

United States Senate

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS

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The Honorable Jim Jones
Assistant Administrator
U.S. Environmental Protection Agency
Office of Chemical Safety and Pollution Prevention (OCSPP)
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Mr. Jones:

On September 30th, the EPA released its final Toxicological Review of Methanol (Non-Cancer) in support of the web posting of summary information for the Integrated Risk Information System, including a set of Appendices with the Agency's response to comments from its External Peer Review Panel as well as public comments. This is one of the first IRIS assessments to be finalized following the 2011 National Academy of Sciences series of recommendations for IRIS improvements. While this final assessment does make some important cosmetic improvements that provide for a more concise and readable report, the scientific rigor of the analysis fails to address the concerns raised by the NAS and members of Congress.

Strikingly, the Agency has chosen to ignore public comments and the criticism of its own external peer review panel. In particular, the external peer review panel raised concern that the assessment employs "Uncertainty Factors" that systematically lead to conclusions that are overly conservative by several orders of magnitude. In its insufficient response to comments, the assessment employs dubious rhetorical arguments such as referring to "unquantifiable effects of uncertain adversity" to justify its rejection of suggested higher "safe" exposure levels. Further, the assessment fails to address a fundamental criticism that external exposures at the oral reference dose and inhalation reference concentration result in methanol levels in humans that are well within normal background levels from dietary exposures.

The final methanol (non-cancer) assessment fails to use the "best available science" on several fronts:

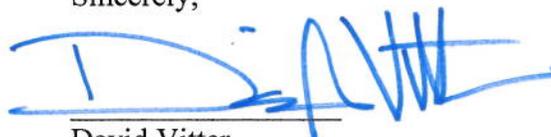
1. Toxic effects are caused by internal levels of methanol in cells, in this case estimated by blood methanol concentration. When there are both internal and external sources of a chemical at play, it is more difficult to determine the individual effect of each on human health. EPA's job – via the IRIS assessment process – is to recommend levels of external exposure which, when combined with internal exposure levels, will not result in adverse effects on human health. *Unfortunately, this assessment does not determine a blood level of methanol that is likely to be without toxic effects.* Rather, the assessment focuses on whether an oral exposure at the RfD combined with inhalation exposure at the RfC results in a blood methanol level that is "*distinguishable*" for a non-externally exposed

person with average endogenous blood methanol levels. All three external peer reviewers and public commenters disagreed with the EPA that EPA's suggested RfD and RfC would lead to a "distinguishable" effect. What is more, by the EPA's own estimates only 20% of the population would show a measurable increase in blood methanol exposure to the Agency's proposed RfD/RfC.

2. On the one hand, the assessment finds that a primate study in the literature is not reliable enough to be used as a basis for establishing the reference concentration, while at the same time the Agency uses the same study to justify their proposed RfD and RfC values. This monkey study suggested methanol effects, but the differences from control groups were not statistically significant. EPA justifies their suggested RfD and RfC values on the basis that if those "uncertain, but potentially adverse effects" in monkeys were real, and the study had been used to derive the RfC and RfD, then the higher values recommended by the external peer review panel could potentially reach these levels associated with uncertain effects. A convoluted argument at best.
3. The assessment used this data to increase the literature database Uncertainty Factor (UF) from "1" to "3," and the same data to raise the animal to human UF from "3" to "10." Both the external peer reviewers and the public commenters recommended against this double counting. The choice of specific Uncertainty Factors appears to result from a desire on the part of the Agency to establish the lowest RfC and RfD that produce blood levels distinguishable from the endogenous background levels. The assessment acknowledges that the database for methanol is extensive, but then assigns a "3" UF for the literature database because there is inconclusive monkey data, even though monkey data is seldom available. The assessment provides extensive PBPK analysis to set pharmacokinetic (PK) animal to human comparison of methanol levels; thus the UF should have been no more than "3" to account for pharmacodynamic (PD) differences. They used a value of "10" (3 for PK and 3 for PD), again, because the monkey data are not fully understood.

This assessment of the non-cancer health effects of methanol by the EPA systematically ratchets down the "safe" exposure levels by providing overly conservative assumptions and uncertainty factors to the point where it provides questionable utility for risk assessment or risk management. The assessment fails to address a fundamental criticism, that exposures at the RfC and RfD result in methanol levels in humans that are well within normal background levels from dietary exposures.

Sincerely,



David Vitter
Ranking Member
Environment and Public Works Committee