

## Reviewer's report

**Title:** A cohort study of in utero polychlorinated biphenyl (PCB) exposures in relation to secondary sex ratio

**Version:** 1 **Date:** 24 January 2008

**Reviewer:** Marc Weisskopf

### Reviewer's report:

Comments on Picciotto et al. "A cohort study of in utero polychlorinated biphenyl (PCB) exposures in relation to secondary sex ratio."

This paper examines the association between maternal serum PCB concentrations and the sex ratio of their children in a cohort of mothers who participated in the Child Health and development Study in the San Francisco Bay Area. It addresses an important question for which there is little good prospective data. As such, the prospective nature of this study with exposure measures from the pregnancy in question this work makes a very important contribution. Overall, it is an excellent paper. There is only one major methodological issue that I see as needing to be addressed.

Major compulsory revisions:

1) The selection process involved selecting all those who scored low on at least one of two cognitive tests or who failed a hearing test, and only a 17% sample of those who did not meet these criteria. The authors indicate that this resulted in selecting more girls because of the relative performance on these tests of boys and girls. Because of this, if there is some association in their data between maternal PCBs and the cognitive and/or hearing tests, this would introduce bias.

To deal with this, I think the authors need to do a weighted analysis such that the test scores (or at least their categorization of them) in their sample reflect those in the population from which selection into their study was made. The authors do do a weighted analysis, but this was with respect to weighting to achieve a sex distribution similar to the original cohort, which I do not believe would accomplish the same thing as weighting based on the cognitive and hearing testing categorization.

As an additional sensitivity analysis, the authors could take a random sample of 17% of the low scorers and look at the result excluding those low scorers not sampled this way. The power would be much less, of course, but the point estimate could be informative.

Minor essential revisions

2) The cutoffs that define low for the cognitive tests (related to the sample selection) should be defined.

3) It would be nice to have a table showing the distribution of some of the covariates by PCB levels. In fact, showing how the cognitive scoring (and in particular whether the categorizations they used related to the sample selection) varies by PCB level would be very informative as this association would be important to possible bias from the sample selection procedure.

4) The authors used an imputation process for PCB congeners below the level of detection. It has been shown that using the actual values obtained (even if below the LOD) leads to less bias. If these are actually available, rather than simply not obtained from the lab, it would be better to use them.

5) In the 3rd paragraph of the results, table 3 should be referenced.

Marc Weisskopf

**What next?:** Accept after minor essential 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.