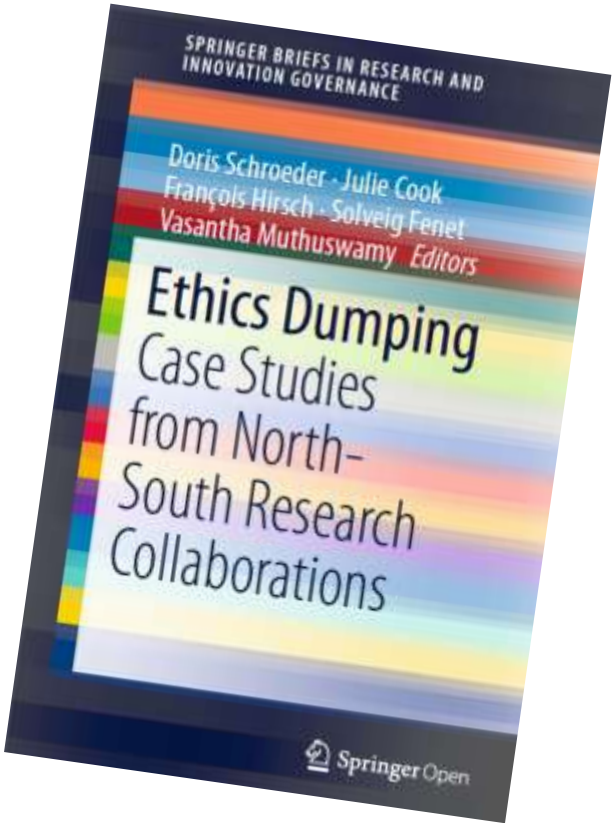
✓ **Why to address this issue?**

Creating and enhancing TRUSTworthy, responsible and equitable partnerships in international research
www.trust-project.eu

- **Our goal:** to catalyse a global collaborative effort to improve adherence to high ethical standards around the world, by proposing tools to the European Commission to avoid/limit ethics dumping.

- we first reviewed the current practices at global level



UK scientist undertakes invasive research on primates in Kenya, forbidden in UK; exploiting legislation gaps in Kenya

78-year-old Chinese woman suffers serious adverse effects after trial, in study of foreign pharma company: compensation for harm only obtained after lengthy legal trials

In open access:
https://www.springer.com/de/book/9783319647302

- we then proposed tools…

San Code of Research Ethics launched!

The 2nd of March 2017 was a historical day for the South African San Communities. They launched their own San Code of Research Ethics.

After decades of bad experience with researchers, TRUST supported the communities in drafting their own Code to avoid further ethics dumping.

THE CONVERSATION

The ethics of research: How to end the exploitation of vulnerable communities

HUFFPOST

San Council launches code of ethics for researchers

news24

San Council launches code of ethics for researchers

Mail&Guardian

San Council launches code of ethics for researchers

genomeweb

Code for Research

Fair Research Contracting
Optimising Global Health Innovation

FAIR RESEARCH CONTRACTING

FRC TOOLKIT

ABOUT THE TOOLKIT

http://frcweb.cohred.org/

TRUST

GLOBAL CODE OF CONDUCT FOR RESEARCH IN RESOURCE-POOR SETTINGS

FAIRNESS

RESPECT

HONESTY

CARE

http://www.globalcodeofconduct.org/

Reference documents

Rules & codes of conduct

- Legal basis - Horizon 2020 Rules for Participation: Ethics Reviews (Article 14)
- Horizon 2020 - Regulation of Establishment: Ethical principles (Article 19)
- Model Grant Agreement: Ethics (Article 34)
- Statements by the Commission on human embryonic stem cell research
- Guide for proposal submission and evaluation
- Charter of Fundamental Rights of the European Union
- European Code of Conduct for Research Integrity
- Global code of conduct for research in resource-poor settings

General guidance

- How to complete your ethics self-assessment

Domain-specific guidance

- Guidance note – Research involving dual use items
- Guidance note – Potential misuse of research results
- Guidance note – Research focusing exclusively on civil applications
- Guidance note – Research on refugees, asylum seekers & migrants
- Ethics and data protection
- Ethics in "Science with and for society"
- Ethics in Social Science and Humanities

