COMMONWEALTH OF PENNSYLVANIA
DEPARTMENT OF ENVIRONMENTAL PROTECTION
BUREAU OF CLEAN WATER

RATIONALE FOR THE DEVELOPMENT OF AMBIENT WATER QUALITY CRITERIA HUMAN HEALTH PROTECTION

1,4-Dioxane

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Executive Summary

States have an obligation under Section 303(c)(1) of the federal Clean Water Act (CWA) to periodically, but at least once every three years, review and revise as necessary their water quality standards. The federal water quality standards regulation at 40 CFR 131.11(b)(1) requires states to adopt numeric water quality criteria that are based on section 304(a) criteria recommendations developed by the United States Environmental Protection Agency (USEPA), section 304(a) criteria recommendations modified to reflect site-specific conditions, or other scientifically-defensible methods. Additionally, the CWA directs states to adopt criteria for toxic pollutants "the presence of which in the affected waters could reasonably be expected to interfere with a state's designated uses." 33 U.S.C. § 303(c)(2)(B).

In December 2020, USEPA completed and published an updated evaluation of 1,4-dioxane under the Toxic Substances Control Act (TSCA) (USEPA 2020). This recent evaluation by USEPA continues to identify 1,4-dioxane as a likely human carcinogen. Following an evaluation of the available scientific data and information on permitted discharges in this Commonwealth, the Pennsylvania Department of Environmental Protection (Department) has developed an ambient water quality criterion recommendation of 0.3 µg/L to protect human health from the toxic effects of 1,4-dioxane.

History of Regulation

As part of its 8th triennial review of water quality standards, the Department evaluated 1,4-dioxane and developed a human health water quality criterion recommendation of 0.35 ug/L. This value was calculated using information available in USEPA's Integrated Risk Information System (IRIS), the Department's policies and regulations for the development of human health-based criteria, and USEPA's *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* (EPA 2000). The recommendation was approved by the Environmental Quality Board (Board) as a proposed rulemaking at its April 17, 2012 meeting and published in the *Pennsylvania Bulletin* on July 7, 2012 (42 Pa.B. 4367). Based on comments received during the public comment period, the Department withdrew its proposed statewide criterion for 1,4-dioxane at the final phase of rulemaking, pending further evaluation, including additional data collection.

Since 2013, the Department has collected additional information regarding various sources and discharges of 1,4-dioxane to surface waters of this Commonwealth. While neither the oral slope factor for 1,4-dioxane in IRIS nor the equation used to calculate water quality criteria to protect human health has changed since 2013, USEPA did publish updated exposure inputs in 2015 which are used in the calculation of human health criteria, including the inputs for human body mass, daily water intake and daily fish intake. The Department adopted these 2015 USEPA updates as part of its 9th triennial review, which was approved by USEPA in 2020. As such, the Department has reevaluated and recalculated a 1,4-dioxane water quality criterion for the protection of human health using USEPA's new exposure inputs for body mass, water intake and fish intake.

Background

1,4-dioxane (CASRN: 123-91-1) is a synthetic, semi-volatile organic compound that is also known as dioxane, p-dioxane, diethylene oxide, diethylene ether, dioxyethylene ether, and 1,4-diethylene dioxide and glycol (USEPA 2013, ITRC 2020). It is a clear, colorless liquid at ambient temperatures with a faint sweet odor similar to that of diethyl ether which mixes easily with water, most organic solvents, aromatic hydrocarbons and oils. 1,4-dioxane has been used as a laboratory reagent; as a chemical intermediate; in plastic, rubber, insecticides, and herbicides; as part of a polymerization catalyst; and as an extraction medium of animal and vegetable oils. However, it is primarily used as a solvent, or solvent stabilizer (ITRC 2020, ATSDR 2012). As a solvent, 1,4-dioxane has various uses in the medical, pharmaceutical, printing inks and paints, automotive, adhesives, and biotechnical industries (ITRC 2020). Historically, it was used as a stabilizer for the solvent 1,1,1-trichloroethane. It can also show up as a contaminant in ethoxylated surfactants. These substances are commonly used in consumer cosmetics, detergents, and shampoos (ATSDR 2012).

