Responses to Major Comments on Technical Support Document

Public Health Goal
For
1,1,2-Trichlorethane
In Drinking Water

Prepared by

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INTRODUCTION

The following are the combined responses to major comments received by the Office of Environmental Health Hazard Assessment (OEHHA) on the public health goal (PHG) technical support document for 1,1,2-trichlorethane, based on the pre-release review draft. Changes have already been made in response to these comments, and have been incorporated into the final PHG posted on the OEHHA website. 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.ca.gov. OEHHA may also be contacted at:

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RESPONSES TO MAJOR COMMENTS RECEIVED

Comments from Reviewer 1 (University of California, Davis)

Comment 1: *Appropriateness of approach:* "The approach taken to determine the PHG is appropriate. The NOEAL derived from the White *et al.* (1985) drinking water study is by far the most appropriate currently available data for the determination of a health-protective value for 1,1,2-TCE."

Response 1: No changes needed.

Comment 2: *Data evaluation and interpretation:* "The available data has been evaluated and interpreted carefully and thoroughly. I agree with the authors on their conclusions regarding the toxicological effects and their data selection for determining the PHG."

Response 2: No changes needed.

Comment 3: *Toxicological Effects in Animals and Plants:* "…headline should be changed to "Toxicological Effects in Mammals", since that is what was reviewed."

Response 3: The header is technically correct since it includes a section on genetic testing in lower organisms, but it differs from most of our other PHG documents. We have removed "…and plants" from the header but retained the more generic "animals" to maintain consistency with our other documents in the series.

Comment 4: *Table 2:* "Numbers do not add up. Is the % Metabolized the sum of Excreta and Expired Air? In that case the numbers for "Metabolized" would have to be 81.5 (rat) and 82.8 (mouse). If % Metabolized is the sum of Excreta, Expired Air (assuming that CO2 is part of Expired Air) and Carcass, the numbers should be 85.4 (rat) and 85.1 (mouse). Also, if fractions are reported this should be done consistently for the whole table. "Recovery" should therefore be 91.5 (rat) and 88.2(mouse)."

Response 4: We added labels identifying biological compartments that the authors (Mitoma *et al.*, 1985) used to report the percentage of dose metabolized. We also extended the Recovery column values by a significant figure to present authors' results more precisely.

Comment 5: "Page 9, line 2: Generally, DNA repair is considered an indicator of toxicity/damage, but if DNA repair mechanisms are not activated in mice (for some reason), the compound can do more damage than otherwise. I don't consider these findings to be contradictory or necessarily "surprising.""

Response 5: The text has been rephrased to indicate that the induced DNA repair provided an apparent contrast between rats and mice, but omitting the "surprising" descriptive.

Comments from Reviewer 2 (University of California, Davis)

Comment 1: "Specifically, this reviewer finds the document to be accurate and complete in terms of appropriate citations, interpretation of published work and conclusions drawn from the results contained in those reports. This reviewer acknowledges that the setting of standards for Public Health Goals for such compounds must be conservative as there are limited data on human exposures and potential species specificities in regard to toxic action is likely. In this regard an inclusive approach has been taken using data from all animal models tested."

Response 1: No changes needed.

Comment 2: "The physical properties of 1,1,2-TCE have been well-characterized and both its pharmacokinetics and pharmacodynamics well-defined in the laboratory rodent animal models. It is known to be absorbed by humans via multiple routes. Taken together the existing data indicate a lower exposure of 1,1,2-TCE is observed for cancer than for non-cancer health risks. Based primarily on the laboratory studies of rodents with cancer as the end point, a new safety of 0.2 ppb is calculated for a risk of one cancer in a million people, 2 ppb for a risk of one cancer in 100,000 exposures and 20 ppb for a risk of one cancer in 10,000 exposures. This is justified on the basis of the rodent data."

Response 2: No changes needed in response to this comment, although it should be noted that we have increased the PHG value to 0. 3 ppb for consistency with another OEHHA risk assessment, as described below, so the values above are obsolete.

Comments from Reviewer 3 (University of California, Davis)

Comment 1: *Appropriateness of data sets:* "Because the cancer endpoint is the driving force behind the development of the PHG, selection of a cancer potency factor is critical in the calculations. The CPF selected for use in the calculation of the PHG is 0.072 mg/kg-d based on OEHHA (1992, 1999). Recently, there is a document from OEHHA (May 2005) that updates the CPFs for numerous compounds. Vinyl trichloride is one of those compounds, and the value of the CPF provided in the update is 0.057 mg/kg-d for both oral and inhalation exposure, the same values used by EPA and all other state and federal agencies. If this CPF is used in the calculations, the value of the PHG changes to 0.3 ppb (rounded from 0.307 ppb), and it is suggested that this value be used as the PHG and 0.057 mg/kg-d be used as the CPF in the calculation. It seems reasonable that the CPF proposed in an OEHHA document be used as the appropriate CPF in the calculation of the PHG. I was unable to obtain the OEHHA documents cited in the PHG document."

Response 1: The commenter is correct that OEHHA recently revised its cancer potency factors for several chemicals, and that 1,1,2-trichlorethane was among them (OEHHA, 2005). The PHG value has been revised accordingly.

Comment 2: *The commenter describes serious reservations about the calculations to establish the Liters/day value used in the equation for the determination of the PHG.*

Response 2: The commenter makes a persuasive point regarding potential flaws in the calculation of equivalent total exposure to drinking water. We agree that this was a needlessly complex calculation. However, this method and others do result in an equivalent value of about 4 L/day for total combined-route exposures to small volatile halogenated hydrocarbons in drinking water, to account for showering and other household uses of drinking water. We have decided merely to accept the 4 L/day value, as cited in our PHG guidelines for such chemicals, and cite one of the methods (the CalTox program), rather than show the chain of calculations. A value of 4 L/day provides a comfortably conservative estimate, and has been used in several other PHGs for chemicals with similar properties.

Comment 3: *Description of uncertainty:* "There is no description of uncertainties for the calculation of the cancer PHG, but there is no need for incorporation of any quantitative estimate of uncertainty. There is a discussion of the uncertainties associated with the study in the Risk Characterization portion of the document. This section clearly states that the finding of carcinogenicity in a single species, with no studies finding carcinogenicity in other species, is a concern and uncertainty."

Response 3: The commenter is correct that while OEHHA discusses potential data quality uncertainties and potential confounding and conflicting information in our PHG documents, we do not affix a level of uncertainty to our calculations of a health-protective concentration. These types of values do not lend themselves to reliable uncertainty estimates.

REFERENCES

Mitoma C, Tyson CA, Riccio ES (1985). Investigation of the species sensitivity and mechanism of carcinogenicity of halogenated hydrocarbons. EPA/OTS, Document #40-842-8424225.

OEHHA (2005). Air Toxics Hot Spots Program Risk Assessment Guidelines; Part II, Technical Support Document For Describing Available Cancer Potency Factors, May 2005. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, California. Accessed at: http://www.oehha.ca.gov/air/hot_spots/pdf/May2005Hotspots.pdf.

White KL, Jr, Sanders VM, Barnes DW, Shopp GM, Jr, Munson AE (1985). Toxicology of 1,1,2-trichloroethane in the mouse. Drug Chem Toxicol 8:333-55.