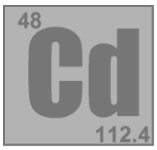
Section of Environmental Epidemiology & Toxicology
Office of Public Health, Louisiana Department of Health
(888) 293-7020; www.seet.dhh.la.gov

INFORMATION FOR HEALTH CARE PROFESSIONALS
CADMIUM EXPOSURE & TOXICITY



Revised: April 2023

This document summarizes information on the sources, exposure pathways, laboratory testing, recognition, and reporting of cadmium exposure and/or poisoning. Louisiana Law requires the reporting of all cases of cadmium poisoning and all cadmium laboratory test results to the Louisiana Department of Health's Office of Public Health.

EXPOSURE TO CADMIUM

Occupational Exposure: Cadmium is a naturally occurring heavy metal found in earth's crust. Most cadmium in the United States is extracted during the production of other metals like zinc, lead, and copper (OSHA, 2022; ATSDR, 2012). Cadmium exposure is most often occupational-related, and can occur in all industry sectors. Due to its non-corrosive properties, it is utilized in batteries, pigments, metal coatings, and plastics. It is also a contaminant of some commercial fertilizers. The most common route of exposure is inhalation of dust and fumes. Workers at the highest risk of exposure are those in manufacturing, followed by construction, wholesale trade, and transportation industry sectors. Workers may be exposed while smelting and refining metal: manufacturing batteries, plastics, coatings, and solar panels; recycling Ni-Cd batteries; electroplating; metal machining; welding; and painting. Workers involved in landfill operations, recycling of electronic or plastic parts, compost workers, and waste collectors are also at high risk (OSHA, 2022; ATSDR, 2012).

Take-Home Exposure: Workers may transport cadmium on shoes, tools, and work clothes into their homes or automobiles with subsequent exposure to their families (NIOSH, 2017).

Steps to prevent "take-home" cadmium contamination:

- Change shoes and clothes at work before getting into the car or going home. Put dirty work clothes and shoes in a plastic bag.
- Wash face and hands prior to leaving work.
- Shower and wash hair immediately upon arriving home (or before leaving work).
- Wash work clothes separately from all other clothes and run the washing machine again to rinse residual cadmium.

Exposure Risks to the General Population: Nonoccupational exposures also occur. Cigarette smoke is the biggest source of non-occupational cadmium exposure (ATSDR, 2015). Studies consistently show that smokers have higher cadmium levels than non-smokers. Food is another source of cadmium exposure. Plants, animals, and seafood accumulate cadmium from water and soil. Foods highest in cadmium include leafy vegetables, potatoes, grains, peanuts, soybeans, sunflower seeds, organ meats (kidney and liver), and some shellfish. Cadmium from smoking cigarettes is more likely to pose a health concern than cadmium in food. One or more packs of cigarettes a day may double the daily exposure of a typical individual. Second-hand smoke is not considered a significant source of cadmium exposure.

Additional exposures to cadmium can occur through sources that may not be readily known or recognized. Hobbies such as jewelry making, ceramics, and metal work could involve cadmium and are potential sources of exposure. People who live near hazardous waste sites, municipal incinerators, or industrial cadmium sources (smelting operations, chemical plants) may also be at an increased risk of exposure through air, food, dust, or water contamination (ATSDR, 2015).

Potential Sources of Cadmium Exposure	
Occupational	**Non-Occupational**
Battery manufacturing	Food
Demolition/wrecking where cadmium is present	Cigarette smoke
Electroplating	Contaminated water
Glasswork	Ceramics and glass glazes
Iron/steel industry	Jewelry making
Landfill Operations	Fabric dyes
Paint production and use	
Petroleum refining	Metal work
Plastics production	Residing near hazardous waste sites-fossil fuel combustion/municipal waste incineration
Pigments, plastics, ceramics, glazes, enamels	
Ship building/repair	
Smelting/refining of metals	
Soldering/welding of metals	

This is not a complete list of exposure sources. The above information was compiled from ATSDR, 2015; OSHA, 2017.