EDCTP

Home | Calls for Proposals | Funded Projects | Prizes | Forum | Get to know us | How we work

Calls for proposals | FAQs on Calls | Guidance | Expert reviewers | Observers

Templates **Guidelines** **Budget** **Legal** **Questions**

Guidelines for application

EDCTP guides

- EDCTP2 Grants Manual for EDCTP2 Calls for proposals
- Preparation of full proposals and annex 1 of the grant agreement (PDF)
- Guidance for applicants for the **online application** procedure
- EDCTP2 policy on clinical trials registration, publication and data sharing (PDF)
- EDCTP2's strategic research agenda

Reference documents

- International Council on Harmonisation – Good Clinical Practice (ICH-GCP)
- Global Code of Conduct for Research in Resource-Poor Settings (PDF)

POLICY BRIEF

Healthy Volunteers in clinical research: making participation safe, fair and transparent

Key Messages

- Every year tens of thousands of healthy volunteers are involved in clinical trials in a wide variety of countries.
- In Low & Middle Income Countries, healthy volunteers are often disadvantaged individuals with low literacy levels who may be coerced to undergo clinical procedures offered.
- The emergence of the "professional volunteer" phenomenon - volunteers who repeatedly participate in clinical trials for financial gain - is a serious challenge.
- "Professional volunteers" may expose themselves to serious medical risks and not communicate the validity of the screening results of the trials.

Recommendations

National Healthy Volunteer Registries can significantly reduce risks for healthy volunteers by monitoring repeated involvement of healthy volunteers in clinical trials.

A harmonized case scheme for financial incentives is a standardized conservative model for participation in clinical trials and provides additional protection.

✓ who are the volunteers (1)

* *Volunteers testing new drugs in Clinical Trials*, e.g.

first-in-humans administration to evaluate tolerance, action on human metabolism, pharmacokinetics, dosage and side effects (Phase 1)

* *Volunteers offering biological samples as control in Clinical Trials*, e.g.

since 2008, Pasteur Institute hosts ICAReB biobank collecting various samples from ~300 healthy volunteers

* *Volunteers participating in cohorts for social science studies*, e.g.

behavioral studies in real-life setting (the Brain Institute (ICM) hosts the PRISME platform which lists ~2000 healthy volunteers available to help, for example, to develop technologies for real life analysis of behaviors in various settings (waiting room, confined environments, public spaces...),

social impact of living in refugees camps (MSF Epicentre follows cohorts of refugees in Ouganda from their arrival)

impact of the 2015 Paris terror attacks: '13-Novembercohort: A Study to Better Understand Traumatic Memory and Resilience'

✓ who are the volunteers (2)

Volunteers for vaccine development:

classical Phase 1 approach (HIV, Ebola, Covid-19…)

- ✓ **who are the volunteers (2)**

‘the Heroes of the pandemia’

IDÉES

Le Monde
VENDREDI 23 AVRIL 2021

« N'oublions pas les volontaires sains, ces héros discrets des pandémies »

Hervé Chneiweiss, *directeur de recherche au CNRS et président du comité d'éthique de l'Inserm;* **Hélène Espérou,** *responsable du pôle de recherche clinique de l'Inserm;* **François Hirsch,** *directeur de recherche honoraire de l'Inserm, membre du comité d'Ethique de l'Inserm;* **Odile Launay,** *professeure en maladies infectieuses à l'Université de Paris, coordinatrice du réseau francais de recherche*

✓ who are the volunteers (2)

Volunteers for vaccine development:

classical approach (HIV, Ebola, Covid-19),

Human challenge trials (Shigella dysenteriae, malaria, flue, dengue)

- ✓ **why to be a volunteer:**

  their activities are close to the research domain, e.g. students in the field of health

  people experiencing the disease of a loved one

  pure altruism ‘to help Science to develop’

  financial motivation

  access to basic health care

✓ is it risky to be a volunteer?

June 2001, study on asthma at John Hopkins University, the volunteer died from lung failure.

March 2006, the German company TeGenero proposed to evaluate the tolerance of an antibody to fight diseases such as rheumatoid arthritis, certain leukemias or multiple sclerosis: six healthy volunteers recruited in UK developed severe multi-organs failures.

