

Dichlorodifluoromethane (DCDFM) – Guidance for Air

The following guidance was developed by the Minnesota Department of Health (MDH) to evaluate a screening chronic provisional reference concentration (p-RfC) for dichlorodifluoromethane derived by EPA.

Risk Assessment Advice for Air

June 22, 2016

Chemical: Dichlorodifluoromethane (DCDFM)

CAS number: 75-71-8

Endpoint: None

Subchronic Value: 10,000 $\mu\text{g}/\text{m}^3$

Source: Stewart et al., 1978; Prendergast et al., 1967

In February of 2016, the Site Assessment and Consultation Unit (SAC) contacted the Health Risk Assessment Unit (HRA) for assistance in evaluating the screening chronic provisional reference concentration (p-RfC) for dichlorodifluoromethane (DCDFM) derived by the EPA in the appendix of their 2010 Provisional Peer-Reviewed Toxicity Value (PPRTV) report. Of concern was the appropriateness of the critical study, and the uncertainty factors, totaling 10,000, that were applied to the point of departure.

The HRA unit has reviewed the available inhalation toxicology literature for DCDFM and based on the available data, is providing Risk Assessment Advice (RAA) for a subchronic duration for DCDFM in air. The recommendation is to use the point of departure from the Stewart et al. (1978) study summarized in the EPA PPRTV rather than the point of departure from the Prendergast (1967) study chosen by EPA as the basis of their provisional RfC. Data are insufficient to develop RAA for the chronic duration. Basic information supporting the derivation of the subchronic RAA is below.

Data Limitations and Basis for the DCDFM air value

The subchronic p-RfC for DCDFM derived in the PPRTV is based on a study by Prendergast et al. (1967) in which multiple species were dosed via the inhalation route. Based on the presentation of study details in both the PPRTV and the manuscript of Prendergast (1967), critical aspects of a well-controlled and conducted inhalation study are absent, along with key data. It is the opinion of HRA that this study, and its reporting, has many substantial flaws. While this study offers the lowest available point of departure, critical questions remain about the findings and

reliability. Undoubtedly, the database of information for DCDFM inhalation toxicity is limited. A clear, well-conducted, and complete study with multiple dose levels is not available. Despite the limited nature of the database overall, the lack of adverse effects in all inhalation studies conducted, except Prendergast, 1967, is difficult to ignore.

The HRA unit recommends a human exposure study, Stewart et al. (1978), as the critical study from which to draw the point of departure for risk assessment advice. While this study does contain significant shortcomings, such as short duration of exposure, single exposure level, and relatively small group sizes, the experiment appears to be well-conducted, the dataset is sufficiently reported, and the study examines sensitive effects in humans in a controlled clinical setting. In addition, the lack of effects in humans after inhalation exposure to DCDFM is consistent with the overwhelming majority of results in animal studies. Therefore, for the purposes of this risk assessment advice, the point of departure recommended by HRA for DCDFM is the time adjusted NOAEL of 1,179,000 $\mu\text{g}/\text{m}^3$ from Stewart (1978). Listed below is the derivation of the subchronic RAA.

$$\begin{aligned} \text{Subchronic Inhalation Risk Assessment Advice (RAA}_{\text{subchronic}}) &= \\ &11,790 \mu\text{g}/\text{m}^3 \text{ rounded to } 10,000 \mu\text{g}/\text{m}^3 \\ &= \frac{\text{Point of Departure (1,179,000 } \mu\text{g}/\text{m}^3)}{\text{(Uncertainty Factors (100))}} \\ &= 11,790 \mu\text{g}/\text{m}^3 \end{aligned}$$

Information from Critical Study (Stewart et al., 1978)

Study population: 8 Caucasian Males in 1000 ppm 4-week exposure group

Exposure method: Controlled-environment chamber

Exposure continuity: 8 hours/day, 5 days/week

Exposure duration: 4 weeks

LOAEL: No effects seen

NOAEL: 1,000 ppm (4,950,000 $\mu\text{g}/\text{m}^3$)

Adjusted Point of Departure: 1,179,000 $\mu\text{g}/\text{m}^3$ (time corrected)

Total Uncertainty Factor: 100

UF Rationale: 10 fold for human variability and 10 fold selected for database insufficiencies including the lack of reproductive/developmental studies with inhalation route of exposure, and studies with multiple dose levels.

Critical effect: None

References

Prendergast, J. A., Jones, R. A., Jenkins, L. J., & Siegel, J. (1967). Effects on experimental animals of long-term inhalation of trichloroethylene, carbon tetrachloride, 1, 1, 1-trichloroethane, dichlorodifluoromethane, and 1, 1-dichloroethylene. *Toxicology and applied pharmacology*, 10(2), 270-289.

Stewart, R. D., Newton, P. E., Baretta, E. D., Herrmann, A. A., Forster, H. V., & Soto, R. J. (1978). Physiological response to aerosol propellants. *Environmental health perspectives*, 26, 275.

Minnesota Department of Health
ESA-EIA
625 Roberts St N
St. Paul, MN 55164
651-201-4899

health.risk@state.mn.us
www.health.state.mn.us

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