Production of 1,4-dioxane was at its highest during the period spanning the 1950s through the mid-1980s (ITRC 2020). Production significantly declined following the 1990 amendments to the Clean Air Act and the Montreal Protocol, which mandated a gradual phase-out of 1,1,1-trichloroethane production in the United States (USEPA 2013).

1,4-dioxane can be released into the environment during its production, the processing of other chemicals, its use, and with its unintentional formation during the manufacture of other substances (ATSDR 2012). Facilities that conduct disposal through incineration can release 1,4-dioxane via emissions. Wastewater treatment plant effluent, landfill leachate and improper waste disposal methods are the most significant contributors of 1,4-dioxane found in surface waters. Groundwater contamination primarily has been associated with 1,1,1-trichloroethane releases, effluent water reuse (e.g., spray irrigation), and sewer line exfiltration issues (ITRC 2020).

Since 1,4-dioxane is a semi-volatile compound, it will exist as a vapor when it enters the air and is expected to volatilize at a moderate rate from water and soil surfaces.

In air, 1,4-dioxane is degraded through photooxidation with an estimated half-life ranging from approximately 6 hours to 3 days.

Based on its estimated K_{oc} value,1,4-dioxane is expected to be highly mobile in soil, which indicates there is a high likelihood of this pollutant reaching and contaminating groundwater aquifers.

The estimated half-life of 1,4-dioxane from a river model is seven days and from a lake model is 56 days. Given that volatilization is hindered in cases of groundwater contamination, 1,4-dioxane is likely to be persistent (USEPA 2013, ATSDR 2012). In water, 1,4-dioxane has been found to be resistant to biodegradation, hydrolysis and direct photolysis. It may undergo indirect photolysis, but degradation through this process is very slow. The half-life for this reaction is approximately 336 days at pH 7 (ATSDR 2012). One author (Roy et al. 1994) did observe biodegradation of 1,4-dioxane by an acclimated microbial culture. However, this observation occurred under very specific and enhanced conditions, and biodegradation was generally not observed under ambient conditions (ATSDR 2012).

In 2017, USEPA collected data on 1,4-dioxane in water as part of its third Unregulated Contaminants Monitoring Rule (UCMR). USEPA uses the UCMR program to collect data for contaminants suspected to be present in drinking water, but that do not have health-based standards set under the federal Safe Drinking Water Act (SDWA). Every five years USEPA develops a new list of UCMR contaminants, largely based on the Contaminant Candidate List (CCL). Sampling indicated that approximately 10% of surface water sources had detections of 1,4-dioxane, and approximately 3% of the sample results were above the reference concentration of 0.35 ug/L (USEPA 2017a).

Discharges and Sources of 1,4-Dioxane in Pennsylvania

When the Department withdrew its recommendation for 1,4-dioxane in 2013, the Board requested the Department collect additional wastewater effluent data and report back to the Board. As a result, the Department determined that it should implement increased monitoring in National Pollutant Discharge Elimination System (NPDES) permits for several pollutants, including 1,4-dioxane, upon issuance or reissuance of an individual NPDES permit. Where the concentration of 1,4-dioxane in a discharge exceeded 10 µg/L and the discharge flow exceeded 0.1 million gallons per day (MGD), Part A of the permit included monitor and report for 1,4-dioxane. Discharges of 0.1 MGD or less were required to monitor and report for 1,4-dioxane if the concentration of 1,4-dioxane in the discharge exceeded 100 µg/L. Following these guidelines, the Department issued 22 NPDES permits containing monitor and report requirements for 1,4-dioxane, and there is currently one active NPDES permit containing numeric permit effluent limitations based on a site-specific criterion for 1,4-dioxane. The 23 permitted facilities are located in five out of six Department regions and include permitted discharges of treated effluent from landfills, wastewater treatment plants, power generating stations and other industrial facilities. The Department also reviewed water quality sample data available for 1,4-dioxane in the Water Quality Portal. The Water Quality Portal is a cooperative service provided by the United States Geological Survey (USGS), USEPA, and the National Water Quality Monitoring Council (NWQMC). A search of the database generated approximately 100 sample results for 1,4-dioxane in Pennsylvania surface waters. Most of the relevant data were collected by the Delaware River Basin Commission (DRBC) in 2021. The samples were primarily collected within the Lehigh River basin, and the results ranged from 0.016 ug/L (i.e., the method detection limit) to 470 ug/L.

