Reviewer's report

Title: Approaches to Informed Consent for Hypothesis-Testing and Hypothesis-Generating Clinical Genomics Research

Version: 1 Date: 6 March 2012

Reviewer: Anne-Marie Tassé

Reviewer's report:

1. Does the debate present a novel argument, or a novel insight into existing work?

Yes, this debate is helpful in exploring a different approach to consent, based on the goal of the research rather than on the research setting. It is a novel way to move the debate forward at both a theoretical and a practical level. This gives rise to certain questions which the article would benefit from addressing. I suggest these are Minor Essential Revisions:

- Since consent nomenclature is already extensive and confusing (implicit, implied, informed, broad, generic, blanket, bridging, etc.), will this paper clarify or complicate the debate?

- Has the authors considered the professional liability related to their new approach? Since the information is available, what if the researcher does not look at the “problematic part” of the genome? What if there is no specific test available in CLIA-certified laboratories?

- Regarding the return of results, which results will be returned to participants? Will negative results be returned? It is also mentioned that only clinically significant results will be returned. Will these results be returned even if not actionable?

- Has the authors considered the feasibility of their new approach? Since genetic research often requires large cohorts (ex. populational studies) and longitudinal studies, is it realistic to expect individual re-contact and re-consent, and individual genetic counseling? Has the authors considered the additional cost of re-testing in CLIA-certified laboratories, individual re-contact and re-consent, and individual genetic counseling?

2. Does the debate address an important problem of interest to a broad biomedical audience?

Yes, consent is a fundamental issue in biomedical research.

3. Is the piece well argued and referenced?

Yes, the piece is well argued but some references are missing (ex. p.18)

4. Has the author used logical arguments and sound reasoning?
Yes.

5. Is the piece written well enough for publication?
Yes.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests