WISCONSIN DEPARTMENT of HEALTH SERVICES

Wisconsin Drinking Water Health Advisory for Molybdenum

Substance overview

Molybdenum (CAS Number: 7439-98-7) is a mineral that occurs naturally in all plants and animals.[1] Low levels of molybdenum are required for good health in humans and animals.[1] Because molybdenum has a very high melting point, it is widely used in industry to make steel alloys.[1]

The Wisconsin Department of Health Services has established a drinking water health advisory level of 200 micrograms per liter (µg/L) for molybdenum.[i]

Health effects

Low levels of molybdenum are essential for good health as it helps the body process materials and break down medications and toxins.[1] The Institute of Medicine's Food and Nutrition Board has recommended dietary molybdenum levels of 45 micrograms per day (µg/d) for adults.[2]

However, high levels of molybdenum can be harmful. Studies in animals suggested that ingesting large amounts of molybdenum can affect the kidneys and may cause liver damage and impact reproduction.[1] These studies also suggest that the severity of these effects may depend on copper levels in diet, with greater toxicity occurring when copper intake is low.[1]

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i This health advisory level supersedes the interim health advisory level established by DHS in 2013.

Exposure routes

Molybdenum is common in the environment. The main way that people can be exposed to molybdenum is by eating food containing molybdenum. People can also be exposed to small amounts of molybdenum by breathing air, drinking water, and touching soil.

Molybdenum can get into the environment through industrial activities like mining, milling, coal-fired power plants, and the production or use of molybdenum compounds. When molybdenum is released into water or soil, it can attach to organic materials such as clay and sand. Once attached to organic materials, molybdenum usually does not move far from the location where it was released.

Wisconsin public health thresholds

NR140 groundwater standards

Wisconsin established public health groundwater standards for molybdenum in 2006.[3,4ii] The enforcement standard of 40 micrograms per liter (µg/L) is based on EPA's draft lifetime health advisory level from 1993.[5] The preventive action limit was set at 20% of the enforcement standard because we did not find any evidence that molybdenum causes carcinogenic, mutagenic, teratogenic, or interactive effects when the standard was established.

To establish their draft Lifetime Health Advisory, they used an oral reference dose of 0.005 milligrams per kilogram per day (mg/kg-d), a body weight of 70 kg, water intake rate of 2 liters per day (L/d) and relative source contribution of 20% to account for potential exposure from other sources. EPA established the oral reference dose in 1992 from a cross-sectional epidemiology study.[6] From this study, they identified a lowest observable effect level (LOAEL) of 0.14 mg/kg-d based on an increased rate of gout-like symptoms and higher uric acid content in blood among the exposed population and used a total uncertainty factor (UF) of 30 to account for differences among people (UF = 3) and using a LOAEL instead of a no observable effect level (NOAEL) (UF = 10; **Equation C-1**).

ii In 2019, DHS recommended revised molybdenum groundwater standards. However, the recommended enforcement standard was calculated erroneously. As such, DHS withdrew these recommendations in 2024.

It should be noted that since EPA finalized the oral reference dose, several reviews have raised concerns regarding the methods used in the Koval'skiy study—these concerns include limited statistical confidence in the ability to establish a cause-effect relationship due to the large difference in sample size between controls (n = 5) and exposed subjects (n = 52); lack of details on how the subjects were chosen; and insufficient information on the analytical methods used. [1,7-9]

Interim drinking water health advisory level

In 2013, the Wisconsin Department of Natural Resource (DNR) requested that DHS review available health information because of the concerns with Koval'skiy et al. study.[10] As a result of this review, DHS established an interim health advisory level of 90 µg/L using the process specified in Chapter 160, Wis. Stats. for establishing recommended public health groundwater standard.[10,11iii]

DHS selected a reproductive toxicity study in rats by Fungwe et al. as the critical study.[12] In this study, the researchers allowed female rats to freely access drinking water that was supplemented with sodium molybdate (0, 5, 10, 50, or 100 mg/L molybdenum) and fed a diet with insufficient copper levels (6.3 mg copper per kg diet). The researchers reported molybdenum intake on a weekly basis. Using this information, we identified a NOAEL of 0.9 mg/kg-d (10 mg/L) based on prolonged estrous cycles and delayed fetal esophageal development at higher levels.[12,13]

To establish the interim health advisory level, DHS used the NOAEL and a total UF of 100 to account for differences between people and research animals (UF = 10) and differences among people (UF = 10; **Equation C-1**). To be consistent with the processes required for establishing groundwater standards, DHS used a body weight of 10 kg, a water consumption rate of 1 L/d, and a relative source contribution of 100% (**Equation C-2**). It should be noted that since the Fungwe et al. study was published, there have been concerns about the accuracy of the dose reporting as the study did not provide details on how the weekly molybdenum intakes were calculated and did not report body weights or water consumption rates..[1,14-19]

iii For more details on this process, see DHS' Setting Groundwater Standards to Protect Public Health guide.

