TECHNICAL SUMMARY

Lithium in Drinking Water
A Resource for Primacy Agencies

Under the Fifth Unregulated Contaminant Monitoring Rule (UCMR 5), EPA is gathering information on the occurrence of lithium in public drinking water. EPA collects nationally representative drinking water occurrence data to support the Agency's future regulatory determinations and, as appropriate, the development of national primary drinking water regulations (NPDWRs) under the Safe Drinking Water Act (SDWA). This monitoring also helps federal, state, and other researchers prioritize studies for health effects information, identify data gaps, and determine the need for future studies to improve our understanding of the possible health risks associated with unregulated contaminants in public drinking water.

EPA has developed this document to help Primacy Agencies interpret the UCMR 5 monitoring results, understand health risks based on available information, and respond to public inquiries.

Background on Lithium

Lithium Sources and Environmental Occurrence

- Lithium is a naturally occurring element and may be found at higher concentrations in certain parts of the country, particularly in groundwater sources in arid locations in the Western U.S. where geologic formations contain lithium salts (EPA, 2008; Lindsey et al., 2021).
- Lithium, in various formulations, has numerous commercial uses including as a pharmaceutical drug, an industrial chemical catalyst, a sanitizing agent for swimming pools and hot tubs, and increasingly, as a component of lithium-ion batteries for electronics and electric vehicles (EPA, 2008; Agusdinata et al., 2018).
- Lithium is likely present in a variety of foods (such as cereal grains, leafy vegetables, and root crops), but it is not clear which foods may be significant sources of dietary lithium (EPA, 2008). There are differing perspectives on whether lithium is beneficial in small amounts (*e.g.*, a micronutrient) (Szklarska and Rzymski, 2019). The U.S. has no current recommended dietary allowance.

Lithium Pharmaceutical Use

- *Lithium salts* (*e.g.*, lithium carbonate [Li_2CO_3], lithium citrate [$Li_3C_6H_5O_7$]) have been used clinically for decades in the United States as a mood-stabilizing medication, primarily for bipolar disorder (NAMI, 2021).
- Therapeutic doses of lithium compounds generally range from 600-1,200 mg/day (NAMI, 2021).
- Therapeutic doses carry the risk of harmful side effects, so therapy strategies are based on a risk-benefit assessment for individual patients (EPA, 2008).

UCMR 5

SDWA requires that every five years EPA publish monitoring requirements for priority contaminants that may be present in drinking water and do not have EPA drinking water regulatory standards. UCMR 5, which includes lithium, spans 2022 – 2026, with sample collection by public water systems (PWSs) from 2023 – 2025 and the completion of data reporting in 2026 (EPA, 2021a; EPA, 2021b). Learn more about UCMR 5.

Lithium is on EPA's Fifth Contaminant Candidate List (CCL 5), a priority list of drinking water contaminants that are known or anticipated to occur in PWSs and may require future regulation under SDWA (EPA, 2022a). The UCMR program typically uses the CCL to identify contaminants without sufficient occurrence data to inform regulatory decision making. Lithium was selected for UCMR 5 through a contaminant prioritization process that considered expected or known occurrence in drinking water and the availability of health effects information (EPA, 2021c).

