Substance report

June 2022

Lead

HBM4EU science and policy for a healthy future

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Authors and Acknowledgements

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Glossary

Abbreviations	
C&L	Classification and Labelling
CLP	The ‘Classification, Labelling, Packaging’ Regulation Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.
EC	European Commission
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EU	European Union
HBM	Human Biomonitoring
HBM4EU	European Human Biomonitoring Initiative
IARC	International Agency for Research on Cancer
OEL	Occupational Exposure Limits
REACH	The ‘Registration, Evaluation, Authorisation and Restriction of Chemicals’ Regulation Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals
WP	Work package

1 Key messages

- Blood lead concentrations showed a decreasing trend in the past decades due to regulations and recently levelled out at concentrations below the reference values set by different organizations.
- However, recent studies reported that lead exposure below the existing reference values is associated with adverse neurodevelopmental effects, and it is suggested that there is likely no safe threshold for lead neurotoxicity. Foetuses and children are the most vulnerable and sensitive group to the adverse effects of lead.
- Occupational exposure at certain workplaces (e.g. e-waste) and environmental exposures in some regions are still of concern.
- While there has been extensive research on lead as a substance, including its toxicology, recent human biomonitoring data is still relatively limited. This hinders interpreting population level exposure to lead across Europe and variations by geography and different key cohort populations.
- Monitoring of the exposure of the vulnerable populations, development of harmonised health-based guidance values and the validation of sensitive and reliable effect biomarkers are needed.

2 Introduction

HBM4EU is a project funded under Horizon 2020 and runs from 2017 until June 2022. It generates knowledge to inform about the safe management of chemicals, and hence protect human health in Europe. HBM4EU uses human biomonitoring (HBM) to monitor the actual human exposure to chemicals and resulting health impacts to build upon existing evidence bases and improve chemical risk assessment. HBM4EU compares data from across Europe which allows an understanding of regional differences and can help to identify vulnerable groups, in order to inform targeted measures to reduce exposure. The results of the HBM4EU project are aimed at supporting policy development, by providing a key evidence base in the understanding of exposure and impacts to toxic chemicals.

If you would like to read more about the project itself, please visit the HBM4EU website.

2.1 How to use this document

This document provides a summary of the known and suspected adverse human health effects of lead and describes the main exposure pathways for humans. It also indicates where HBM could be of value in the development of EU policy, along with the remaining challenges in determining human lead exposure. This substance report is intended to inform scientists, relevant stakeholders and policy makers on the value of HBM to establish the EU population's exposure to lead.

This substance report is based largely on the HBM4EU scoping document for lead, first draft produced in 2019 and updated regularly, as well as the accompanying reports on legislative mapping and policy questions. Where necessary, additional information has been used from the European Chemical Agency (ECHA) documents including the classification and labelling (C&L) Inventory, and legislative text for relevant EU policy areas, have also been used for this report.

2.2 Overview of lead

Lead, a silvery grey metal, has some unique properties, like soft softness, high malleability, low melting point, ductility and resistance to corrosion, which contributed to its widespread use. Lead

occurs naturally in the environment and, to a greater extent, from anthropogenic activities such as mining, smelting and battery manufacturing.

Lead exists in elemental, organic and inorganic forms which have different chemical and toxicological properties. The inorganic form of lead poses the greatest risk for human health and predominates as an environmental contaminant (ECHA, 2019).

Growing understanding of toxicity of lead resulted in the use of lead being phased out of petrol, paints, ceramic products, caulking, and pipe solder in the second half of the 20th century. However, lead is still extensively mined and used in the smelting industries, construction, plumbing, batteries, bullets and shot, weights, solders, pewters, fusible alloys, and radiation shielding (ECHA, 2019). In 2020, leaded petrol is used in only one country worldwide, Algeria (UNEP, 2020).

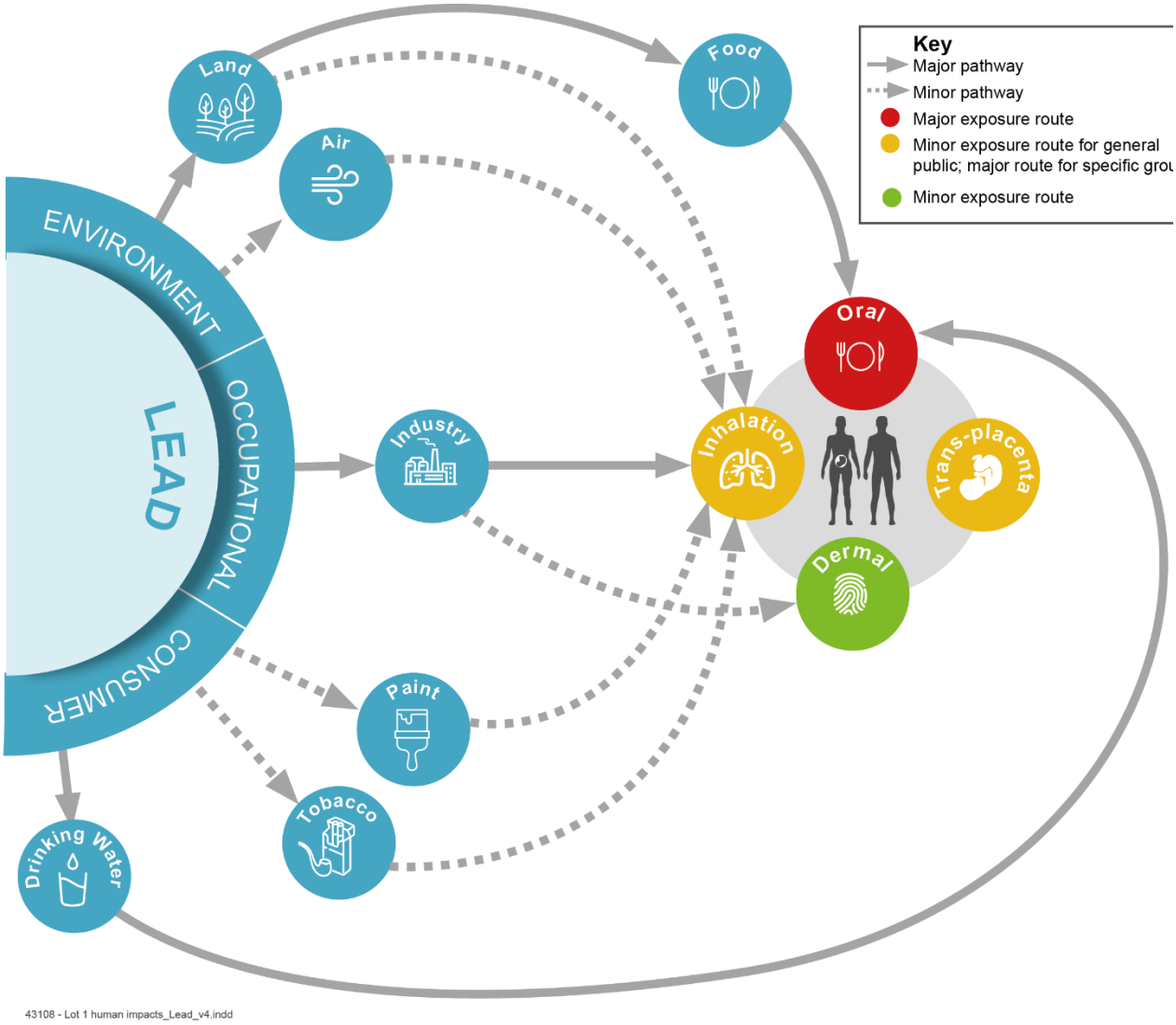
3 Human exposure to lead

Whereas the exposure to lead in Europe is expected to be decreasing due to various regulations which are presented in Section 5, the global consumption is increasing as the demand for storage batteries for electric vehicles is increasing (WHO 2010). Exposure levels vary geographically. People living in low-income regions where there are industrial uses of lead are more exposed. The most important source of exposure for the general population in Europe to lead is through the diet. The consumption of drinking water due to leaded water pipes in old houses might also increase the exposure levels. Additionally, the ingestion of contaminated soil and settled dust can be an important exposure source for children.