Available health thresholds

When establishing state drinking water health advisory levels, DHS follows the groundwater standards process that is specified in Chapter 160, Wis. Stats.[11] We start by reviewing the relevant scientific information available. For molybdenum, we looked for public health thresholds and peer-reviewed research studies published since DHS established the groundwater standards in 2006. We identified an intermediate oral minimum risk level established by the Agency for Toxic Substances and Disease Registry (ATSDR) in 2020 and two peer-reviewed toxicology studies.

Guidance values

In 2020, ATSDR recommended an intermediate-duration oral minimal risk level (MRL) of 0.06 mg/kg-d for molybdenum.[1] ATSDR derived this value from a subchronic toxicity study in rats conducted by Murray et al. in which male and female rats were fed diets containing various levels of sodium molybdate for 90 days.[17] The study found that molybdenum affected body weight, weight gain, and food conversion efficiency, and caused kidney damage in female rats. Based on these findings, ATSDR established the MRL using a NOAEL of 17 mg/kg-d molybdenum. To calculate the MRL, ATSDR applied an uncertainly factor of 100 to account for differences between people and research animals (UF = 10) and differences among people (UF = 10). An additional modifying factor (UF = 3) was included to address concerns regarding increased sensitivity to reproductive and developmental effects in populations with lower copper intakes.[1] The resulting MRL is calculated based on the assumption of healthy dietary levels of molybdenum and copper and represents the level of exposure above normal dietary intake.

Peer-reviewed scientific studies

To ensure that Wisconsin drinking water health advisories are based on the best available information, DHS searches for relevant peer-reviewed health studies. We used the Web of Science and PubMed databases to look for studies related to molybdenum's toxicity and effects on a disease state. We focused our literature search on studies published since ATSDR finalized their toxicological profile for molybdenum in 2020.

Approximately 310 studies were returned by the search engines. We excluded studies that did not meet the Population, Exposure, Comparator, and Outcome (PECO) criteria for key studies (**Tables A-1 and B-1**). After applying these criteria, we identified three key toxicity studies and 14 key epidemiology studies (details in **Tables A-2** and **B-2**).

To be considered a critical study and evaluated for use in establishing the recommended standard, the study must meet the PECO criteria for critical studies (**Tables A-1** and **B-1**). We identified two critical toxicology studies and no critical epidemiology studies (details in **Tables A-3** and **B-3**).

Critical toxicology studies

To compare results between studies, we calculated acceptable daily intake (ADI) values for each study/effect (**Equation C-1**). The ADI is the estimated amount of molybdenum that a person can be exposed to every day and not experience health impacts. The ADI equals the toxicity value divided by the total uncertainty factor. Uncertainty factors were included to account for differences between humans and research animals, differences in sensitivity of health effects within human populations, using data from short-term experiments to protect against effects from long-term exposure, and using data where a health effect was observed to estimate the level that does not cause an effect.

In 2023, Aveyard et al. examined the systemic and reproductive toxicity of molybdenum in rats.[14] In this study, the researchers exposed pregnant rats (GD6-20) to different concentrations of sodium molybdate (0, 80, 120 mg molybdenum/kg-d) in a diet with more than adequate copper levels (13.3 ppm). We identified a LOAEL of 80 mg/kg-d based on effects on body weight and development. We obtained a candidate ADI of 0.027 mg/kg-d based on the LOAEL of 80 mg/kg-d and a total uncertainty factor of 3000 to account for differences between people and research animals (UF = 10), differences among people (UF = 10), and using an LOAEL (UF = 10), and the limited data on reproductive effects and the quantitative relationship between copper and molybdenum (UF = 3). The researchers identified several benchmark dose levels based on data from this study and from a reproductive study conducted in 2014 by the same group in which no adverse effects were observed at levels up to 40 mg/kg-d.[14,18]. We obtained a candidate ADI of 0.12 mg/kg-d based on the continuous benchmark dose lower confidence at 0.5 standard deviation (37 mg/kg-d) and a total uncertainty factor of 300 to account for differences between people and research animals (UF = 10), differences among people (UF = 10), and deficiencies in the dataset (UF = 3).

