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NORTH CAROLINA
Environmental Quality

Secretaries' Science Advisory Board
Official Recommendation

Subject: **PFMOAA Toxicology Literature Review for Appropriateness to Derive a Reference Dose or Health-Based Value**
Date: **March 15, 2023**

Summary:
During the August 1, October 3, and December 5, 2022, Secretaries' Science Advisory Board (Board) meetings, the Board discussed two PFMOAA peer-reviewed publications (Yao et al. 2020 and Woodlief et al. 2021) to determine if the existing data is of high enough quality and presents adequate results to derive a reference dose. The questions posed by the NC Department of Environmental Quality (NCDEQ) and the Board's summarized discussions are provided below. The DEQ conducted two literature reviews (summer 2022 and winter 2023) to retrieve any PFMOAA studies which might inform a reference dose; these searches yielded only the two papers brought to the Board for review.

The questions posed to the Board by NCDEQ during the June 6, 2022, meeting were:
1- Review the PFMOAA studies in detail.
- *assess the quality of the studies (low, moderate, high)*
- *based on sample sizes, dose regimes, endpoints measured*

2- Do the studies provide sufficient scientific information to determine a point of departure to derive a reference dose now?

The Board's response:
The two studies were of high quality but had limitations that would preclude their use to derive a reference dose. The Woodlief et al. study examined immunotoxicity endpoints relevant to effects observed for other PFAS. The paper presented mostly no effects data (effects not statistically significantly different from controls), so higher doses may be required to evaluate the immunotoxic potential of PFMOAA using similar endpoints. In addition to being evaluated for benchmark dose modeling, this study could be useful for dose range-finding to inform the consent order studies.

The Yao et al. study is a cross-sectional epidemiogical study examining PFMOAA among 13 perfluoroalkyl ether carboxylic and sulfonic acids in 311 of 977 serum samples collected from residents living near a fluorochemical plant in China. The study's inclusion of cholesterol and liver function markers is relevant to effects associated with many PFAS chemicals. Only one statistically significant association (between PFMOAA and glucose) was observed when data from the lowest third of the ranked PFMOAA data was compared to the upper two thirds of the data. No statistically significant associations were seen between PFMOAA and other blood biochemistry endpoints.

These two studies examined different biologically plausible effects of PFAS and have acceptable data quality. However, these two studies do not provide an adequate foundation from which to derive a reference dose for PFMOAA.

PFMOAA is one of the compounds subject to mammalian (mouse and rat) toxicological testing under the consent order with Chemours, but those results may be years away. Dr. Jamie DeWitt noted that she is working on a manuscript describing PMFOAA exposures to mice with a different dose range and which includes serum chemistry for PFMOAA; the paper will have dose-response data suitable for benchmark dose modeling as well as a NOEL and LOEL.

The Board recommends that NCDEQ pause derivation of a reference dose until the referenced manuscript in preparation is published and available for review. Also, the Board understands from DEQ that there are no other North Carolina regulatory protective values that can be derived without a reference dose. In the interim, the Board encourages NCDEQ to continue with their analyses of the Yao et al. 2020 and Woodlief et al. 2021 papers (and periodically refresh their PFMOAA literature search for other relevant papers) for inclusion in a toxicological synthesis with the expected new information.

The recordings of the three Board discussions of the topic are here: NC DEQ and DHHS Secretaries' Science Advisory Board 08/01/2022 - YouTube (at 1:28:00), NC DEQ and DHHS Secretaries' Science Advisory Board 10/03/2022 - YouTube (at 0:22:50), NC DEQ and DHHS Secretaries' Science Advisory Board 12/05/2022 - YouTube (at 00:47:33)

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References:

Woodlief T, Vance S, Hu Q, DeWitt J. 2021. Immunotoxicity of per- and polyfluoroalkyl substances: Insights into short-chain PFAS exposure. *Toxics* 9(5):100.

Yao J, Pan Y, Sheng N, Su Z, Guo Y, Wang J, Dai J. 2020. Novel perfluoroalkyl ether carboxylic acids (PFECAs) and sulfonic acids (PFESAs): Occurrence and association with serum biochemical parameters in residents living near a fluorochemical plant in China. *Environmental Science & Technology* 54 (21): 13389-13398.