Screening Levels and Reporting Limits for Drinking Water

- EPA has not established a non-regulatory drinking water Health Advisory or any regulatory standard for lithium in public drinking water supplies. EPA calculated a provisional oral reference dose (p-RfD) of 2 µg/kg-day using the Provisional Peer-Reviewed Toxicity Value (PPRTV) process. A PPRTV is defined as a toxicity value derived for use in the Superfund Program when such a value is not available from EPA's Integrated Risk Information System (IRIS). This PPRTV process involves a more limited assessment compared to those conducted under EPA's IRIS process. The provisional value for lithium is based on adverse effects observed in patients administered lithium therapeutically (generally 600-1,200 mg/day of lithium compound) (EPA, 2008; NAMI, 2021).
    - EPA's fifth Candidate Contaminant List (CCL 5) Health Reference Level (HRL) of 10 µg/L is based on the p-RfD, consideration of the general population risk, a daily drinking water ingestion rate of 33.8 ml/kg-day, and a "default" assumption that drinking water accounts for 20% of daily lithium intake compared with other sources (EPA, 2022b). The U.S. Geological Survey (USGS) also published a 10 µg/L screening level for lithium (USGS, 2018).
    - As an alternative non-regulatory screening level, the USGS published a "drinking water only" benchmark (*i.e.*, based on an assumption that drinking water is the only source of daily lithium intake) of 60 µg/L to provide context for evaluating lithium concentrations in groundwater (Lindsey et al., 2021).
- The U.S. Food and Drug Administration (FDA) has not established a standard for lithium in bottled water at this time. The FDA bottled water resources are available on the Bottled Water Everywhere: Keeping it Safe web page.
- The UCMR 5 program established a minimum reporting level (MRL) of 9 µg/L for lithium based on laboratory analytical measurement capability using EPA Method 200.7 (EPA, 1994; EPA, 2021a). UCMR MRLs are not associated with contaminant health effects information. Analysis using EPA Method 200.7 provides a concentration of total lithium, accounting for lithium from all compounds present in the water.

Adverse Effects Observed in Humans at Therapeutic Doses

Adverse human health effects based on exposure at therapeutic doses have been observed in several organs and body systems of treated patients. The types of health effects are consistent with the limited number of available toxicology studies (EPA, 2008).

- Renal (kidney-related) effects: Lithium pharmaceutical treatment can interfere with the kidney's ability to concentrate urine, resulting in excessively dilute urine and feelings of thirst. Severe kidney disease may result from long-term treatment at higher doses (EPA, 2008).
- Neurologic (nervous system) and other effects: Lithium pharmaceutical treatment can cause lethargy, fatigue, weakness, tremor, and cognitive impairment, as well as impairment of endocrine gland function such as the thyroid and parathyroid. Other severe but rarer effects, including developmental effects, have also been associated with lithium therapy (EPA, 2008; Tondo et al., 2019).

Uncertainties Associated with Risk Estimates for Drinking Water

There are uncertainties associated with risk estimates based on the findings in the PPRTV assessment (EPA, 2008).

- Despite the abundance of information on patients receiving lithium at *therapeutic* levels, there has historically been limited information available to evaluate health risks in people at the levels associated with typical drinking water consumption.
- EPA derived the p-RfD of 2 µg/kg-day for lithium from a lowest-observed-adverse-effect level (LOAEL) because a no-observed-adverse-effect level (NOAEL) was not established for lithium. Therefore, there is uncertainty about the therapeutic lithium dose at or below which there are no adverse effects in humans or experimental systems. Additional data gaps include the lack of information about adverse human health effects resulting from long-term exposure to lithium and the populations or life stages with increased susceptibility to lithium exposure.
- To account for these uncertainties, EPA applied a composite uncertainty factor of 1,000 to the lowest therapeutic dose associated with adverse effects in human patients to develop the p-RfD.

Example risk statements based on health screening levels and uncertainties:

- Health risk information is limited for lithium exposures from drinking water only (≤60 µg/L) and from drinking water when considering all exposure sources (≤10 µg/L). However, EPA has applied a standard health-protective multiplier to account for this uncertainty; therefore, estimated exposures to these concentrations are unlikely to result in increased potential for human health concern based on the available health risk information.
- At present, EPA cannot confidently estimate the risk for people with lithium exposures from drinking water between 10 µg/L and the much higher concentration equivalent to a therapeutic dose from lithium compounds.

Drinking Water Treatment

Lithium cannot be removed by heating, boiling, or disinfecting water. Certain drinking water treatment approaches can reduce exposure. Available literature, based largely on bench- and pilot-scale data, suggests ion exchange is effective for removal of lithium from drinking water. Adsorption using certain novel media may also be effective. EPA continues to review treatment literature and publish details regarding the removal efficiencies for various technology types for lithium via its Drinking Water Treatability Database (EPA, 2023).

