

Reviewer's report

Title: Serum dioxin-like activity of Inuits across Greenlandic districts

Version: 1 **Date:** 26 December 2006

Reviewer: Linda Birnbaum

Reviewer's report:

General

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

MAJOR COMPULSORY REVISIONS

I have a major problem with this paper. The authors, in a previous paper (ref 26) state that their methodology does not discriminate between true "dioxins" – i.e., those compounds which are structurally related to TCDD, persistent and induce a common spectrum of biochemical as well as adverse effects, and chemicals which are non-persistent ligands of the Ah receptor, such as PAHs. The levels observed in this population, as well as in another one of their recent studies (ref 41), of AhR-TEQ are unacceptably high to reflect the true AhR TEQ as defined by the international community in the dioxin TEQ approach (ref 1 as well as the more recent WHO update - Vandenberg et al 2006, which should also be cited). In fact, they are NOT only measuring dioxin-TEQ with their assay! While there may be value in their comparisons of different levels of AhR ligand activity across various populations, there is no explanation of what the compounds involved are! These are serious issues which MUST be addressed and require major revisions.

The volume of serum used make it highly unlikely that the assay is measuring ANY ligand activity from PCDDs/DFs or even co-planar PCBs.

It is a serious problem that larger volumes were not used AND that PCDDs, PCDFs, and coplanar PCBs were not measured analytically.

High concentrations of weak agonists can lead to antagonism. Also, there may be other forms of antagonism when there are large concentrations of other compounds relative to high affinity ligands.

Another serious comment is that it is very hard to state whether you have synergism or antagonism UNLESS dose/response studies are conducted.

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

MINOR ESSENTIAL REVISIONS

1. How are lipids determined in these samples? The values are presented as both wet weight and lipid adjusted but there is no explanation of how the lipid adjustment was done. Gravimetric? Clinical Chemistry? Please explain.

The recent studies clearly demonstrate that PBDEs do NOT bind with high affinity to the AhR.

There are studies demonstrating that PCBs 126 and 169 DO biomagnify up the food chain.

Discretionary Revisions (which the author can choose to ignore)

DISCRETIONARY REVISIONS

The lack of an effect of age of BMI on their "AhR-TEQ" values is a surprise - but really supports the fact that they are NOT measuring persistent ligands alone in this study.

I agree with the statement in the discussion that the total POPs may not be a suitable proxy for DLC levels -

but NEITHER are the assays reported here!

Non-dioxin-like PCBs can both antagonize and/or synergize the effects of DLCs. It depends on the response, the dose, and the concentrations.

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: No, the manuscript does not need to be seen by a statistician.