

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for carbon tetrachloride (CAS #56-23-5)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: Screening levels for carbon tetrachloride

DATE: August 12, 2015

The screening levels for carbon tetrachloride are as follows:

- ITSL = 480 ug/m³, annual averaging time
- IRSL = 0.17 ug/m³, annual averaging time
- SRSL = 1.7 ug/m³, annual averaging time

The basis for these SLs is the EPA (2010; IRIS) assessment, with an adjustment made by AQD to the total uncertainty factor (UF_T) that was utilized by EPA (2010). The previous AQD ITSL was 100 ug/m³ with a 24-hour averaging time (AT), established on 4/1/2010. That ITSL value was based on and identical to the EPA RfC established by EPA (2010) utilizing a UF_T = 100. The EPA (2010) UF_T consisted of UF_H = 10, UF_A = 3, and UF_D = 3. EPA explained that the use of the latter UF_D for database gaps was due to the lack of an adequate multigeneration study, although the available inhalation and oral bioassays investigating the potential for developmental effects did not identify developmental effects as a sensitive critical effect. "On balance, the available information suggests that further developmental toxicity testing would not likely result in a POD smaller than that based on liver toxicity. The database lacks an adequate multigeneration study of reproductive function by any route of exposure; therefore, a UF of 3 was applied." (EPA, 2010). It is not AQD's current policy and practice to apply a UF_D value other than "1" purely as a default value, but to only apply or adopt a value other than "1" when it is justified based on chemical-specific information indicating that a potential critical effect has not been adequately tested. Based on the EPA (2010) database assessment, their application of a UF_D = 3 is a default policy decision that is applied despite the availability of findings indicating that the potential for developmental effects was not a sensitive endpoint. Therefore, the EPA (2010) UF_D value of 3 will not be utilized by AQD; this is allowed under Rule 229(1)(c). A UF_T = 30 will be applied, consisting of UF_H = 10 and UF_A = 3, consistent with EPA (2010). Also, in setting the AT for the ITSL in 2010, AQD applied a 24-hour AT to the ITSL, which is the default procedure per Rule 232(2)(b). The AT is being changed now to annual because the RfC was derived by EPA (2010) from a key study using a chronic exposure protocol (EPA, 2010), as allowed under Rule 229(2)(b) based on toxicological grounds.

EPA (2010) based the RfC on a key study involving rat inhalation exposure (Nagano et al., 2007; JBRC, 1998), with a BMCL_{10[HEC]} = 14.3 mg/m³ for fatty changes in the liver of rats using PBPK modeling for interspecies extrapolation, to derive the RfC = 100 ug/m³. The ITSL of

480 ug/m³ (rounded from 477 ug/m³) is based on the same POD (14,300 ug/m³) divided by a UF_T = 30 as discussed above.

EPA (2010) found that carbon tetrachloride is, “likely to be carcinogenic to humans” based on sufficient evidence of carcinogenicity in animals with both the oral and inhalation routes of exposure, with findings of hepatic tumors in multiple species (rat, mouse and hamster) and pheochromocytomas (adrenal gland tumors) in mice. Regarding the possible mode of action (MOA) for carcinogenicity, EPA (2010) noted that, “...the MOA for carbon tetrachloride carcinogenicity across all exposure levels is unknown at this time.” EPA (2010) provided a unit risk = 6E-6 per ug/m³, representing an upper bound, continuous lifetime exposure risk estimate. Based on this unit risk estimate (URE), the IRSL and SRSL are derived as follows:

$$\text{IRSL} = \frac{1\text{E-}6}{6\text{E-}6 \text{ (ug/m}^3\text{)}^{-1}} = 0.17 \text{ ug/m}^3 \text{ (annual AT)}$$

$$\text{SRSL} = \frac{1\text{E-}5}{6\text{E-}6 \text{ (ug/m}^3\text{)}^{-1}} = 1.7 \text{ ug/m}^3 \text{ (annual AT)}$$

References

EPA. 2010. IRIS database. Chemical entry for carbon tetrachloride. Chronic inhalation RfC assessment and carcinogenicity assessment. Last revised 3/31/2010.

JBRC (Japan Bioassay Research Center). 1998. Subchronic inhalation toxicity and carcinogenicity studies of carbon tetrachloride in F344 rats and BDF1 mice. Unpublished report to the Ministry of Labor. As cited in : EPA (2010).

Nagano, K. et al. 2007. Inhalation carcinogenicity and chronic toxicity of carbon tetrachloride in rats and mice. Inhal. Tox. 19:1089-1103.

RS:lh