Biological Exposure Index (BEI) review

LEAD
(CAS NO: 7439-92-1)

September 2021

Te Kāwanatanga o Aotearoa
New Zealand Government

WORKSAFE
Mahi Haumaru Aotearoa

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Summary

Biological Exposure Index for lead (CAS: 7439-92-1):

	CURRENT	PROPOSED
BEI	20**µg/dL** (0.97**µmol/L**)	–
Suspension (removal) level[a]	10µg/dL (0.48µmol/L)	
Suspension (removal) level[b]	30µg/dL (1.45µmol/L)	–
Biological Agent Reference Value[a]	–	29µg/L (2.9µg/dL; 0.14µmol/L)
BEI[b]	–	100µg/L (10µg/dL; 0.48µmol/L)
Notations		***oto***

Note: All values are for lead (**Pb**) in whole blood

TABLE 1: Current and proposed Biological Exposure Index (BEI) for lead

Recommendation and basis for BEI

It is proposed that WorkSafe:

1. adopt a Biological Agent Reference Value (**BRV**) for lead in whole blood of females of reproductive capacity of 29µg/L (0.14µmol/L) as an indicator that workplace exposure may exist and should be investigated as ideally pregnant women, breastfeeding women, or women planning to become pregnant should have no exposure to lead at all
2. adopt a BEI for lead in whole blood of all other workers of 100µg/L (10µg/dL; 0.48µmol/L)
3. remove suspension level for females of reproductive capacity, and those pregnant or breastfeeding
4. remove suspension level for all other workers
5. suspension (removal) of workers should be determined by a suitably qualified medical practitioner and should consider the BEI and BRV as factors in determining risk.
6. adopt an ***oto*** notation for lead.

Discussion

Lead is widely used due to its properties of high resistance to corrosion; softness and low melting point; high density; relatively low energy conductivity; sound and vibration absorber; and, radiation shield. Inorganic lead compounds are also widely used in industry. Lead smelting, refining and recycling industries; battery manufacturing; steel welding or cutting; construction; painting and printing; firing ranges; vehicle radiator-repair and other uses of lead solder are all workplaces associated with potential for high lead exposures (**ACGIH®**, 2017).

Terms that are **bold** (first occurrence only) are further defined in the Glossary.

a. For females of reproductive capacity, and those pregnant and/or breastfeeding.

b. For all other workers.

Cancer risks

The International Agency for Research on Cancer (**IARC**) evaluation of inorganic and organic lead compounds concluded that:

> There is *limited evidence* in humans for the carcinogenicity of inorganic lead compounds.
>
> There is *sufficient evidence* in experimental animals for the carcinogenicity of inorganic lead compounds.
>
> There is *sufficient evidence* in experimental animals for the carcinogenicity of lead acetate, lead subacetate, lead chromate, and lead phosphate.
>
> There is *inadequate evidence* in experimental animals for the carcinogenicity of lead oxide and lead arsenate.

With an overall evaluation that:

> Inorganic lead compounds are *probably carcinogenic to humans* (**Group 2A**). (IARC, 2006).

The US National Toxicology Program (**NTP**) Report on Carcinogens (**RoC**), Fourteenth Edition concluded that:

> Lead and lead compounds are *reasonably anticipated to be human carcinogens* based on limited evidence of carcinogenicity from studies in humans and sufficient evidence of carcinogenicity from studies in experimental animals. (NTP RoC, 2016).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of elemental lead and its inorganic compounds in the workplace environment noted that the critical effects were cardiovascular, neurological, renal and reproductive effects (ACGIH®, 2017). The ACGIH recommended a BEI of 200µg/L whole blood and note that in applying this BEI, female workers of child-bearing age should be counselled on the risk of delivering a child with a blood lead exceeding the **CDC** reference value of 50µg/L (5µg/dL; 0.24µmol/L) (ACGIH 2017).

The ACGIH® noted that the toxicity of lead had been well studied with a number of extensive summaries (ACGIH®, 2017):

> "Lead affects a number of systems in the body and is associated with a variety of health impairments. The BEI has been set at a level to prevent or minimize effects that are believed to result in persistent functional impairment of the worker or the worker's offspring. Certain effects may be seen at **PbB** below the BEI. These effects are not believed to be significant impairment either because the effect is reversible or transient and it is not likely to result in permanent impairment or because the body's reserve capacity sustains normal function despite a slight enzyme deficit." (ACGIH®, 2017).

