

Memo to: Norm Birchfield, National Center for Environmental Assessment Office of Research and Development U.S. EPA

From: NCEH/ATSDR, Centers for Disease Control and Prevention

Regarding: Interagency review of EPA's Final Draft Toxicological Profile for Hydrogen Cyanide and Cyanide Salts

Date: July 7, 2010

CDC's National Center for Environmental Health (NCEH) and the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the final draft Toxicological Profile for Hydrogen Cyanide (HCN) and Cyanide Salts. We appreciate the opportunity to comment on this document as well as the report from EPA's External Peer Review Meeting. Overall, the Toxicological Profile provides an excellent review of HCN and cyanide salts, with well-defined routes of exposure and thorough coverage of all peer-reviewed literature. EPA provides a sound scientific basis for its derivation of both the RfD for Cyanide Salts and the RfC for Hydrogen Cyanide, while clearly explaining the use of uncertainty factors. Major points of note from our reviewers include:

1. - Summary statements at the end of each section are extremely helpful given the length of this document. We encourage the continued use of this format in future toxicological assessments.
2. - An uncertainty factor (UF) of 3000 was applied to the point of departure of 1.9 mg/kg-day for BMD modeling of an oral reference dose for Cyanide Salts. The authors did a good job describing in detail the justifications behind each uncertainty factor: 10 for extrapolation from animal to human studies, 10 for human interspecies variability, 10 for extrapolation from subchronic to chronic exposure duration, and 3 to account for deficiencies in the hydrogen cyanide database. We acknowledge that the method for UF selection was appropriate and consistent with an EPA risk assessment approach. However, an UF of 3000 does raise some concern over the usefulness of the resulting RfD.
3. - We suggest replacing the word "killed" on page 41 of the Toxicological Profile with the term "sacrificed." The authors are consistent in their use of the term "sacrificed" throughout the rest of the document.
4. - External peer reviewers suggested that EPA include additional information on carbon monoxide and perchlorate as potential sources of co-exposure. We agree with the usefulness of this approach, particularly as it relates to exposure from house fires, industrial processes and the burning of plastics.
5. - EPA's determination of inadequate data to assess the risk of carcinogenicity from HCN and cyanide salts is appropriate given the lack of information on cancer risk.