

Nitrite; CASRN 14797-65-0

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR Nitrite

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

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Last Revised — 01/31/1987

The 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. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

NOTE: The oral RfD for nitrite may change in the near future pending the outcome of a further review now being conducted by the RfD/RfC Work Group.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Methemoglobinemia	NOEL: 10 ppm of drinking water or 10 mg/L converted to 1.0 mg/kg/day	1	10	1E-1 mg/kg/day
Infant Chronic Exposure to Drinking Water	LOAEL: 11-20 ppm			
Walton, 1951				

*Conversion Factor: 1 L drinking water/day 10 kg child; thus, 10 mg/L x 1 L/day / 10 kg = 1.0 mg/kg/day

I.A.2. Principal and Supporting Studies (Oral RfD)

Walton, G. 1951. Survey of literature relating to infant methemoglobinemia due to nitrate-contaminated water. Am. J. Public Health. 41: 986-996.

This is an epidemiologic study on the incidence of methemoglobinemia in infants routinely fed formula prepared from nitrate-contaminated water. This study analyzed all known cases of infant methemoglobinemia occurring in 37 U.S. states irrespective of date or type of water supply. Nitrate (nitrogen) content ranged from 10 ppm to over 100 ppm. No incidences of methemoglobinemia were found to occur in drinking water containing less than or equal to 10 ppm (10 mg/L) nitrate (nitrogen). A NOEL of 10 mg/L was derived from these studies.

Exposure of hemoglobin to nitrite results in the oxidation of the hemoglobin to methemoglobin. Animals do not provide a good model for methemoglobin formation because many species lack nitrate-reducing bacteria. Infants are, however, particularly susceptible due to their high gut

content of nitrate-reducing bacteria, their lower enzymatic capacity to reduce methemoglobin to hemoglobin, and to the presence of hemoglobin F, which is more susceptible to oxidation.

Several more recent studies support Walton's (1951) 10 mg/L NOAEL for infant methemoglobinemia (NAS, 1977; Winton, 1971; Calabrese, 1978).

Using the NOAEL from the Walton study and a modifying factor of 10, the RfD for nitrite was calculated (U.S. EPA, 1985) for a 10-kg child drinking 1 L of water/day as 0.1 mg/kg/day or 1 mg/day.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — No uncertainty factor was used in the derivation of the RfD because the NOEL was of the critical toxic effect (i.e., methemoglobinemia) in the sensitive human population (i.e., infants). The length of exposure encompassed both the critical effect and the sensitive population.

MF — A modifying factor of 10 was applied because of the direct toxicity of nitrite.

I.A.4. Additional Studies/Comments (Oral RfD)

An RfD of 0.2 mg/kg/day could be calculated from the Walton (1951) study using the body weight of 4 kg and fluid consumption of 0.64 L/day for infants. The lower value of 0.1 mg/kg/day is maintained, however, because of the uncertainties in the changing fluid consumption and body weight as a neonate (4 kg) ages to a 2-year-old child (10 kg). While there are some data to the contrary, it is most likely that older children do not respond with increased methemoglobin to nitrate in drinking water. For example, Craun et al. (1981) reported that 64 children aged 1-8, consuming water with nitrate nitrogen concentrations of 22 to 111 mg/L, had an average methemoglobin concentration of 1.13%. This is not considered to be elevated and was in fact no different from the level (0.98%) observed in 38 children who drank water contaminated with less than 10 mg nitrate/L.

I.A.5. Confidence in the Oral RfD

Study — High

Database — High

RfD — High

Confidence in the study is high because the NOEL is determined in the known sensitive human population. The database contains several recent supporting epidemiologic studies for the critical

effect in the sensitive population (infants); therefore, a high confidence rating is given to the database. High confidence in the RfD follows.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1985

Agency Work Group Review — 11/21/1985, 02/05/1986, 02/26/1986, 06/24/1992

Verification Date — 02/26/1986

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Nitrite conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Nitrite

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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Nitrite
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Not available at this time.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Nitrite
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VI.A. Oral RfD References

Calabrese, E.J. 1978. Drinking Water Standards. In: Methodological Approaches to Deriving Environmental and Occupational Health Standards. John Wiley and Sons, Inc., New York, NY. p. 165-169.

Craun, G.F., D.G. Greathouse and D.H. Gunderson. 1981. Methemoglobin levels in young children consuming high nitrate well water in the United States. *Int. J. Epidemiol.* 10: 309-317.

NAS (National Academy of Sciences). 1977. *Drinking Water and Health*. Washington, DC.

U.S. EPA. 1985. *Drinking Water Criteria Document for Nitrates/Nitrites*. Office of Drinking Water, Washington, DC.

Walton, G. 1951. Survey of literature relating to infant methemoglobinemia due to nitrate-contaminated water. *Am. J. Public Health.* 41: 986-996.

Winton, E.F., R.G. Tardiff and L.J. McCabe. 1971. Nitrate in drinking water. *J. Am. Water Works Assoc.* 63: 95-98.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Nitrite

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Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Nitrite

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Last Revised — 01/31/1987

- 14797-65-0
- Nitrite
- Nitrous acid, ion(1-)