The ACGIH® noted for adults/workers: cognitive function decrements at PbB of 370 to 520µg/L (Seeber et al., 2002 cited in ACGIH®, 2017); reversible neurological effects at PbB of 107 to 175µg/L (Murata et al., 2002 cited in ACGIH®, 2017); neurobehavioral and peripheral nervous system effects at PbB threshold of about 180µg/L (Schwartz et al., 2001, 2005 cited in ACGIH®, 2017); postural sway PbB threshold of 121 to 173µg/L (Iwata et al., 2005 cited in ACGIH®, 2017);

peripheral nerve conduction reduction at PbB > 300µg/L (Schwartz et al., 1988 cited in ACGIH®, 2017); increased risk of circulatory and cardiovascular mortality at PbB of 200 to 290µg/L (Lustberg and Silbergeld, 2002 cited in ACGIH®, 2017); increased risk of kidney disfunction (ACGIH®, 2017); reduced sperm counts and increase abnormal sperm at PbB > 400µg/L (Assennato et al., 1986 cited in ACGIH®, 2017); and, reduced fertility at PbB > 250µg/L (Bellinger, 2005 cited in ACGIH®, 2017).

The ACGIH® also noted that from the second trimester to 2 years of age the individual appears to be more sensitive to the neurotoxicity of lead (ACGIH®, 2017). The US CDC has concluded that there is no apparent threshold for the adverse effects of lead to children, and that follow-up should occur at maternal PbB ≥ 50µg/L (CDC, 2010 cited in ACGIH®, 2017). The ACGIH® recommended that women of child-bearing age, who are potentially exposed to lead in the workplace, be counselled about the risk of delivering a child with a PbB over the current US CDC reference value (PbB ≥ 50µg/L), the importance of closely monitoring the child's PbB, and the need to minimize the child's post-natal exposure to lead (ACGIH®, 2017).

With regards to the utility of blood lead as an exposure biomarker, ACGIH® noted that it has limitations:

> "Only about 1% of an individual's total body Pb burden resides in blood. Furthermore, blood consists of several compartments. More than 90% of Pb in whole blood is bound to red cell proteins such as **ALAD**, with the balance in plasma."
>
> "Another limitation of blood Pb as an exposure biomarker is that the kinetics of Pb in blood is relatively fast compared to the kinetics of Pb in bone, and therefore, of the whole body burden. Thus, a high blood Pb concentration measured at any given time does not necessarily indicate a high body Pb burden. Similarly, individuals who have the same blood Pb level will not necessarily have similar body burdens of exposure histories. The rate at which blood Pb changes with time and age depends on exposure history due to the changing equilibrium of Pb stored in the various body pools (**U.S. EPA**, 2013)." (reference cited in ACGIH®, 2017).

The ACGIH® **BEI®** review concluded that:

> "The BEI Committee recommends that lead (Pb) exposure be assessed by determining the concentration of lead in blood. A BEI of 200µg/L in a blood sample obtained at any time during the work shift or work week is recommended. Sample time is not critical to the results. Care must be taken to ensure that the blood sample is not contaminated with lead from the workplace or laboratory equipment or supplies. The BEI is intended to reduce the risk of neurological and neurobehavioral effects and reproductive effects associated with lead exposure ... Because Pb crosses the placenta and is present in breast milk, it is possible that a pregnant or nursing worker may transfer Pb to their fetus or child. Children of workers potentially exposed to lead should be closely monitored according to the CDC Guideline (CDC, 2010). This BEI applies only to exposures to inorganic compounds of lead. This BEI cannot be applied to exposure to tetraethyl lead or other organic lead compounds." (reference cited in ACGIH®, 2017).

The ACGIH® recommended that action should be taken to control exposure to lead at the first signs of an increase in PbB in workers, especially among individuals with many years of exposure, due to the long clearance mechanism for lead (ACGIH®, 2017).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of lead and its compounds (except for lead arsenate, lead chromate and alkyl lead compounds) recommended a Biologische-Arbeitsstoff-Referenzwerte (Biological Reference Value, **BAR**) of 70µg/L blood for women. The BAR was based on a 95th percentile PbB for women (18–69 years) from a 1998 survey of the existing background exposure to lead in the general population of Germany (DFG **BAT**, 2013).

The DFG noted that the previous Biologische Leit-Werte (Biological Guidance Value, **BLW**) for women of less than 45 years of age at 100µg/L blood could not exclude the possibility of impairment of foetal development at PbB of 100 to 150µg/L (DFG BAT, 2013).

The DFG re-evaluation of lead and its compounds (except for lead arsenate, lead chromate and alkyl lead compounds) recommended a BLW for men at 400µg/L blood, based on research that decreased performance in neurobehavioural test can generally be reproduced at PbB ≥ 400µg/L (DFG BAT, 2005).

SCOEL

The Scientific Committee on Occupational Exposure Limits (SCOEL) evaluation of lead and its inorganic compounds noted that the critical effects were impaired performance in neurobehavioural tests (SCOEL, 2002).