An overview of main sources of exposure (environmental, occupational, consumer) and exposure pathways (oral, inhalation, dermal) is provided in Figure 3.1 below.

Additional information on these sources and pathways is provided in Appendix 1.

Figure 3.1 Overview of exposure routes and pathways for lead



3.1 Environmental exposure

Before phasing out lead in petrol, inhalation of contaminated air was the main exposure route for the general public. The latest EMEP/CCC report[1] states that the lowest lead levels in the air in the EU in 2018 can be found in Scandinavia (< 1 ng/m^3) and the highest concentrations in Central Europe (5 ng/m^3).

Lead accumulates in the top layer of soils. The contamination varies geographically depending on nearby anthropogenic sources releasing lead and the accumulation of atmospheric lead particles. The WHO considers the EU median value of lead in soil as uncontaminated (WHO 2007).

[1] European Monitoring and Evaluation Programme/Chemical Coordinating Centre report on the assessment of transboundary pollution by toxic substances is available at http://en.msceast.org/reports/2_2020.pdf

3.2 Occupational exposure

Lead is manufactured and/or imported in the European Economic Area in 1 000 000 – 10 000 000 tonnes per year (ECHA, 2018). Lead mining in the EU accounted for 6.1 % of the total worldwide production of lead from mining in 2012, with Poland and Sweden mining the most. At the same time the EU accounted for 15.6 % of the world's refined lead, with Germany refining the most (ECHA, 2019).

According to the Roadmap on carcinogens initiative, 1.5 million workers in the EU are estimated to be potentially exposed to lead through inhalation of lead fumes and dusts and through ingestion due to hand to mouth activity at the workplace. Dermal absorption is considered as minimal. The initiative considers the potential exposure as critical since workers may not know that they are exposed as lead does not have an odour. If you would like to read more about the initiative's opinion on lead, please visit their website

3.3 Consumer exposure

The major source of exposure for the general population in Europe to lead is through the diet with cereal products, potatoes, leafy vegetables, tea, beverages, and milk products being the main contributors. Since phasing-out leaded petrol, a decrease of lead levels in food products was observed (EFSA 2010). Canned food products can additionally be exposed through lead solder.

If you would like to read more about on current EU policies on lead in food products, please refer to Section 5 of this report.

In addition to exposure through the diet, consumers can be exposed to lead through drinking water due to lead pipes or pipes joined with lead solder. Lead is no longer used in modern construction, with lead pipes now mainly replaced, but it may still exist in older houses where repairs are yet to be completed, it may also still be found in some replacement products made of recycled materials. As outlined in Section 5 the EU is strengthening water policies with regards to lead.

As lead accumulates in tobacco leaves, smoking is another potential lead exposure source. In this context, studies indicate that children can be significantly exposed to lead through passive smoking. In addition, please note that increased lead exposure is strongly related to the poverty index (EFSA 2010).

4 Overview of key health impacts from lead

Once lead is inhaled, it is rapidly transferred to the blood where it can harm many of the body's internal organ and systems. The absorption is influenced by physiological factors such as age and pregnancy and the characteristics of the lead particles such as size (Jakubowski, 2012). Overall, lead poisoning can affect every organ of the body. A very high proportion of lead accumulates in bone tissue, where it remains for long periods of time. The Institute for Health Metrics and Evaluation estimated that 1.06 million people died due to lead exposure worldwide in 2017 (IHME, 2017). The human health effects due to the exposure to lead are presented in Figure 4.1. [2]

[2] An explanation of the categorisation of the strength of evidence for the health effects presented in Figure 4.1 is provided in Appendix 2.