January 2016, the Portuguese company Bial proposed to test a molecule supposed to relieve pain and anxiety: among the 128 healthy volunteers recruited in France, on the fifth day of the administration of a daily dose of the candidate-drug, one died and five suffered irreversible brain damage and mental handicaps.

✓ is it risky to be a volunteer (2)

GULF | MENA | ASIA | AFRICA | UK | EUROPE | US | THE AMERICAS | OCEANIA

Thousands of Indians die in unethical clinical trials

► 'We can't treat Indians as guinea pigs,' head of Indian Society for Clinical Research

Samanth Subramanian
The National News
September 17, 2018

Tenofovir trials on HIV transmission

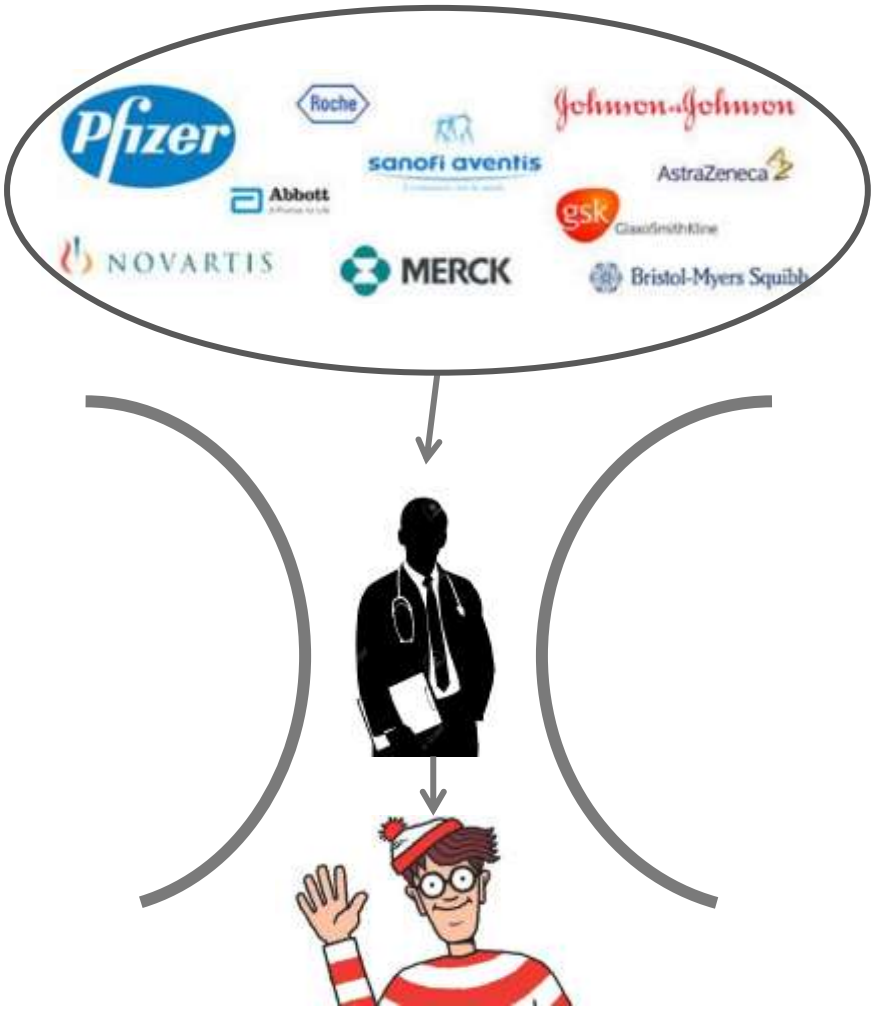
Drugs:	Tenofovir (Viread)
Treatment:	Prevention of HIV transmission
Sponsors:	Gilead, US CDC, Bill and Melinda Gates Foundation
Research organization:	Family Health International (FHI) in Africa, US NIH in Cambodia
Period:	2004 – 2005
Location:	Cameroon, Thailand, Nigeria

Unethical aspects:
In Cameroon five women became HIV-infected while enrolled in the Tenofir-study. Non-governmental organisations (NGOs) claim the 400 sex workers participating in the trial were not adequately informed about the risks and only English information was given to mostly French speaking volunteers. There was a lack of ARVs for patients infected during the trial.

