Author's response to reviews

Title: Inverse Association of Colorectal Cancer Prevalence to Serum Levels of Perfluorooctanoate (PFOA) and Perfluorooctane Sulfonate (PFOS) in a Large Appalachian Population

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Author's response to reviews: see over
Dear Dr. Solera,

Attached is our manuscript with the revisions included as requested (changes highlighted on pages 2 and 4). Specific responses to editorial and reviewer concerns, including those detailed in our July 17th, 2013 email response, are given below.

**Editorial Concerns (10/16/2013)**

1) Please include in the Methods section the full name of the IRB who approved the study.

The full name is now included.

As per email from Dr. Solera, 7/10/2013:

Your explanation regarding your lack of involvement in the court settlement sounds reasonable, however there are a couple of aspects that we would like you to clarify:

1) You mention below that “West Virginia University Dept of Community Medicine investigators were granted access to the deidentified data from the C8 Health Project, but played no role in the design or implementation of the original study”. However we note that two of the authors on this manuscript, Frisbee and Ducatman, are both authors on the 2009 article describing the C8 Health Project. This would seem to indicate to us that they must have been involved in the C8 Health Project, could you please comment on this?

The C8 health project began testing on July 27, 2005 and delivered its final raw data to the court for filing on May 16, 2008 (see http://www.hpcbd.com/C8%20Brookmar%20Health%20Project.html). Dr Ducatman (Dept of Community Medicine, now the WVU School of Public Health) was responsible for arranging access to the original deidentified C8 data and for establishing a key role of Dept of Community Medicine (now School of Public Health) in constructing the data set for analysis. Dr. Frisbee, the first author on this paper, was (as a PhD student), in part responsible for cleaning and coding the raw deidentified data. In collaboration with Paul Brooks, MD (co-founder of Brookmar, Inc. an entity that was created for purposes of conducting the C8 health project as directed by the court), 2 members of the Science Panel, and other colleagues, Dr. Frisbee prepared the first publication regarding this project— a description of the project design and methods. However, as stated in my earlier email (see below), neither Dr. Frisbee nor Dr. Ducatman played any role in designing or implementing the original study.


2) Also are the data from the C8 study (and which you have used in your analysis) publicly available? If not, we would be grateful if you could provide details of who granted permission to use it and include these details in the manuscript’s Methods section. Please note that the link you provide to access the project webpage doesn’t seem to be working.
Following completion of the C8 Health project, investigators in the WVU Department of Community Medicine (now the WVU School of Public Health) were granted formal access to the raw deidentified project data by Brookmar, the organization responsible for conducting the C8 study. Although the C8 Health project data will eventually be shared with the broader scientific community (see Brookmar web link below), access is currently available only to the Science Panel (data with identifiers) and WVU investigators (deidentified data). We now provide these details, including the updated web links.

3) **It also seems like the data from the C8 project has been used to look at various different outcomes, which have been reported in different articles. Could you please clarify why these were not all reported in one article?**

As indicated on the The Brookmar C-8 Health Project website (http://www.hpcbd.com/C8%20Brookmar%20Health%20Project.html), this study is, if not the largest, certainly among the largest human health projects (in terms of participant numbers, richness of the data collected, etc) ever conducted. As with other large cohort and cross-sectional studies (e.g., National Health Interview Survey, National Inpatient Sample, National Health and Nutrition Examination Survey, Pregnancy Risk Assessment Monitoring System, Behavioral Risk Factor Surveillance System, Nurse’s Health Study, Women’s Health Initiative, etc.), there will likely be numerous publications based on this very complex database. As in the case of other publications stemming from other large health studies, these papers will target many different questions, associations, and outcomes depending on the research interests and expertise of the authors. Even if it were possible (and publishable, given the page limits in virtually all journals), combining all outcomes in a single paper would be infeasible for many additional reasons, including differences in sample (case-control) selection; evaluation of potential confounders, mediators, and effect modifiers; ancillary analyses and other methodological issues; rational and discussion focus, etc.

**Reviewer 2 Comments:**

'Conclusion paragraph of the abstract should be modified so as to be consistent with the Conclusions section in the end of the paper.'

We have modified the abstract conclusion as requested.

Thank you for your consideration, and we look forward to hearing from you.

Best regards,

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