Appendix to comments on animal studies in section 3.3.3.5

RIVM acknowledges that the animal studies indicate a large uncertainty in the data set. We have the following questions concerning the animal data.

- EFSA states that the animal studies (Peden-Adams 2008; Dong 2009) are subject to high uncertainty in their dose-response due to an unavailable zero-dose group. However RIVM notes that in these animal studies the response at the lowest 2-3 dose groups levels off enabling an estimate of the background response (parameter a). The accuracy of the estimate of the BMD CI could be further improved by setting constraints to the background response, which could be obtained from historical data (i.e. experiments with different substances than PFASs, but with similar experimental setups). This approach is illustrated by the right figure of the Peden-Adams data, see text with fig 1.

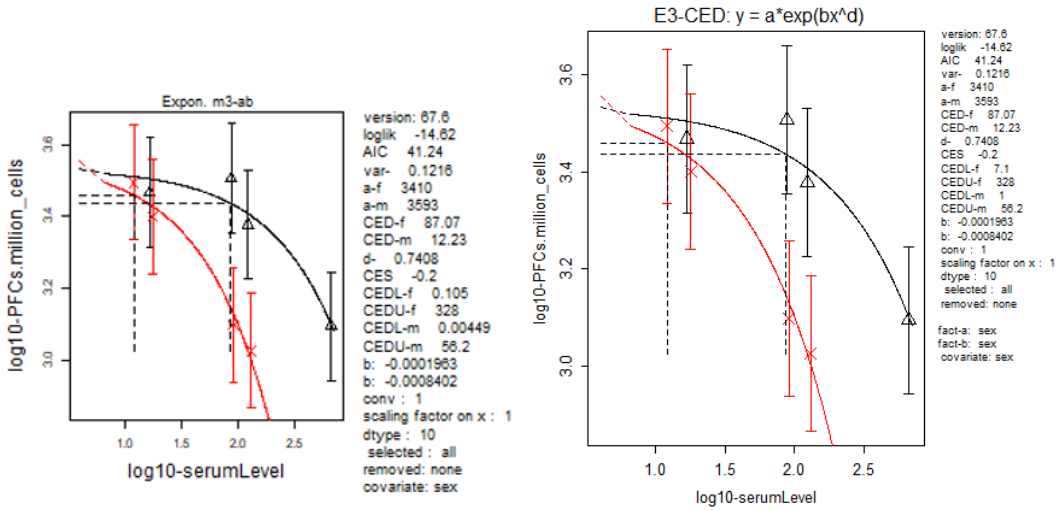

Figure 1: Peden-Adams, CES=20% red line=male, black=female: Left unrestricted parameter a, right restricted between 2500 and 4500 (on log10-scale: 3.40-3.65), serum level in ng/g ~ ng/mL

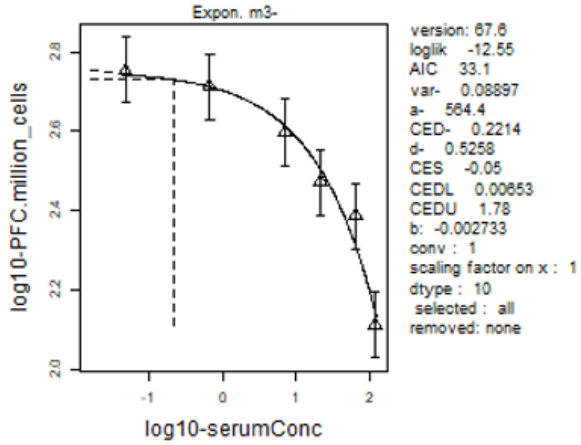

Figure 2: Dose-response analysis of the Dong 2009 data with CES=5%, serum level in mg/L = ug/mL. Resulting BMD_{05} CI has a BMDL of 6.5 ng/mL and BMDU of 1780 ng/mL.
When CES is set to 10% the BMD_{10} CI ranges from 80 to 5300 ng/mL.

Please note that in the analyses above different critical effect sizes were used. This analyses were merely performed for illustrative purposes.