The SCOEL recommended a biological limit value (**BLV**) for PbB of 300µg/L, with a long-term PbB of 400µg/L considered a **LOAEL** for neurobehavioural effects in adults. The SCOEL noted that the recommended BLV was not necessarily protective of the offspring from exposed female workers as no threshold for potential **CNS** effects in new-born and infants had been identified. The exposure of fertile women to lead should therefore be minimised, the review noted (SCOEL, 2002).

The SCOEL recommended an **OEL**, 8-hour **TWA**, of 100µg/m^3 which was consistent with the BLV. It was noted that the setting of an OEL for airborne lead was problematical as only part of the occupational exposure occurs by inhalation and a considerable portion is due to ingestion. The extent of lead ingestion was a function of personal hygiene and the overall cleanliness of the work environment (SCOEL, 2002).

Safe Work Australia

The Safe Work Australia health monitoring guidance for inorganic lead noted:

> "The adverse health effects of lead have been well documented over the years in both occupational and non-occupational studies ...
>
> "Research in non-occupational settings has indicated:
>
> - increased risk of spontaneous abortion and potential for post-natal developmental delay at maternal blood lead levels ≥ 5µg/dL (50µg/L)
> - hypertension and kidney dysfunction at blood lead levels ≥ 5µg/dL (50µg/L)
> - reduced birth weight and potential for subclinical neurocognitive deficits at maternal blood lead levels ≥ 10µg/dL (100µg/L)
> - increased non-specific symptoms at blood lead levels ≥ 30µg/dL (300µg/L)
> - neurocognitive effects, sperm abnormalities nephropathy, anaemia, colic, gout at blood lead levels ≥ 40µg/dL (400µg/L), and
> - encephalopathy and peripheral neuropathy at blood lead levels ≥ 80µg/dL (800µg/L).

> "Medical conditions that may be exacerbated with continued exposure to lead include chronic renal dysfunction, hypertension, neurological disorders, and cognitive dysfunction.
>
> "Non-specific symptoms may include headache, fatigue, sleep disturbance, anorexia, constipation, arthralgia, myalgia, and decreased libido." (Safe Work Australia, 2020)."

Safe Work Australia defines "lead risk work" as any "lead process" that is likely to cause PbB in the involved worker to exceed:

- 5µg/dL (50µg/L; 0.24µmol/L) for females of reproductive capacity, and
- 20µg/dL (200µg/L; 0.97µmol/L) for all other workers. (Safe Work Australia, 2020).

A worker must be immediately removed from carrying out lead risk work if biological monitoring of the worker shows that the worker's blood lead level is:

- greater than or equal to 30µg/dL (300µg/L; 1.44µmol/L) for females not of reproductive capacity and males, and
- greater than or equal to 10µg/dL (100µg/L; 0.48µmol/L) for females of reproductive capacity. (Safe Work Australia, 2020).

Safe Work Australia noted that the workplace exposure standard for dusts and fumes of inorganic lead was an 8-hour TWA of 0.05mg/m^3, which was estimated to result in an average PbB of approximately 23µg/dL (230µg/L) with an upper bound of 46µg/dL (460µg/L) if inhalation was the primary route of exposure (Safe Work Australia, 2020).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current BEI of 200µg/L (20µg/dL) for lead in whole blood, to be inadequate to manage health risks to the whole workforce from possible workplace exposure.

It is recommended for lead and inorganic lead compounds, measured as Pb, that a Biological Agent Reference Value (BRV) of 29µg/L (0.14µmol/L) in whole blood is adopted for females of reproductive capacity as an indicator that workplace exposure may exist and should be investigated, as ideally pregnant women, breastfeeding women, or women planning to become pregnant should have no exposure to lead at all. The BRV is derived from population data and includes people not exposed to lead at work. The BRV is the 95th percentile in women aged 18–69 as extracted from the New Zealand Biological Monitoring Program, 2014–2016 ('t Mannetje et al., 2018). Blood lead values exceeding the BRV is an indicator that occupational exposure may not be controlled and should be investigated as there is no recognised threshold for neurotoxicity for new-borns and infants. It is important for a suitably qualified medical practitioner to evaluate trends (where possible) in blood lead levels as part of the investigation of the source of the elevated blood lead level(s) and determine if suspension from work where lead exposure might occur, is warranted. Workers in these cases should be counselled by a suitably qualified medical practitioner as to the associated health risks.

A BEI of 100µg/L (10µg/dL; 0.48µmol/L) in whole blood is adopted for all other workers to protect against neurotoxicity and neurobehavioural effects, based on information from ACGIH® and DFG.

Lead is a known ototoxin (OSHA, 2018; EU-OSHA, 2009).

The WorkSafe New Zealand 8-hour TWA for Lead (inorganic dusts and fumes) of 0.05mg/m^3 for exposure via the inhalation route does not take into account exposure via ingestion.