SOMO briefing paper on ethics in clinical trials
#1: Examples of unethical trials
February 2008 (updated)
Centre for Research on Multinational Corporations, NL

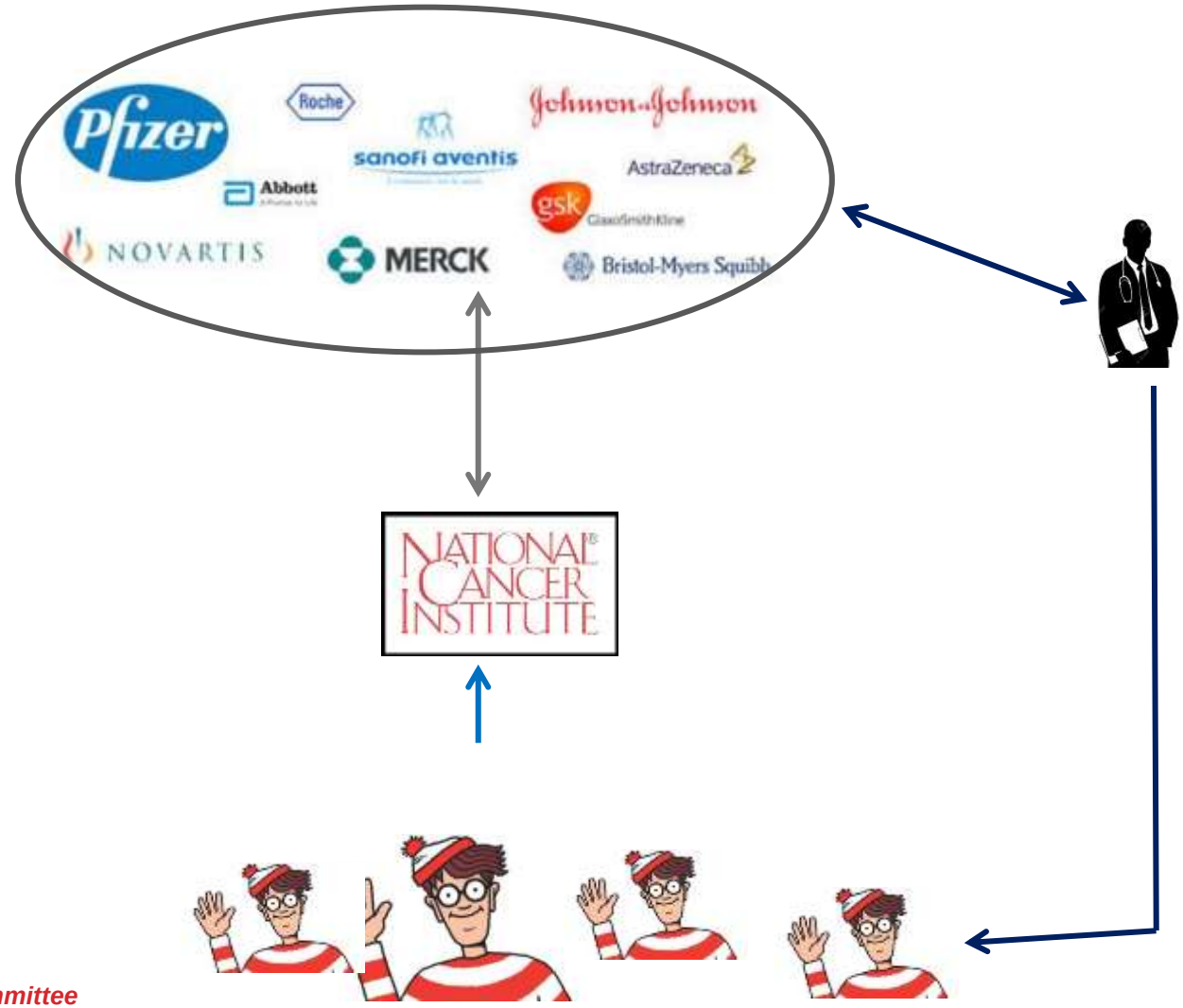
another potential risk:
the new ways of enrolling volunteers

