

**STATE OF MICHIGAN
Rick Snyder, Governor**



**DEPARTMENT OF ENVIRONMENTAL QUALITY
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August 14, 2017

**Response to Public Comments for
1,3-Butadiene (CAS# 106-99-0)**

Summary:

Based on public comments, the Air Quality Division (AQD) has reviewed the Initial Threshold Screening Level (ITSL) for 1,3-butadiene. As a result of that review, the AQD is changing the ITSL from 2 ug/m³ with a 24 hr averaging time to 33 ug/m³ with annual averaging time.

Background:

Revisions to the Air Pollution Control Rules¹ were promulgated December 22, 2016. Subsequently, the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) published toxic air contaminant screening levels and their basis as required by Rule 230(1). Pursuant to Rule 230(2), the AQD solicited and received public comments on these screening levels for 60 days: February 14 through April 14, 2017. The AQD must respond to these comments within 180 days; the latest date for response is October 11, 2017.

¹ Air Pollution Control Rules in Michigan Administrative Code promulgated pursuant to Article II Pollution Control, Part 55 (Sections 324.5501-324.5542), Air Pollution Control, of the Natural Resources And Environmental Protection Act, 1994.PA 451, as amended (NREPA).

Comments and Responses:

Comment:

One comment was received by AQD on the ITSL for 1,3-butadiene (BD). They stated that the basis for the current ITSL (2 ug/m³ with a 24 hr averaging time based on the EPA (2002) RfC of the same value) should be replaced by the more recent chronic health benchmark of the TCEQ (2008), which is a chronic Reference Value (ReV) of 33 ug/m³. The commenter suggested that AQD evaluate this TCEQ (2008) benchmark and base the ITSL on this more up-to-date and thorough assessment.

Response:

A review of TCEQ (2008) reveals that they initially based their evaluation on the EPA (2002) assessment, with the same key study and critical effect as EPA (2002), but with supplemental dose-response modeling to discern the appropriate point of departure. TCEQ (2008) utilized a 5% response level (BMCL₀₅) rather than the 10% response level (BMCL₁₀) as utilized by EPA (2002). They reasoned that the BMCL₀₅ has generally been considered a conservative NOAEL surrogate whereas the BMCL₁₀ may be analogous to a NOAEL or a LOAEL. As a result, TCEQ (2008) utilized a lower uncertainty factor for LOAEL-to-NOAEL conversion (UF_L) of 1, whereas EPA (2002) utilized a value of 10. Also, TCEQ (2008) accounted for the interspecies differences between the test species (mice) and humans, with regard to the ability to metabolize 1,3-butadiene to the presumptive toxic diepoxide metabolite (DEB). EPA (2002) also agreed with this concept, but defaulted to an interspecies toxicokinetic uncertainty factor (UF_{A-TK}) of 1: "There is strong evidence that the diepoxide metabolite (1,2:3,4-diepoxibutane, DEB) is required to elicit ovarian atrophy (U.S. EPA, 2002; Chapter 5), and it is expected, based on pharmacokinetic data, that humans produce less DEB than mice (U.S. EPA, 2002, Chapter 3). However, DEB levels cannot be quantified without an adequate physiologically-based pharmacokinetic (PBPK) model. Thus, default dosimetry (i.e., 1,3-butadiene exposure concentration) was used for dose-response modeling, and the default value of 1 for the pharmacokinetic portion of the interspecies uncertainty factor for inhalation exposures was retained." (EPA, 2002). TCEQ (2008) Toxicology Section (TS) found that, "However, there is empirical evidence to indicate that the toxicokinetic UF is considerably less than 1 because mice metabolize BD to the reactive metabolite DEB much more than humans as discussed in Section 4.1.2 MOA Analysis. Although the experimental data are not sufficient to develop a chemical-specific adjustment factor (CSAF) for BD, it would support a UF_A substantially less than 1. The toxicokinetic UF_A that will be used by the TS is 0.3, although it may be substantially less than 0.3, as discussed below. If a BD-specific toxicokinetic UF = 0.3 is used with the standard toxicodynamic UF = 3, the total UF_A = 1."

