Responses to Major Comments on Technical Support Document

Public Health Goal
For
Trichloroethylene
In Drinking Water

Prepared by

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INTRODUCTION

The following are responses to major comments received by the Office of Environmental Health Hazard Assessment (OEHHA) on the proposed public health goal (PHG) technical support document for trichloroethylene as discussed at the PHG workshop held on October 6, 1998, or as revised following the workshop. Some commenters provided comments on both the first and second drafts. For the sake of brevity, we have selected the more important or representative comments for responses. Comments appear in quotation marks where they are directly quoted from the submission; paraphrased comments are in italics.

These comments and responses are provided in the spirit of the open dialogue among scientists that is part of the process under Health and Safety Code Section 57003. For further information about the PHG process or to obtain copies of PHG documents, visit the OEHHA web site at www.oehha.org. OEHHA may also be contacted at:

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RESPONSES TO MAJOR COMMENTS RECEIVED

Wilmer, Cutler & Pickering

Comment 1. *Could OEHHA address whether and why it disagrees or rejects the statement in Lofgren v. Motorola (1998) that* "the scientific community ….. does not accept the theory that [TCE] is causally linked to any of the specific diseases at issue in this case".

Response 1: The actual quotation in the cited opinion referred to a California Supreme Court case (*People* v. *Shirley*) : "If a fair overview of the literature discloses that scientists significant either in number or expertise publicly oppose [the theory] … as unreliable, the court may safely conclude that there is no such consensus at the present time." One of the diseases claimed in the Lofgren v. Motorola case was kidney disease. OEHHA's technical support document (TSD) for the proposed public health goal (PHG) for trichloroethylene (TCE) provides an evaluation of current health and safety data relevant to establish a safe concentration of TCE in drinking water pursuant to the specific criteria set forth in the Health & Safety Code Section 116365. Our analysis includes a quantitative risk assessment based on the induction of liver tumors in mice by TCE. We also reviewed the limited human epidemiology, in particular a recent study of German cardboard workers chronically exposed to TCE. This study is the only one we could find that claimed a causal association between TCE exposure and a specific human cancer, in this case kidney cancer. Our TCE TSD included a summary of published criticisms of this study; however, OEHHA believes the findings are plausible albeit not conclusive.

With respect to the judicial opinion in *Lofgre*n v. *Motorola*, we believe that a causal association of chronic human TCE exposure and kidney disease, including cancer, is plausible based on our interpretation of the current scientific data. The establishment of a public health protective environmental criterion such as the PHG does not require "proof" of such effects in humans, but rather is more often based on plausible extrapolation from effects seen in animal studies. Our TSD also derives a safe level for noncancer effects; in this case kidney nephropathy seen in rats chronically exposed to TCE. Since the judicial opinion does not refer to any specific scientific studies it is difficult to know what the scientific community acceptance criterion for TCE is based on. More importantly, OEHHA has a specific legislative mandate in section 116365 to conduct its evaluation of TCE (and all chemicals for which it is developing a PHG) in a very specific manner. OEHHA has complied with this mandate in setting the PHG for TCE. OEHHA has no specific information about the evidence or scientific data the court relied on in Lofgren. Nor does OEHHA have authority to take just the judicial opinion into account.

Halogenated Solvents Industry Alliance, Inc. (HSIA)

Comment 1. We would like to request an extension of the December 14 deadline for comments. Our brief review of the document suggests that it does not incorporate the latest scientific information available. For example, a considerable amount of information has been collected as part of the U.S. Environmental Protection Agency's reassessment of trichloroethylene that is not included in the draft technical support document (TSD).

Response 1. The draft TSD was first made available on the OEHHA homepage in September 1998. It was the subject (along with other proposed PHGs) of a public workshop held in Oakland, CA on October 6, 1998. Following revision the TSD draft was reposted in mid November 1998 for a 30 day comment period ending 12/14/98. The law mandates that OEHHA adopt 25 or more PHG each year and this mandate and our schedule does not allow extensions or delays for the benefit of interested parties. The reassessment of TCE by U.S. EPA is still in progress and is not expected to be completed until the third quarter of 1999 or later. Our draft TCE TSD was reviewed by staffs of the U.S. EPA's Office of Water and NCEA without significant adverse comment. Our law requires reassessment or update of state PHGs at least every five years.

Comment 2. The EPA's reassessment aside, there is a great deal of recent published scientific information that should be taken into account in any current review of trichloroethylene. Two studies in particular should be cited, an epidemiological investigation of occupationally exposed workers (Morgan et al., Epidemiology 9:424(1998)) and a biochemical study on formic acid and the kidney effects of TCE (Green et al., Toxicology 127:39(1998)).