Figure 4.1 Overview of health effects associated with exposure to lead

Target organ of the body	Effects	Relevant Substances	Adults (men)	Adults (women)	Infants / Foetuses
Brain/ neurological system 	Disturbance of neurodevelopment e.g. cognitive deficits	Lead	●	●	●
	Cancer	Lead	●	●	●
Stomach 	Cancer	Inorganic lead	●	●	●
		Organic lead	●	●	●
Lung 	Cancer	Inorganic lead	●	●	●
		Organic lead	●	●	●
Kidney 	Cancer	Inorganic lead	●	●	●
	Cancer	Organic lead	●	●	●
	Chronic kidney disease	Lead	●	●	●
DNA 	Reproductive toxicity	Lead	●	●	●
Cardiovascular System 	Increase of blood pressure	Lead	●	●	○
Blood system 	Anaemia	Lead	●	●	●

Key: ● Strong evidence ● Suspected ● Evidence lacking ○ Not applicable

An overview of current EU (ECHA C&L Inventory) classifications of lead is provided in the table below. If you would like to read more about lead, please visit the referenced ECHA info card in Table 4.1. below.

Table 4.1 Overview of CLP classifications for lead

Substance	Properties of concern				Category according to CLP criteria							ECHA info card
	Carcinogenicity	Mutagenic	Skin sensitising (SS)	Reproductive Toxicity	Carcinogenicity	Acute Toxicity	Specific target organ tox (repeated exposure)	Reproductive Toxicity	Mutagenic	Eye Damage/ Eye Irritation	Skin Sensitivity	Skin Corrosion/ Irritation	
Lead					1A / 2 (C&L) 2A/2B/3 (IARC)**	4	1, 2	1A*	2				Link

* Harmonised classification under the CLP Regulation. (Other classifications are those notified to the CLP inventory but without harmonised EU classification.); ** Based on IARC classification (IARC classified lead (in general) as possibly carcinogenic to humans (Group 2B), inorganic lead compounds as probably carcinogenic to humans (Group 2A) and the evidence for organic lead compounds was considered to be inadequate in humans and animals (Group 3). Blank cells denote a lack of classification.

4.1 Vulnerable target groups

Children are the most vulnerable and sensitive group to adverse effects of lead. In addition, pregnant and lactating women and hence, foetuses and very young children may be more vulnerable and sensitive to the effects of lead as these are the periods of the human brain development. Lead can cross the placental barrier and enter the bloodstream of the foetus (Baeyens et al., 2014).

Socioeconomically deprived people are more likely to be exposed to lead as they are more likely to live on marginal land (near landfills and polluted sites), to live in substandard housing with ageing and deteriorating lead-based paint or water pipes and to live near industrial sites where waste is burned and heavy traffic occurs (WHO, 2010).

4.2 Societal concerns

Societal concerns are mainly related to economic costs associated with IQ loss due to childhood exposure. The indirect costs due to loss of intelligence and the lifelong decrements in economic productivity that result from it (lost opportunity costs) are considered as substantial. According to the WHO, each 1 µg/dL increase in the blood lead level decreases the IQ by 0.25 points. Further, each lost IQ point is linked to a decline of the lifetime economic productivity by 2.4 % (WHO, 2010).

Besides the aforementioned indirect costs, lead exposure additionally results in direct costs such as the provision of medical care to children with acute lead poisoning or adults with chronic cardiovascular diseases (Landrigan et al., 2002).

The Roadmap on Carcinogens Initiative demands to replace lead-containing products and more training for workers that are potentially exposed to lead. If you would like to read more about the initiative's opinion on lead, please visit their website.

5 EU policies on lead

Several policy measures have already been introduced in the EU to address human exposure to lead and managing risks. In general, the existing EU policies cover i) regulations on chemicals; ii) the environment; iii), consumer products and iv) occupational exposure. An overview of these regulatory measures at EU level is provided in Table 5.1.

Table 5.1 Overview of EU policies related to lead

<table>
<tr>
<td>Chemicals</td>
<td>

Lead is registered under REACH (Regulation (EC) No 1907/2006). Specific uses of lead are further restricted under Annex XVII (restriction); and Lead has been identified as a substance of very high concern and included in the candidate list for authorisation.
Lead is subject to EU harmonised classification and labelling under CLP (Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures) – see list of classifications above.

