Reviewer’s report

Title: Neuropsychological effects of chronic low-dose exposure to polychlorinated biphenyls (PCBs)

Version: 1 Date: 19 April 2005

Reviewer: Susan L Schantz

Reviewer’s report:

General
This manuscript presents findings relating to the neuropsychological impact of exposure to PCBs from indoor air. The issue is an important one that has received little attention in the literature. The assessment procedures used to measure neuropsychological function are appropriate. However, there are a number of problems with the manuscript and the study. These include a lack of statistical power due to a very small sample size, the relatively low level of PCB exposure in the sample that was studied, the limited analysis of just a few “marker” PCB congeners, a questionable statistical approach, and over interpretation of results that were either not significant or only marginally significant. The PCB literature is also rather selectively cited in the introduction, which could lead to some false perceptions for readers who do not know the field.

The introduction needs to be better organized and better referenced. It would be better to cite review articles rather than selectively referencing a subset of publications from a subset of the individual studies. Also, several statements are misleading or incorrect.

The reference to PCB 105, 118 and 156 as the most frequently detected congeners in the US population is not correct. These may be the most frequently detected congeners with AhR activity, but they are not the most frequently detected over all. A statement like this should be based on an overview of the literature, not one isolated article. A summary of various studies would show that PCB 138, 153 and 180 are the most frequently detected and are also present in the highest amounts.

It is also misleading to say that neurodevelopmental effects are noted primarily in the striatum, prefrontal cortex and cerebellum. This may be due to a lack of studies on other brain regions rather than a lack of effects. Many brain areas have not yet been studied for PCB effects.

The small sample size in this study together with the relatively low PCB exposure from air is a big concern. As a result, the study is seriously lacking in power to detect an effect. As the authors themselves note a sample size of 200-500 PCB-exposed individuals would have been needed and this study included only 30 exposed subjects. It is hard to draw any useful conclusions from such an under-powered study.

Another limitation is the decision to analyze only a few “marker” PCB congeners. It is unclear what percentage of the total PCBs in air these congeners typically represent or whether they are actually good markers that can be used to accurately estimate total airborne PCB exposure. The authors state that more extensive analyses were not feasible for technical and practical reasons. However, many research labs routinely analyze for much larger numbers of PCB congeners and provide detailed congener profiles for various matrices including air and blood.

The statistical approach of using one-tailed significance tests and a p value of 0.10 is questionable and not well justified, and it seems especially unusual to take this approach and then apply the very conservative Bonferoni correction procedure.
Regarding the methods, what was the order of administration for the neuropsychological tests and how long did the entire battery take to administer?

Given the lack of power and the relative lack of effects, there is a tendency in the discussion to over-interpret the study.

A number of words, such as dopamine for example, are misspelled throughout the ms.

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

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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?:** Reject because scientifically unsound

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I have no competing interests