In 2023, Murray et al. examined the systemic and reproductive toxicity of molybdenum in rats.[14] In this study, the researchers exposed pregnant rats (GD6-20) to different concentrations of sodium molybdate (0, 80, 120 mg molybdenum/kg-d) in diet with adequate copper levels (6.3 ppm). They found no treatment-related effects on

mortality, clinical observations, body weight, body weight gain, food consumption, estrous cycling, reproductive performance, maternal macroscopic pathology, ovarian or uterine parameters, litter size, resorptions, fetal sex ratio, fetal weight, or external fetal malformations or variations. The researchers identified a NOAEL of 40 mg/kg-d based. We obtained a candidate ADI of 0.13 mg/kg-d based on the NOAEL of 40 mg/kg-d and a total uncertainty factor of 300 to account for differences between people and research animals (UF = 10), differences among people (UF = 10), and deficiencies in the dataset (UF = 3).

Health advisory determination

In our review, we found a guidance value from ATSDR and two peer-reviewed critical toxicology studies. Candidate ADIs from the critical studies were higher than ATSDR's intermediate oral minimum reference level.

Wisconsin's drinking water health advisory level for molybdenum is 200 µg/L.

To establish this level, we utilized the exposure factors indicated in Chapter 160 (body weight: 10 kilograms; water consumption rate: 1 liter per day; relative source contribution: 100%), ATSDR's oral intermediate minimum risk level (0.06 mg/kg-d) with an additional uncertainty factor of three to ensure adequate protection for copper deficient populations (**Appendix C** shows the equations used in this process).[1,10,11][iv] We included this additional uncertainty factor because dietary copper status affects the toxicity of molybdenum and copper deficiency in humans is not as rare as previously indicated.

Studies in research animals have shown that, when dietary copper levels are low, molybdenum causes severe effects – including decreased body weight gain and weight loss, anemia, fertility and reproduction impacts, and mortality.[12,20-23] When dietary copper levels are adequate, the occurrence or severity of molybdenum-induced toxic effects are lessened but not eliminated.[14-18,23-33] While the exact mechanism for these effects has not been elucidated, researchers have found that molybdenum exposure increases the copper levels in the plasma, liver, and kidneys and that this copper is in a tightly bound form.[34,35] These changes occur even when the animals are maintained on

iv For more details on this process, see DHS' Setting Groundwater Standards to Protect Public Health guide.

a copper-adequate diet.[14-18] Together, these results indicate that molybdenum exposure can cause biochemical changes even when diets provide adequate copper.

In establishing their minimum risk level, ATSDR did not consider studies in which animals were fed inadequate levels of copper because they stated that the average copper intake of the U.S. population exceeds the dietary requirements. Recent studies have reported that dietary copper intakes are declining with one study estimating that a quarter of adults in North America consume less copper than the estimated average requirement. [36,37] Furthermore, studies have indicated that copper deficiency in humans may be more prominent than previously thought. [38] Copper deficiency results most frequently from hereditary diseases, insufficient intake, increased demands, malabsorption, increased losses, and hereditary diseases (**Table 1**).[38] [36] For these reasons, we included an additional uncertainty factor to ensure adequate protection from molybdenum toxicity for populations at risk for copper deficiency.

Table 1. Causes and Examples of Copper Deficiency in Humans

Cause	Examples
Diseases/conditions	Menkes disease, familial hypoceruloplasminemia, nephrotic syndrome, protein-losing enteropathy, Celiac disease
Inadequate intake	Anorexia, malnutrition, poverty, vegetarian diets, parental hyperalimentation
Increased demand	Pregnancy, lactation, pre-mature infants, wound healing
Malabsorption	Inflammatory bowel disease, ulcerative colitis, colitis, Crohn's disease, bariatric surgery
Medications/diet	Excessive zinc ingestion; iron supplements; excessive dietary fructose

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Appendix A. Toxicology literature search criteria and results

Table A-1. Population, exposure, comparator, and outcome (PECO) criteria for key and critical toxicology studies

Element	Key Study	Critical Study
Population	Non-human mammalian animal species of any life-stage.	*No additional criteria.*
Exposure	Exposure to only the substance of concern via oral routes for more than a single or acute exposure duration.	Exposure to only the substance of concern via oral routes for at least 28 days.*
Comparator	A concurrent control group exposed to vehicle-only treatment or untreated control.	Two or more doses of the substance of concern.
Outcome	All health outcomes.	Health outcomes relevant to humans and consistent with other studies with identifiable toxicity value.