</td>
<td>
Food

Regulation (EC)1881/2006 set maximum levels for lead in foodstuffs (e.g., milk 0.020 mg/kg, crustaceans 0.50 mg/kg).

</td>
<td>Consumer</td>
</tr>
<tr>
<td>Environmental</td>
<td>
Water

The Drinking Water Directive (98/83/EC) limits the concentration of lead in water for human consumption to 10 µg/L.

Air

Directive (EC) 2008/50 sets a regulatory limit value for lead in air as 0.5 µg/m^3 per calendar year.

Soil

Directive (EEC) 86/278 sets a regulatory limit value of lead in soil as 50 – 300 mg/kg, in sludge for agriculture as 750 – 1200 mg/kg.

</td>
<td>

Occupational exposure is regulated by Directive (EC) 98/24 containing both a binding Occupational Exposure Limit (0.15 mg/^{m3}) a Biological Limit Value (70 µg/dL).

</td>
<td>Occupational</td>
</tr>
</table>

In 2018, the European Commission adopted a proposal on the revision on the Drinking Water Directive. This includes a strengthening of the limit value of lead in drinking water as it has to be reduced by half (5 µg/L) at the latest ten years after the Directive[3] enters into force.

[3] https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1519210589057&uri=CELEX:52017PC0753

6 Policy questions for lead

6.1 Introduction

For each of the HBM priority substances, stakeholders were asked to identify policy related questions that HBM4EU should address in order to contribute to the strengthening of policy ambitions on lead. Further background detail on lead and how the policy questions were selected is available in the scoping document and the report on stakeholder consultation and mapping of needs.

6.2 What is the concentration of lead in the human blood nowadays (after phasing out leaded petrol) in the countries of Europe?

Information on blood lead levels in children and young people after 2015 is limited; however, the decreasing trend that started following the phasing out of leaded petrol came to a halt more or less in 2010 in the countries with regular nationwide surveys and levelled out at approximately 10 µg/L. Although, the blood lead concentrations were below the reference values set by different organizations, the most recent studies reported health outcomes at lower concentrations, and it was suggested that there is likely no safe threshold for lead neurotoxicity.

6.3 Do blood lead levels of both adults and children still indicate permanent existence of lead exposure?

The data collected in HBM4EU showed the decreasing exposure of the European population over the past decades that levelled off in 2010 which indicates permanent existence of Pb exposure. However, data on the most recent exposure is lacking for Europe.

6.4 What are the sources of still existing lead exposure in different countries of Europe?

Based on the literature review, it is assumed that some foods, particularly cereals and grain-based products, still may contain lead at non-negligible levels when the raw materials had been grown at contaminated sites. Tap water from lead pipes in non-renovated, old houses can also be sources of lead exposure. Old paint can contain lead. Household dust can also be important sources. Exposure to lead occurs through smoking and inhaling particles from burning waste. Certain workplaces may present risk of occupational exposure. Furthermore, herbal and traditional medicines or cosmetics could be sources for people using these products. Lead can accumulate in certain parts of the body, thus the transplacental and breast milk mediated exposure of successors of employed European women with relatively high age at childbirth is of concern. The high variation in breast milk Pb levels and the relatively high concentrations found in some studies suggest that breast milk can pose a source of exposure for infants in some areas.

6.5 What kind of exposure sources are the most important for the children of various age groups and the younger or older adult population?

Based on the literature review, milk and cereals are the most important sources of lead for children, and grain-based foods for adults.

In some more deprived and polluted areas children's Pb exposure can be of concern.

6.6 Taking the hazard from transplacental lead exposure of the unborn child into consideration, what are the blood lead levels of pregnant women?

Based on the literature review, the mean maternal and cord blood Pb concentrations did not exceed the EFSA BMDL01 value of 12 µg/L in the European surveys implemented after 2005 (Gundacker et al. 2021). Lead concentrations were only slightly lower in cord than in maternal blood, indicating that the placenta does not constitute a barrier for Pb transfer from the maternal to the foetal compartment.

