

MICHIGAN DEPARTMENT OF ENVIRONMENT, GREAT LAKES, AND ENERGY

INTEROFFICE COMMUNICATION

TO: File for Benzoic acid (CAS # 65-85-0)
FROM: Doreen Lehner, Toxics Unit, Air Quality Division
DATE: May 6, 2024
SUBJECT: Screening Level for Benzoic acid (CAS # 65-85-0)

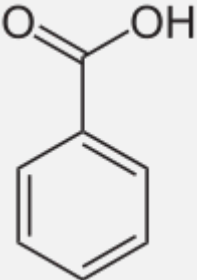
Summary

The initial threshold screening level (ITSL) for benzoic acid (CAS# 65-85-0) is 5 µg/m³ (8-hour averaging time).

Uses and Physical Chemical Properties

Benzoic acid is a naturally occurring plant and algal metabolite. Benzoic acid is used in industry as a precursor for the synthesis of many organic substances. Benzoic acid salts are used as a food preservative due to its antimicrobial and antifungal properties. Benzoic acid destroys microbes and fungi by inhibiting their ability to grow or reproduce; it specifically inhibits triacylglycerol and arachidonate 15-lipoxygenase. Benzoic acid was historically used as an insecticide and an herbicide.

Table 1. Physical/Chemical Properties of Benzoic acid

Structure	
CAS Number	65-85-0
Synonyms	Carboxybenzene, Dracylic acid, and Benzenecarboxylic acid
Appearance/Odor	White crystalline solid or powder with a faint urine, almond odor
Molecular Weight	122.12 g/mol
Melting Point	122.4°C

Boiling Point	249.2°C @ 760 mmHg
Flash Point	121°C (closed cup)
Autoignition Temperature	570°C
Solubility: Water	2.9 g/L @ 20°C
Density	1.316 g/cm ³ @ 24°C
Vapor Pressure	0.00083 mm Hg at 20°C
Log Kow	1.87 at pH 7

Literature Search

The literature was searched to find relevant data to assess the toxicity of these compounds. The following references or databases were searched: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Levels (RELs), International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) SciFinder (searched 11/14/2023), U.S. EPA ChemView, California Office of Environmental Health Hazard Assessment (OEHHA), the U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry (ATSDR), European Chemical Agency (ECHA), and the U.S. National Toxicology Program (NTP).

Key Study

In 1988, the EPA developed a chronic oral reference dose (RfD) of 4 mg/kg/day for benzoic acid but did not develop a chronic inhalation reference concentration (RfC). The RfD was developed even though no critical adverse effects were observed. The EPA used a study from Wiley and Bigelow (1908) which "...observed irritation, discomfort, weakness, and malaise in humans given oral bolus doses of less than or equal to 1.75 g/day over a 20-day period (25 mg/kg/day)" (EPA, 1988). The EPA also used a study by "Gerlach (1909) [who] reported no externally visible effects in humans ingesting benzoic acid at 0.5 -1.0 g/day for 44 consecutive days or for 88/86 or 88/92 days. Assuming a body weight of 70 kg, this level corresponds to a dose of 14 mg/kg/day... The RfD (4 mg/kg/day) is well below these doses" (EPA, 1988). This evaluation is for oral exposure only and is not protective against inhalation exposure. The previous memo (Lehner, 2012; see attachment), which provided an adequate explanation on how the screening level was evaluated as a particulate. It was determined that the National Ambient Air Quality Standards (NAAQS) for PM_{2.5} was more protective of public health including sensitive subgroups.

ACGIH set a TLV-TWA of 0.5 mg/m³ (inhalable fraction and vapor). The TLV-TWA of 0.5 mg/m³, inhalable fraction and vapor was recommended to minimize the potential for eye and respiratory irritation and lung damage. "The reports of human effects, although

extensive, are insufficient to characterize dose-response effects, hence the TLV for [this] substance [is] based on animal studies” (ACGIH, 2021).

“The TLV-TWA concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effect” (ACGIH, 2021). The TLVs are derived for workers who are typically healthy adults that are exposed during work hours and do not consider long-term exposures or their effects on susceptible subpopulations such as infants, children, the elderly, sensitive individuals, or those with illnesses. Therefore, TLVs may generally be divided by 100 to derive an acute ITSL that may be presumed to be protective of the general population including sensitive subgroups.

ITSL Derivation

The ACGIH TLV-TWA of 0.5 mg/m³ is used to derive a screening level using Rule 232(1)(c) using the following equation:

$$ITSL = \frac{\text{occupational exposure level}}{100} = \frac{0.5 \text{ mg/m}^3}{100} = 0.005 \text{ mg/m}^3 = 5 \text{ }\mu\text{g/m}^3$$

Based on Rule 232(s)(a) the averaging time for a screening level derived from an occupational exposure level is 8-hours.

The initial threshold screening level (ITSL) for benzoic acid (CAS# 65-85-0) is 5 µg/m³ (8-hour averaging time).

References

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environment, Great Lakes, and Energy.

ACGIH. 2021. Benzoic Acid and Alkali Benzoates. TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. ACGIH Signature Publications.

EPA. 1988. Integrated Risk Information System (IRIS). Benzoic acid; CASRN 65-85-0. Retrieved data 5/6/2024. Available online at:
[Benzoic acid CASRN 65-85-0 | IRIS | US EPA, ORD](#)

Gerlach, V. 1909. VII. Summary of the results. In: Physiological Activity of Benzoic Acid and Sodium Benzoate, V. Gerlach, Ed. Verlag von Heinrich Stadt, Wiesbaden. P. 90-92. (Cited in Informatics, Inc., 1972).