These differences and other comparisons between EPA (2002) and TCEQ (2008) are shown below in Table 1.

Table 1. Comparison of the EPA (2002, IRIS) RfC and the TCEQ (2008) chronic ReV for 1,3-butadiene.

Agency:	EPA (2002)	TCEQ (2008)
Key study	NTP (1993) 2-yr mouse inhalation study	same
Critical Effect	Ovarian atrophy in B6C3F1 mice	same
NOAEL or LOAEL	LOAEL = 6.25 ppm, 6 hr/d, 5 d/wk	same
BMC	BMC ₁₀ = 1.05 ppm (2320 ug/m ³) ¹	BMC ₀₅ = 0.607 ppm (1341 ug/m ³)
BMCL	BMCL ₁₀ = 0.88 ppm (1945 ug/m ³) ¹	BMCL ₀₅ = 0.462 ppm (1021 ug/m ³)
Composite UF	1000	30
UF _H	10	10
UF _A	3 (UF _{A-TK} = 1; UF _{A-TD} = 3)	1 (UF _{A-TK} = 0.3; UF _{A-TD} = 3)
UF _L	10 ²	1 ⁴
UF _D	3 ³	3 (agreement with EPA (2002))
Final benchmark	RfC = 2 ug/m ³	Chronic ReV = 15 ppb = 33 ug/m ³

¹ 1 ppm = 2.21 mg/m³ = 2210 ug/m³

² “An extrapolation factor for effect level is applied because the 10% response level used as a point of departure is an adverse effect level. Therefore, a factor analogous to the LOAEL-to-NOAEL factor is needed to attempt to extrapolate to a level closer to a no effect level.” (EPA, 2002)

³ “Finally, a factor of 3 was used to reflect an incomplete database, in particular the absence of a multigeneration study and a developmental neurotoxicity study.” (EPA, 2002)

⁴ TCEQ utilized a UF_L = 1 because the BMC modeling was performed to determine a Point of Departure (POD) based on the BMCL₀₅, which is considered to be a conservative NOAEL surrogate (TCEQ, 2008).

It may be noted that TCEQ (2008) also derived a 24-hr ReV = 430 ppb (968 ug/m³) based on a mouse developmental toxicity study. This value is 29 times higher than the chronic ReV of 33 ug/m³.

Following this review of EPA (2002) and TCEQ (2008), AQD agrees with the commenter that TCEQ (2008) is a more appropriate basis for the ITSL. TCEQ (2008) performed more refined modeling of the low dose-response relationship to develop a surrogate no-effect level, and utilized the available data on interspecies differences to account for the relatively lower formation of the toxic metabolite in humans as compared to mice. AQD agrees with the TCEQ (2008) derivation of their ReV. AQD will be consistent with TCEQ (2008) by assigning an annual averaging time to this ITSL; the TCEQ (2008) 24-hr ReV is much higher and does not suggest and a shorter averaging time is appropriate or necessary for an ITSL of 33 ug/m³.

Summary and Conclusions:

Based on public comments, the Air Quality Division (AQD) has reviewed the Initial Threshold Screening Level (ITSL) for 1,3-butadiene. As a result of that review, the AQD is changing the ITSL from 2 ug/m³ with a 24 hr averaging time to 33 ug/m³ with annual averaging time.

The primary AQD reviewer for these comments was Robert Sills, AQD Toxics Unit Supervisor. The secondary (peer) reviewer was Mike Depa, Senior Toxicologist, AQD Toxics Unit.

References:

EPA. 2002. Integrated Risk Information System (IRIS database). 1,3-Butadiene. RfC last revised 11/5/2002.

Texas Commission on Environmental Quality (TCEQ). 2008. 1,3-Butadiene. Development Support Document. August 7, 2008.