The toxicokinetics of lead have been studied extensively using experimental studies and modelling and different toxicokinetic models are available to predict blood lead concentrations. The extension of the physiologically based pharmacokinetic model to pregnancy would be needed to fully assess the foetal exposure.

6.7 Taking the presumably low concentration of lead in blood, is it feasible to measure blood lead levels in children from as small amount of blood as it can be gained from capillary samples? What criteria should be applied in order to avoid contamination from outside sources?

As lead is not investigated in the HBM4EU aligned studies this question could not yet be addressed.

6.8 As it is difficult to connect later outcomes with exposures, which biomarkers of effects can be used in relation to effects caused by lead exposure?

There is not sufficient information for mandatory inclusion of specific effect markers in future HBM studies concerning lead exposure associated with neurodevelopmental disorders. Reduced brain-derived neurotrophic factor (BDNF) is a potential biomarker of Pb-induced neurotoxicity that should be further investigated.

BDNF is a key regulator of brain development and neural plasticity and is involved in the pathophysiology of diverse neurological and psychiatric disorders. BDNF can be assessed in different biological matrices and at different exposure levels. Environmental chemicals, including bisphenols, phthalates and polycyclic aromatic hydrocarbons can also influence the expression and regulation of this protein.

Epigenetic changes due to environmental exposures, including DNA methylation, can influence BDNF expression and regulation, thus the DNA methylation status of the BDNF gene seems to be another (more stable) biomarker of neurotoxical effects caused by lead exposure.

7 HBM4EU outputs to date

7.1 Categorisation

Substances under HBM4EU have been categorised depending on availability of HBM data. The categorisation indicates the information gaps hence allowing to develop targeted activities to fill the knowledge gaps. Substances will pass from Category E over D, C, B towards Category A as more information becomes available. Fully characterised substances should end up as category A substances.

Table 7.1 Categorisation of lead

Category		Priority substance(s)	Details
A	HBM data are sufficient to provide an overall picture	Lead	The health impacts of lead are well documented. Data on total lead exposure from different countries across Europe are available. However, several countries lack recent data or data on vulnerable populations, such as children. Also, in most instances, sampling is not representative of the population.

7.2 Key outputs

Lead levels

A systematic literature review was performed in the bibliographic database PubMed to identify human biomonitoring studies focusing on children's, pregnant women's, and young people's exposure to lead. In total, 58 publications from European countries were included in the review.

The European HBM dashboard has 23 datasets with lead exposure data integrated and in IPCHEM metadata for 43 datasets with lead data are available.

The exposure of e-waste workers, among others, to lead was assessed in 8 countries (Belgium, Finland, Latvia, Luxembourg, the Netherlands, Poland, Portugal and the United Kingdom).

Sources

A literature review was performed to answer the policy question on the recent exposure sources of the European population.

Furthermore, principal representatives of 20 studies from 6 countries agreed to provide individual data for analysis. The protocol has been elaborated for the statistical analysis.

Furthermore, several materials (e.g., questionnaires) to provide support for future studies to be able to comprehensively investigate the associations between lead levels and potential sources were developed.

Health aspects

The available health-based guidance values were reviewed.

The environmental burden of disease expressed as disability-adjusted life years (DALYs) was calculated, based on human biomonitoring data of children and adults obtained from different EU countries, regions and hot spot areas. In children, DALYs were estimated for developmental neurotoxicity (lost cognitive development attributable to blood lead levels above 20 µg/L. In adults, DALYs were estimated based on a recent dose–response relationship and corresponding hazard

ratios (relative risk) between blood lead levels above 10 µg/L and premature mortality (all causes of deaths).

The available human physiologically based pharmacokinetic (PBPK) models were reviewed.

A review was published on the biomarkers of effect associated with lead exposure.

7.3 Key data gaps

HBM4EU is a five-year project, that kicked off in 2017 and will run until June 2022. HBM4EU has helped to identify a number of specific data gaps that are needed to give policy makers relevant and strategic data to establish appropriate regulations and improve chemical risk management. However, some gaps will remain after the end of HBM4EU which should be addressed in the future:

- Long-term monitoring of exposure levels to evaluate differences between countries and population groups, time trends, and age-related differences in exposure.
- More research is needed for the validation of sensitive and reliable effect biomarkers to assess the exposure.