TOXICITY OF CADMIUM

Cadmium is a heavy metal that causes adverse health effects at very low exposure levels. Cadmium affects many organ systems and induces toxicity following acute and chronic exposures. The degree and severity of effects depend on the amount of cadmium present. Toxicity is also related to the form of cadmium (cadmium oxide, cadmium chloride), the particle size (fume or aerosol), length of exposure, and route of exposure (inhaled cadmium is more readily absorbed than ingested cadmium).

Possible Cadmium-Induced Health Effects in Adults	
Acute	Chronic
Mild/severe irritation of the upper respiratory tract, coughing, shortness of breath, pulmonary edema, pneumonitis	Kidney damage: kidney stones, proteinuria, aminoaciduria, glycosuria, renal tubular damage
GI disturbances; vomiting, abdominal pain, diarrhea, nausea, cramps	Bronchiolitis, COPD, emphysema, fibrosis
Flu-like symptoms: chills, headache, aching and/or fever	Calcium deficiency, osteoporosis, osteomalacia
	Prostate and lung cancer

Information compiled from: ATSDR, 2015; EPA, 2016; OSHA, 2017.

Acute Toxicity*:* Inhalation of high levels of cadmium fumes or dust may severely irritate respiratory tissue (e.g. nasopharyngeal or bronchial irritation). Acute pneumonitis may occur with symptoms such as fever and chest pain. In extreme exposure cases pulmonary edema may develop. Respiratory symptoms may linger for several weeks, and impairment of pulmonary function may persist for months. At lower levels of exposure, non-specific symptoms such as headache, chills, muscle aches, nausea, vomiting, and diarrhea can occur (ATSDR, 2015). Metal fume fever can also occur from inhalation of cadmium oxide fumes that are produced when cadmium metal and cadmium compounds are heated to high temperatures. Metal fume fever causes flu-like symptoms. Particle size is a more important determinant of respiratory toxicity than chemical form (the smaller cadmium particles in fumes are more potent toxicants than the larger particles in dusts).

Chronic Toxicity*:* With chronic exposure, cadmium accumulates primarily in the kidneys, with smaller amounts accumulating in the liver and muscles. 1) Renal effects: Kidney damage is the critical health effect associated with long-term cadmium exposure. Cadmium damages the proximal tubules and is characterized by increased urinary excretion of low-molecular-weight proteins including β2-microglobulin or intracellular tubular enzymes. Over time, cadmium may also affect glomerular function. 2) Pulmonary effects: Long-term inhalation exposure at low levels can lead to decreased lung function and emphysema. 3) Bone effects: Bone disorders have been reported following chronic exposure to high levels of cadmium in food. Bone disorders include osteoporosis and osteomalacia (adult rickets). In Japan, long term ingestion of cadmium-contaminated water and food was associated with a crippling condition known as "itai-itai" (ouch-ouch) disease. The affliction is characterized by pain in the back and joints, osteomalacia, and bone fractures.

Carcinogenesis: Several inorganic cadmium compounds are associated with malignant tumors in animals. Occupational exposure to cadmium has been implicated in an increase of risk in developing lung and prostate cancer. The IARC has determined that there is sufficient evidence in humans for the carcinogenicity of cadmium and cadmium compounds.

Mechanism of Cadmium Toxicity: Cadmium affects many organ systems primarily by binding to proteins within cells and interfering with enzymes requiring zinc. Cadmium is very similar to zinc in structure and function and may replace zinc in many physiological and enzymatic functions. The zinc/cadmium ratio influences cadmium toxicity and storage; zinc deficiency increases toxicity while adequate levels of zinc can reduce cadmium-related tissue damage. Zinc deficiency and cadmium toxicity are more likely to occur in diets high in refined grains and flours because the zinc/cadmium ratio may be altered during the refining of grains.

