LEAD

Heavy metal

Contamination source

Lead (Pb) (CAS # 7439-92-1) is a soft, heavy and non-essential metal (atomic weight 207.2), shiny silver in appearance, but quickly becomes covered with a dull gray-blue layer of insoluble lead carbonate on contact with air or water. Lead is found in low concentrations in the Earth's crust, predominantly as lead sulfide (*galena*) (IARC, 2006).

Lead is an environmental contaminant that occurs naturally and mainly comes from anthropogenic activities such as mining, smelting and battery manufacturing. The historical use of lead in herbicides, gasoline, pipes, welds and paints, has contributed to the contamination of the environment (Carlisle et al., 2009). Lead is a metal found in both organic and inorganic form, the latter being the predominant form in the environment (EFSA, 2010).

Human exposure to lead can come from food, water, air, soil and dust. According to EFSA (2010), food is the major source of lead exposure, but it should be noted that for children, ingestion of soil particles and dust may represent an important source of lead exposure. Among children 1 to 3 years, it has been suggested that the activity "hand to mouth" account for 50% or more of the total intake of lead (Davies et al. 1990; source LDAI, 2008).

Lead contamination of food arises mainly from the environment or from food processing, food handling and food packaging. Atmospheric lead can contaminate food through deposition on agricultural crops. Water is another source of lead contamination of food (WHO, 2011).

Analytical method

The analytical methods for the determination of lead in foods are well established. Performance characteristics for analytical determination of lead are set in Regulation (EC) N° 333/2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo[a]pyrene in different foodstuffs.

The sample preparation procedure used most frequently for the determination of lead in food is acid digestion in the presence of strong oxidants in open or closed vessels. Microwave-assisted acid digestion has been extensively employed, which allows the use of large sample masses (1–2 g) under controlled temperature and pressure of the system, reducing contamination and avoiding losses of the element during mineralization (WHO, 2011).

The main techniques for the analysis of lead in food are atomic absorption spectrometry (AAS), atomic emission spectrometry (AES) and mass spectrometry (MS). For the analysis of high concentrations, X-ray fluorescence spectroscopy (XRFS) is also applicable (EFSA, 2010).
Flame AAS (FAAS) and graphite furnace AAS (GFAAS) are two techniques used for measurement of trace elements in food (EFSA, 2010).
Inductively coupled plasma atomic emission spectrometry (ICP-AES) and inductively coupled plasma mass spectrometry (ICP-MS), are techniques that allow analysis of several elements (up to 75 items) (EFSA, 2010).

Toxicity

The absorption of (soluble) lead compounds ingested appears to be higher in children than in adults. Lead accumulates in soft tissues, and over time in bone. The half-life of inorganic lead in the blood and bones are approximately 30 days and 10-30 years, respectively. Excretion occurs mainly through urine and faeces (EFSA, 2010).

Due to a high half-life in the body, chronic toxicity of lead is more worrying when one considers that the potential risk to human health (EFSA, 2010).

Lead exposure is associated with a wide series of effects, including many neurodevelopmental outcomes, mortality (mainly due to cardiovascular disease), decreased renal function, hypertension, impaired fertility and adverse consequences on pregnancies (WHO, 2011).

In humans, the central nervous system is the main target organ for lead toxicity.

In adults, the neurotoxicity associated with lead affects the central information processing, especially for organizing visuo-spatial and verbal memory in the short term, because of psychiatric symptoms and decreased manual dexterity. There is a considerable amount of evidence showing that the developing brain is more vulnerable to the neurotoxicity of lead than the mature brain. In children, an elevated blood lead level was inversely associated with scores of intelligence quotient (IQ) and reduced cognitive function reduced until the age of 7 years. There is some evidence that this later led to a volume of gray matter reduced adult, especially the prefrontal cortex (EFSA, 2010).

A number of studies in adults have found an association between blood lead, elevated systolic blood pressure and chronic kidney disease at relatively low blood lead (EFSA, 2010).