8 Future recommendations

- Establishment of a harmonised health-based guidance value, especially for the vulnerable target groups.
- Establishment of standardised non-invasive methods for assessing lead exposure, especially in the case of children.

9 References

HBM4EU, 2019, Scoping document for lead, v1 part of the D4.9 Scoping document set.

HBM4EU, 2019, Prioritised substance group: Lead – not updated, policy-related questions.

HBM4EU, 2020, Legislative mapping for lead, summary document prepared by RPA on behalf of the European Environment Agency.

Baeyens, W. et al. (2014). Trace metals in blood and urine of newborn/mother pairs, adolescents, and adults of the Flemish population (2007-2011). *Int J Hyg Environ Health*, 217(8), p.p. 878-90.

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UNEP (2020). The Lead Campaign, https://www.unenvironment.org/explore-topics/transport/what-we-do/partnership-clean-fuels-and-vehicles/lead-campaign.

WHO (2007). Regional Office for Europe & Joint WHO/Convention Task Force on the Health Aspects of Air Pollution. (2007). Health risks of heavy metals from long-range transboundary air pollution. Copenhagen : WHO Regional Office for Europe. https://apps.who.int/iris/handle/10665/107872

WHO (2010). Childhood lead poisoning, WHO, Geneva. Available at: https://www.who.int/publications/i/item/childhood-lead-poisoning

Appendix 1: Additional information on exposure

Source of exposure	References
Environmental • Release to soil and air through man-made sources.	WHO 2007, Health risks of heavy metals from long-range transboundary air pollution. Copenhagen: Joint WHO/Convention Task Force on the Health Aspects of Air Pollution.
Occupational • Used in industrial processes e.g. smelting. • Used in the following products: pigments and other compounds, rust inhibitors, rolled and extruded products, cable sheathing, alloys, radiation shielding, ceramic glazes, plastic stabilisers, jewellery making, soldering, crystal products, fishing weights, shot and ammunition, electronic waste, use in water pipes, and fuel additives.	WHO 2010. Childhood lead poisoning, WHO, Geneva.
Consumer • Present in food. • Present in drinking water.	WHO 2010. Childhood lead poisoning, WHO, Geneva.

Route of exposure	References
Oral • Primary source of human exposure to lead is the diet. • Contaminated drinking water is another exposure source. Major route of exposure for the general population.	EFSA 2010. Scientific Opinion on Lead in Food, https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1570.
Dermal • Dermal uptake of lead may occur in industrial processes. Minor route of exposure for the general population but can be more significant in specific occupational settings.	ECHA 2019. ECHA scientific report for evaluation of limit values for lead and its compounds at the workplace, https://echa.europa.eu/documents/10162/68cf7011-9c04-2634-efa6-b712f1b34a85.
Inhalation • Inhalation of lead may occur in industrial processes. • The general population may be exposed to lead inhalation through dust from e.g. paint. Minor route of exposure for the general population but can be more significant in specific occupational settings.	ECHA 2019. ECHA scientific report for evaluation of limit values for lead and its compounds at the workplace, https://echa.europa.eu/documents/10162/68cf7011-9c04-2634-efa6-b712f1b34a85.
Trans-placenta • Lead might cross the placenta and results in foetal exposure. Possible major route of human exposure.	Baeyens W. et al. 2014. Trace metals in blood and urine of newborn/mother pairs, adolescents, and adults of the Flemish population (2007-2011). Int J Hyg Environ Health 217(8):878-90.