Susceptible Populations: The greatest potential for above average exposure of the general population to cadmium is from smoking. Smokers who are exposed to cadmium in the workplace are at the highest risk (CDC 2005). Individuals living near zinc or lead smelting operations, municipal incinerators, or other industrial processes emitting cadmium to the air will also have above average exposure (ATSDR, 2012). While there are few reports of cadmium poisoning in children, health effects are expected to be similar to the effects seen in adults (kidney, lung, and intestinal damage depending upon route of exposure). These effects are mostly seen in acute high-level exposure situations. Harmful effects on child development or behavior have not generally been observed in populations exposed to cadmium but more research is needed (ATSDR, 2015). Children who do not get enough iron, calcium, zinc, or protein may absorb more cadmium from their diet. It remains unclear if cadmium causes birth defects. A limited number of epidemiology studies suggest effects on birth weight, neurobehavior, and the developing immune system. However, further confirmation of these findings is needed. Studies in animals exposed to high levels of cadmium during pregnancy have resulted in harmful effects to the developing nervous system, leading to behavioral and learning deficits. There are also some animal data suggesting that high cadmium exposures before birth can lower birth weight and affect the developing skeleton. However, dose levels used in these animal studies are higher than human exposures and people may respond differently. Pregnant women with low levels of calcium, iron, or zinc, may absorb more cadmium. Cadmium can be transferred to offspring through breast milk. Cadmium levels in breast milk range from 5 to 10% of the levels found in the mother's blood.

EVALUATION OF CADMIUM POISONING

Assessment of a patient for cadmium poisoning requires the following -

- Work history and identification of possible cadmium exposure sources
- Medical history
- Laboratory testing for cadmium

Work and Exposure History: Often, patients do not recognize that they have been exposed to cadmium unless directly asked about their work environment and activities. A detailed occupational and environmental exposure history is a fundamental step toward acquiring information on possible exposures to cadmium.

- A full work history is necessary to identify workplace exposures. Ask patients about their job (where they work and what they do), potential exposure occurring in current and previous jobs, hygiene practices in the workplace, and use of personal protective equipment. If the worker is employed in a job that may involve exposure to cadmium, further questions on length of time at the job, frequency of tasks handling cadmium

materials, and descriptions of how they carry out their work, (e.g., are fumes generated from high heating, are there dusts or other factors that would influence exposure) should be asked.

- An environmental history can identify non-occupational exposure sources. Ask patients about their smoking habits; exposure to second hand smoke; dietary intake (shellfish, liver, kidney); the presence of cadmium-containing items around the home (e.g. batteries, fabric dyes, ceramic and glass glazes); hobbies; sources of drinking water; and proximity of their residence to hazardous waste sites, smelting operations, or other industries.

The Agency for Toxic Substances & Disease Registry (ATSDR) offers a self-instructional module on "Taking an Exposure History" which provides an exposure history form in Appendix 1.

Medical History: A medical history may help identify possible symptoms that could be associated with cadmium poisoning. Early symptoms of acute cadmium poisoning include nausea, vomiting, and abdominal pain. Symptoms of chronic low-level cadmium exposure include chronic obstructive pulmonary disease, emphysema, and chronic renal tubular disease. Most of these symptoms have many other causes, but may provide useful information for diagnosis when coupled with the exposure history. It may take a period of time for symptoms from cadmium exposure to occur and symptoms may last months or years. Laboratory testing for cadmium exposure should be considered if the exposure history indicates possible cadmium sources and/or the patient is experiencing symptoms that suggest possible cadmium poisoning.

Laboratory Tests

- **Cadmium in Blood (CdB)** Cadmium levels in blood are reflective of both acute and chronic exposures (CDC, 2016). Blood levels of cadmium decrease with two distinct half-lives (OSHA, 2017). The first half-life of a few months is thought to reflect the turnover rate of cadmium-bound red blood cells. The second halflife is several years long and is likely to reflect body burden (cadmium stored in kidneys, liver, and muscle). Among currently exposed individuals, CdB increases during the first four to six months of exposure and then levels off, which is likely to reflect the average exposure during those months. In individuals with a history of chronic exposure who have accumulated significant stores of cadmium, a portion of the CdB can be attributed to body burden. When these individuals are removed from exposure, CdB may remain elevated, possibly for years.