Genotoxicity, carcinogenicity

Inorganic lead derivatives are classified as probable human carcinogen (in group 2A) by IARC (2006) based on animal data (renal tumors) and limited data in humans. Lead has a low mutagenic activity but promote the genotoxicity of radiation and chemical agents ("co-carcinogenic effect") (Lauwerijs, 2007).
In humans, an increased risk of lung cancer, gastric or bladder cancer has been suggested (Fu and Boffetta, 1995; Steenland and Boffetta, 2000). Even if they are partially metabolized to inorganic lead, organic lead compounds are not classifiable as carcinogenic to humans (Group 3).

Establishment of Health Based Reference Values

The CONTAM Panel identified the following potential adverse effects of lead, the developmental neurotoxicity in young children, cardiovascular effects and nephrotoxicity in adults as the basis for the risk assessment (EFSA, 2010). The BMDL approach has been used by EFSA to characterize the dose-response relationship. The BMDL dietary intake values derived from lead concentration in blood from epidemiologic study were 1.50 µg/kg bw/day for cardiovascular effects, 0.63 µg/kg bw/day for renal effects and 0.50 µg/kg bw/day for developmental neurotoxicity.
JECFA has characterized the dose-response for the neurodevelopmental effects and cardiovascular effects. The dose–response modelling for blood lead levels and children's IQ is based on estimates in the Lanphear et al. (2005). Dietary exposures associated with a range of decreases in IQ (i.e. 0.5–3 IQ points) were calculated by combining the dose–response models with the toxicokinetic data, using a Monte Carlo simulation (WHO, 2011). For adults, increased systolic blood pressure was selected as the most sensitive end-point. A linear slope relating increases in systolic blood pressure as a function of blood lead level was derived by averaging the estimates from four different studies. Blood lead levels were converted to dietary exposures using the range of values previously used by the Committee for adults. Dietary exposure corresponding to an increase in systolic blood pressure of 1 mmHg (0.01333 kPa) was estimated to be 80 (5th–95th percentiles 34–1700) µg/day, or about 1.3 (5th–95th percentiles 0.6–28) µg/kg bw/day (WHO, 2011).

Occurrence in food

Food categories with the highest frequency of detectable lead include meat, especially offal, organ meats and wild game, shellfish (particularly bivalves), cocoa, tea, cereal grains and products, and vegetables (WHO, 2011).

Dietary exposure assessment

The median (P50) dietary lead exposure of the Belgian adult population was estimated by the probabilistic approach (middle bound scenario) to 0.13 µg/kg bw/day and the exposure at the 95th percentile was estimated at 0.36 µg/kg bw/day (Sci Com, 2009).
The median (P50) and the 95th percentile lead dietary exposure of the children was estimated by the probabilistic approach to 0.42 and 1.07 µg/kg bw/day, respectively (Sci Com, 2009).
Dietary lead intake of the Belgian population estimated by SCOOP in 2004 was 4.4 µg/kg bw/week.

Mean and the 95th percentile lead dietary exposure estimated recently by EFSA (2012) for different age group in the European Union are presented in table 1. Middle bound mean lead dietary exposure estimated recently by EFSA (2012) for the Belgian population are 1.54 µg/kg bw/day for toddlers in Flanders, 1.27 µg/kg bw/day for other children in Flanders, 0.54 µg/kg bw/day for adolescent, 0.51 µg/kg bw/day for adults, 0.48 µg/kg bw/day for elderly and 0.46 µg/kg bw/day for very elderly.

Table 1: Lower (LB), middle (MB) and upper (UB) bound mean and 95th percentile (P95) lead dietary exposure in µg/kg bw per day for each age groups and as a mean and 95th percentile average lifetime exposure calculated by weighting the contribution of each age group according to the number of years covered (different range of countries covered in the respective age group). (Source EFSA, 2012)

Age group	Mean			P95		
	LB	MB	UB	LB	MB	UB
Infants	0.73	0.91	1.09	1.39	1.80	2.22
Toddlers	1.10	1.32	1.54	1.95	2.28	2.56
Other children	0.87	1.03	1.18	1.46	1.68	1.92
Adolescents	0.46	0.55	0.63	0.84	0.97	1.11
Adults	0.43	0.50	0.57	0.74	0.85	0.97
Elderly	0.42	0.48	0.55	0.72	0.82	0.92
Very elderly	0.40	0.47	0.53	0.71	0.79	0.89

For the total/adult population, mean exposures reported by JECFA ranged from 0.02 to 3 µg/kg bw/day (WHO, 2011). The estimated high exposures reported by JECFA ranged from 0.06 to 2.43 µg/kg bw/day (WHO, 2011). Children's mean exposures reported by JECFA ranged from 0.03 to 9 µg/kg bw/day (WHO, 2011). The estimated exposures for children who were defined by the country as consumers with high exposure ranged from 0.2 to 8.2 µg/kg bw/day (WHO, 2011).

