

## Reviewer's report

**Title:** Inter-individual variations of human mercury exposure biomarkers

**Version:** 2 **Date:** 16 August 2005

**Reviewer:** Alan Stern

### 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) Review of "Inter-individual variations of human mercury exposure biomarkers"

General

This is an important and useful MS that provides timely data on the relationship among the various biomarkers of MeHg and IHg exposure. It will be particularly helpful in resolving some of the current controversy regarding the use of these biomarkers. The MS deserves to be published with relatively minor changes (as indicated below).

Specific Comments.

pg. 2, second to last line - Something has been omitted from this sentence.

pg. 5 and ff. - The Methods section does not contain any information on the determination of the number of amalgams or the number of fish meals. This information should be included. Also, the distribution of these parameters in the population is not described.

Figure 1 - Directional arrows showing direction of flow would be helpful.

pg. 10, - The percent IHg in the reference material (23-79%) seems unusually high. Also, it is unclear from Table 1 which are the whole blood samples and which are the RBC samples.

While Table 3 gives LOD, it does not make the case for the specific role of the "cleanup step" in the LOD reduction.

pg. 11, 3 - The intent of the first sentence ("The distribution of OHg and IHg ...") is not clear.

What does the abbreviation, "B-EVF" mean?

pg. 12, equations 1 and 2 - What is being calculated with these equations? There is no equivalence (i.e., no equal sign).

1 - I assume that the CI means a 95% confidence interval, but this should be explicitly stated.

2 - "The average percentage of RBC-IHg of RBC-THg..." This is awkward. A better formulation would be, "RBC-IHg was 6.8% of RBC-THg..." Likewise, later in the paragraph, "RBC-IHg was 7.2% of RBC-OHg?" However, it is not quite clear what this means since O-Hg does not include I-Hg. Is this a simple ratio?

"In a person with no dental amalgam fillings, the percentage of RBC-IHg..."

Does this refer to the average percentage?

pg. 13, 2 - "In our previous study of women with a high fish... in individuals with 10 fillings or more (included data from our previous study.)"

It is sufficient to merely say that these results are nearly identical to those from the earlier study. The citation should be provided.

"The difference was not statistically significant (Student t-test, p=0.4)?"

After stating that I-Hg in hair was not associated with amalgams, this is largely superfluous and merely adds to the general thicket of numbers.

"... but not with the number of dental amalgam fillings (Table 4).?"

This was already stated earlier in the paragraph.

pg. 14, 3 - I suggest inserting the word "moderately" with respect to the association of dental amalgams with IHg in urine. the r of 0.49 is meaningful but not overwhelming.

pg. 15, 2, second line - substitute "including" for "as well as." Demethylation is part of MeHg

kinetics, not a separate concept.

3 - ?The inter-individual variation was relatively low (about 15%).?

What exactly does this value represent? Is it a coefficient of variation (cv). The same question applies to subsequent descriptions of inter-individual variation.

pg. 16, 2 - ?This can explain the larger inter-individual variation in the distribution of IHg...?

It is not obvious how the above explains the inter-individual variability in the distribution of IHg between RBC and plasma.

pg. 17, 1 - ?... the average degree of demethylation in the hair follicles would be on average 4%.?

Is this a rate? If so, what is the time factor?

2 - This is an insightful analysis. I think that a bit more can be gleaned from it with respect to the fact that (it appears to me) the coefficient represents the underlying inherent relationship between HHg and BHg at steady state.

pg. 18, 2 - Add the words ?with this method? after ?sample preparation and analysis...?

pg. 19 - It seems, therefore, that these data support the conclusion that, in general, HHg provides a better measure of long-term average MeHg exposure than any of the blood measures. In light of the ongoing discussion of the of the relative usefulness of the various biomarkers, it would be worthwhile to make this point explicitly.

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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?:** Accept after discretionary revisions

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**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.