

National Institute of Environmental Health Sciences (NIEHS)
Comments on the Interagency Science Consultation (Step 3)
Draft IRIS Toxicological Review of Perfluorononanoic Acid (PFNA) and Related Salts
Hepatic Effects Section and Modeling Results for Liver Toxicity

Dated December 2023

(Date Received December 7, 2023)

3.2.4 Hepatic Effects – new epidemiological data and summary

General comments:

- As part of literature updates, EPA identified new epidemiological studies of liver/hepatic effects wherein the incorporation of the new studies into the draft resulted in changes to draft conclusions that, taken together, are viewed as substantial. These additions and revisions are well supported and documented. Overall, the scientific rationale and analysis is sufficient to include the new data and indeed strengthens the overall RfD.
- Previously the hepatic data were not sufficient to support an RfD and were largely based on animal studies. The updated and revised draft develops lifetime RfD that are in support of the overall RfD from developmental endpoints, thus strengthening the assessment.
- It is appropriate that the cross-sectional studies were correctly classified as informative and of medium confidence because of the long half-life of PFNA and short-term response in liver enzymes (section 3.2.4 lines 22-32).

Specific suggested revision:

- Section 3.2.4 line 30-31 – while the issue of long half-life of PFNA and short-term response in liver enzymes is introduced here there is a lack of specificity that could be addressed with a few more details. Specifically, is the short-term response on the order of days, weeks, months, or longer? For example, is it important for study participants to have maintained a residence for more than one year for the exposure in a cross-sectional study to be adequately addressed relative to the time for biological response for liver enzymes or is short-term response in the liver enzymes something that happens in days, weeks, or months?

Very minor editorial comments:

- Note, it would have been helpful to reviewers if EPA was more explicit at which studies were new and which were part of the previous writeup.