

Fluorine (soluble fluoride); CASRN 7782-41-4

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 Fluorine (soluble fluoride)

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)

Substance Name — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

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.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Objectionable dental fluorosis, a cosmetic effect	NOAEL: 1 ppm (converted 0.06 mg/kg/day LOAEL: 2 ppm	1	1	6E-2 mg/kg/day
Epidemiologic Study in Children				
Hodge, 1950, cited in Underwood, 1977				

*Conversion Factors: see text

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

Hodge, H.C. 1950. The concentration of fluorides in drinking water to give the point of minimum caries with maximum safety. *J. Am. Dent. Assoc.* 40: 436. Cited in: Underwood, E.J. 1977. *Trace Elements in Human and Animal Nutrition*. Academic Press, NY.

Fluoride-related compounds are used in the prevention of dental caries. Extensive human epidemiologic studies with large populations have been carried out over the last 40 years. The NOAEL (1 ppm) and LOAEL (2 ppm) in drinking water are defined within a narrow dose range.

Hodge (1950) studied children consuming fluoride in their drinking water. Fluoride levels of 0-14 ppm were investigated. Dental mottling was the parameter of interest. Fluoride levels of 2-10 ppm produced a linear dose- response curve (increasing mottling with increasing dose). Fluoride levels of 0.1-1.0 ppm produced no observable effect. An assumption of 20 kg bw and 1 L/day water consumption for children was used, since the children studied were 12-14 years old. It is

further assumed that a 20-kg child consumes 0.01 mg of fluoride/kg bw/day in the diet (50 FR 20164). Thus, a total intake would be approximately 0.06 mg/kg/day.

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

UF — Uncertainty factors were not deemed necessary since the NOAEL is that of the critical effect (i.e., dental fluorosis) in a sensitive population of humans (i.e., children) for a length of exposure that encompasses both the critical effect and the sensitive population.

MF — None

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

Dental fluorosis results from excess exposure to fluoride during the age of calcification of the teeth (up to about 8 years of age for anterior teeth). Dental fluorosis in its mild form is characterized by white opaque areas covering 50% of a given tooth; in its severe form, dental fluorosis is characterized by brown to black stains and pitting (50 FR 20164). There is considerable controversy over whether objectionable dental fluorosis (moderate and severe) is a toxic and/or adverse health effect. However, the U.S. EPA has determined that objectionable dental fluorosis is a cosmetic effect and not a toxic and/or adverse health effect (50 FR 47142). Numerous epidemiologic studies have been conducted in the U.S. concerning the relationship between dental fluorosis and fluoride levels in drinking water (50 FR 20164). Based on these studies, the NOAEL for objectionable dental fluorosis is approximately 1.0 ppm fluoride in drinking water. Assuming that a child weighs 20 kg, drinks 1.0 L of water/day and ingests fluoride at 0.01 mg/kg/day in the diet (50 FR 20164), a NOAEL of 1 ppm fluoride in drinking water corresponds to 0.06 mg/kg/day. Since data are available for the only susceptible population (children), an uncertainty factor of 1 is appropriate.

It has been estimated that the development of crippling skeletal fluorosis in man requires the consumption of 20 mg or more of fluoride/person/day over a 20-year period, i.e., 0.28 mg/kg/day (U.S. EPA, 1985). While the NOEL for crippling skeletal fluorosis in humans is unknown, a safe level of fluoride exposure can be determined. No cases of crippling skeletal fluorosis have been observed in the United States associated with the consumption of 2 L of water/day containing 4 ppm fluoride (50 FR 20614). Assuming a 70 kg adult ingests 0.01 mg fluoride/day in the diet and consumes 8 mg fluoride/day in drinking water (2 L/day containing 4 ppm fluoride), this would correspond to a total intake of 0.12 mg/kg/day. Thus, 0.12 mg fluoride/kg/day is a safe exposure level for this more severe endpoint in adults.

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

Confidence in both the study and the database is high because the large number of studies conducted in children all support the chosen NOAEL. Confidence in the RfD is high because little uncertainty remains in the toxicity database.

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

Source Document — U.S. EPA. 1985. Federal Register, Vol. 50, p. 20164, 47142.

ECAO-Cincinnati Internal Review, July 1985.

Other EPA Documentation — None

Agency Work Group Review — 08/05/1985, 02/05/1986, 02/26/1986

Verification Date — 02/26/1985

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 Fluorine (soluble fluoride) conducted in November 2001 identified one or more significant new studies. IRIS users may request the references for those studies from 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 — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

VI.A. Oral RfD References

Hodge, H.C. 1950. The concentration of fluorides in drinking water to give the point of minimum caries with maximum safety. J. Am. Dent. Assoc. 40: 436.

Underwood, E.J. 1977. Trace elements in human and animal nutrition. Academic Press, New York. p. 347-369.

U.S. EPA. 1985. Federal Register. Vol. 50, p. 20164, 47142.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

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

VIII. Synonyms

Substance Name — Fluorine (soluble fluoride)

CASRN — 7782-41-4

Primary Synonym — Fluoride

Last Revised — 01/31/1987

- 7782-41-4
- Fluoride
- Fluoride ion
- Fluoride ion(1-)

- Fluorine
- Fluorine, ion
- Hydrofluoric acid, ion(1-)
- Perfluoride