UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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SUBJECT: Existing Chemical Exposure Limit (ECEL) for Occupational Use of 1,4-Dioxane

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EPA calculated an 8-hour existing chemical exposure limit (ECEL) as a summary value to represent occupational exposure scenarios and the most sensitive health endpoints. This calculated ECEL may be used in support of risk management efforts on 1,4-dioxane under TSCA section 6(a), 15 U.S.C. §2605. EPA calculated the ECEL to be 0.055 ppm (0.20 mg/m^3) for inhalation exposures to 1,4-dioxane as an 8-hour time-weighted average (TWA) and for use in workplace settings (see Appendix 0 of the 2023 Draft Supplement to the Risk Evaluation for 1,4-Dioxane). This ECEL is based on the Inhalation Unit Risk (IUR) for lifetime cancer risks based on multiple tumor types observed in rodents, including nasal cavity squamous cell carcinoma, Zymbal gland adenoma, hepatocellular adenoma or carcinoma, renal cell carcinoma, peritoneal mesothelioma, mammary gland fibroadenoma, and subcutis fibroma.

This calculated ECEL value represents the exposure concentration below which workers and occupational non-users are not expected to exhibit any appreciable risk of adverse toxicological outcomes, accounting for potentially exposed and susceptible subpopulations (PESS). It is derived based

on the most sensitive and relevant human health endpoint, a cancer benchmark of 1 x 10^{-4}, and standard occupational scenario assumptions of 8 hr/day, 5 day/week exposures. While this calculated ECEL is a useful limit to consider for risk management, unreasonable risk determinations and subsequent risk management actions may also incorporate uncertainties, feasibility considerations, and additional factors as described in the Risk Evaluation Procedural Rule (82 FR 33726).

EPA expects that the lifetime cancer ECEL of 0.055 ppm (0.20 mg/m^3) would keep excess lifetime cancer risk resulting from occupational exposure ≤ 1x10^{-4} benchmark value. This ECEL is also protective of liver toxicity and effects in the olfactory epithelium resulting from acute and chronic occupational exposures, respectively. EPA has not separately calculated a short-term exposure limit (STEL) or ceiling for 1,4-dioxane.

Identified occupational monitoring data for 1,4-dioxane demonstrates measured workplace air concentrations below the calculated ECEL. These data support the feasibility of monitoring air concentrations below the calculated ECEL. EPA searched for available monitoring methods from the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and EPA and identified one NIOSH method, summarized in Appendix B. Table Apx B-1 presents the validated NIOSH method and is not intended to be a comprehensive list of available air monitoring methods for 1,4-dioxane. The monitoring method identified by EPA can be sensitive enough to detect concentrations below the ECEL, but the limit of detection for this method varies depending on how it is applied.

OSHA set a permissible exposure limit (PEL) as an 8-hour TWA for 1,4-dioxane of 100 ppm (https://www.osha.gov/annotated-pels). However, as noted on OSHA's website, "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970 and have not been updated since that time." In addition, OSHA's PEL must undergo both risk assessment and feasibility assessment analyses before selecting a level that will substantially reduce risk under the Occupational Safety and Health Act. EPA's calculated ECEL is a lower value and is based on newer information and analysis from this risk evaluation.

Recommended exposure limits have also been established for 1,4-dioxane by other governmental agencies and independent groups. The American Conference of Governmental Industrial Hygienists (ACGIH) set a Threshold Limit Value (TLV) at 20 ppm TWA. California OSHA set a PEL of 0.28 ppm (https://www.osha.gov/annotated-pels/table-z-1). This chemical also has a NIOSH 30-minute Recommended Exposure Limit Ceiling (REL-C) of 1 ppm (https://www.cdc.gov/niosh/npg/).

Appendix A ECEL and Other Exposure Limit Calculations

This appendix presents the calculations used to estimate the ECEL and other exposure limits used for comparison. The values used in the equations below were originally derived in the 2020 risk evaluation and are summarized in Table 4-1 of the 2023 Draft Supplement to the Risk Evaluation for 1,4-Dioxane.