The Department's data collection and water quality data review efforts indicate that 1,4-dioxane is found in select surface waters as well as wastewater discharges across the Commonwealth. Thus, statewide ambient water quality criteria for 1,4-dioxane are appropriate to protect human health and the protected water uses listed in §93.3.

Human Health and 1,4-Dioxane

1,4-dioxane is known to enter the human body through inhalation, dermal absorption, intravenous injection, and ingestion. As a semi-volatile compound, 1,4-dioxane can be quickly taken into the human body via the lungs. This exposure route is primarily of concern to those who work with 1,4-dioxane in a laboratory or industrial setting. Adsorption through the skin is another route of concern, both for workers who handle 1,4-dioxane directly in a professional capacity and by consumers through the use of deodorants, shampoos or cosmetics which may have been contaminated. Some studies indicate that much of the 1,4-dioxane will evaporate before absorption through the skin can take place; however, USEPA noted there are significant data gaps for the potential carcinogenic effects of 1,4-dioxane from dermal exposure in humans and animals (USEPA 2020, ATSDR 2012). Ingestion, or oral exposure, to 1,4-dioxane can occur by eating food products contaminated with pesticides containing 1,4-dioxane, drinking contaminated water or through unintentional ingestion of consumer products (e.g., cosmetics, mouthwash and other personal care products). Upon exposure, 1,4-dioxane is bioavailable and will be absorbed, particularly when exposure occurs via the oral and inhalation pathways.

Most of the available scientific data that has been published on the toxic effects of 1,4-dioxane has been obtained through animal toxicity studies. Although the available data on toxic effects in humans is limited, acute and chronic exposures to 1,4-dioxane via the oral exposure pathway are known to negatively affect the liver and kidneys in both laboratory animals and humans. Furthermore, it has been documented that acute exposures to high concentrations of 1,4-dioxane may result in death, and chronic exposures may also cause cancer.

Factors influencing 1,4-Dioxane levels in the body

Certain subpopulations and individuals with pre-existing conditions may be biologically more susceptible to exposure than others. For example, variations in CYP enzyme expression can affect the body's ability to metabolize 1,4-dioxane, and it is known that there are large variations in CYP expression and functionality in humans, especially for the CYP2E1 enzyme (USEPA 2020). Diseases of the liver, kidney, upper respiratory system and other organs may also impair 1,4-dioxane metabolism and make individuals susceptible to toxic effects. For example, fatty liver disease has been associated with reduced CYP function, and there is some evidence of the potential for developmental toxicity as a result of gestational exposures to 1,4-dioxane (USEPA 2020). As a subpopulation, children may experience increased exposure to 1,4-dioxane when compared to that of an adult. Children generally drink more fluids, eat more food, and breathe more air per kilogram of body weight. They have a larger skin surface in proportion to their body volume and their diet often differs from that of adults. In addition, children crawl on the floor, put things in their mouths, intentionally or unintentionally eat inappropriate things (including consumer products such as baby shampoo, etc.) and spend more time outdoors. Children also are closer to the ground, and they do not have the judgment of adults to avoid hazards (ATSDR 2012).

Regarding the potential for 1,4-dioxane to bioaccumulate in organisms or biomagnify through food webs, USEPA has determined that 1,4-dioxane has a low bioconcentration and bioaccumulation potential due its hydrophilic properties and short half-life in animals following uptake. Using The EPI Suite™ BCFBAF model, USEPA estimated a bioaccumulation factor of 0.9 for 1,4-dioxane (USEPA 2020).

Guidelines for 1,4-Dioxane

Health-based Guidelines

USEPA's IRIS database provides human health assessment information on chemical substances following a comprehensive review of toxicity data as outlined in the IRIS assessment development process. An oral reference dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The oral RfD for 1,4-dioxane was last revised in 2010. The current oral RfD for 1,4-dioxane is 0.03 mg/kg-day based on liver and kidney toxicity.

