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Toxicological Summary for: Strontium

CAS: 7440-24-6

Synonyms: Strontianite, celestine, celestite, strontium carbonate, strontium sulfate, strontium chloride, strontium acetate, strontium citrate

Strontium and calcium are chemically similar, and strontium toxicity is mainly due to strontium mimicking calcium within the body. A high calcium to strontium ratio (>100:1) in drinking water and diet reduces the risk of harmful health effects from strontium exposure. As nearly all Minnesotans are estimated to have a high calcium to strontium ratio, water guidance for strontium is presented as Risk Assessment Advice tailored for specific situations where calcium intake is known or suspected to be deficient.

Acute Non-Cancer Risk Assessment Advice (nRAA) = Not Derived (Insufficient Data)

Short-term Non-Cancer Risk Assessment Advice (nRAA_{Short-term}) = 3000 µg/L

$$\begin{aligned} & \frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Short-term Intake Rate, L/kg-d})} \\ &= \frac{(1.4 \text{ mg/kg-d}) \times (0.6)^* \times (1000 \text{ µg/mg})}{(0.285 \text{ L/kg-d})^{**}} \\ &= 2947 \text{ µg/L rounded to } \mathbf{3000 \text{ µg/L}} \end{aligned}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1. MDH applied an RSC of 0.6 by using the subtraction method instead of the default 0.5 for non-volatile chemicals. Based on unpublished MDH data, formula-fed infants are potentially exposed up to 20% of the RfD from the powdered formula itself. Subtracting 20% to account for formula exposures from the maximum RSC of 0.8 leaves 0.6 remaining for water ingestion for short-term exposures.

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration: HED/Total UF = 431 mg/kg-d / 300 = 1.4 mg/kg-d (Sprague-Dawley rat)
Source of toxicity value: Determined by MDH in 2019
Point of Departure (POD): 431 mg/kg-d (NOAEL_{HED}, Chiu et al., 2019)
Dose Adjustment Factor (DAF): Chemical-specific DAF=1, based on recognition that the Ca/Sr ratios used in the animal study were artificially low, maximizing strontium uptake and internal animal exposure

resulting in greater experimental effects. This low Ca/Sr ratio is not representative of human exposures.

Human Equivalent Dose (HED): $POD \times DAF = 431 \text{ mg/kg-d} \times 1 = 431 \text{ mg/kg-d}$
Total uncertainty factor (UF): 300
Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty for lack of an adequate 2-generation study as well as concerns over possible endocrine effects.
Critical effect(s): Fetal malformations (anophthalmia, absent sternebra, wavy ribs)
Co-critical effect(s): None
Additivity endpoint(s): Developmental, Skeletal

Subchronic Non-Cancer Risk Assessment Advice ($nRAA_{\text{Subchronic}}$) = $nRAA_{\text{Short-term}}$ = 3000 $\mu\text{g/L}$

$$\begin{aligned} & \frac{(\text{Reference Dose, mg/kg-d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic Intake Rate, L/kg-d})} \\ &= \frac{(1.4 \text{ mg/kg-d}) \times (0.7)^* \times (1000 \text{ } \mu\text{g/mg})}{(0.070 \text{ L/kg-d})^{**}} \\ &= 14000 \text{ } \mu\text{g/L} \end{aligned}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1. MDH applied an RSC of 0.7 by using the subtraction method, instead of the default 0.2 for non-volatile chemicals. For subchronic exposures, food is the only other major source of strontium and accounts for 6-8% of the RfD (Rose et al., 2010; Pennington and Jones, 1987). Subtracting 10% to account for food exposures from the maximum RSC of 0.8 leaves 0.7 remaining for water ingestion.