✓ « classical » recruitment



Dr F. Eisinger, Inserm ethics committee

✓ new recruitment



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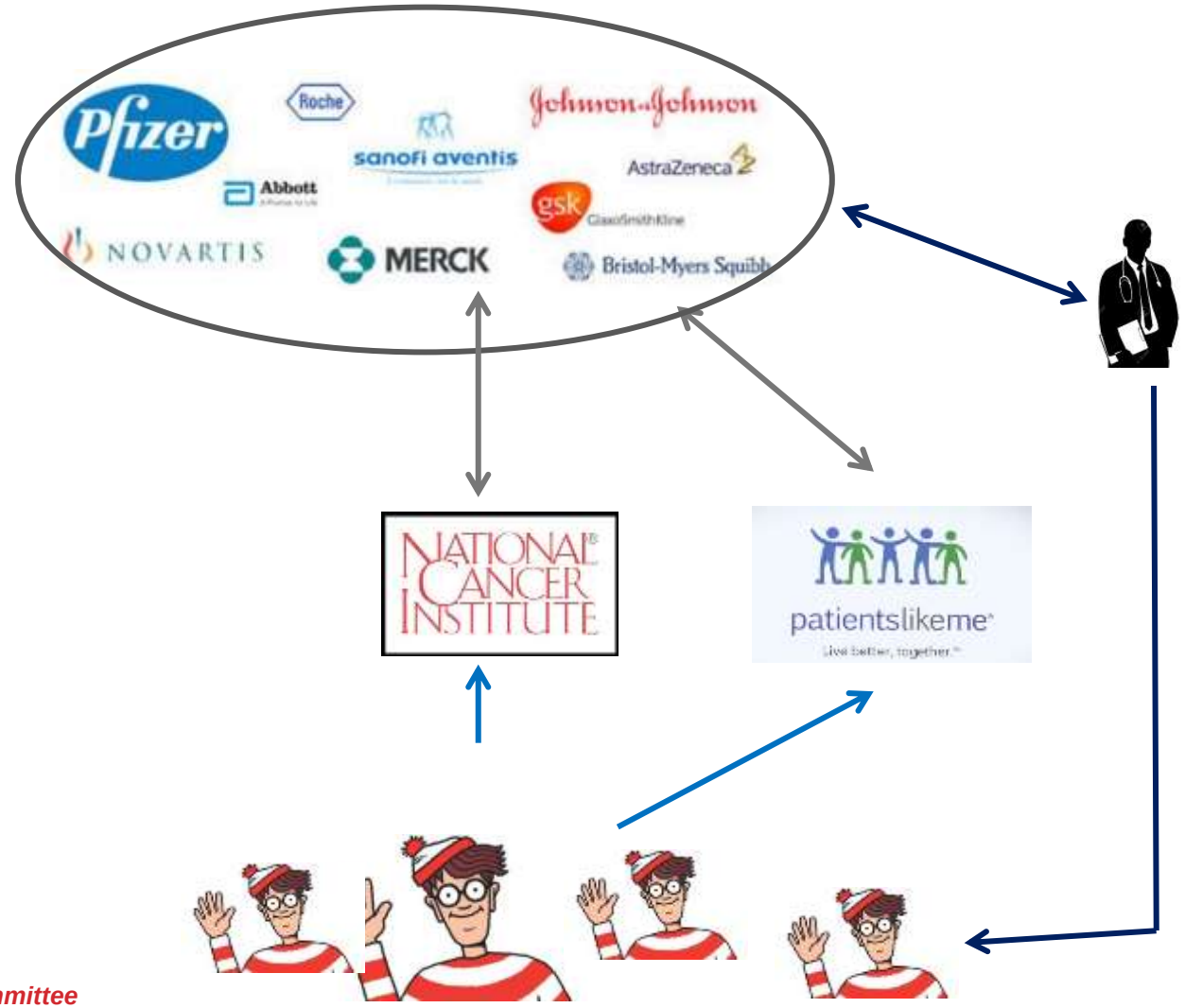

