JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 2, No. 8, August 2006 "Can You Handle the Truth?"

The Two Dimensions of Subject Vulnerability

By Norman M. Goldfarb

Informed consent requires a clinical research subject to freely agree to participate in a study based on an informed decision without undue influence or coercion. Special care must be taken with vulnerable persons. The requirements in Exhibit 1 do not limit vulnerable people to specific, defined categories; anyone can be vulnerable.

When obtaining informed consent from a potential study subject, an investigator must consider that specific person's vulnerability in two dimensions:

- Capability, i.e., the ability to understand the informed consent information and make a sound decision whether or not to participate
- Autonomy, i.e., the ability to resist undue influence and coercion

(Undue influence and coercion are related but somewhat different concepts: Undue influence is the inappropriate use of promise or threat by someone who is influential to persuade a person to do something. Coercion is unethically using the threat of harm or otherwise pressuring a person to do something.)

Not everyone has the same vulnerabilities, even in the same population. However, by looking at each vulnerable population in Chart 1 on the next page, we can identify the measures likely to be effective for people in that group (and similar groups) and how rigorously we should apply them. For example:

- A parent is more likely to resist coercion and undue influence when giving informed consent for his/her child than for himself/herself. On the other hand, he/she is inherently limited in his/her ability to make a decision for another person.
- A site employee should be relatively well-equipped to make an informed decision, but susceptible to undue influence and coercion by his/her employer.
- A depressed person may not have the energy and focus to make a complex decision, but may resist anything new.
- A comatose person is completely unable to give informed consent, but is also completely resistant to undue influence and coercion.
- A poorly-educated person may not have the skills to make decisions based on complex information. On the other hand, he/she may have high respect for educated persons such as physicians.

Exhibit 1. Vulnerable Subject Regulatory Examples

21 CFR 56.111(3) says that IRBs "should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons."

ICH E6 3.1.1 says that "an IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects."

If someone is in two (or more) vulnerable sub-populations, e.g., a critically-ill good Samaritan, we must take both vulnerabilities into consideration when obtaining informed consent.

Chart 1. Subject Vulnerability

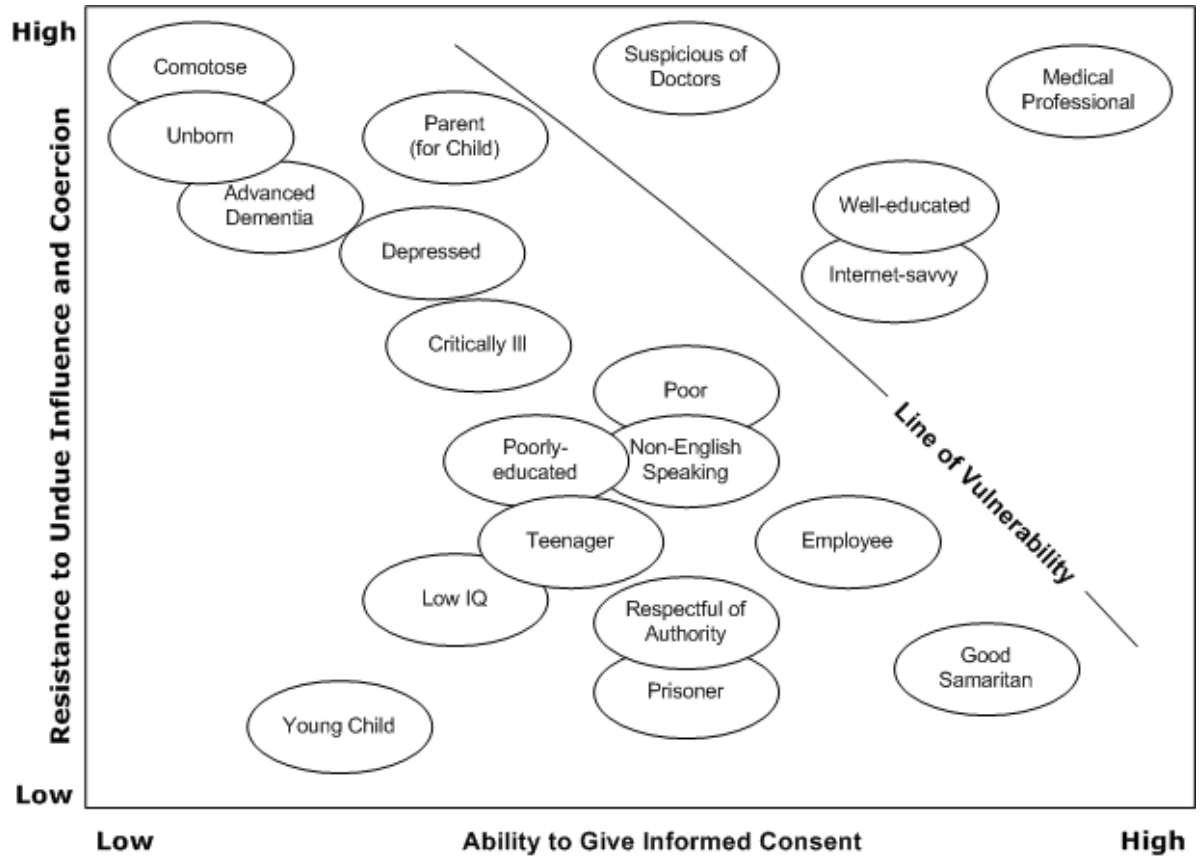

Chart 2 presents measures that can be taken to protect vulnerable populations.

Chart 2. Protection Measures

Measure	Increases Capability	Increases Autonomy
Write informed consent form in understandable language	+	+
Reduce stipend		+
Have person without pre-existing relationship obtain informed consent		+
Solicit & answer questions	+	+
Administer informed consent quiz and review misunderstandings	+	
Include family & friends in decision process	+	+
Allow 72-hour waiting period	+	+

Author

Norman M. Goldfarb is Managing Director of First Clinical Research LLC, a provider of clinical research best practices information, consulting and training services. Contact him at 1.650.465.0119 or ngoldfarb@firstclinical.com.

