Reviewer's report

Title: Consenting the Vulnerable: The Informed Consent in Advanced Cancer Patients in Mexico

Version: 4 Date: 22 November 2006

Reviewer: Neema Sofaer

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General
I would like to congratulate the authors on making such substantial and effective revisions. The discussion section in particular is a pleasure to read. The abstract and background is still unclear in places, and the language must be checked thoroughly. I have suggested quite a few minor revisions. These should be implemented. The points in red are the most important.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Abstract
Background
(1) “the enforcement of a valid Informed Consent”. This phrase is confusing, because one can’t enforce a consent. Do you mean the enforcement of a requirement that informed consent should be obtained or the provision of valid informed consent? Also: there is no need to capitalize “I” and “C”.

(2) “However, a valid procedure…”. Should be reworded as something like: “The procedure is valid only if the individual is competent to understand the risks and benefits of participating, actually understands them, and consents to participate.”

Methods
(1) Put a comma after ‘Mexico’.
(2) Switch “four steps” to “four-step”
(3) (1) should report a process. SE and educational level is not a process.
(4) switch “ten points” to “ten point”
(5) “no patient knew the IC was to protect their rights”.
   a. If you use the acronym “IC”, you must first define it.
   b. Incomplete sentence: I think you mean “no patient knew that a function of informed consent was to protect their rights”. “A function” is missing.
   c. For your information, that the primary rationale for the requirement of informed consent in the Nuremberg Code and most subsequent guidelines and regulation is to safeguard voluntary consent. The Nuremberg Code does not state that there is a right to voluntary consent. So I’m not quite sure why you asked the subjects whether they knew that the function of informed consent was to protect their rights.

Background
(1) The “thin line” metaphor is confusing. I think you mean that researchers are often faced with a dilemma: either they do the trial, in which case they exploit the participants or unduly induce them, or they don’t do it, in which case they don’t give the people the opportunity to participate, and either option is morally problematic. By the way, I think that the first horn of the dilemma - that research, if conducted, necessarily exploits or unduly induces participants - is false, so you may need to weaken your point and say simply that both conducting research and choosing not to conduct it can be morally problematic.
(2) The paragraph indentation should be consistent.
(3) Thank you for making the point that IC is considered necessary, but not sufficient, for research to be ethical. However, you still left in the question “What makes research…ethical?”. This is naturally understood as meaning “What has to happen for research to be ethical?” You then quote Emanuel as saying that researchers, bioethicists, and IRB members say that informed consent makes research ethical. He does not say this! What he does say is that informed consent is a necessary condition for research to be ethical. Please change the question, as it’s very misleading, even with the subsequent clarification.
Methods
Informed Consent Documents
(1) Define ‘CF’ before proceeding to use this acronym
(2) Switch “presence of language” to “use of language”
Enrolment into the clinical trials…
(1) “each and every one of the patients that read”. Switch “that” to “who”
(2) Put a full stop after “lengthy” and start a new sentence. The sentence is too long.
(3) “The most important reasons to accept enrolment”. Switch to “the reasons that were cited as the most important for enrolling in trials”.
(4) 7th paragraph: switch “cannot be giving” to “cannot be given”
(5) I don’t understand the meaning of “--among others--”. Do you mean that members of vulnerable populations are not the only persons who, according to O’Neill, cannot give IC? The grammar is unclear.
(6) Third paragraph from the end ends with two full stops (‘.’)

Conclusions
(1) The conclusion should not include substantially new information. The practical recommendations should therefore be made before the conclusion. You should footnote the Flory article when you give this recommendation. (I see that you’ve footnoted it elsewhere.)

Discretionary Revisions (which the author can choose to ignore)

Thank you for adding the different rationales for IC in the Background. You may like to put this information in a footnote. My main concern was that you should not simply assume that IC has one rationale. I no longer have this concern.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

As before. I write on the ethics of research on human subjects. I am also working on an NIH-funded research project on the experiences of participants in clinical trials. My focus is compensation and post-trial access, not informed consent.