

Vulnerability

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Vulnerability

- Definitions and lists
- Problems
- Possible solutions

Definitions

Declaration of Helsinki (DoH), Paragraph 9

‘Some research populations are particularly vulnerable and need special protection. These include...’

CIOMS, Commentary on Guideline 13

‘Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interest’

ICH-GCP (1.61) Vulnerable Subjects

‘Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate’

Lists

Declaration of Helsinki:

...These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.

US (Common Rule) 45 CFR 46:

- children, prisoners, pregnant women and foetuses

ICH-GCP:

- members of a group with hierarchical structure (medical students, hospital and laboratory personnel, employees in the pharmaceutical industry), unemployed or impoverished persons, ethnic minority group, homeless persons, nomads, refugees, minors

Problems

Definitions:

Incomplete: *incapacity to protect one's interests, susceptibility to coercion*

Lists:

Absence of an explicit organizing principle leads to confusion (pregnancy does not remove the capacity to consent for example)

Incompleteness, obsolescence, absurdity, labeling

General:

Lack of clarity as to what protection of vulnerable persons mean, potentially counterproductive effects.

Declaration of Helsinki

Paragraph 9

‘Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.’

Paragraph 16

The responsibility for the protection of research subjects must always rest with the physician or other health care professional and never the research subjects, even though they have given consent.

Inconsistent

Implicitly states – without justification- that vulnerability is inherently based on a deficit on the part of the vulnerable person.

Options

Dissolve: Vulnerability is a matter of degree. The same protections should apply. Although they will require greater effort, this does not require any *additional* principles.

Problem: invisibility, inappropriate uniformity in protocol design and REC review.

List: Attempt to devise a list of vulnerable groups or persons which adheres to an appropriate –and explicit- organizing principle.

Problem: ... incompleteness, obsolescence, absurdity, labeling

Instruct: provide clarification of vulnerability and the required protections.

Vulnerability

A greater likelihood of incurring a wrong in the context of research.
Any wrong. For any reason.

<i>Requirements</i>	<i>Examples of vulnerability</i>
Social or scientific value	<ul style="list-style-type: none"> • Lack of access to either benefit or knowledge derived from research
Scientific validity	<ul style="list-style-type: none"> • Rare disease, leading to difficulties in reaching statistical power to demonstrate therapeutic effectiveness
Fair subjects selection	<ul style="list-style-type: none"> • All persons likely to be victims of discrimination
Favorable risk-benefit ratio	<ul style="list-style-type: none"> • Potentially higher risks: unstable patients, emergency research, foetuses, pregnant women • Potentially lower benefits: subjects in phase I studies, terminally ill patients • Subjects whose risk-benefit ratio might sometimes be the object of lesser concern to those responsible for protection: terminally ill patients, disenfranchised persons, poor subjects in developing countries, subjects without access to health care outside of research.
Independent review	<ul style="list-style-type: none"> • All persons likely to be victims of discrimination, if those responsible for review share discriminatory views.
Informed consent	<ul style="list-style-type: none"> • Difficulties in receiving or understanding the relevant information: not knowing the language used, or how to read • Lack of decision-making capacity: some children, some patients with mental disorders, comatose patients. • Lack of freedom to make a voluntary choice <ul style="list-style-type: none"> ○ Through limited freedom: prisoners ○ Through social weakness: minorities, refugees, sometimes women ○ Through hierarchical weakness: lab employees, students
Respect for potential and enrolled subjects	<ul style="list-style-type: none"> • Health care providers, researchers and students close to the study team who are at increased risk of faulty confidentiality • Groups and communities at risk of stigmatisation in the interpretation of study results

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16. *Researchers' Ethical Obligations:*

16.0: Researchers have an obligation to implement the principles contained in the present declaration at all stages of research. This implies a duty to guarantee equal protection for vulnerable participants, whose health and rights are more difficult to protect.

Possible concerns

Virtually all studies will recruit vulnerable persons

This is not *per se* a problem, if the protections extended to them are appropriate.

We lose subsidiarity

Protection against being recruited in exploitative research is required for all

As is protection against non-existence of research targeting one's needs

Protection against sloppy protections is easier with clearer standards

We lose protections associated with REC structure

Protection against conflicts of interests in RECs should also apply to everyone.

Conclusion

- Don't list the vulnerable
- Provide a clear guidance: vulnerability is a matter of degree.
 - Protecting vulnerability *implies a duty to guarantee equal protection for vulnerable participants, whose health and rights are more difficult to protect*
- Stick to the general guidance: require a case by case specification but don't do it within the DoH.
- As far as vulnerability is concerned, scrap the rest: all other so-called protections of vulnerability should really apply to everyone.