Author's response to reviews

Title: "Snake-oil," "quack medicine," and "industrially cultured organisms:" Biovalue and the commercialization of human microbiome research

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Author's response to reviews: see over
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Dear Adrian Aldcroft, Daniel Vallero, and Joyce Ikingura:

Please find attached the revised version of the manuscript ““Snake-oil,” “quack medicine,” and “industrially cultured organisms:” Biovalue and the commercialization of human microbiome research.”

We would like to sincerely thank the reviewers for their thoughtful and extremely helpful comments. We have addressed each comment below.

Daniel Vallero, Reviewer 1:

Comment 1: Indicate what is meant by semi-structured, particularly to show the extent to which responses were led versus spontaneous.

- We have added a description of semi-structured interviews in the text: “Semi-structured interviews allowed us to set the agenda in terms of the topics we wanted to cover, while providing investigators flexibility in their discussions and interpretations of these topics.” [Methods section, Page 6, Paragraph 2, Lines 4-6]
- We have also included the interview guide [see comment 3 below]

Comment 2: Explain the expert elicitation process. For example, were all 63 respondents of the same discipline, or were they selected on the bases of expertise, interests, or simply availability at a conference?

- In this study, we did not employ the expert elicitation method. In contrast to the expert elicitation method, which seeks to reach consensus through the quantification of uncertainty, our goal was to explore and describe a range of issues related to the ethical, legal, and social dimensions of human microbiome research.
- To address issues of recruitment highlighted by the reviewer, we have described our recruitment process in more detail: “Initially, using a purposive sampling strategy [23], we identified 140 potential investigators from a publicly accessible list of HMP Research Network Meeting Participants. Subsequent snowball sampling [23] supplemented our recruitment efforts, allowing us to interview investigators who, for example, were not directly involved in the HMP but were involved in human microbiome research. Eighty-eight agreed to participate, 41 did not respond, and 11 declined. Of the 88 investigators who agreed to participate, 63 were interviewed in 60 distinct interviews (the remaining 25 were not interviewed due to scheduling conflicts). Investigators represented a range of academic disciplines, including genetics, pathology, microbiology, virology, gastroenterology, and medicine.” [Methods section, Page 7, Paragraph 1, Lines 5-13]

Comment 3: Include the interview guides and questionnaires as appendices or supplemental materials.
We have included the interview guide.

Comment 4: Some statistical interpretation is needed. Is \( n = 63 \) sufficient for inference from a judgment sample? In fact, is this more of a fishing expedition than an expert elicitation? I do not know, but someone like Ken Reckhow, formerly at Duke, or Igor Lindov at US Army can likely give insights as to the appropriateness and sufficiency of the study design.

The study design is neither a fishing expedition nor expert elicitation. The design of this study adhered to a standard qualitative research framework: exploratory and inductive. Given this study design, statistical inferences concerning sample size and power are beyond the scope. Sample size, as in most qualitative research, is contingent on the information received from interview participants. This is commonly understood as saturation, or the point at which new data no longer provide new information. Additionally, the purpose of exploratory, qualitative research is not to make inferences; the data presented in this manuscript consistently emerged across the interviews we conducted with investigators.

Discretionary Revisions:

Comment 1: Include a table of disciplines/expertise represented (e.g. ethicists, microbiologists, etc.)

- Given that our sample size is small, the number of investigators representing various disciplines even smaller, and groups such as this are often close-knit, providing detailed information about investigator characteristics has the potential to breach our assurances of confidentiality. To address this issue, we have included in the methods section examples of the disciplines represented in our sample. [Methods section, Page 7, Paragraph 1, Lines 12-13]

Comment 2: Describe the factors and weightings of expert elicitation. For example, were the interviews conducted in the same way for life scientists as for social scientists? Were the instruments developed to ascertain information about certain factors, e.g. \( X \) questions for safety, \( Y \) questions for environmental considerations, \( Z \) questions for professional ethics, etc.?

- Again, we did not employ the expert elicitation method; therefore we cannot address comments about the use of this particular method. We did not interview social scientists.
- The interview guide was developed to ascertain information about ethical, legal, and social dimensions of human microbiome research. Interview guide items are listed in the methods section [Methods section, Page 7, Paragraph 1, Lines 1-4], and we have included the interview guide as supplemental material.

Joyce Ikingura, Reviewer 2

Question 3: Are the data sound? Data is sound and derived from the methods used. However I
could not see where exactly the authors were teasing out legal challenges in the methodology and results. Under Methods section para 3, the authors state ‘We limit our findings to ethical and social considerations….. ‘This seems to show that although initially they wanted to cover also legal issues, they did not. This should therefore be reported under the study limitations.

- Given that we are addressing regulation and policy issues, the omission of the word “legal” was an oversight on our part. We thank the reviewer for catching this error.

Question 5: Are the discussions and conclusions well balanced and adequately supported by the data? Yes. The authors discussions are well balanced. (1) However I felt there was a need to include in this study the views of the representatives of the general public as consumers of these commercialized products. They would have provided information that would add social value of this study results.

- We agree with the reviewer that consumers’ perceptions would be interesting and valuable information. However, while we interviewed those who participated in the Human Microbiome Project at Baylor College of Medicine, this was not a theme that emerged within this group. This is definitely an issue in need of further exploration.

The legal challenges in this study would relate to the information that must be passed on to the consumers to know exactly what they are engaging in. The manufacturers of these products should take a legal responsibility of ensuring that what they are selling promotes good health, in the real sense and not to create hype. The information should be backed by the manufacturers for safety and better health and regulated by the regulatory authorities.

- We agree with the reviewer’s comments. We discuss these issues in terms of product and marketing regulation, or lack thereof. [Results section, Pages 13-15; Conclusion section, Page 17] We believe it would be interesting to study this issue in the future.

Question 6: Are the limitations of the work clearly stated? The limitations of the legal aspects were not well reported and therefore should have been mentioned under this section.

- We have addressed this comment by more clearly framing regulation and policy change in terms of legal concerns [please see response to question 8].

Question 8: Do the title and abstract accurately convey what has been found? More, so but they should add on legal issues in the methodology and results.

- We have addressed this issue by more explicitly framing the part of our discussion of regulation and policy: “Investigators’ primary legal concern centered on regulation and policy change.” [Conclusion section, Page 17, Paragraph 2, Line 1]

Discretionary Revisions
Comment 1: On results last paragraph before Public Awareness of the benefits..... section The authors may consider to add

.... within this new paradigm of health, the marketing strategies should ensure they inform the consumers what they are selling and what the consumers should expect. The information to be passed on must be backed by science and ethical, without which the ethical issue of therapeutic misconception may arise.

- We would like to thank the reviewer for engaging with the material presented in this manuscript. To avoid introducing a new concept (therapeutic misconception) into the results section, we added the following text [in purple] to a discussion point about safety and effectiveness: “Under the current paradigm of health that encourages individual responsibility, we need to consider why individuals begin or continue to use dietary supplements even when faced with evidence questioning safety or effectiveness, as well as the ethical implications of therapeutic misconception.” [Conclusion section, Page 16, Paragraph 2, Line11]