Summary Information

- Lithium is a naturally occurring metal, has numerous commercial uses including as a main component of batteries, and is likely found in a variety of foods. Lithium is also used as a pharmaceutical to treat certain medical conditions.
- Lithium is on EPA's Fifth Contaminant Candidate List (CCL 5), a priority list of drinking water contaminants that may require future regulation under the Safe Drinking Water Act. Lithium was selected for the Fifth Unregulated Contaminant Monitoring Rule (UCMR 5) to better inform research and determine whether lithium poses health risks to people through drinking water from public water systems.
- EPA continues to assess the literature for health effects information, identify data gaps, and determine the need for future studies to improve our understanding of the possible health risks associated with lithium in public drinking water.
- Research on the use of lithium as a pharmaceutical indicates that exposure at certain levels may be connected to adverse effects on the body's kidneys and nervous system. While the health effects in patients receiving lithium at therapeutic levels have been documented, there is limited information available to evaluate health risks for people exposed to lower levels of lithium via drinking water.[1]
    - EPA does not currently have an EPA Health Advisory for lithium in drinking water. The screening Health Reference Level (HRL) of 10 µg/L from CCL 5 is based on adverse effects observed in patients administered lithium therapeutically, not at levels expected to be found in drinking water. The occurrence data gathered by UCMR 5 will help inform future steps the Agency may take to protect public health.
- Lithium cannot be removed by heating, boiling, or disinfecting water. Certain drinking water treatment approaches can reduce exposure. The U.S. Food and Drug Administration (FDA) has not established a standard for lithium in bottled water.

Additional Information about UCMR 5

PWSs inform their customers about their UCMR 5 monitoring results via the established Tier 3 Public Notification (PN) [40 CFR 141.207] and Consumer Confidence Report (CCR) [40 CFR 141.153(d)(7)] requirements. PWSs are required to notify their customers about the availability of all UCMR results no later than 12 months after they are known by the PWS. Community water systems (CWSs) are required to report UCMR results in their annual CCR when unregulated contaminants are found (*i.e.*, measured at or above minimum reporting levels). CWSs must report the average and range of the year's monitoring results. EPA resources for PWSs are available on the CCR and PN Compliance Help web pages.

[1] Based on the concentration range (third quartile – maximum) of lithium observed in 1,464 public-supply wells (21 – 396 µg/L) (Lindsey et al., 2021), the average daily consumption of 2.5 L/day amounts to a maximum daily ingestion of 0.05 – 1.0 mg (as compared to the lower end of the therapeutic dose range for lithium compounds, 600 mg) (NAMI, 2021).

Glossary of EPA Technical Terms

Health Advisory (HA): HA levels are non-regulatory concentrations of a contaminant in drinking water at which adverse health effects and/or aesthetic effects are not anticipated to occur over specific exposure durations (*e.g.*, 1-day, 10 days, a lifetime). EPA's HA documents provide technical information on chemical and microbial contaminants that can cause human health effects and are known or anticipated to occur in drinking water. *[non-regulatory]*

Health Reference Level (HRL): Derived during the CCL 5 process for screening purposes. HRLs are used in EPA's Regulatory Determination process as risk-derived concentrations against which to evaluate the occurrence data to determine if contaminants occur at levels of public health concern. HRLs are not final determinations about the level of a contaminant in drinking water that is necessary to protect any particular population and, in some cases, are derived prior to development of a complete exposure assessment. *[non-regulatory]*

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level of a contaminant at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group. *[non-regulatory]*

Minimum Reporting Level (MRL): Determined using data from multiple laboratories that participate in EPA's UCMR MRL-setting studies and are not associated with contaminant health effect information. The MRL is the lowest level of a contaminant that is considered measurable, with 95% confidence, by at least 75% of laboratories nationwide using a specified analytical method (recognizing that individual laboratories may be able to measure or quantify analytes at lower levels). EPA's MRL for lithium is 9 µg/L. *[regulatory]*

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level of a contaminant at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects. *[non-regulatory]*

Oral Reference Dose (RfD): An estimate, with uncertainty spanning perhaps an order of magnitude, of a daily oral exposure of a contaminant to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. *[non-regulatory]*

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