

Phthalic anhydride

85-44-9

Hazard Summary

Exposure to phthalic anhydride may occur during its use as a chemical intermediate in the plastics industry. The acute (short-term) effects from exposure to phthalic anhydride in humans consists of irritation to the eyes, respiratory tract, and skin, but no permanent injury is observed. Chronic (long-term) effects observed in workers exposed to phthalic anhydride included conjunctivitis, rhinitis, rhinoconjunctivitis, bronchitis, and irritation of the skin and mucous membranes of the respiratory tract. Animal studies indicate that chronic exposure to phthalic anhydride vapor causes congestion, irritation, and injury to lung cells. No studies are available on the reproductive, developmental, or carcinogenic effects of phthalic anhydride in humans. EPA has not classified phthalic anhydride for carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information Service (IRIS) (4), which contains information on oral chronic toxicity of phthalic anhydride and the RfD, and the National Cancer Institute's Bioassay of Phthalic Anhydride for Possible Carcinogenicity. (1)

Uses

- Phthalic anhydride is an important chemical intermediate in the plastics industry from which are derived numerous phthalate esters that function as plasticizers in synthetic resins. Phthalic anhydride itself is used as a monomer for synthetic resins such as glyptal, the alkyd resins, and the polyester resins. (1)
- Phthalic anhydride is also used as a precursor of anthraquinone, phthalein, rhodamine, phthalocyanine, fluorescein, and xanthene dyes. (1)
- Phthalic anhydride is used in the synthesis of primary amines, the agricultural fungicide phaltan, and thalidomide. Other reactions with phthalic anhydride yield phenolphthalein, benzoic acid, phthalylsulfathiazole (an intestinal antimicrobial agent), and orthophthalic acid. (1)

Sources and Potential Exposure

- Exposure to phthalic anhydride may occur during the manufacture of phthalate-derived products. (1)
- It has been suggested that exposure to phthalic anhydride may occur from the use of plastics from which phthalate plasticizers are leached, specifically certain medical plastics such as blood bags, plastic syringes, and plastic tubing. (1)
- Phthalate esters have been identified as environmental pollutants. (1)

Assessing Personal Exposure

- There is no known medical test available to determine whether someone has been exposed to phthalic anhydride. (2)

Health Hazard Information

Acute Effects:

- Phthalic anhydride is irritating to the eyes, respiratory tract, and the skin in humans, but no permanent injury is observed. Since phthalic anhydride has no effect on dry skin, but burns wet skin, it has been

suggested that the actual irritant is phthalic acid, which is formed on contact with water. (2)

- Tests involving acute exposure of rats have shown phthalic anhydride to have moderate acute toxicity. (3)

Chronic Effects (Noncancer):

- Conjunctivitis, rhinitis, rhinoconjunctivitis, bronchitis, and irritation of the skin and mucous membranes of the respiratory tract have been observed in workers exposed to phthalic anhydride. Other effects observed in workers chronically exposed to phthalic anhydride were occasional bloody sputum, emphysema, lower blood pressure, and minor signs of central nervous system (CNS) excitation. (1,2,9)
- Animals exposed to heated phthalic anhydride experienced congestion, irritation, and injury of lung cells. (2)
- Hypersensitivity of guinea pigs to phthalic anhydride dust has been reported, with bronchoconstriction, transiently increased respiratory rate, and elevated IgG antibodies observed following an inhalation challenge. (9)
- Decreased body weight, increased incidence of lung and kidney lymphocytosis, bile duct inflammation, adrenal atrophy, and mineralization of the thalamus were reported in mice exposed to phthalic anhydride in the diet. (1,4)
- EPA has calculated a provisional Reference Concentration (RfC) of 0.12 milligrams per cubic meter (mg/m^3) for phthalic anhydride based on respiratory effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. The provisional RfC is a value that has had some form of Agency review, but it does not appear on IRIS system. (5)
- EPA has established a Reference Dose (RfD) of 2.0 milligrams per kilogram body weight per day ($\text{mg}/\text{kg}/\text{d}$) for phthalic anhydride based on lung and kidney effects in mice. (4)
- EPA has high confidence in the study on which the RfD is based because the study is a well-designed feeding study in two species that defines a no-observed-adverse-effect level (NOAEL) and lowest-observed-adverse-effect level (LOAEL); medium confidence in the database because teratogenicity has not been tested adequately; and, consequently, medium confidence in the RfD because of the lack of reproductive toxicity data. (4)

Reproductive/Developmental Effects:

- No studies regarding reproductive or developmental effects in humans were available.
- Phthalic anhydride was reported to be teratogenic in mice following intraperitoneal injection. (4)
- Decreased spermatozoa motility time was reported in one study in which male rats were exposed via inhalation. (9)

Cancer Risk:

- No studies were available on the carcinogenic effects of phthalic anhydride in humans.
- A bioassay of phthalic anhydride for possible carcinogenicity was conducted by administering phthalic anhydride in feed to groups of male and female rats and mice. It was observed that no tumors occurred in the rats or mice of either sex at incidences that could be clearly related to the administration of phthalic anhydride. (1)
- EPA has not classified phthalic anhydride regarding carcinogenicity. (4)