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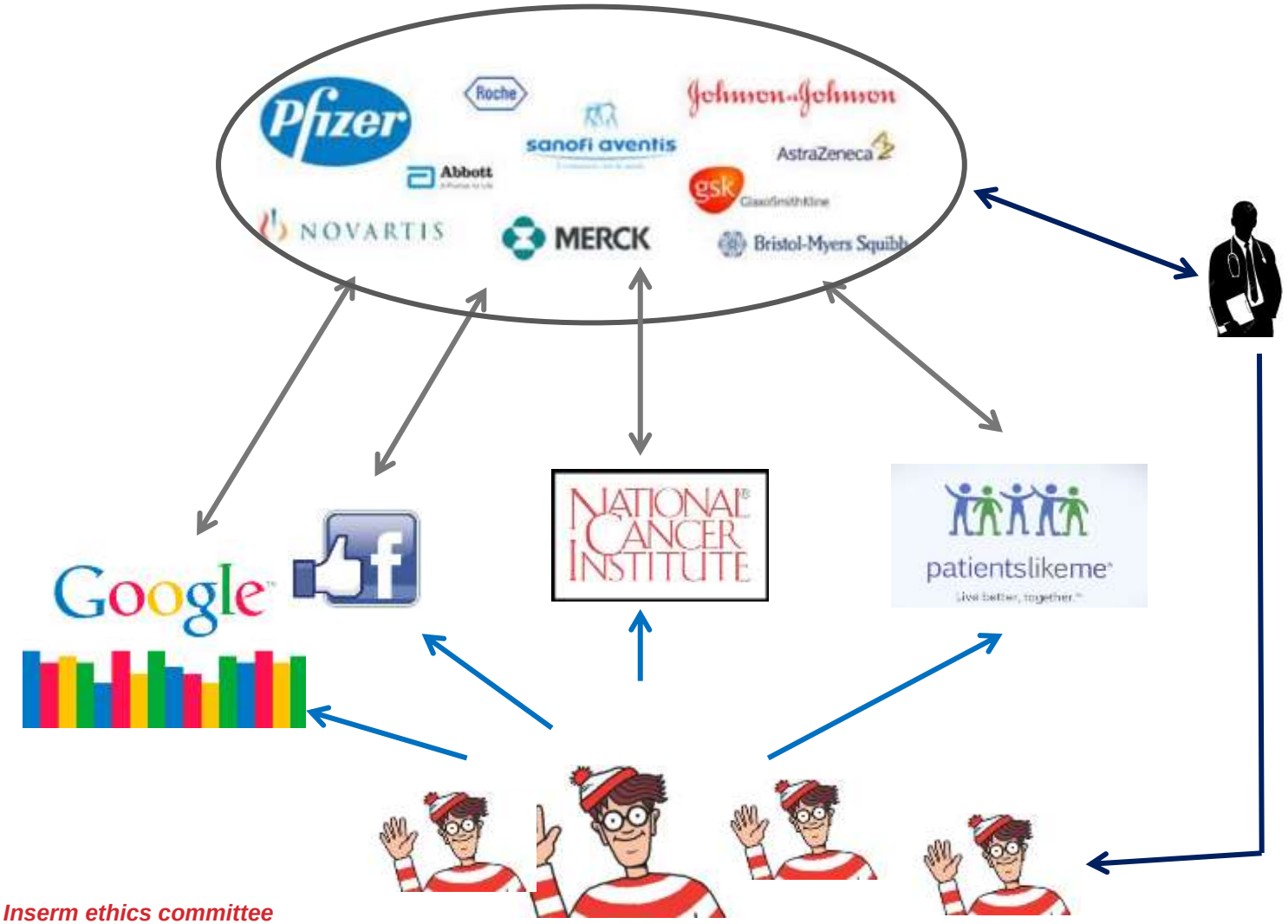