- **Cadmium in Urine (CdU)** Urine levels primarily reflect body burden (mainly kidney burden) and chronic exposures (CDC, 2016; OSHA, 2017). In the general population, CdU is both small and constant. For low to moderate exposures, CdU concentrations rise slowly and decrease very slowly due to its long half-life in the kidney (10-30 years). With high cadmium exposures, increased CdU reflects recent exposure. For an individual exposed over a long period of time, sufficient cadmium may be present to saturate renal binding sites. In these cases, CdU will then reflect both recent exposure and body burden. If a patient suffers from cadmium-induced kidney disease, CdU may increase dramatically with no direct relationship to body burden or current exposure.

- **Beta-2-microglobulin (B^2-M)** (proteinuria and other small molecular weight proteins) present in urine is an indication of damage to the proximal tubules. B^2-M is normally filtered out of the blood by the kidney's glomeruli, and then reabsorbed back into the blood in the renal tubules. When the tubules fail, they can not reabsorb B^2-M resulting in elevated B^2-M levels in the urine. Finding excess B^2-M proteins in urine in conjunction with elevated cadmium body burden, as indicated by elevated CdU and CdB, is evidence of cadmium-related kidney disease.

HEALTH-BASED REQUIREMENTS, RECOMMENDATIONS & GUIDELINES

Occupational Safety and Health Administration: The Occupational Safety and Health Administration (OSHA) promulgates and enforces regulations for toxic substances in the workplace. These regulations are enforceable by law. OSHA regulations are based on both air monitoring and biological monitoring of the worker. Air monitoring provides data on work place conditions, guides industrial hygiene measures, and serves as the basis for requiring medical/biological monitoring of workers. Biological monitoring measures the uptake of cadmium into the body, reflects actual exposure, and is used to assess health risk to workers (OSHA, 2017).

- Workers exposed to levels of airborne cadmium > 2.5µg/m^3 (eight-hour time-weighted average) for more than 30 days per year must be placed in a medical surveillance program.
- Medical surveillance is also required for veteran workers who have been previously exposed to cadmium for more than 5 aggregate years.
- Medical surveillance involves monitoring of biological indicators of cadmium exposure and toxicity. This includes cadmium in blood (CdB), cadmium in urine (CdU), and beta-2-microglobulin levels in urine (B^2-M).

Three categories of exposure are defined based on the biological monitoring results. The "Monitoring Result Category" a patient falls into guides the frequency and type of medical surveillance:

- Category **A**- All three laboratory test results fall at or below levels shown
- Category **B**- One laboratory test result falls within the range shown.
- Category **C**- One laboratory test result falls above the levels shown.

Exposure Categories for Cadmium			
Biological marker	Monitoring results categories		
	A	B	C
Cadmium in urine (CdU) (µg/g creatinine)	< = 3	> 3 & < = 7	>7
B2-microglobulin (B2-M) (µg/g creatinine)	< = 300	> 300 & < =750	>750
Cadmium in blood (CdB) (µg/liter whole blood)	< = 5	> 5 & < = 10	>10

The frequency of biological monitoring and medical examinations increase with each higher category.

Requires Actions Based on Monitoring Results			
Required Actions	Monitoring Results Category		
	A	B	C
Biological Monitoring			
Annual	X		
Semiannual		X	
Quarterly			X
Medical Examination			
Biennial	X		
Annual		X	
Semiannual			X
Within 90 days of monitoring results		X	X
Discretionary Medical Removal		X	X
Mandatory Medical Removal			X

Guidelines for medical removal are as follows:

- Medical removal is discretionary for category B
- Medical removal is mandatory for category C if at least one of the following criteria is true
    1) CdU is greater than 7 µg/g creatinine, or
    2) CdB is greater then 10 µg/L whole blood, or
    3) B^2-M value is greater than 750µg/g creatinine and either the employees CdU level is >3 µg/g creatinine, or the CdB level is above >5 µg/liter whole blood.