Physical Properties

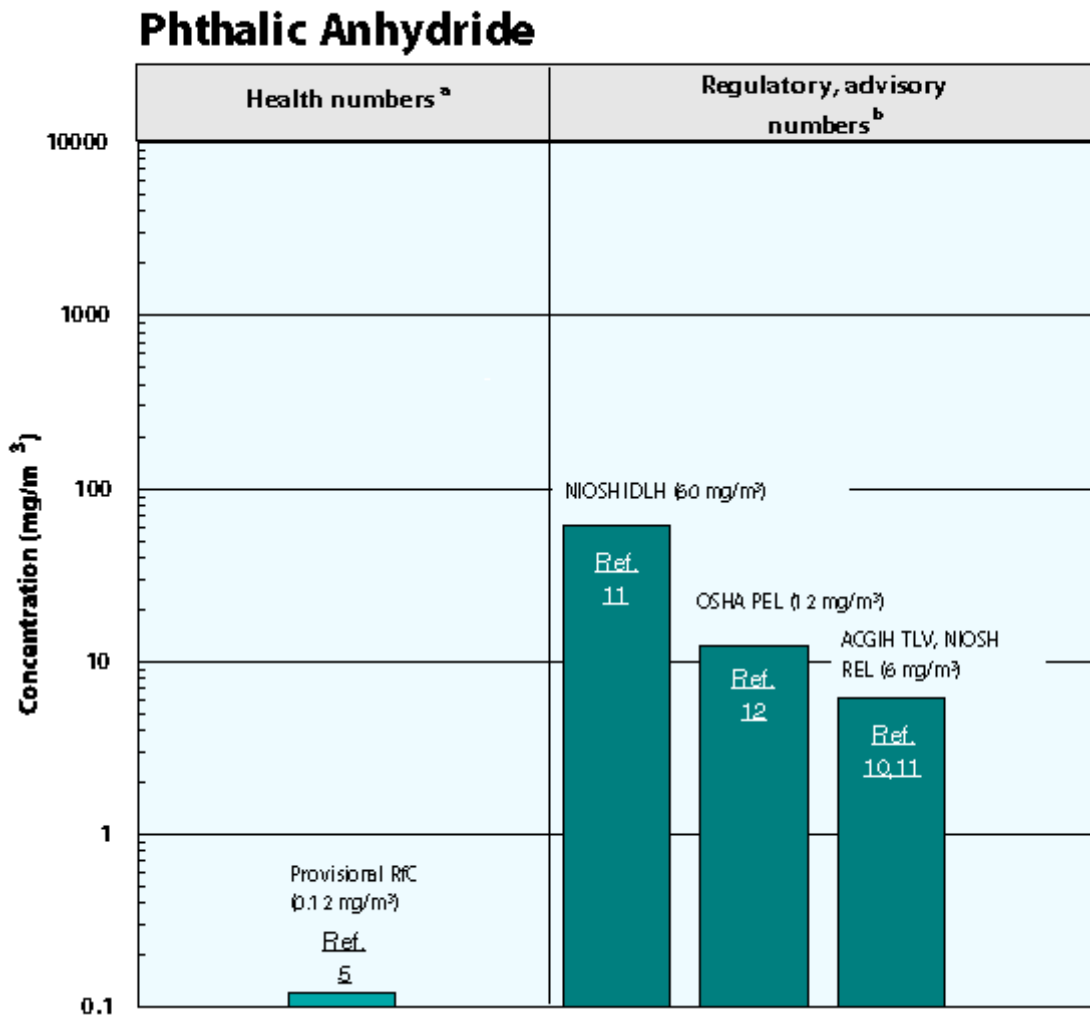
- Phthalic anhydride is a white (lustrous needles) solid that is slightly soluble in water. (6,8)
- Phthalic anhydride has an odor threshold of 0.053 parts per million (ppm). (7)
The chemical formula for phthalic anhydride is $\text{C}_8\text{H}_4\text{O}_3$, and it has a molecular weight of 148.12 g/mol.

- The chemical formula for phthalic anhydride is $C_8H_4O_3$, and it has a molecular weight of 148.12 g/mol. (3,6)
- The vapor pressure for phthalic anhydride is 5.14×10^{-4} mm Hg at 25 °C. (2)

Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m^3 : $mg/m^3 = (ppm) \times (\text{molecular weight of the compound}) / (24.45)$. For phthalic anhydride: 1 ppm = 6.1 mg/m^3 . To convert concentrations in air from $\mu g/m^3$ to mg/m^3 : $mg/m^3 = (\mu g/m^3) \times (1 \text{ mg} / 1,000 \mu g)$.

Health Data from Inhalation Exposure



ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.

NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH -- NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; OSHA allowable level in workplace air averaged over an 8-h shift.

The health and regulatory values cited in this factsheet were obtained in December 1999.

^a Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

^b Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

References

Summary created in April 1992, updated in January 2000

1. National Cancer Institute. Bioassay of Phthalic Anhydride for Possible Carcinogenicity. Technical Report 159. Public Health Service, Bethesda, MD. 1979.
2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, [online database](#)). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, [online database](#)). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
4. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on Phthalic Anhydride. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.
5. U.S. Environmental Protection Agency. Health Effects Assessment Summary Tables. FY 1997 Update. Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC. EPA/540/R-97-036. 1997.
6. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th ed. Ed. S. Budavari. Merck & Co., Inc., Rahway, NJ. 1989.
7. J.E. Amooore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.
8. R.C. Weast and M.J. Astle, Eds. CRC Handbook of Chemistry and Physics. 63rd ed. CRC Press, Inc., Boca Raton, FL. 1982.
9. California Environmental Protection Agency (CalEPA). Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.
10. American Conference of Governmental Industrial Hygienists (ACGIH). 1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 1999.
11. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards*. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.
12. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations 29 CFR 1910.1000. 1998.