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration: $HED/Total \text{ UF} = (425 \text{ mg/kg-d})/300 = 1.4 \text{ mg/kg-d}$
(Sprague-Dawley rat)
Source of toxicity value: Determined by MDH in 2019
Point of Departure (POD): 425 mg/kg-d (NOEL_{HED}, Marie et al., 1985)
Dose Adjustment Factor (DAF): Chemical-specific DAF=1, based on recognition that the Ca/Sr ratios used in the animal study were artificially low, maximizing strontium uptake and internal animal exposure resulting in greater experimental effects. This low Ca/Sr ratio is not representative of human exposures.
Human Equivalent Dose (HED): $POD \times DAF = 425 \text{ mg/kg-d} \times 1 = 425 \text{ mg/kg-d}$
Total uncertainty factor (UF): 300
Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty for lack of an adequate 2-generation study as well as concerns over possible endocrine effects.
Critical effect(s): Decreased bone calcification rate

Co-critical effect(s): Fetal malformations (anophthalmia, absent sternebra, wavy ribs), inhibition of bone calcification

Additivity endpoint(s): Developmental, Skeletal

The Subchronic nRAA must be protective of the short-term exposures that occur within the subchronic period and, therefore, the Subchronic nRAA is set equal to the Short-term nRAA of 3000 µg/L. Additivity endpoints: Developmental, Skeletal.

Chronic Non-Cancer Risk Assessment Advice (nRAA_{Chronic}) = nRAA_{Short-term} = 3000 µg/L

(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)
(Chronic Intake Rate, L/kg-d)

$$= \frac{(0.43 \text{ mg/kg-d}) \times (0.7)^* \times (1000 \text{ µg/mg})}{(0.044 \text{ L/kg-d})^{**}}$$

$$= 6840 \text{ µg/L rounded to } 7000 \text{ µg/L}$$

*Relative Source Contribution: MDH 2008, Section IV.E.1. MDH applied an RSC of 0.7 by using the subtraction method, instead of the default 0.2 for non-volatile chemicals. For chronic exposures, food is the only other major source of strontium and accounts for 6-8% of the RfD (Rose et al., 2010; Pennington and Jones, 1987). Subtracting 10% to account for food exposures from the maximum RSC of 0.8 leaves 0.7 remaining for water ingestion.

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81

Reference Dose/Concentration: HED/Total UF = 425/1000 = 0.43 mg/kg-d (Sprague-Dawley rat)

Source of toxicity value: Determined by MDH in 2019

Point of Departure (POD): 425 mg/kg-d (NOAEL_{HED}, Marie et al., 1985) (subchronic exposure)

Dose Adjustment Factor (DAF): Chemical-specific DAF=1, based on recognition that the Ca/Sr ratios used in the animal study were artificially low, maximizing strontium uptake and internal animal exposure resulting in greater experimental effects. This low Ca/Sr ratio is not representative of human exposures.

Human Equivalent Dose (HED): POD x DAF = 425 mg/kg-d x 1 = 425 mg/kg-d

Total uncertainty factor (UF): 1000

Uncertainty factor allocation: 3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 10 for database uncertainty for lack of an adequate 2-generation study as well as concerns over possible endocrine effects, and a 3 for use of a subchronic study for the chronic exposure duration.

Critical effect(s): Decreased bone calcification rate

Co-critical effect(s): Fetal malformations (anophthalmia, absent sternebra, wavy ribs), inhibition of bone calcification

Additivity endpoint(s): Developmental, Skeletal

The Chronic nRAA must be protective of the short-term and subchronic exposures that occur within the chronic period and, therefore, the Chronic nRAA is set equal to the Short-term nRAA of 3000 µg/L. Additivity endpoints: Developmental, Skeletal.

Cancer Health Based Value (cRAA) = Not Applicable

Cancer classification: Not Classified
 Slope factor (SF): Not Applicable
 Source of cancer slope factor (SF): Not Applicable
 Tumor site(s): Not Applicable

Volatile: No.

Summary of Guidance Value History: There is no previous MDH guidance for strontium.

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	Yes	No	Yes	Yes	No
Effects observed?	No ¹	-	Yes ²	Yes ³	-

¹A limited study investigated organ weights of various endocrine glands but did not monitor endocrine function. A more thorough study of endocrine toxicity is required. This contributed to the database uncertainty factor of 10.

²The short-term RfD is based on fetal skeletal malformations observed in a limited developmental study. The lack of an adequate two-generation study and a developmental study with strontium exposure throughout the entire skeletal development period contributed to the database uncertainty factor of 10.

³A reproductive study showed no effect on female rat reproduction at doses approximately 700 times higher than the short-term RfD. Male rats exhibited increased epididymis and testes weight at doses 350 times higher than the current short-term RfD; the magnitude of weight changes were not reported and reproductive behavior/success was unaffected.

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