Reviewer’s report

Title: Biomarkers of naphthalene in pregnant women: an investigation of personal and indoor air sources.

Version: 1 Date: 6 December 2013

Reviewer: Stuart Batterman

Reviewer’s report:

Major compulsory Revisions

This paper tries to relate exposure sources measured via urinary and breast milk biomarkers from pregnant women to indoor and personal measures measured via surveys and monitoring. While the data collection plan is interesting, few associations or exposure sources were identified, which seems surprising and which may call into question data quality, or suggest that the exposure contrasts were small. The contribution of the paper is to show, for unknown reasons, that naphthalene levels increase slightly post-partum in the studied residences, and that urinary biomarker levels are uncorrelated to indoor air and personal air measures. This is interesting, but both require further explanation prior to publication.

1. The study showed very strong correlation (> 0.80) between personal and indoor air levels, indicating that indoor naphthalene sources are present and account for the bulk of inhalation through the inhalational route. How much time was spent in the residence for this population -- probably more than average? But no significant or apparently even borderline associations were found between air or biomarker naphthalene levels and potential sources reported in the questionnaires. This does not appear reasonable and suggests the possibility of sampling or other errors. Or the biomarkers used are not unique, as suggested in a limited case.

2. No convincing source of exposure or metabolic pathway producing the same biomarkers are suggested. No calculations relate airborne to biomarker levels are performed, though at least 5 PBPK models are available for rats or mice.

3. The statistical analyses and data interpretation are very limited. Median, Q1, Q3, Min and Max statistics are essentially all that is provided. Min and Max are unreliable. Q1 and Q3 statistics suggest a 2-3 fold range in airborne concentrations, and possibly a slightly larger range for the urine measures and a smaller range for breast milk. A more complete analysis should look at the distribution, correlation, and dependencies of the data.

4. Given that a non-random sample was selected, the paper should limit its claims with respect to representing naphthalene exposure. Moreover, the very low enrollment percentage indicates a high likelihood for non-random selection.
5. Quality assurance requires more attention. The OVM samplers are known to have blank contamination. Background subtraction is an inferior method. The 50% criterion for blank subtraction is flawed. Describe the distribution of errors. What were the maximum field blank levels? The lack of biomarker field blanks is a potential issue and might explain the lack of correlation with air samples. There do not seem to be any replicates. The QA for the biomarkers is also inadequate. Performance for breast milk analytes is not described. If the data quality cannot be understood, this should preclude publication.

6. On p. 17 the finding that levels are higher post-partum is interesting. The text should quantify how much higher. Also, did the survey ask about the use of sanitizers, deodorizers, air fresheners, etc? If so, I am surprised an association was not found, but it appears that this information was not requested.

7. The paper does not provide an adequate discussion of temporal variability. Are single measurements sufficient to capture exposure that is representative? Was there correlation between the pre- and post-partum measurements?

8. The conclusion is weak and incorrect. We already know that indoor and personal measurements are highly correlated for many compounds. Sources of naphthalene have been identified. Can you conclude that the urinary biomarkers do not reflect exposure of this compound, rather than stating that there is variability.

Minor essential revisions

Abstract:

1. The objective should not be stated in Methods.

2. The authors should explain why this study selected pregnant women as participants.

3. Statistical methods were not described in the Methods. The exact methods used are not clear.

4. A more detailed analysis of correlation among pregnancy and post-birth samples would be useful.

Methods:

1. Page 11: Does “simple linear regression models” indicate univariate regression models? Since the following section mentioned many independent variables (or covariates), I think it should be multiple regression models rather than “simple”. Also, did the authors test ethnicity? The use of naphthalene, e.g., mothball, may differ by culture.

2. Page 11: I am not sure if the authors put personal and indoor air naphthalene levels in a model at the same time. If so, there might be an issue on colinearity due to the high correlation between personal and air levels. Other variables may
present similar problems if they are highly correlated.

Results and Discussion:

1. Table 2: What is the unit for air samples?

2. Table 2: Maybe the authors can added some information about sign rank tests.

3. Although there is no significant finding of linear regression models, some tables still may be worth show as supplemental materials.

4. Some graphical displays, like a distribution of levels or box plots, scatterplots might be informative and show outliers and other data features difficult to discuss.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

No competing interests