Informatics, Inc. 1972. GRAS (Generally Recognized as Safe) Food Ingredients; Benzoic Acid and Sodium Benzoate. P. 75-79.

Lehner. 2012. File for Benzoic acid (CAS# 65-85-0): From Doreen Lehner, Screening Level Determination for Benzoic acid: Dated: July 26, 2012.

Wiley, H.M. and Bigelow W.D. 1908. Influence of benzoic acid and benzoates on digestion and health. Bulletin 84, pt. IV, Bureau of Chemistry, U.S. Dept. Agriculture. (Cited in Informatics, Inc., 1972).

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Attachment

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Benzoic acid (CAS# 65-85-0)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Determination for Benzoic acid

DATE: July 26, 2012

An initial threshold screening level (ITSL) for benzoic acid will not be set due to a lack of sufficient toxicity data. This compound is a solid with a relatively low oral toxicity and therefore, emissions may be evaluated based on the National Ambient Air Quality Standards (NAAQS) for PM_{2.5}.

Benzoic acid [CAS# 65-85-0] (also known as benzenecarboxylic acid and benzoate) is an aromatic carboxylic acid with a molecular weight of 122.12 g/mol. It is a colorless crystalline solid. Benzoic acid is used as a precursor for the synthesis of many organic substances including: benzoyl chloride; benzoate plasticizers; and phenol. Benzoic acid is also used as a food preservative, a growth inhibitor for mold, yeast, and bacteria, skin antifungal treatment, antiseptic, and in inhalant decongestants (Wikipedia, 2012).

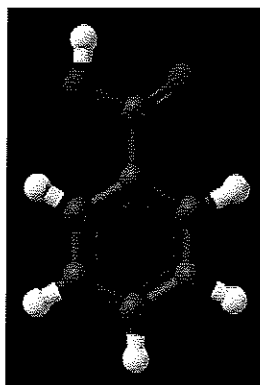


Figure 1. Benzoic acid ball and stick model.

A literature review was conducted to attempt to derive an initial threshold screening level (ITSL) for benzoic acid. The following references and databases were searched: Chemical Criteria Database (CCD), United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2010 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online (searched 8/22/11), National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, US EPA TSCATS database, and Hazardous Substances Data Bank (HSDB).

No inhalation toxicity data were found which could be used to establish an ITSL. However, benzoic acid is regarded to have a relatively low order of oral toxicity. In 1973 the FDA evaluated the health effects of benzoic acid and determined it to be Generally Recognized as Safe (GRAS) in food based on an estimated average daily intake of 0.1-1.4 mg/kg (0.6 – 34 mg/day) for benzoic acid and 2 – 17 mg/kg (10 – 328 mg/day) for sodium benzoate (FDA, 1973). The EPA has set an oral RfD for benzoic acid at 4 mg/kg/day based on a NOAEL of 34 mg/day benzoic acid and 328 mg/day for sodium benzoate (converted to 312 mg/day benzoic acid). "In the stomach, both benzoic acid and sodium benzoate exist in their ionized form, benzoate, which is absorbed rapidly and completely by the GI tract" (EPA, 1993). Since the molecular weight for sodium benzoate differs from benzoic acid the following conversion factor is needed to determine total exposure of both compounds to calculate the RfD listed below:

$$328 \text{ mg/day sodium benzoate} \times \frac{122.12 \text{ (MW benzoic acid)}}{144.11 \text{ (MW sodium benzoate)}} \\ = 278 \text{ mg/day (benzoic acid from sodium benzoate)}$$

$$278 \text{ mg/day} + 34 \text{ mg/day (benzoic acid)} = 312 \text{ mg/day}$$

Assuming adult human body weight of 70 kg, the EPA (1993) RfD was derived as:

$$\frac{312}{70} = 4.4 \text{ mg/kg/day}$$

According to Rule 232(1)(b), an ITSL can be determined by an oral reference dose

$$ITSL = Oral \text{ RfD} \times \frac{70 \text{ kg}}{20 \text{ m}^3} \\ \text{potential ITSL} = 4 \text{ mg/kg/day} \times \frac{70 \text{ kg}}{20 \text{ m}^3} = 14 \text{ mg/m}^3 = 14,000 \text{ } \mu\text{g/m}^3$$

Rounded to one significant figure the potential ITSL is 10,000 $\mu\text{g/m}^3$. According to Rule 232(2)(b) the averaging time is 24 hours. As benzoic acid is considered a solid, the ITSL determined above exceeds the NAAQS for $\text{PM}_{2.5}$ therefore, an ITSL will not be determined and emissions of benzoic acid will be evaluated using the NAAQS standard for $\text{PM}_{2.5}$.

References:

Act 451 of 1994. Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

EPA. 1993. Integrated Risk Information System. Benzoic acid. Retrieved data on 7/18/2011 (<http://www.epa.gov/iris/subst/0355.htm>).

EPA. 2006. National Ambient Air Quality Standards (NAAQS) 71FR61144, October 17, 2006. Available online at <http://www.epa.gov/air/criteria.html>

FDA. 1973. Evaluation of the health aspects of benzoic acid and sodium benzoate as food ingredients. Federation of American Societies for Experimental Biology, U.S. Food and Drug Administration. PB-223-837.

Wikipedia, 2012. Benzoic acid. Available online at:
http://en.wikipedia.org/wiki/Benzoic_acid

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