January 3, 2023

Barbara Losey, Executive Director
The Alkylphenols & Ethoxylates Research Council (APERC)
1250 Connecticut Avenue, NW
Suite 700
Washington, DC 20036

MDH RESPONSE TO APERC REGARDING NONYLPHENOL COMMENTS

Dear Ms. Losey:

We thank the Alkylphenols & Ethoxylates Research Council (APERC) for their comments on nonylphenol and for sharing their expertise with us. In their comments from May 13, 2022 and virtual presentation to the Minnesota Department of Health (MDH) on December 15, 2022, APERC disagreed with MDH's point-of-departure (POD) for subchronic and chronic critical noncancer effects upon nonylphenol exposure. MDH selected a 3-generation rat study by the National Toxicology Program (NTP) 1997 that was reported by Chapin 1999 as the critical subchronic and chronic study with renal mineralization in young male rats as the critical effect. It is a thorough study performed by a highly reputable group (NTP). NTP reported a dose response for renal mineralization in not only the male parental rats, but also in the 1st generation male progeny, and the 2nd generation male progeny. Usually, renal mineralization in young male rats is a rare effect, however, this effect was a nonylphenol-induced effect observed at the lowest dose tested. Although, the effect was reportedly minimal at this dose, there were other renal effects occurring at this dose including renal degeneration, which indicates a true treatment induced effect on the kidneys. APERC suggests identifying the lowest dose tested as the NOAEL of the study (13 mg/kg-d).

MDH's published risk assessment methods direct risk assessors to use a benchmark dose (BMD) approach to evaluate critical effects when possible. EPA supports the use of BMD modeling and wrote technical guidance for BMD modeling in 2012. BMD modeling uses the entire range of doses in a study and corresponding data from all of these doses to calculate a lower BMD (BMDL) confidence limit for a dose associated with a predefined effect level (example, a 10% change). This approach uses all of the data to derive a POD instead of using a study-selected NOAEL or LOAEL. The dose response for the F1 males was modellable and produced a $BMDL_{HED10\%}$ = 0.49 mg/kg-d and a $BMD_{HED10\%}$ = 1.1 mg/kg-d. The BMD/BMDL are lower than the

lowest dose used in the study (13 mg/kg-d), suggesting that nonylphenol-induce effects are likely occurring at doses below those used in the study. MDH used the BMDL as the POD in accordance with EPA 2012 technical guidance.

It is MDH's mission to protect the health of all Minnesotans, including sensitive populations and the most vulnerable. Although APERC suggests a higher POD using weight-of-evidence from other animal studies and a 2001 Health Canada Report, discounting the young male rat data and MDH modeling produced from the NTP 1997 study because effects occur at a lower dose than other studies contradict MDH's mission. Young males may be the most sensitive population to nonylphenol effects and selecting a higher POD would not protect younger animals that showed increased sensitivity. A subsequent 3-generation study by Tyl supports possible kidney effects at lower doses, however, the study is incomplete and cannot be used to assess a POD. Therefore, in order to be protective for all populations, MDH will retain the POD defined by BMD analysis without modification.

Sincerely,

/s/ Sarah Johnson

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