Lifetime Cancer Existing Chemical Exposure Limit

The $ECEL_{cancer}$ is the concentration at which the extra cancer risk is equivalent to the benchmark cancer risk of $1x10^{-4}$:

$$EL_{cancer} = \frac{Benchmark_{Cancer}}{IUR} * \frac{AT_{IUR}}{ED * EF * WY} * \frac{\text{IR}_{\text{input}}}{\text{IR}_{\text{workers}}}$$

$$= \frac{1X10^{-4}}{3.7 \times 10^{-3}\ per\ ppm} * \frac{8\frac{h}{d} * \frac{260d}{y} * 78y}{8\frac{h}{d} * \frac{250d}{y} * 40y} * \frac{0.6125\ \text{m}^3/hr}{0.6125\ \text{m}^3/hr} =$$

$$= 0.055 \text{ ppm} = 0.20\ \frac{\text{mg}}{\text{m}^3}$$

Where:

Molar Volume	=	24.45 L/mol, the volume of a mole of gas at 1 atm and 25 °C
MW	=	Molecular weight of 1,4-dioxane (88.11 g/mole)

Acute Non-Cancer Exposure Limit

The acute exposure limit (EL_{acute}) is based on the occupational human equivalent concentration for acute liver toxicity. The EL_{acute} was calculated as the concentration at which the acute MOE would equal the benchmark MOE for acute occupational exposures using the following equation:

$$\text{EL}_{\text{acute}} = \frac{\text{HEC}_{\text{acute,occupational}}}{Benchmark\ MOE_{acute}} * \frac{\text{AT}_{\text{HEC acute}}}{ED} * \frac{\text{IR}_{\text{input}}}{\text{IR}_{\text{workers}}} = \frac{78.7 \text{ ppm}}{300} * \frac{\frac{8h}{d}}{\frac{8h}{d}} * \frac{0.6125\ \frac{\text{m}^3}{hr}}{0.6125\ \frac{\text{m}^3}{hr}}$$

$$= 0.26 \text{ ppm} = 0.95\ \frac{\text{mg}}{\text{m}^3}$$

Chronic Non-Cancer EL

The chronic non-cancer exposure limit ($EL_{chronic}$) is based on the occupational human equivalent concentration for effects in the olfactory epithelium. The $EL_{chronic}$ was calculated as the concentration at which the chronic margin of exposure (MOE) would equal the benchmark MOE for 8-hour chronic occupational exposures with the following equation:

$$\text{EL}_{\text{inhal,occupational}} = \frac{\text{HEC}_{\text{chronic,occupational}}}{Benchmark\ MOE_{chronic}} * \frac{\text{AT}_{\text{HEC chronic}}}{ED*EF*WY} * \frac{\text{IR}_{\text{input}}}{\text{IR}_{\text{workers}}}$$

$$= \frac{3.6 \text{ ppm}}{30} * \frac{\frac{8h}{d} * \frac{260d}{y} * 40\ y * 0.6125\ \text{m}^3/hr}{\frac{8h}{d} * \frac{250d}{y} * 40\ y * 0.6125\ \text{m}^3/hr} = 0.13 \text{ ppm}$$

$$EL\ \left(\frac{\text{mg}}{\text{m}^3}\right) = \frac{EL\ ppm * MW}{Molar\ Volume} = \frac{0.13 \text{ ppm} * 88.11 \frac{g}{mol}}{24.45 \frac{L}{mol}} = 0.45\ \frac{\text{mg}}{\text{m}^3}$$

Where:

$AT_{HECchronic}$	=	Averaging time for the POD/HEC used for evaluating non-cancer, chronic occupational risk, based on study conditions and/or HEC adjustments (8 hrs/day for 260 days/yr) and assuming the number of years matches the high-end working years (WY, 40 yrs) for a worker (2020 RE Section 3.2.6.2.4)
$AT_{HECacute}$	=	Averaging time for the POD/HEC used for evaluating non-cancer, acute occupational risk, based on study conditions and/or any HEC adjustments (8hrs/day) (2020 RE Section 3.2.6.2.1)
AT_{IUR}	=	Averaging time for the cancer IUR, based on study conditions and any adjustments (8 hrs/day for 260 days/yr) and averaged over a lifetime (78 yrs) (2020 RE Section 3.2.6.2.5)
Benchmark MOE_{acute}	=	Acute non-cancer benchmark margin of exposure, based on the total uncertainty factor of 300 (2020 RE Table 4-4; Supplement Table 5-1)
Benchmark $MOE_{chronic}$	=	Chronic non-cancer benchmark margin of exposure, based on the total uncertainty factor of 30 (2020 RE Table 4-4; 2023 Supplement Table 5-1)
$Benchmark_{Cancer}$	=	Benchmark for excess lifetime cancer risk
ECEL	=	Existing chemical exposure limit (ppm)
EL_{acute}	=	Exposure limit based on acute liver toxicity
$EL_{chronic}$	=	Exposure limit based on chronic effects in olfactory epithelium
ED	=	Exposure duration (8 hrs/day) (2020 RE Appendix G.2; Table 4-4)
EF	=	Exposure frequency (250 days/yr), (2020 RE Appendix G.2; Table 4-4)
$HEC_{acute\ or\ chronic,\ occupational}$	=	Human equivalent concentration for acute or chronic occupational exposure scenarios (2020 RE Table 4-4; Supplement Table 5-1)
IUR	=	Inhalation unit risk (per ppm) (2020 RE Table 4-4; Supplement Table 5-1)
IR	=	Inhalation rate (for 1,4-dioxane, EPA used an inhalation rate of 0.6125 m^3/hr for both workers and the general population at rest)
WY	=	Working years per lifetime at the 95^{th} percentile (40 yrs) (2020 RE Table 4-4)

Unit conversion:

1 ppm = 3.6 mg/m^3 (based on molecular weight of 88.11 g/mol for 1,4-dioxane)

Appendix B Summary of Air Sampling Analytical Methods Identified

EPA conducted a search to identify relevant NIOSH, OSHA, and EPA analytical methods used to monitor for the presence of 1,4-dioxane in air (see Table_Apx B-1). This table covers validated methods from governmental agencies and is not intended to be a comprehensive list of available air monitoring methods for 1,4-dioxane. The sources used for the search included the following:

1) NIOSH Manual of Analytical Methods (NMAM); 5th Edition
   - URL: https://www.cdc.gov/niosh/nmam/default.html
2) NIOSH NMAM 4th Edition
   - URL: https://www.cdc.gov/niosh/docs/2003-154/default.html
3) OSHA Index of Sampling and Analytical Methods
   - URL: https://www.osha.gov/dts/sltc/methods/
4) EPA Environmental Test Method and Monitoring Information
   - URL: https://www.epa.gov/measurements-modeling/index-epa-test-methods

Table_Apx B-1. Limit of detection (LOD) and Limit of Quantification (LOQ) summary for air sampling analytical methods identified.

Air Sampling Analytical Methods	Year Published	LOD[a]	LOQ	Notes	Source
NIOSH Method 1602[b] https://www.cdc.gov/niosh/docs/2003-154/pdfs/1602.pdf	1994 (issue 2)	0.10 to 21 mg/m^3 (0.028 to 5.8 ppm)	n/a	Method reports the LOD as 0.01 mg per sample and provides procedures for collecting air samples between 0.5 and 15 L with a flow rate of 0.01 to 0.2 L/min. Multiple media change-outs will be required in order to achieve the minimum LOD based on a maximum sampling volume of 15L.	NIOSH NMAM 4th Edition https://www.cdc.gov/niosh/docs/2003-154/default.html

ppm = parts per million; ppb = parts per billion; ppt = parts per trillion

[a] These sources cover a range of LOD including both below and above the ECEL value. This method provides the LOD based on sample size. For a sample size range of 0.5L to 15L, the LOD would be 0.67 mg/m^3 to 20 mg/m^3, however the LOD listed in the table can be achieved through changeouts of media across an 8-hr period.

[b] Note: It is common for laboratories to acquire updated equipment and for the modern equipment to offer dramatically greater performance than the equipment available when NIOSH Method 1602 was published resulting in significantly lower LOQ/LODs. However, NIOSH does not necessarily continually update the method since the labs are using the same general procedures with just modified/better equipment. Therefore, the lab is permitted to report their method as "modified NIOSH Method 1602". The lab will include a record of how it modifies the method in their results.