Studies evaluating the relationship between airborne lead and blood lead concentration indicate that a both inhalation and ingestion are important routes of entry and the relying solely on airborne concentration to evaluate risk may severely underestimate actual exposure (ACGIH, 2017; SCOEL, 2002). Biological monitoring is recommended for workers potentially exposed to lead and investigation of elevated blood lead concentrations should include ingestion as a possible major contributing route of exposure.

Appendices

IN THIS SECTION:

Appendix 1: Additional information

Appendix 2 Glossary

Appendix 3: References

Appendix 1: Additional information

Glossary	Definition of terms used in this document (Appendix 2)
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/5352425#section=Chemical-and-Physical-Properties
CAS Number	7439-92-1 [Elemental lead, Pb]
Conversion factors	1µg/L = 4.8 **nmol/L** 1µg/L = 0.1µg/dL
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/7D9276E8-66C9-4AD6-842A-AA8D8285383D Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

PubChem 2021; **EPA**, 2021

Appendix 2: Glossary

TERM	MEANING
ACGIH®	The American Conference of Governmental Industrial Hygienists (ACGIH®) is a member-based organisation, established in 1938, that advances occupational and environmental health. Examples of this include their annual edition of the **TLVs®** and BEIs® book and work practice guides. Store at: https://portal.acgih.org/s/store#
ALAD	The enzyme δ-aminolevulinate dehydratase; also known as porphobilinogen synthase (PBGS).
BAR	Biological Reference Value – a DFG term.
BAT	Biologische Arbeitsstoff-Toleranzwerte [Biological Tolerance Value], a DFG term.
BEI®	Biological Exposure Indices – ACGIH® term. Please see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®
BEI	Biological Exposure Index.
Biological Agent Reference Value	See BRV, below.
BLV	Biological Limit Value.
BLW	Biologische Leit-Werte are derived for carcinogenic substances and for substances without sufficient data to establish a BAT, a DFG term.
BRV	Biological Agent Reference Value – a WorkSafe term. Represents the 95th percentile or upper reference level of a biological agent expected in the general population (non-workplace exposures). The BRV is intended to indicate when occupational exposure may not be controlled and should be investigated.
CDC	Centers for Disease Control and Prevention. The U.S. health protection agency.
CNS	Central nervous system.
DFG	Deutsche Forschungsgemeinschaft (German Research Foundation), the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Federal Republic of Germany. The science-based **MAK** values are recommended to the German Minister of Labour and Social Affairs for possible adoption under the German Hazardous Substances Ordinance.
EPA	The New Zealand Environmental Protection Authority.
Group 2A	IARC designation: The agent is probably carcinogenic to humans. There is strong evidence that it can cause cancer in humans, but at present it is not conclusive.
HSNO	Hazardous Substances and New Organisms Act 1996, New Zealand.
IARC	The International Agency for Research on Cancer – an agency of the World Health Organisation.
LOAEL	Lowest Observed Adverse Effect Level.
µg/dL	Microgram or one millionth of a gram per decilitre [1/10th of a litre].
µg/L	Microgram or one millionth of a gram per litre.
µmol/L	Micromole of substance per litre of the matrix.
nmol/L	Nanomoles of substance per litre of the matrix.
NTP	National Toxicology Program, US Department of Health and Human Services.
MAK	Maximale Arbeitsplatz-Konzentration, (maximum workplace concentration) is defined as the maximum concentration of a chemical substance (as gas, vapour or particulate matter) in the workplace air which generally does not have known adverse effects on the health of the employee nor cause unreasonable annoyance (e. g. by a nauseous odour) even when the person is repeatedly exposed during long periods, usually for 8 hours daily but assuming on average a 40-hour working week. A value set by the DFG.

TERM	MEANING
OEL	Occupational Exposure Limit (equivalent to a **WES**).
oto	Ototoxic. The substance may alone, or in concert with noise, result in hearing loss.
Pb	Lead.
PbB	Blood lead concentration.
RoC/ROC	Report on carcinogens.
SCOEL	The Scientific Committee on Occupational Exposure Limits is a committee of the European Commission, established in 1995 to advise on occupational health limits for chemicals in the workplace within the framework of Directive 98/24/EC, the chemical agents directive, and Directive 90/394/EEC, the carcinogens at work directive.
TLV®	Threshold Limit Value [see TLV-C, TLV-STEL and TLV-TWA below]. An ACGIH® term. Please see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®
TWA	Time-weighted average exposure.
WES	Workplace Exposure Standard – WESs are values that refer to the airborne concentration of substances, at which it is believed that nearly all workers can be repeatedly exposed to, day after day, without coming to harm. The values are normally calculated on work schedules of five shifts of eight hours duration over a 40-hour week. A WorkSafe term.

Appendix 3: References

American Conference of Governmental Industrial Hygienists (ACGIH®). (2017). *Lead and Inorganic Compounds BEI®*. Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission.

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Notes

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