Livsmedelsverket
National Food Agency

Enclosure

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Risk Benefit Assessment Department
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Comments and questions on the opinion on dioxins an DL-PCB from the Swedish National Food Agency

Confounding of HCB and HCH
HCB- and HCH-exposure are important confounders in the Russian Children's study and have been shown to be associated with onset of puberty expressed in an earlier paper from the study (Lam *et al* 2014, 2015). Is it possible that onset of puberty has an impact on semen quality and therefore should be included as a confounder in the semen parameters study?

Uncertainty in reference point and model calculations
As discussed in the opinion, the critical effect used for the derivation of TWI (semen quality) is likely to be causal since it has been replicated (Seveso and Russian Children's study), has support from experimental animal studies and is significant also after adjustment for important confounders. However, the exact reference point used (7 pg TEQ/g fat) is probably uncertain due to the modest size of the Russian Children's study (only 133 men provided semen samples), and unknown confounders that have not been accounted for etc.
In addition, there are also uncertainties in the model calculations that are not sufficiently indicated. How will e.g. the TWI be affected if variation in the parameters included in the model is addressed? Based on uncertainties in reference point and model calculations, we would prefer if the TWI was presented as a range based on e.g. a sensitivity analysis.

Applying the TWI on different age groups
The proposed TWI is based on an estimated intake in women that is stated to be sufficiently low to keep the levels in breast milk on a safe level. However, it is also stated that the TWI is not applicable on children. But at what age should the intake be restricted to 0.25 pg/kg bw/day in girls/women to secure the levels in breast milk? What is the TWI for children, is it 0.5 pg/kg bw/day, i.e. the level used in the model calculation? Is there a difference between boys and girls in terms of tolerable intake?

Using data on PCDD/F-TEQ as the basis for a total-TEQ TWI
We are hesitant to the derivation of a TWI for total-TEQ because of the fact that the DL-PCBs do not have a statistically significant association with semen quality in the Russian cohort. If the observed effect is caused solely by PCDD/F, it might be more correct to designate the TWI for PCDD/F-TEQ and leave the DL-PCBs out. Alternatively, if we

suppose that the effect is caused by PCDD/Fs and DL-PCBs together, it might be wise to use the results for total-TEQ (median level of Q1) to calculate a TWI, despite the fact that there is no significant association between total-TEQ and sperm concentration. The lack of a significant association may have several reasons, e.g. lack of power. Both these suggested approaches will result in a higher TWI.