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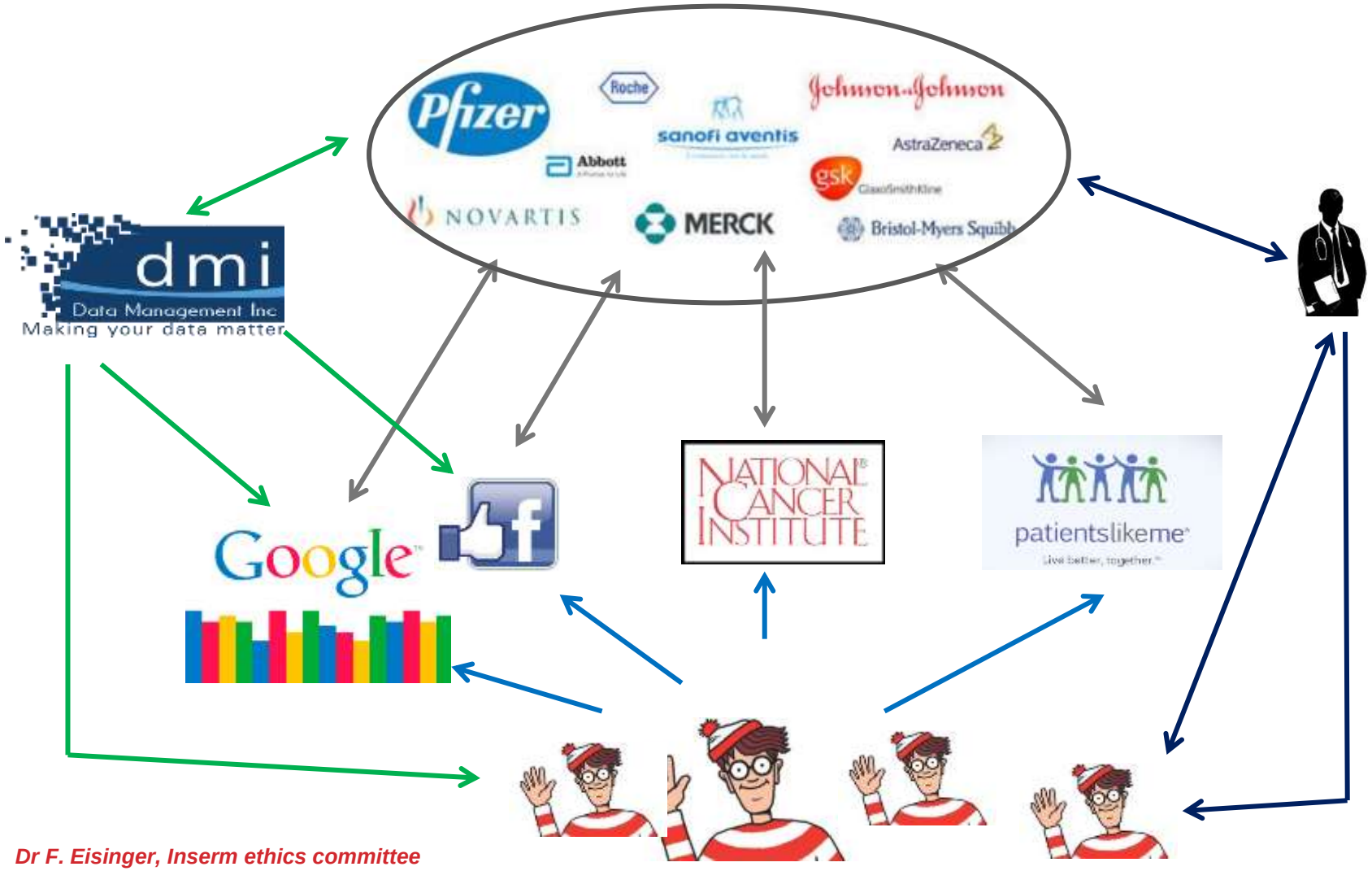

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✓ new recruitment: our conclusions

- Allows faster recruitment for more patients

✓ new recruitment: our conclusions

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Vulnerable populations may be induced to participate through misleading messages

✓ new recruitment: our conclusions

Allows faster recruitment for more patients

Vulnerable populations may be induced to participate through misleading messages

→ Need for better control of the messages

→ Need for better oversight of the CoI

- ✓ several questions to be discussed:

  Should we name these research participants ‘healthy volunteers’ or ‘healthy participants’ ?

  Should it be allowed to recruit participants who are in a context of vulnerability or should all clinical studies be condemned when the context of vulnerability is evident ?

  Is it necessary, prior to any clinical studies, to precisely assess the context of vulnerability and implement measures to reduce it? But who would be in a position to define the boundaries of vulnerability ?

  How to provide a true information to people in vulnerable condition ?

- ✓ our next steps:

Development of good practices guideline to assist investigators in the conduct of research involving healthy volunteers/participants.

Discussing the guideline during a 2-day workshop: ‘Toward good ethical practices to protect the healthy volunteers in biomedical research’

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Merci!!

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