Uncertainties in the critical effects, dose-response assessment and derivation of an HBG

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181. The EFSA CONTAM Panel have considered uncertainties in their Opinions (EFSA 2018; EFSA, 2020). “Overall, the CONTAM Panel considered the impact of the uncertainties on the risk assessment for the sum of PFOA, PFOS, PFHxS and PFNA is high” (EFSA, 2020).

182. The COT had reviewed the two studies (Abraham et al., 2020 and Grandjean et al., 2012) used by EFSA for the derivation of a TWI for PFASs. The endpoints used were the indications of a decrease in vaccine response in children. The results from the studies were not entirely consistent for the PFASs compounds studied. It was also noted that the cohort in the Abraham et al. study was relatively small.

183. The immune effects of PFASs have been seen in both experimental animal and human studies. The Grandjean and Abraham studies are the only studies suitable for undertaking BMD modelling and only one of these (Abraham et al 2020) provided a BMDL suitable for risk assessment. Both studies are still less than ideal, and it would be helpful to have a more robust point of departure (POD). The modelling used seems to take account of the critical toxicokinetic effects. The pathological consequences of the reduction in vaccine response in these children are unknown. It is unknown how this effect relates to the TWI.

184. The EFSA opinion indicated that when antibody titres are diminished, the level of protection from vaccines might be compromised. However, it was not clear what decrease in antibody levels could cause such an effect. It was noted that there were also natural fluctuations in vaccine titres over time.

185. The Committee was of the view that information on the impact of vaccinating against diphtheria in the UK should be available. As most children in the UK are vaccinated, the fact that there were almost no cases of diphtheria (10 cases in England in 2019 (Vaccine Knowledge Project)) would suggest that any effect of PFASs on vaccine response was non-linear. However, as there is no cohort of infected subjects (due in part to the effectiveness of vaccination) any effect on impairment of the vaccine response would not necessarily be seen, as only a small percentage of the population would be at risk. Currently there does not appear to be any discernible impact.

186. The COT agreed that, on the basis of the information reviewed by EFSA, qualitatively the appropriate health endpoint had been selected but quantitatively, questioned the calculations. Overall, there were some reservations about the choice of the critical study and the specific effect selected. However, the COT agreed that the critical study was the best available. It was not unreasonable that this study was selected, and, in the absence of more appropriate studies, its use was understandable.

187. The COT considered whether there was a real effect or not.

188. The Grandjean et al cohort had initially been studied to assess the effects of polychlorinated biphenyls (PCBs) and the results for PFASs had been compared after correcting for confounding by PCBs. However, the Committee questioned how effective this correction would be when the major source of exposure for both groups of chemicals was the same, i.e., seafood. It was noted that the assessment was multi-faceted and that the two groups of chemicals were not necessarily confounders because they were on the same causal pathway. However, it would not be possible to put both PCBs and PFASs in the model at the same time and it would also not be possible to fully adjust the model for one group of chemicals for the other.

189. The COT discussed the benchmark dose (BMD) modelling that had been carried out by EFSA. This had originally been carried out by Abraham et al. and then replicated by EFSA. A relatively small set of data was used in the modelling. A number of the fitted models showed no threshold, indicating that there was no ‘no effect level’. However, there did not appear to be anything in the EFSA Opinion to explain this. There had also been difficulties with the BMD modelling, for example, model averaging did not provide plausible results and was not further discussed by the EFSA panel although model averaging is their preferred approach in BMD modelling. Instead, the lowest value from an individual model was used. It was presumed that this was for a non-threshold

dose response. It was noted that the data set could be very difficult to model.

Summary of uncertainties and recommendations

190. The CONTAM Panel identified several uncertainties and had a number of recommendations to decrease these uncertainties. To improve the exposure assessment, data obtained by more sensitive analytical methods with high levels of quality control (to avoid matrix effects or impact of background contamination) are needed in order to increase the proportion of quantified results and thus reduce uncertainty in the dietary exposure assessment. This is needed for all PFASs and a broad range of widely consumed food products.

191. For the determination of the total amount of PFASs, sensitive and accurate methods, which facilitate determination of the total amount of PFASs in samples of food and drinks are needed. Exposure assessment should be frequently updated, especially when analytical data obtained from more sensitive methods become available. Additional studies on the relative contribution of sources other than food are needed, especially for PFASs which are present in the highest concentrations in indoor air and house dust, such as n:2 FTOHs and PAPs.

192. More studies on the effect of cooking and food processing, in particular in relation to transfer to food from food contact materials that contain PFASs, are needed, given that most food is consumed after cooking/processing, and the fact that data reported in the scientific literature are inconsistent regarding the impact this has on exposure. Therefore, more data is needed on the transfer of PFASs along the food chain.

193. Furthermore, additional studies on paired human samples are needed to identify the relevant matrices for biomonitoring of various PFASs (this is not further explained, but presumably relates to pairs of serum/plasma and tissue samples).