Reviewer’s report

Title: A Case-Control Study of GST Polymorphisms and Arsenic Related Skin Lesions

Version: 1 Date: 27 June 2006

Reviewer: David J. Thomas

Reviewer’s report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1- The design of the study is described as a case/control comparison but it is not, as the authors note on page 6, a standard case/control design. The authors need to provide more detail on how the controls who are also exposed to arsenic in drinking water are differentiated from the cases who apparently have skin lesions. Also, are there controls with skin lesions? Stating that the design is valid and highly efficient is not sufficient to explain the design or to allay concerns of the reader. This issue must be addressed in the Methods.

2- The analytical procedures used must be described in more detail. The paragraph on page 7 describing water collection and analysis is not intelligible. Also, if toenail arsenic concentrations were used in this study then one must describe collection, processing, and analysis.

3- For clarity and accuracy, the authors should avoid stating that the formation of arsenic-glutathione complexes is dependent on the catalytic activity of some glutathione transferase. As far as I am aware, there is no direct evidence that the reaction is catalyzed by this enzyme. Certainly expression of glutathione transferases affects the kinetic behavior of arsenic but this does not prove the action depends on catalysis of conjugation. Although this issue does not go to the validity of the data reported here, an unsubstantiated hypothesis for the mode of action of the glutathione transferases may mislead readers.

4- The description of the change in a commonly held opinion about the role of metabolism in the actions of arsenic is not a paradigm shift. Thomas Kuhn’s careful description of a real paradigm shift (e.g., the Copernican revolution) describes a global change in thinking about a fundamental characteristic of the physical world. In the case of assessing the role of metabolism of arsenic, what occurred was a self-correcting process in which investigators tried to falsify a hypothesis (that metabolism of arsenic is only detoxification) and found they could do so. Here, paradigm shift is scientific hyperbole.

5- Table 2 contains an error in the footnote. I believe that both arsenic concentration in well water and arsenic concentration in nails were used for adjustment of the crude model.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.