Reviewer's report

Title: Unexpectedly long half-lives of blood 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) levels in Yusho patients

Version: 2 Date: 13 May 2015

Reviewer: Lesa Aylward

Reviewer's report:

The article is a concise, straightforward and useful presentation of the observed changes in concentration of 2,3,4,7,8-PeCDF in 395 Yusho patients. The paper is quite good as written. Following are my comments.

Minor Essential Revisions
1. In the review copy I received, there are two copies of Figure 2 and no Figure 1. Please provide Figure 1 in the final manuscript.

2. In the discussion of other literature on "dioxin" half-lives presented from lines 120 to 133, the distinction between different dioxin, furan, and PCB compounds is completely lost. The current manuscript describes data for one congener, 2,3,4,7,8-PeCDF. However, other than the Milbrath review, the remaining cited studies (Ritter, Aylward, and Grandjean) all deal with either PCB compounds (Ritter and Grandjean) or PCDD compounds (Aylward). The pharmacokinetic behavior (distribution and elimination) of 2,3,4,7,8-PeCDF is known to be much more extreme than most of the PCB and PCDD compounds described in these other papers. The authors need to rewrite the section to be more precise and also should provide citation to additional studies that examine the excretion rates of 2,3,4,7,8-PeCDF including Flesch-Janys et al. 1996 (J. Toxicol. Environ. Health 47:363).

Discretionary Revisions
1. The authors may wish to discuss briefly the possible role that the strong binding of 2,3,4,7,8-PeCDF to CYP1A2 proteins in the liver may play in slowing the overall apparent elimination rate for the compound at long time periods following exposure. Animal models demonstrate that at elevated exposure levels, a majority of the body burden is sequestered in the liver through binding to induced CYP1A2 protein. A slow equilibrium may exist between the bound compound in liver and the lipid reservoir, resulting in replenishment of the lipid reservoir as compound is eliminated. As a result, measured lipid-adjusted concentrations may change very slowly or not at all, even though compound is being eliminated.

2. On Figures 1 and 2 it would be helpful to either include regression lines to show any trend with age or concentration, or to state that there was no significant trend with these two factors.
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.

Declaration of competing interests:

I have conducted analysis and research on the toxicokinetics of 2,3,4,7,8-PeCDF for various organizations that have an interest in the topic. I have no other relationships that could be considered competing interests.