In 1994, OSHA released a Windows-based system, **GOCAD 2.0,** directed at assisting the general public with applying the biological monitoring provisions of the OSHA Cadmium Standard.

American Conference of Governmental Industrial Hygienists: The American Conference of Governmental Industrial Hygienists (ACGIH) is a non-profit, nongovernmental scientific organization, which develops peer-reviewed guidelines for workplace exposures. BEIs are the opinion of the scientific community, not standards. The ACGIH develops Biological Exposure Indices (BEIs®) as guidance values for assessing biological monitoring results. The BEI® generally indicates a concentration below which nearly all workers should not experience adverse health effects. ACGIH adopted a BEI® for cadmium and inorganic cadmium compounds in urine of 5µg/g creatinine and a BEI in blood of 5 µg/L (ACGIH and OSHA, 2012).

National Report on Human Exposure to Environmental Chemicals: The "Fourth National Report on Human Exposure to Environmental Chemicals" (CDC, 2017) provides an assessment of the exposure of the U.S. population to environmental chemicals using biomonitoring. One of the primary purposes of this report is to establish reference ranges that can be used by physicians to determine whether an individual has been exposed to higher levels than are found in the general population. Cadmium levels in blood and urine samples from a random sample of participants from the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics are shown in the table below. People who are occupationally exposed may have higher background levels then those found in the general population.

		Background Cadmium Levels				
		1-5 yrs	6-11 yrs	12-19 yrs	≥ 20 yrs	Current Smokers ≥20 yrs*
Blood (µg\L)	Geometric Mean (95% conf. interval)	NC	NC	.138 (.131-.145)	0.295 (0.280-0.311)	NC
	95th percentile (95% conf. interval)	.190 (.180-.210)	.220 (.190-.250)	.360 (.320-.440)	1.44 (1.22-1.67)	NC
Urine (µg\L)	Geometric Mean (95% conf. interval)	NC	NC	.064 (.057-.071)	.179 (.162-.197)	.275 (.242-.314)
	95th percentile (95% conf. interval)	NC	.148 (.110-.181)	.206 (.185-.292)	.919 (.838-1.00)	1.48 (1.28-1.70)
Urine (µg\g creatinine)	Geometric Mean (95% conf. interval)	NC	NC	.057 (.530-.062)	.189 (.175-.205)	.274 (.247-.305)
	95th percentile (95% conf. interval)	NC	.156 (.119-.260)	.177 (.124-.264)	.807 (.730-.935)	1.29 (1.11-1.57)

Average background levels in representative sample of the US population, 2017-2018

NC= Not calculated: proportion of results below limit of detection was too high to provide a valid result

*Special Sample of tobacco smoke exposure for certain chemical groups starting with NHANES 2011-2016

Louisiana Cadmium Poisoning Reporting Requirements

The State of Louisiana mandates that all cases of cadmium poisoning and all laboratory cadmium test results (regardless of the cadmium result) be reported to the Louisiana Office of Public Health. Cadmium poisoning cases are defined as, "any medical condition/visit resulting from exposure as determined from the exposure history or patient statement and/or acute, subacute, or chronic illness or injury resulting from inhalation, ingestion, dermal exposure or ocular contact."

Cases of cadmium poisoning must be reported to the Office of Public Health's Section of Environmental Epidemiology and Toxicology using one of the following methods: fax (504)568-8149
telephone 888-293-7020 (business hours) Reporting Form

SOURCES OF INFORMATION

The **Agency for Toxic Substances and Disease Registry** is a federal public health agency focused on providing trusted health information to prevent harmful exposures and diseases related to toxic substances. Succinct fact sheets, detailed documents, educational resources, and chemical interaction profiles can be found on their website. Much of this information is available in English and Spanish.