The food categories that the most contribute to lead exposure of the Belgian adult population are beverages, cereals products, vegetables and potatoes (Sci Com, 2009).

The highest contributors as averaged across all age groups for the middle bound results reported by EFSA (2012) were "grains and grain-based products" at 16.3% followed by "milk and dairy products" at 10.6%, "non-alcoholic beverages" at 10.3 %, "vegetables and vegetable products" at 8.4%, "drinking water" at 7.0% and "alcoholic beverages" at 6.7 %. However, the exposure profile will vary with age group and location reflecting differences in eating patterns across Europe.

Risk characterization

The MOE approach was used to characterize the risks of the Belgian population to lead. BMDL values determined by EFSA for the critical effects systolic blood pressure, chronic kidney disease and scores of intelligence quotient (IQ) were divided by the values of dietary exposure estimates for the Belgian population (Adult, Children, baby) (Table 2). Dietary exposures to lead are lower than the BMDL intake value for effects on systolic blood pressure (1.50 µg/kg bw/day) and for effects on the prevalence of chronic kidney disease (0.63 µg/kg bw/day). MOEs range from 1.8 to 11,5.
Estimated exposure at P95 in children exceeds the $BMDL_{01}$ intake level of 0.50 µg/kg bw/day for neurodevelopmental effects. Therefore, the possibility of effects in some children cannot be excluded.

Table 2: Estimated MOE for the Belgian population (adult, children, baby) on basis of dietary lead exposure determined by the Scientific Committee (Sci Com, 2009).

Population	Toxicological effect	MOE	
		Mean dieatary exposure	95eme percentile dieatary exposure
Adults	Cardiovascular effect ($BMDL_{01}$ = 1.50 µg/kg bw/day)	11.5	4.2
	Nephrotocixity ($BMDL_{10}$ = 0.63 µg/kg bw/day)	4.8	1.8
Chlidren from 2,5 to 6,5 years	Neurodevelopmental effect ($BMDL_{01}$ = 50 µg/kg bw/day)	1.2	0.5
Baby's 3 month	Neurodevelopmental effect ($BMDL_{01}$ = 50 µg/kg bw/day)	1.2	

Risk characterization by the CONTAM panel (EFSA, 2010)

Dietary exposures to lead based on lower bound and upper bound assumptions for average adult consumers in Europe are lower than the BMDL intake value for effects on systolic blood pressure ($BMDL_{01}$ = 1.50 µg/kg bw/day), but vary from above to below the BMDL intake value for effects on the prevalence of chronic kidney disease, ($BMDL_{10}$ = 0.63 µg/kg bw/day). The respective MOEs range from 1.2 to 4.2 and from 0.51 to 1.8, respectively. Hence, if exposure were closer to the upper bound estimates, the possibility of effects in some consumers cannot be excluded.

Estimated exposure in children up to age seven exceeds the $BMDL_{01}$ intake level of 0.50 µg/kg bw/day for neurodevelopmental effects. The MOE in average 1 to 3 year old child consumers ranged from 0.16 to 0.45, and was only slightly higher in 4 to 7 year old children. Therefore, the possibility of effects in some children cannot be excluded. It was not possible to estimate the potential numbers of children who might be affected, as even in average consumers the MOE was <1.

Breast-fed 3-month old infants are predicted to have a lead exposure that is below the $BMDL_{01}$ intake value of 0.50 µg/kg bw/day. Lead exposure based on lower bound assumptions in both average and high 3-month old infant consumers of infant formula is below the $BMDL_{01}$ intake value, but may exceed this level, based on upper bound estimates. Therefore, the possibility of an effect in some infants cannot be excluded.

Risk characterization by JECFA (WHO, 2011)

The Committee of JECFA reaffirmed that because of the neurodevelopmental effects, fetuses, infants and children are the subgroups that are most sensitive to lead.

