Reviewer’s report

Title: Use of Next Generation Sequencing Technologies in Research and Beyond: are participants with mental health disorders fully protected?

Version: 3 Date: 11 May 2012

Reviewer: Annelien L. Bredenoord

Reviewer’s report:

In this paper the authors review the use of NGS technology for mental disorders. Next to the ‘general’ ethical issues raised by the emergence of NGS technology, applying these techniques in the field of mental disorders raises some additional issues in view of the vulnerability of the target group. The authors provide a useful overview of the main ethical issues, but I think the manuscript could substantially improve when the authors would focus on and explain what makes the use of NGS technology in the context of mental disorders ethically different.

Major compulsory revision
- As said above, I think this manuscript could be greatly improved when the authors would focus on what they promise to be the subject of this review: NGS for mental disorders. What are the specific challenges of NGS for this group of participants/patients? In the current version the authors give a too general discussion of the ELSI aspects of NGS technology (which has already been done elsewhere). An explanation of the specific challenges for this group would be the real added value of this manuscript. For example, participants with bipolar disorders are usually considered vulnerable. There has been debate on who should be considered ‘vulnerable’ in research and for what reason, but the potential diminished capacity to consent and the context of being for example institutionalized are generally considered as inferring a need for special protection in medical research. Psychiatric patients are considered to be “cognitively vulnerable” – there is plenty of literature demonstrating that “mental incapacity to make decisions on treatment is common in people admitted to psychiatric wards”, This is a theme the authors could further explore. I enclosed one of our papers (van der Baan et al, in press) that discusses consent in psychiatric biobanks – the topic and references may be useful.

Minor essential revisions
- In each paragraph, the authors discuss a relevant issue but the different paragraphs are lacking some focus –it’s a bit of a blur of information. For example, the Consent paragraph provides the reader with a large amount of information not only related to consent (for example on data sharing and confidentiality). Why do you not discuss those issues in a separate paragraph? In addition, it remains unclear what exactly is the main ethical challenge of Consent in NGS for BD. What makes consent issues in BD research different from other NGS studies? A short summary finalizing each paragraph may be helpful here.
- Throughout the manuscript it is sometimes not clear whether the authors give an overview of the debate or whether they express their own opinion.

- Regarding the methods: could the authors give a motivation / explain how they came to selection of those 6 issues and why they chose to focus on NGS for BD in particular?

- The genetic background information is useful but quite extensive – perhaps too extensive for an ethics journal?

- Please check the entire text for typos and incorrect sentences.

Under Consent
- “Clear understanding….stigmatization”: what do the authors mean with ‘reducing pre-conception’?
- What is the TCPS 2nd Edition? Please explain the abbreviation.

Feedback, Return of results and Incidental Findings
- The authors mention that return of results could distort the aim of the research by generating therapeutic misconception, but I think an ethically more salient aspect of the therapeutic misconception is that people become research participant for the wrong reason and that they do not take autonomous, informed decisions. Could the authors comment on that?
- In most countries REB is not a well-known abbreviation.
- In this paragraph the authors do not clarify what’s new or specific for feedback in the context of BP disorders.

Clinically relevant ethical challenges
- Also in this paragraph, the authors give a too general discussion of NGS. Again, I would suggest they focus on NGS for BP disorders.
- The authors mix several types of genetic testing, e.g. prenatal, postnatal, adult. These different timings however evoke different ethical questions. I think the authors should concentrate on one of these, and that will most likely be NGS for adults.

**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, the manuscript does not need to be seen by a statistician.