Department of Energy (DOE)
Comments on the Interagency Science Consultation (Step 3)
Draft IRIS Toxicological Review of Perfluorononanoic Acid (PFNA) and Related Salts
Dated July 2023
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Thank you for the opportunity to review. Overall, the analysis was clear and the conclusions were well supported. We were impressed with the quality of the meta-analysis conducted on developmental outcomes.

For clarity, we would suggest calculations derived from uncertainty factors to determine developmental osRfD on Tables 5-15 and 5-16 on pages 5-30 – 5-33 are cited on pages xxi-xxii. It is a bit difficult to follow how the value 6 x 10(-9) was reached in this section.

The study selected to calculate the developmental osRfD (Sagiv 2018) has a cohort selected between 1999 and 2002. Given that PFNA serum levels have decreased over time, does this impact the evidence from older studies? To us, it seems likely that although sampling occurred during a time of higher human exposure and thus this exposure cohort may not be representative of the current exposure levels, effects associated with exposure may still be relevant to understanding potential associations. However, the relevance of the older studies to current population exposure trends should be discussed in the text.

Page 29 line 20-21: which NPL site? Or is this an average of several sites on the NPL?

Page 46, lines 8-9: "PFNA is excreted in urine and feces. When dosed by i.v. or i.p. injection, the majority of PFNA is excreted in urine by rats, approximately 10 times as much as was excreted in feces. While roughly 1/3 of oral doses were excreted in feces, this could result from incomplete absorption."

These sentences are very difficult to follow. When dosed by iv or ip, excretion in feces exceeded that in urine by 10 fold whereas excretion in feces following oral exposure was about 1/3 of the oral dose. It is not easy to compare those two metrics. Is it 10% versus 33%? We suggest rephrasing to make clarify the difference in excretion after different dosing paradigms.

Page 64, line 15: The epidemiological section switches between using the term "female" and "woman" and "male" and "men". We recommend using "women" and "men" when referring to humans, rather than males and females. Aligning changes are needed in several places in this section.

Page 96, fetal growth restriction summary: Since the effect on growth restriction seems to most strongly associated with birth weight, but not length or head circumference, has EPA

considered that this effect could be indicative of placental dysfunction during the last few weeks of pregnancy? The last few weeks of pregnancy are when the fetus gains the most mass. This reviewer wonders if the effects of PFNA (and other pfas) on the placenta may be greatest at the end of pregnancy, or perhaps the effects on placenta increase with pregnancy duration.