Response 2. We have incorporated summaries of the noted studies and cited as much of the meaningful recent study data on TCE as was feasible in view of our mandated deadline. The objective of the technical support document is to provide the key support for the determination of the PHG and not to provide detailed review of all of the available literature on TCE.

Comment 3. In its review of non-carcinogenic effects, we urge OEHHA to place no reliance on the teratogenicity data of Dawson et al. (1993).

Response 3. OEHHA is aware of the limitations of the Dawson et al. (1993) study which is mentioned in the text of the technical support document. This study was not relied upon in evaluating benchmark doses (Table 7) or estimating potential safe drinking water for non-cancer effects (Table 10) from the more reliable studies. As noted, we chose the kidney nephropathy endpoint as reported by Haag-Gronlund et al. (1995) as the basis for the non-cancer value for safe concentration of TCE in drinking water.

Department of the Air Force

Comment 1. *OEHHA should use a mode of action based framework for implementing dose response assessment for TCE. Specifically for liver and lung cancer use the MOE approach instead of the linear plus nonlinear dose response approach based on TCA and chloral dose metrics. For kidney cancer use linear plus nonlinear instead of linear only based on GST metabolites dose metric.*

Response 1. OEHHA did use a mode of action based framework for assessing dose response options for TCE. The commenter claims or assumes that a mode of action (MOA) for each cancer site has been clearly established, namely: (1) TCA induced peroxisome proliferation in the case of liver cancer; (2) chloral hydrate as a tumor promoter in the lung; and (3) GST metabolites through a genotoxic MOA in the kidney. In each case the commenter proposes a less health conservative dose response approach than that chosen by OEHHA. OEHHA's interpretation of the carcinogen dose response methodology proposed by U.S. EPA in their 1996 Guidelines is as follows. When there is data clearly supporting a linear approach (e.g., genotoxicity) or insufficient information on the MOA then the linear approach is

used. When there is equivocal evidence of linear and nonlinear MOAs both approaches are used. When there is clear and convincing evidence that the only MOA is nonlinear then that approach is used. Since we are mandated to determine a specific value for the PHG and not a range, the MOE approach is of limited use. To apply the nonlinear approach we use the LED_{10} point of departure as a LOAEL for cancer. For TCE OEHHA has chosen the linear approach for kidney cancer and the linear plus nonlinear approaches for liver and lung cancers. OEHHA concludes that the nonlinear MOAs of these latter cancers have not been definitely established and our assessment reflects this uncertainty. Of these three sites the lung and liver tumors presented sufficient data sets to allow adequate dose-response assessment. The rat kidney tumor data was considered inadequate. Similarly, of the dose metrics evaluated, the metabolized dose (AMET) metric seemed to fit the tumor incidence data better than other mode of action based metrics used.

Comment 2. "The uncertainty factors applied include one for potential carcinogenicity. First this is totally inappropriate because this is the noncancer assessment and cancer is being addressed."

Response 2. The alternate cancer calculation for the safe drinking water concentration used the nonlinear approach and the LED10 as a LOAEL. The additional 10-fold uncertain factor for cancer was applied for severity of effect possibly an irreversible cancer. In this and other technical support documents, OEHHA has applied and interpreted proposed U.S. EPA cancer guidelines which are not yet finalized and which OEHHA has not fully adopted. For chemical carcinogens for which adequate quantitative data exist, we calculate cancer potencies after considering the appropriateness of several models. In these cases, OEHHA's convention is not to further modify the non-cancer risk value with a factor for potential carcinogenicity. For TCE, a chemical for which there is sufficient data to calculate a cancer potency, no modifying factor should have been applied in the non-cancer risk assessment. The calculation based on the non-cancer endpoint has been revised to exclude a factor for cancer.

Comment 3. "Finally, though much effort has gone into preparing the current draft, it is curious that OEHHA did not directly use the PBPK models that have been prepared. Upon request, their developers have readily shared these models or reported the values of the relevant dose metrics."

Response 3. We did request, via email, additional model simulations from Dr. Jeffery Fisher of Wright-Patterson Air Force Base in Ohio for the AUC metrics as a function of applied dose in different target tissues but did not receive these data and we assumed the work required was too great. As noted above, the metabolized dose metric (AMET) seemed to fit the tumor data better than the AUC based metrics that we derived from published literature. As noted elsewhere in these responses the timeframe of the PHG mandate does not allow extensive evaluations but rather adopts a five year periodic reassessment to incorporate significant new information.

Comment 4. *A list of 14 additional recent references is attached. These should be included in the technical support document*.

Response 4. The articles noted plus others were obtained and reviewed and the findings incorporated where appropriate into the text and references of the technical support document.