*Exceptions are studies that are conducted during reproduction and/or development.

Table A-2. Summary of key toxicology studies

Reference	Species	Route	Doses (mg/kg-d)	Duration	Endpoints	Copper Status*	Toxicity Value (mg/kg-d)
Aveyard et al., 2023[14]	Rat	Diet	80, 120	GD0-20	Decreased body weight. Reduced fetal body weight. Decreased anogenital distance.	Adequate (13.3 mg/kg)	NOAEL: N/A LOAEL: 80
Murray et al., 2023[15]	Rat	Water	20, 40	GD6-20	No effects on all endpoints evaluated.	Adequate (6.3 mg/kg)	NOAEL: 40
Zhou et al., 2024[39]	Mouse	Gavage	0.01, 1	56 d	No significant effects on body weight, organ coefficients, and histopathological examinations.	Not reported	NOAEL: N/A LOAEL: 0.01

* Adequate copper levels in diet for rats are 5 milligrams copper per kilogram diet (mg/kg) for growth and 8 mg/kg female reproduction are 6 mg/kg for growth and 8 mg/kg for pregnancy and lactation.[40] Adequate copper levels for mice are 6 mg/kg for growth and 8 mg/kg for pregnancy and lactation.

Table A-3. Critical toxicology study selection

Reference	Appropriate duration	Consistent with other studies	Effects relevant to humans	More than one dose	Toxicity value identifiable	Critical study
Aveyard et al., 2023[14]	Yes	Yes	Yes	Yes	Yes	Yes
Murray et al., 2023[15]	Yes	Yes	Yes	Yes	Yes	Yes
Zhou et al., 2024[39]	Yes	Yes	No*	Yes	Yes	No

* Direct relevance of metabolomic findings to adverse human health effects are not clear at this time.

Appendix B. Epidemiology Literature Search Criteria and Results

Table B-1. Population, exposure, comparator, and outcome (PECO) criteria for key and critical epidemiology studies

Element	Key Study	Critical Study
Population	Any population and life-stage (occupational or general population, including children and other sensitive populations).	*No additional criteria.*
Exposure	Any exposure to the substance of concern via oral routes.	*No additional criteria.*
Comparator	A comparison or referent population exposed to lower levels (or no exposure/ exposure below detection limits) of the substance of concern.	Dose response relationship between exposure and health endpoint(s) is identified.
Outcome	All health outcomes.	Health outcomes consistent with other studies with identifiable toxicity value.

Table B-2. Summary of key epidemiology studies

Reference	Study type	Outcomes	Results
Chi et al., 2025[41]	Cross-sectional	Analyze how individual metals and their mixtures contribute to infertility risk.	Nonlinear relationship between urinary Mo and infertility.
Fang et al., 2024[42]	Prospective birth cohort	Explore the association between neighborhood walkability and hormones in pregnant women.	Placental Mo levels linked to decreased testosterone levels.
Jiang et al., 2026[43]	Prospective birth cohort	Evaluate the effects of toxic metals and trace elements on child behavioral problems.	Mo concentrations in the second trimester positively associated with internalizing symptoms scores, externalizing symptoms scores and total problems score.
Kuang et al., 2024[44]	Cross-sectional	Investigate the relationships between urinary metals and clinical health indicators.	Kidney and cystatin-C emerged as the most sensitive organ and critical effect indicator of molybdenum exposure, respectively.
Lipner et al, 2022[45]	Case-control	Identify water-quality constituents that influence odds of nontuberculous mycobacteria (NTM) infection among persons with cystic fibrosis.	Consistent association with molybdenum in the source water and M. abscesses group species infection.
Lipner et al., 2026([46])	Retrospective cohort	Examine the effect of trace metals in public distribution system water on nontuberculous mycobacterial (NTM) pulmonary infection among susceptible persons.	Increases in Mo in treated drinking water significantly increased the risk of NTM pulmonary infection.
Long et al., 2022[47]	Cross-sectional	Explore the associations of multiple plasma metals with homocysteine levels.	Plasma Mo levels were positively associated with homocysteine levels – risk factor for cardiovascular disease.

