Reviewer’s report

Title: Prevalence and Mortality of Cryptococcal Disease in Adults with Advanced HIV in an Urban Tertiary Hospital in Sierra Leone: A Prospective Study

Version: 1 Date: 27 Jan 2020

Reviewer: Lianne Sheppard

Reviewer's report:

Overall I found the author was very responsive to the reviews and made valuable improvements to the paper, which have strengthened its contribution. Clearly some of my requests involved more effort than I anticipated; the additional documentation included is very valuable so I appreciate they were addressed. In a few places the revision falls short of my hopes for improvement and I defer to the editor to address these remaining details. (In particular, I find it difficult to ensure I understand the contributions made by the authors (vs. other researchers) when their paper is written in passive voice. I won't belabor this further.) Here are additional comments that I suggest be addressed in the final version.

1. The author should correct the errors I found in the current draft and look carefully to ensure no others remain.
   a. The number of significant findings in the abstract differs from the main text
   b. Equation (2) is missing an i subscript.
   c. Takahashi is Study E not Study L

2. Add a concluding paragraph to the discussion. Right now the paper falls flat at the end. I think a few key points are worth restating at the end of the paper, for instance
   a. The regulatory bodies aren't doing their own analyses and this is leading them to miss important evidence.
   b. Summary statements highlighting the organs/systems where there is clear evidence that glyphosate is causing cancer, with some mention about those that are particularly compelling given the other evidence reviewed in this paper.
   c. The tumors with "clear evidence" where regulatory bodies reached different conclusions or did not consider them at all.

3. Consider revising the abstract to incorporate more of the distilled findings summarized in Table 6 and some of the most important points made in the discussion. Also in the abstract please consider these suggestions:
a. Glyphosate is the most widely used agricultural chemical of any kind worldwide and also the most widely used pesticide (of which a subset are herbicides).

b. I think the abstract can be reworded to not repeat the idea of consistency across sex, species, strain in two consecutive sentences.

4. Consider a bit more elaboration on the NTP criteria to bring along readers unfamiliar with them. While the cancer evaluation criteria are clearly referenced, the paper does not give good insight into any of the terms. (For example, I don't consider a statement like "Clear evidence (CE) indicates it is clear that glyphosate caused these tumors" a particularly informative definition.)

5. Table 6 (e.g. in a footnote) or the text describing it does not say anything about Table 6's blank cells. What do they mean?

6. As a reviewer not familiar with animal carcinogenicity tests, I don't know how to put into context when there is evidence of a certain type of cancer in a single gender, species or strain, but not in other subgroups. For instance, there is clear evidence for adrenal cortical carcinoma, but only for one gender, species and strain subgroup. How is a reader unfamiliar with animal carcinogenicity testing supposed to think about this evidence when it isn't replicated in any of the other subgroups? Are there some cancers where we expect specific strains to be more likely to show clear evidence? Some comment about these points would be helpful. This was the gist of my general comment number 4.c.iii. in my first review that Dr. Portier did not understand and thus did not appear to respond to.

7. Is it worth making a comment in the introduction about the unusually large number of animal carcinogenicity studies available for glyphosate, at least compared to other compounds? (This is my understanding; please correct me if I am wrong.)

8. P 3: There are some generic statements that could be made more specific in the last paragraph of the introduction. I think it is important to say that all known studies were reviewed for this review (add number), and that those with the raw data available in the public domain were included in the reanalyses done in this review.

a. line 10: Is it fair to say this study reviewed all available studies of pure glyphosate? The wording is currently so generic as to not help readers understand the magnitude and context of this contribution.

b. Line 11: "data is available" is very generic. The point is that there are studies where the data are not in the public domain in any way, and these are omitted. The number of these studies could be given.

9. Methods

a. P 3 line 30: Many readers may not understand that the full laboratory reports are often not available to the public.
b. P 3 Line 39: I suggest adding a sentence that gives the most important reasons for exclusion.

c. There are two Takahashi 1999 studies; they should be distinguished, e.g. 1999a, 1999b. The study L reference on p 6 line 2 appears to be incorrect. I'm unclear if there are other details for discussion of references [15] and [33] that need to be corrected in the text and tables. For instance, Table 1 has no mention of JMPR, but Table 2 does, but the text seems to be making a different point.

d. P 7 line 10: Add Ha

10. Discussion

a. P 20: I had trouble following the paragraph starting on line 35 so please revise for greater clarity. Tables 3-5 don't address preneoplastic lesions.

b. P 21: EPA also excluded findings for doses above the limit dose. The discussion implies that EFSA did this but not EPA. This should be clarified.

c. P 22 l 21-3: This is an important comment that should be brought into the summary at the end and the probably also into the abstract.

11. It would be really helpful to provide websites for some of the references, e.g. to regulatory guidance documents such as the NTP Cancer Evaluation Criteria [100].

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