The mean dietary exposure estimates for children aged about 1–4 years range from 0.03 to 9 µg/kg bw/day. The health impact at the lower end of this range is considered negligible by the Committee, because it is below the exposure level of 0.3 µg/kg bw/day calculated to be associated with a population decrease of 0.5 IQ point. The higher end of the exposure range is higher than the level of 1.9 µg/kg bw/day calculated to be associated with a population decrease of 3 IQ points, which is deemed by the Committee to be a concern. For adults, the mean dietary lead exposure estimates range from 0.02 to 3 µg/kg bw/day. The lower end of this range (0.02 µg/kg bw/day) is considerably below the exposure level of 1.2 µg/kg bw/day calculated by the Committee of JECFA to be associated with a population increase in systolic blood pressure of 1 mmHg (0.1333 kPa). The Committee considered that any health risk that would be expected to occur at this exposure level is negligible. At the higher end of the range (3 µg/kg bw/day), a population increase of approximately 2 mmHg (0.3 kPa) in systolic blood pressure would be expected to occur. An increase of this magnitude has been associated, in a large meta-analysis, with modest increases in the risks of ischaemic heart disease and cerebrovascular stroke. The Committee of JECFA considered this to be of some concern, but less than that for the neurodevelopmental effects observed in children. The Committee of JECFA stressed that these estimates are based on dietary exposure (mainly food) and that other sources of exposure to lead also need to be considered. The Committee of JECFA concluded that, in populations with prolonged dietary exposures to lead that are at the higher end of the ranges identified above, measures should be taken to identify major contributing sources and foods and, if appropriate, to identify methods of reducing dietary exposure that are commensurate with the level of risk reduction.

Legislation

Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs (Official Journal L364/5-24, 20-12-2006)

Royal Decree of 2 December 1991 setting maximum levels in food for some heavy metals

Recommandations

Recommendations of the scientific Committee in advice 07-2011 (Sci Com, 2011)

- The Scientific Committee recommended to extend the monitoring of lead in infant formula and follow-up formula and in baby foods for infants and young children.
- The Scientific Committee recommended to increase the analysis sensitivity for some matrices such as infant formula, beverages (juice), etc. The limits of detection and quantification are sufficient to control compliance with maximum levels but are not sufficient for a correct risks analysis.
- The Scientific Committee agreed that all measures should be taken to reduce lead exposure in order to limit the risk. In particular, information campaigns could be organized to raise

awareness of the non-food sources of exposure (dust, soil particles, old paintings, ...) and to better inform users of kitchen utensils and cosmetics craft (tajines, teapots and artisan kohl). The Scientific Committee recommended to control the migration of lead in kitchen craft (cf. joint opinion, and CSS Sci Com No. 06-2011 8726).
- The Scientific Committee also recommended to keep pressure on controlling lead in drinking water.
- The Scientific Committee recommended a specific study on the occurrence of trace elements in foods for infants and young children and on the estimated exposure of infants and young children to these trace elements. The study should include specific scenarios such as consumption of soy milk for infants allergic and food intake for babies and preparations of rice cereal by infants and young children .
- The Scientific Committee recommended the implementation of biomonitoring studies targeted on risk groups (eg infants, children, ethnic groups), coupled with investigations of sources of exposure to determine their respective share of the total exposure to lead. The Scientific Committee encourages the initiatives of the Authority to raise awareness of the risk factors for lead exposure linked to housing, occupational exposures and recreation. People must be informed of the importance of good hygiene such as hand washing to limit lead exposure via ingestion of soil particles and dust inhalation in smokers that contaminate their cigarettes (bioavailability inhalation).
- The Scientific Committee recommends that companies ensure water supply to maintain the lead concentrations in water as low as possible.

Recommendations of the scientific Committee in advice 36-2009 (Sci Com, 2009):
- The Scientific Committee recommends further identify food matrices analyzed in the database Foodnet and to ensure that the crossing with the consumption data is facilitated. For example, specify the type of bread (white bread, wholemeal bread, ...) as is the case in the consumer database (available on the internet http://www.iph.fgov.be/epidemio/epifr/foodfr / food04fr/fooda32fr.pdf). It is also recommended to differentiate into Foodnet fish, shellfish, and depending on the source (farmed or wild).
- The Scientific Committee recommends to analyze lead in offal (liver and kidney) of cattle and liver pastes and other food groups such as chocolate, coffee and biscuits.
- The Scientific Committee draws attention to the fact that existing methods for estimating exposure to contaminants are aware of some limitations, especially for the most at risk groups. Therefore, the Scientific Committee recommends that a standardized method was developed and validated.