Su et al., 2024[48]	Case–control	investigate the associations between metals in blood and follicular fluid and endometriosis risk.	Mo levels are significantly greater among the cases than among the controls, with a positive association with endometriosis risk.
Vrijheid et al., 2020[19]	Cross-sectional cohort	Assess the association between early -life environmental exposures and childhood obesity.	Child blood levels of molybdenum were associated with lower BMI.
Wang et al., 2022[49]	Prospective	Evaluate the associations of plasma multiple metals with the decline in kidney function.	Mo plasma concentrations were significantly associated with the decline in kidney function.
Wen et al., 2025[50]	Cross-sectional	Investigate the association between plasma concentrations of metals and serum immunoglobulin (Ig) levels.	Higher Mo levels in urine are positively associated with IgG.
Wu et al., 2025[51]	Cross-sectional	Evaluate the association between urinary metals and metabolic dysfunction-associated steatotic liver disease (MASLD).	Urinary Mo levels positively correlated with the risk of MASLD.
Yang et al. 2025[52]	Prospective cohort	Evaluate the relationships between multiple metal exposures and incident anemia.	Elevated plasma Mo levels are associated with higher risks of incident anemia.
Yu et al., 2025[53]	Cross-sectional	Evaluate the association between exposure to metals and dyslipidemia.	Mo levels linearly associated with total cholesterol levels, after adjusting for confounders.

Table B-3. Critical Epidemiology Study Selection

Reference	Consistent with other studies	Dose-Response relationship	Toxicity value identifiable	Critical study
Chi et al., 2025[41]	Yes	No	No	No
Fang et al., 2024[42]	Yes	No	No	No
Jiang et al., 2026[43]	Yes	No	No	No
Kuang et al., 2024[44]	Yes	Yes	Yes	Yes
Lipner et al, 2022[45]	Yes	No	No	No
Lipner et al., 2026[46]	Yes	No	No	No
Long et al., 2022[47]	Yes	No	No	No
Su et al., 2024[48]	Yes	No	No	No
Vrijheid et al., 2020[19]	Yes	No	No	No
Wang et al., 2022[49]	Yes	No	No	No
Wen et al., 2025[50]	Yes	No	No	No
Wu et al., 2025[51]	Yes	No	No	No
Yang et al. 2025[52]	Yes	No	No	No
Yu et al., 2025[53]	Yes	No	No	No

Appendix C: Wisconsin Drinking Water Health Advisory Level Calculations

Equation C1: Acceptable daily intake determination

$$\text{Acceptable Daily Intake} = \frac{\text{Toxicity Value}}{\text{Total Uncertainty Factor}}$$

Where:

- Acceptable Daily Intake: Estimate of a daily oral exposure to that is likely to be without an appreciable risk of deleterious effects (milligrams substance per kilogram body weight per day; mg/kg-d)
- Toxicity value: No observable adverse effect level (NOAEL), lowest observable adverse effect level (LOAEL), or benchmark dose (BMD).
- Total uncertainty factor = used to account for scientific uncertainty that is inherent in the type of data used to establish human health advisory. Sum of the following uncertainty factors:
    - Interspecies - Accounts for differences between people and research animals
    - Intraspecies - Accounts for difference among people
    - Study duration – Accounts for using data from a shorter-term study to protect from long term effects
    - Endpoint – Accounts for using a value that caused a health effect to protect public health
    - Database – Accounts for extrapolating from valid results in experimental animals when the data set is incomplete.

Equation C2: Health advisory level determination

$$\text{Health Advisory Level} = \frac{\text{Acceptable Daily Intake} \times \text{Body Weight} \times \text{Relative Source Contribution}}{\text{Water Consumption}}$$

Where:

- Acceptable Daily Intake: Estimate of a daily oral exposure to that is likely to be without an appreciable risk of deleterious effects (milligrams substance per kilogram body weight per day; mg/kg-d)
- Body weight: Weight of young child (10 kg)[v]
- Relative source contribution: Percent of daily exposure that is attributed to drinking water (100%)[v]
- Water consumption rate: Amount of water consumed each day (1 L/d)[v]

v Specified in Chapter 160, Wisc. Stat., for establishing recommended public health groundwater enforcement standards – used to establish health advisory levels for consistency. More information on these equations is available in DHS' Setting Groundwater Standards to Protect Public Health guide.