Reviewer's report

Title: Polymorphisms in xenobiotic metabolizing genes (EPHX1, NQO1 and PON1) in lymphoma susceptibility: a case control study

Version: 2 Date: 30 January 2013

Reviewer: Kathryn Barry

Reviewer's report:

Major Compulsory Revisions

1. The authors state that an aim of the paper was to compare the genotype distribution in non-exposed and exposed subjects and they mention the possibility of genotype selection in the exposed population (see 5th paragraph of the Discussion section). However, it is unclear why the genotype distribution would be related to exposure. Please elaborate.

2. Please add a description of the results for all genetic models evaluated. For example, there should be some mention of the results with the dominant genetic model, even if non-significant. The methods section should also mention the various genetic models considered.

3. The study conclusion in the abstract that “this study demonstrates that the PON1 GG genotype is a risk factor for B-cell lymphomas…” is overly strong given the relative small size of the study compared to genome-wide association studies and the need for replication. The authors mention the need for replication in relation to the finding of a possible association with differential carcinogen exposure, but should also emphasize this for the overall association of the PON1 GG genotype with lymphoma outcomes.

Discretionary Revisions

1. Recommend removing discussion/references for cancer outcomes other than lymphoma because the association for a particular SNP with cancer risk could potentially vary by the type of cancer and therefore findings for other cancers than lymphoma may not be relevant to the current paper.

2. In the Discussion section (paragraph 5), the authors state the limited sample size did not allow testing of gene-environment interactions and that “in order to take into account the possible environmental influence we stratified both cases and controls according to exposure,” which is essentially the same idea. Instead of stating that testing of gene-environment interactions was not possible, suggest re-wording along the lines that the authors attempted to account for the possible influence of environmental exposures by stratifying according to exposure, but the analysis was limited by small numbers.

3. Did participation rates or any other factors differ between the cases included
from the previous study and the cases diagnosed in 2011? Also, it would be helpful if the Methods section could include the specific numbers of participants drawn from different sources.

Minor Revisions

1. There are some grammatical issues, for example a fragment in paragraph 2 of the Background section: "And, in particular...".

2. In the Methods section, suggest writing out the title for the WHO document and defining WHO.

**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.

**Declaration of competing interests:**

I declare that I have no competing interests.