Reviewer’s report

Title: The Best Interests of the Child and the Return of Research Results: International Comparative Perspectives

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Reviewer: Lainie Ross

Reviewer’s report:

The authors have written an interesting manuscript about the best interest of the child and its application to the return of research results. The manuscript is divided into international norms and national norms.

The authors note that there is very little guidance about the return of research results to children. They then discuss international norms that define and provide criteria about the best interest of the child by examining the rights of children in various international documents. I do not see how they extrapolate from these rights to any of their claims about what these rights say about best interest in the context of returning research results. In contrast, some of the national norms do discuss the best interest of children and the return of research results and this part is much easier to follow. Below I provide specific concerns that need to be addressed.

- Major Compulsory Revisions

1) p. 3 “After many years of exclusion”… What is this referring to? Exclusion from research? Actually, even before there were guidelines, children have participated in research for 100s of years (look at the history of vaccine research). Also see Lederer and Grodin, “Historical Overview: Pediatric experimentation.” In: Grodin and Glantz (eds.), Children as Research Subjects: Science Ethics and Law., Or is the exclusion from guidelines. Please clarify.

2) p. 3: The UNESCO Human rights is about the “results of genetic examination.” This whole manuscript seems to conflate genetic testing in the clinical setting and genetic testing in the research setting. It is not clear to me that the two are equivalent. You will need to argue why this is the case.

3) p. 3 the CRC: the highest attainable standard of health. There are a few cases where research did offer the highest attainable standard of health (early days of AZT for HIV), but in general, research does not necessarily offer the highest attainable standard and it is not clear that the CRC is meant to be applied to research. Can you please show why it should apply in the research setting.

In fact, all of the international documents except OECD Guidelines for Human Biobanks and Genetic Research Databases and Council on Europe’s “Additional protocol on biomedical research” focus on clinical care. What is the justification of
extrapolating to research context? The manuscript seems to be on better footing in the laws of each European country (pp 11ff) which focuses on research context.

4) On page 6, you write,” but this should go without saying”. Actually, inferring an idea when it is not stated may not be accurate as the rules may differ between clinical care and research. I will point out additional places where you make claims that need to be proven.

5) Page 7: “A link can surely be made between this right (child’s right to health) and the return of research results.” Actually I don’t agree. Please make an argument for the link. The right to health is a right because it is known to be in the child’s best interest. We don’t know if research is in the child’s best interest nor if the return of results is in the child’s best interest. You cannot assert this link, you must show it. You insinuate the research can prevent or treat, but the more we learn about genomic data, the more we learn it is probabilistic and treatment may

6) Page 8: “The same principles for assessing the BIC likely apply to genomic research.” Why? Again an argument is needed

7) Page 9: where you show law cases all involving clinical care. So a question, what degree of maturity or decisional capacity do you need to make health care decisions or research decisions? I would argue that the bar is lower for clinical care because doctor and patient’s interests are aligned in serving the patient’s best interest. However, research is not about maximizing patient well-being but advancing science. The therapeutic misconception is real and may be reflected in the authors’ willingness to extrapolate from the clinics to the research setting.

8) p. 10 does Convention on Human Rights and Biomedicine apply to research?

9) p. 10: as you note, the focus on the ESHG is that “parents should be notified about early onset diseases providing the findings are subject to assessment of clinical validity and utility . Research often does not reach that level of clinical validity and utility. SO at minimum, the authors need to explore when is research findings like clinical care and meet certain levels of clinical validity and when does it not. In the European paper that they cite [35], it was only for Mendelian early onset conditions. The ESHG norms on whole genome sequencing want validity, utility and actionability, which again would limit disclosure to early onset conditions. The authors need to make clear what genetic research results they are discussing.

10) p. 14 I am confused by the case of AC v Manitoba as the citation on p 14 seems to focus on when to listen to the child and not how to define BIC.

Minor Compulsory Revisions

1) Second sentence in background of abstract needs to be rewritten: Guiding decision making concerning the child is the best interests of the child framework. This sentence is unclear. I think you mean that The guiding principle in
decision-making about children is the best interest of the child standard.

2) There is too much jargon: on page 5 the authors write “Obviously” when it is not necessarily obvious. On page 6, the authors write,” but this should go without saying”. Actually, inferring an idea when it is not stated may not be accurate as the rules may differ between clinical care and research. I will point out additional places where you make claims that need to be proven.

3) (p. 8 when you first write out Convention on Human Rights and Biomedicine put {CHBR} next to it as you use the initials thereafter.

Discretionary Revisions

1) p. 17 With respect to rights, the authors state there are 3 actors; the state the family and the child. They want to add a fourth, the researcher. How different is this than adding the clinician?

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

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'