USEPA completed its initial cancer risk assessment in 1980s and classified 1,4-dioxane as a probable human carcinogen. When threshold level toxic effects were evaluated in 2010, USEPA updated its classification for 1,4-dioxane, identifying it as "likely to be carcinogenic to humans." An oral cancer slope factor of 0.1 mg/L was published in 1988 and this recommended value did not change following USEPA's updated review of 1,4-dioxane in 2013. USEPA's characterization of 1,4-dioxane is based on inadequate evidence of carcinogenicity in humans, but sufficient evidence in animals (USEPA

2013). USEPA cited evidence of hepatic tumors in three strains of rats, two strains of mouse, and in guinea pigs. In addition, mesotheliomas of the peritoneum, mammary, and nasal tumors were observed in rats following 2 years of oral exposure to this chemical. The oral slope factor of 0.1 mg/kg-day is based on the incidence of liver cancer in female mice exposed to 1,4-dioxane in drinking water for 2 years (USEPA 2013).

USEPA's Drinking Water Health Advisory Program, sponsored by the Health and Ecological Criteria Division of the Office of Science and Technology (OST), Office of Water (OW), provides information on the health and organoleptic (e.g., taste, odor, color) effects of contaminants in drinking water. A health advisory level (HAL) is not an enforceable standard, but rather provides technical guidance to assist Federal, State and local officials when emergency spills or contamination situations occur. HALs are generally determined for one-day, ten-day and lifetime exposure if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The current HAL for 1,4-dioxane was published in 2012 (USEPA 2012) and is based on the current oral RfD and cancer slope factor published in IRIS. The one-day and ten-day HALs for a 10-kg child are 4 mg/L and 0.4 mg/L, respectively. The lifetime HAL for adults and children is 0.2 mg/L and was calculated using the oral reference dose for noncancer effects published in IRIS, which was last revised in 2010. USEPA also included a cancer risk level drinking water concentration of 0.035 mg/L at the 10^{-4} cancer risk level, which corresponds to an excess estimated lifetime cancer risk of 1 in 10,000 persons.

The World Health Organization (WHO) assessed 1,4-dioxane in 2004 and subsequently published a guideline value for drinking water of 0.05 mg/L in the third edition of its *Guidelines for Drinking-water Quality* (WHO 2008). This guideline was retained in WHO's 4th edition of the guidelines.

Scientific Literature and Data Related to the Human Health Effects of 1,4-Dioxane

USEPA published its *Final Risk Evaluation for 1,4-Dioxane* in December 2020 (USEPA 2020). Given the recentness of this comprehensive evaluation, little information on this subject can be found in recent academic reviews that has not already been covered in the 2020 USEPA report.

Evaluation of Available Recommendations and Scientific Data

The Department has reviewed and considered the available scientific data and recommendations in accordance with 25 Pa. Code Chapter 16. Water Quality Toxics Management Strategy – Statement of Policy and 25 Pa. Code Chapter 93. Human health criteria are based on one of two approaches – either threshold level or non-threshold level toxic effects (carcinogens). Department guidelines for the development of threshold level toxic effect human health-based criteria are found specifically at 25 Pa. Code §16.33 (relating to non-threshold effects (cancer)). In establishing water quality criteria for carcinogens, the Department makes a determination as to whether a substance is a carcinogen based upon USEPA's identification of the substance. For toxic substances for which oral slope factors (i.e., cancer slope factors) have been developed by USEPA and published in IRIS, the Department will use one of the following approaches in establishing water quality criteria for this Commonwealth. The Department will use USEPA-developed 304(a) water quality criteria recommendations as amended and updated in USEPA's *National Recommended Water Quality Criteria – Human Health Criteria Table* if they are available. If 304(a) criteria recommendations are not available, the Department will develop water quality criteria based upon USEPA's oral slope factors using USEPA's *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* (USEPA 2000). For carcinogens or suspected carcinogens for which oral slope factors have not been developed by USEPA, the Department will use threshold level effects toxicity data, if available, and apply an additional safety factor of 10 to develop a protective human health water quality criterion.

In accordance with this policy, the Department has reviewed the available scientific data and recommendations. Since USEPA does not currently have a 304(a) water quality criterion recommendation for 1,4-dioxane, the Department has determined that USEPA's oral slope factor as published in IRIS represents the best available data to calculate an ambient water quality criterion for 1,4-dioxane that is protective of human health.