The **Electronic Library of Construction Occupational Safety and Health** (eLCOSH), developed and maintained by The Center for Construction Research and Prevention, provides accurate, user-friendly information about the safety and health of construction workers including a detailed guide for physicians and other health care providers entitled "What Physicians Need to Know About Occupational Cadmium Exposure" and a document directed at employees "Important Information for Workers Exposed to Cadmium: Your Cadmium Level"

The US **Environmental Protection Agency** provides the general public and professionals with information about cadmium hazards in drinking water and their prevention. Information is available in English and Spanish.

The **National Institute for Occupational Safety and Health** (NIOSH) is a federal agency established to help assure safe and healthful working conditions by providing research, information, education, and training in the field of occupational safety and health. Information about occupational cadmium exposure and prevention can be found on their website.

The US **Department of Labor's Occupational Safety & Health Administration** (OSHA) develops and enforces regulations for toxic substances in the workplace. Occupational standards and medical monitoring standards for occupational cadmium exposure can be found on their website. OSHA also provides access to the Windows-based system OSHA Cadmium Biological Monitoring Advisor directed at assisting the general public with applying the biological monitoring provisions of the OSHA Cadmium Standard. For each employee, the cadmium advisor analyzes the biological-monitoring results and prepares and saves a letter to the employee, a memorandum for the employer, and notes for the physician's records.

REFERENCES

ACGIH and OSHA. 2012. *Biological Exposure Guidelines (ACGIH BEI and OSHA Expanded Standards Only)*. American Conference of Governmental Industrial Hygienists and Occupational Safety and Health Administration. ISBN 1-882417-49-6. Cincinnati (OH). Available at <https://www.osha.gov/dts/osta/otm/otm_ii/pdfs/otmii_chpt2_appb.pdf> [accessed 8/23/2017]

ATSDR. 2015. *Agency for Toxic Substances and Disease Registry (ATSDR).2012*. Toxicological profile for Cadmium. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry. Atlanta (GA). Available at <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=48&tid=15> [accessed 8/23/2017]

CDC. 2015. *Fourth National Report on Human Exposure to Environmental Chemicals Update*. Centers for Disease Control and Prevention. Atlanta (GA). Available at <http://www.cdc.gov/biomonitoring/pdf/FourthReport_UpdatedTables_Feb2015.pdf> [accessed 8/25/2017]

CDC, 2016. *National Biomonitoring Program: Cadmium Biomonitoring Summary*. Centers for Disease Control and Prevention. Atlanta (GA). Available at <https://www.cdc.gov/biomonitoring/Cadmium_BiomonitoringSummary.html> [accessed 8/28/2017]

EPA. 2016.*Health Effects Notebook for Hazardous Air Pollutants: Cadmium Compounds*. US Environmental Protection Agency. Available at <https://www.epa.gov/sites/production/files/2016-09/documents/cadmium-compounds.pdf > [accessed 8/25/2017]

OSHA. 2017. *Cadmium: OSHA Standards*. US Department of Labor, Occupational Safety and Health Administration. Available at <https://www.osha.gov/SLTC/cadmium/index.html>. [accessed 8/25/2017]

McKelvey et al. 2007. A Biomonitoring Study of Lead, Cadmium, and Mercury in Blood of NYC Adults. Env Health Perspectives 115(10); 1435-1441. Available at <https://www.ncbi.nlm.nih.gov/pubmed/> [accessed 8/25/2017]

NIOSH. 2017. *Reproductive Health and the Workplace: Take-Home Exposures.* National Institute for Occupational Safety and Health. Centers for Disease Control and Prevention. Department of Health and Human Services. Atlanta (GA). Available at <http://www.cdc.gov/niosh/topics/repro/takehome.html> [accessed 8/25/2017]