



Memorandum

Date: August 22, 2011

From: Agency for Toxic Substances and Disease Registry

Subject: Comments on EPA's Toxicological Review of Tetrahydrofuran

To: Environmental Protection Agency

We appreciate the opportunity to review EPA's Toxicological Review of Tetrahydrofuran. Overall, we found the document well-written and easy to read. We have no comment on the Oral RfD and inhalation RfC or on selection of endpoints, UFs for intraspecies and interspecies differences.

We agree with the statements made by peer-reviewers with respect to EPA's cancer risk assessment that, "THF is not genotoxic/DNA reactive, its metabolism is rapid and doesn't form a reactive metabolite, it doesn't cause irreversible damage, it induced a weak tumor response at high doses, and it doesn't induce proliferative lesions considered to be pre-neoplastic; concluding that the application of a non-threshold model will overestimate cancer risk."

However, we understand why EPA selected the default policy: "The linear approach is recommended if the mode of action of carcinogenicity is not understood (U.S. EPA, 2005a). In the case of THF, although there is some information available, the data are inadequate to establish the mode of carcinogenic action for kidney and liver tumors."