Recommendations of the CONTAM panel of EFSA (EFSA, 2010):
- Further efforts should be made to increase the understanding of the lead dose-response relationship.
- At the same time, work should continue to reduce exposure to lead, from both dietary and non-dietary sources.
- When results are reported as below LOD, LOQ or as non-detected, the respective numerical values should be reported.
- An additional recommendation is that the EFSA food category database should be expanded and refined.

Recommendations of EFSA (EFSA, 2012):
- It is considered important to confirm the seemingly decreasing lead levels in food by future testing. A standardised data collection system now in place for reporting of European analytical test results of chemicals in food to EFSA will facilitate a more accurate future trend analysis. As part of this system it is required to always report the LOD and LOQ of the analytical methods used and to clearly indicate whether sample results were below the detection or below the quantification limit.
- It is suggested that the on-going work to collect harmonised occurrence and consumption data from across the European Union should continue with results pointing to the importance of using refined tools for calculating exposure.
- For a few food categories rather high limits of detection and quantification were reported. To increase precision and accuracy in calculating exposure, it would be important to lower such limits as much as possible. WHO recommends that the LOQ for lead analysis of food should

not exceed 10 µg/kg.

References

Carlisle J.C., Dowling K.C., Siegel D.M., Alexeeff G.V. 2009. A blood lead benchmark for assessing risks from childhood lead exposure. Journal of Environmental Science and Health, Part A 44, 1200–1208.

EFSA, Panel on Contaminants in the Food Chain (CONTAM) 2010. Scientific Opinion on Lead in Food. EFSA Journal 2010; 8(4):1570.[147pp.] doi :10.2903/j.efsa.2010.1570. Available online : www.efsa.europa.eu. http://www.efsa.europa.eu/fr/scdocs/doc/1570.pdf

EFSA (European Food Safety Authority). 2012. Lead dietary exposure in the European population. EFSA Journal 10(7):2831. [59 pp.] doi:10.2903/j.efsa.2012.2831. Available online: www.efsa.europa.eu/efsajournal

Fu H., Boffetta P. 1995. Cancer and occupational exposure to inorganic lead compounds: a meta-analysis of published data. Occup. Environ. Med., 52(2), 73-81.

IARC. 2006. Inorganic and Organic Lead Compounds - Summary of Data Reported and Evaluation . IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 87.

Lauwerys R., Haufroid V., Hoet P., Lison D. 2007. Toxicologie industrielle et intoxications professionnelles, 5e édition, Masson, Paris.

LDAI. 2008. Voluntary risk assessment report on lead and some inorganic lead compounds – human health section – final draft status 4 March 2008. Prepared by ILZRO and EBRC Consulting under contract of the LDAI Lead Risk Assessment Working Group. Beschikbaar via: http://echa.europa.eu/chem_data/transit_measures/vrar_en.asp.

SCI COM. 2009. Avis 36-2009 Estimation de l'exposition au plomb par la population belge (dossier Sci Com N°2009/14). http://www.favv-afsca.fgov.be/comitescientifique/avis/_documents/AVIS36-2009_FR_DOSSIER2009-14_000.pdf

SCOOP. 2004. Reports on tasks for scientific cooperation. Task 3.2.11. Assessment of the dietary exposure to arsenic, cadmium, lead and mercury of the population of the EU Member states. European Commission, Directorate-General Health and Consumer Protection, March 2004. Available: http://ec.europa.eu/food/food/chemicalsafety/contaminants/scoop_3-2-11_heavy_metals_report_en.pdf

Steenland K., Boffetta P. 2000. Lead and cancer in humans: where are we now? Am. J. Ind. Med., 38(3), 295-9.

WHO (World Health Organization). 2011. Evaluation of certain food additives and contaminants Seventy-third report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Technical report series 960. http://whqlibdoc.who.int/trs/WHO_TRS_960_eng.pdf