Development of 1,4-Dioxane Water Quality Criteria

Criteria for the Protection of Human Health from Toxic Substance

As described above, the Department develops human health-based criteria in accordance with its Water Quality Toxics Management Strategy – Statement of Policy. Human health criteria development considers various exposure pathways including exposures from drinking water and fish consumption and may include exposures from inhalation or dermal absorption. The inclusion of multiple exposure pathways and the toxicity risk of the substance make development of human-health-based criteria different than the development of other types of water quality criteria, such as Potable Water Supply use criteria.

Development of a Human Health Criterion based on IRIS

USEPA identified 1,4-dioxane as a likely human carcinogen and developed the current oral slope factor in 1988. USEPA also published an RfD for 1,4-dioxane based on threshold level toxic effects to the liver and kidneys. Since USEPA has information available in IRIS for both threshold level and non-threshold toxic effects, the Department must evaluate both recommendations and develop an ambient water quality criterion that will provide the highest level of protection. The Department determined that use of the oral slope factor results in the most protective value when calculating an ambient water quality criterion for 1,4-dioxane. Thus, the Department used USEPA's oral slope factor to calculate an ambient water quality criterion for 1,4-dioxane in accordance with its Water Quality Toxics Management Strategy – Statement of Policy. The Department uses a 1×10^{-6} cancer risk level as specified in § 93.8a(d) (relating to water quality criteria for toxic substances). Expressing this another way, the probability of an individual getting cancer from ambient water exposure to a carcinogen is increased by a factor of one in one million.

<u>Calculation of the Risk-Specific Dose (RSD)</u>

RSD = (Target Incremental Cancer Risk)/m

Where:

RSD = Risk-specific dose (mg/kg-day)
Target = 1×10^{-6} (in accordance with Department policy)
Incremental
Cancer Risk
m = cancer potency factor or oral slope factor $(mg/kg\text{-}day)^{-1}$

<u>Calculation of Risk-Specific Dose for 1,4-Dioxane</u>

$RSD_{1,4\text{-dioxane}} = (1 \times 10^{-6})/0.1$ mg/kg-day
= 0.00001 mg/kg-day

In accordance with the USEPA *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* (USEPA 2000) using the Department's updated exposure input values (body weight, drinking water intake, and fish consumption) and Chapter 93 guidelines, the Department derived the following human health criterion for 1,4-dioxane. Based upon USEPA's review, 1,4-dioxane is not expected to bioaccumulate in freshwater fish or mussels. USEPA modelling has suggested that a bioaccumulation factor of 0.9 for 1,4-dioxane is appropriate. Thus, a bioaccumulation factor of 1 has been used in this calculation. The following equation is used for the calculation of ambient water quality criteria for carcinogens where an RSD is obtained from a linear approach:

<u>Calculation of an Ambient Water Quality Criterion for 1,4-dioxane</u>

$AWQC_{1,4\text{-dioxane}} = RSD \times (BW \div [DWI + (FI \times BAF)])$

Where:

RSD = 0.00001 mg/kg-day
Body Weight (BW) = 80 kg
Drinking Water Intake (DWI) = 2.4 L
Fish Intake (FI) = 0.022 kg/day
Bioaccumulation factor (BAF) = 1

$AWQC_{1,4\text{-dioxane}}$ = 0.00001 x (80 ÷ [2.4 + (0.022 kg/day x 1)])
$AWQC_{1,4\text{-dioxane}}$ **= 0.0003 mg/L (0.3 µg /L)**

Conclusion

In accordance with the Commonwealth's regulations and polices, the Department has calculated an ambient water quality criterion for 1,4-dioxane of 0.3 µg/L to protect human health from non-threshold level toxic effects (i.e., cancer). This water quality criterion shall be achieved in all surface waters at least 99% of the time as specified in 25 Pa. Code §96.3(c). Water quality based effluent limits (WQBELs) for 1,4-dioxane will be developed using the design flow conditions for non-threshold (cancer) human health criteria contained in 25 Pa. Code §96.4, Table 1.

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