

August 31, 2010

Ms. Rebecca Clark  
Acting Director  
National Center for Environmental Assessment  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, N.W.  
Washington, DC 20460

RE: Docket ID No. EPA-HQ-2010-0396

Draft Toxicological Review of Formaldehyde in Support of Summary Information on the Integrated Risk Information System

Dear Ms. Clark:

The Methanol Institute appreciates this opportunity to comment on the draft IRIS toxicological review of formaldehyde. As the trade association for the global methanol industry, the Methanol Institute works closely with our downstream customers in the formaldehyde industry. On a global basis, nearly 16 million metric tonnes of methanol will be used as a feedstock for the production of formaldehyde this year, representing one-third of total methanol consumption. Here in the United States, it is estimated that over two million metric tonnes of methanol was consumed for formaldehyde production in 2009. The current housing market slump and the global economic recession have already reduced formaldehyde demand by 20-40%, placing a severe strain on both the formaldehyde and methanol industries. Since both chemical commodities are essential building blocks for hundreds of products that touch our daily lives, we would strongly urge caution in any assessment that may adversely impact these important industries.

In preparing draft IRIS toxicological assessments, NCEA staff are guided by two sets of guidelines, the Information Quality Act (IQA) Guidelines and the EPA's own Guidelines for Carcinogen Risk Assessment (March 2005). Unfortunately, in its draft formaldehyde assessment, the review strays considerably from the rigors of both sets of guidelines, and therefore fails to provide an accurate and objective view of the best available science. It is our deep concern that these failures could form the basis of policy decisions that may have a negative and lasting impact on the U.S. and global economies.

As we believe was also the case with the draft methanol IRIS assessment, the formaldehyde review in several instances incompletely or incorrectly reports a study's findings to support what clearly seem to be pre-determined conclusions. The IQA requires the Agency to fully, objectively and accurately report on the underlying science used to develop the assessment, not to "cherry-pick" individual data points that support a particular finding or ignore other valid research that would point the assessment in a different direction. Under the EPA's Cancer Guidelines, in order to apply the "Carcinogenic to Humans" descriptor in the absence of convincing epidemiological evidence of a causal association between human exposure and cancer, there must be strong and convincing evidence of all of the following four items:

- (1) association between human exposure and either cancer or the key precursor events of the agent's mode of action, but not enough for a causal association; and
- (2) extensive evidence of carcinogenicity in animals; and
- (3) the mode(s) of carcinogenic action and associated precursor events have been indentified in animals; and
- (4) key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information.

We find that the EPA's proposed conclusions regarding Leukemia and Hodgkin's lymphoma fail to provide convincing epidemiological evidence, offer insufficient Mode of Action data and are contradicted by negative animal data. The Hauptmann et al, 2003, is one of two studies used as the basis for linking exposure to formaldehyde with leukemia and Hodgkin's lymphoma, but the Agency fails to note that Beane-Freeman et al, 2009, found that the Hauptmann study missed 1,000 deaths. Further, the EPA did not include the more recent meta-analysis by Bachand et al, 2010, which is the only study that assessed all cohort, case-control, and proportional mortality ratio studies conducted to date, including Beane-Freeman and the corrected Hauptmann data.

The Agency also relied on the controversial Zhang et al, 2009 study, which employed an unconventional methodology, and reported findings that are at odds with three other meta-analysis of much of the same data (Collins 2004, Bosetti 2008, and Bachand 2010). When describing the Lu et al, 2010 study, the assessment notes only that endogenous formaldehyde-DNA adducts are found in all tissues examined, but completely ignores the key finding that NO inhaled exogenous formaldehyde gets past the nasal epithelial tissues to form exogenous formaldehyde-DNA adducts. Without this formation of exogenous formaldehyde-DNA adducts there can be no effects on distant sites and therefore no biological plausibility for formaldehyde induced leukemia.

Further, the draft assessment completely ignores the findings that there is a threshold effect associated with the proposed MOA for nasopharyngeal cancer, which have been accepted by other authoritative bodies in Canada, Germany, EU, Australia, and by the NAS. The draft assessment "cherry-picks" one finding from Meng et al, 2010, but omits the study's major conclusion which is the absence of p53 mutations at increasing formaldehyde doses following 13 weeks of exposure. The animal data chosen by EPA places more weight on the single dose toxicogenomic study by Hester et al, 2003 and 2005, which used inappropriate administration (nasal instillation) and extremely high dose, than on a toxicogenomic study by Andersen et al, 2008, using multiple doses and multiple durations.

We find that an objective review of ALL of the best available science strictly following the Information Quality Act and the EPA's own Cancer Guidelines would fail to support a classification of formaldehyde as being "Carcinogenic to Humans." Given the importance of formaldehyde as a basic chemical building block for hundreds of products that touch our daily lives, the Agency has an obligation to do a very careful weight of evidence assessment of all the available data that studiously avoids a pre-conceived result. We would strongly urge the EPA to carefully consider all of the comments received, and the views of the NAS peer review panel, and revise this draft assessment to more accurately reflect such a careful weighing of the best available science.

Sincerely,



Gregory Dolan  
Executive Director  
Americas/Europe