Sources of Exposure

Toxicokinetics and **Biomonitoring**

Biomarkers/Environmental Levels

General Populations

- the consumption of certain vegetables; those particularly high in nitrate include celery, lettuce, and spinach.
- Selected meats and meat products contain sodium nitrate and/or sodium nitrite as preservatives and can be a source of overexposure to sodium nitrate and/or sodium nitrite.
- Drinking water from water supplies contaminated by nitrate from fertilizer runoff, animal waste, and/or nitratecontaining substances at waste disposal sites may result in overexposure to nitrate.
- Release of nitrate and/or nitrite to soil from fertilizer runoff, animal waste. and/or waste disposal sites could result in increased uptake by plants used for human consumption.

Occupational Populations

Workers who are employed in occupations where fertilizer use is common (e.g., farming, greenhouse operations) may be exposed to nitrate and nitrite through dermal routes and inhalation of dust particles.

Toxicokinetics

- Most dietary intake of nitrate comes from
 There is no information regarding the toxicokinetics of nitrate or nitrite following inhalation or dermal exposure.
 - Gastrointestinal absorption of nitrate and nitrite occurs after drinking water or eating food that contain these compounds.
 - Some of the nitrate in your body moves from blood to the salivary glands where some of it is changed to nitrite. Both nitrate and nitrite can be produced inside the body.
 - Nitrate and nitrite are widely distributed in the body.
 - Most of the nitrate that you take into your body each day leaves in the urine the same day it enters your body.
 - Some nitrite in the stomach forms other substances called nitrosamines, some of which may be harmful.

NHANES Biomonitoring

■ The geometric mean level of urinary nitrate was 46.3 mg/L (2007–2008).

Biomarkers

- There are no biomarkers specific to nitrate or nitrite exposure because these substances are also produced in the body.
- Methemoglobinemia has been used as a biomarker of nitrate and nitrite toxicity; however, this effect is not specific to nitrate and nitrite.

Environmental Levels

Air

There are no recent monitoring data for air levels nitrate or nitrite in the United States.

Sediment and Soil

Nitrate levels in humid temperate U.S. soils typically range from 25 to 150 kg/hectare (as nitrogen), although much higher levels have been reported.

Water

Naturally occurring levels of nitrate in streams and ground water in the United States were estimated at 0.24-1.0 mg/L; anthropogenic activity may result in much higher levels.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2017. Toxicological Profile for Nitrate and Nitrite. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

ToxGuideTM for

Nitrate (NO₃-) CAS# 14797-55-8 and Nitrite (NO₂-) CAS# 14797-65-0

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U.S. Department of Health and **Human Services Public Health Service** Agency for Toxic Substances and Disease Registry www.atsdr.cdc.gov



Chemical and Physical Information

Routes of Exposure

Relevance to Public Health (Health Effects)

Nitrate and nitrite

- Nitrate and nitrite are naturally occurring ionic species. They are part of the earth's nitrogen cycle, whereby some nitrogen gas in air is converted to nitrite and nitrate, which can be used by plants and animals and returned to the air as nitrogen gas.
- Nitrate and nitrite are chemicals that combine with other chemicals such as sodium or potassium; these combinations are known as salts.
- Nitrate and nitrite salts are highly watersoluble and completely dissociate in aqueous environments.
- Nitrate is used in inorganic fertilizers.
- Nitrate and nitrite are used in food preservation and in the production of munitions and explosives.

- Inhalation exposure is not a likely route of concern for the general population.
- Oral exposure is the dominant route of exposure for the general population through ingestion of a normal diet.
 Over-exposure is possible by consumption of nitrate-rich diets and/or nitrate-contaminated drinking water.
- Dermal exposure is not a likely route of concern for the general population.

Nitrate and nitrite in the Environment

- Nitrate and nitrite occur naturally in the environment as part of the nitrogen cycle.
- Fertilizers, industrial processes, and animal waste products contribute to nitrate and nitrite in the environment.
- Nitrite combines readily with oxygen to form nitrate. Nitrate is generally stable in the environment; however, it may be changed to nitrite through biological processes involving plants, microbes, etc.
- Nitrate can be removed from the air by wet and dry deposition.
- Nitrate and nitrite have the potential to rapidly migrate through soil to surface water and groundwaters.
- In soil and water, nitrate may be removed by denitrification to atmospheric nitrogen and by plant uptake.
- Under anaerobic conditions, degradation of nitrate into atmospheric nitrogen is an important removal process.

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

Minimal Risk Levels (MRLs)

Inhalation

No acute- (≤14 days), intermediate- (15–364 days), or chronic- (≥365 days) duration inhalation MRLs were derived for nitrate or nitrite.

Oral

- MRLs of 4 mg/kg/day have been derived for acute- (≤14 days)-, intermediate- (15– 364 days)-, and chronic- (≥365 days) duration oral exposure to nitrate.
- MRLs of 0.1 mg/kg/day have been derived for acute- (≤14 days), intermediate- (15– 364 days), and chronic- (≥365 days) duration oral exposure to nitrite.

Health Effects

- Exposure to high levels of nitrite can cause methemoglobinemia, a change to hemoglobin that decreases its ability to transport oxygen to tissues. Related symptoms include decreased blood pressure, increased heart rate, headaches, abdominal cramps, vomiting, and even death.
- Thyroid dysfunction has been reported in rats that were orally treated with nitrate and nitrite.
- The International Agency for Research on Cancer (IARC) noted that the presence of nitrite and some types of amines or amides in the acid environment of the stomach may result in the production of some cancer-causing N-nitroso compounds; under these conditions, IARC determined that ingested nitrate and nitrite is probably carcinogenic to humans (Group 2A). The U.S. Environmental Protection Agency (EPA) has not classified nitrate or nitrite for carcinogenicity.

Children's Health

- Young infants (<6 months of age) appeared to be particularly sensitive to the effects of nitrite on hemoglobin. These effects were seen after consuming formula prepared with drinking water that contained higher than recommended nitrate levels; some of these infants died.
- It is not known whether nitrate or nitrite can cause birth defects.