Appendix 2: Additional information on health effects

Human health effect	Category	Justification for category	References
Disturbance of neurodevelopment	Strong	As noted on the scoping report The Panel on Contaminants in the Food Chain (CONTAM Panel) of the European Food Safety Authority (EFSA) identified developmental neurotoxicity in young children and cardiovascular effects and [toxicity in the kidneys] in adults as the critical effects for the risk assessment [of lead].	Scoping report EFSA (2010)
Cancer (Brain)	Suspected (inorganic lead) Evidence lacking (organic lead)	IARC classification of inorganic lead compounds as probably carcinogenic to humans (Group 2A) and organic lead compounds were not classifiable as to their carcinogenicity to humans (Group 3). As noted in scoping report - epidemiological studies indicate higher risk of cancers of the stomach, lung, kidney, and brain in workers exposed to inorganic lead (Steenland, 2019, Barry et al, 2019).	Scoping report IARC (2006)
Cancer (Stomach)	Suspected (inorganic lead) Evidence lacking (organic lead)	IARC classification of inorganic lead compounds as probably carcinogenic to humans (Group 2A) and organic lead compounds were not classifiable as to their carcinogenicity to humans (Group 3). As noted in scoping report - epidemiological studies indicate higher risk of cancers of the stomach, lung, kidney, and brain in workers exposed to inorganic lead (Steenland, 2019, Barry et al, 2019).	Scoping report IARC (2006)
Cancer (Lung)	Suspected (inorganic lead)	IARC classification of inorganic lead compounds as probably	Scoping report

	Evidence lacking (organic lead)	carcinogenic to humans (Group 2A) and organic lead compounds were not classifiable as to their carcinogenicity to humans (Group 3). As noted in scoping report - epidemiological studies indicate higher risk of cancers of the stomach, lung, kidney, and brain in workers exposed to inorganic lead (Steenland, 2019, Barry et al, 2019).	IARC (2006)
Cancer (Kidney)	Suspected (inorganic lead) Evidence lacking (organic lead)	IARC classification of inorganic lead compounds as probably carcinogenic to humans (Group 2A) and organic lead compounds were not classifiable as to their carcinogenicity to humans (Group 3). As noted in scoping report - epidemiological studies indicate higher risk of cancers of the stomach, lung, kidney, and brain in workers exposed to inorganic lead (Steenland, 2019, Barry et al, 2019).	Scoping report IARC (2006)
Chronic kidney disease	Suspected	As noted on the scoping report The Panel on Contaminants in the Food Chain (CONTAM Panel) of the European Food Safety Authority (EFSA) identified developmental neurotoxicity in young children and cardiovascular effects and [toxicity in the kidneys] in adults as the critical effects for the risk assessment [of lead].	Scoping report EFSA (2010)
Reproductive toxicity (e.g. damage fertility, damage to unborn child, reduced foetal growth and disturbed maturation, pre-term delivery)	Strong	Based on harmonised listing of Repr.1B, and evidence presented in the scoping report.	See Table 4.1 Scoping report

Hypertension/ Increase in blood pressure	Suspected	As noted in the scoping report A previous systematic review evaluating the evidence on the associations between lead exposure and cardiovascular endpoints in human populations concluded that the evidence is sufficient to infer a causal relationship of lead exposure with hypertension.	Scoping report EFSA (2010)
Anaemia	Suspected	As noted in the scoping report The severity and prevalence of lead-induced anaemia correlate directly with the blood lead concentration. Younger and iron deficient children are at higher risk of lead-induced clinical anaemia	Scoping report EFSA (2010)

For the categorisation of the strength of evidence for human health effects, the following criteria has been used:

- **Strong –** where the health effect is confirmed by either a harmonised classification indicating that there is a known effect (e.g. 1A or 1B for CMRs) (see Table 4.1), or where there is no applicable C&L classification, a statement in the Scoping Document that concludes there is strong evidence (or where a significant body of evidence is presented in the scoping document).
- **Suspected –** where there is either (a) a harmonised classification indicating that there is a suspected effect (e.g. category 2 CMRs or similar); (b) notified classification for that effect, or (c) where there is no applicable C&L classification, a statement in the Scoping Document (or other references presented in the Table above) that there is a suspected health impact.
- **Evidence lacking –** where a health effect is noted in the Scoping Document (or other evidence sources referenced in the Table above), but it is stated that evidence is currently lacking or there are uncertainties or inconsistencies in the available evidence.
- **Not applicable –** where a health effect does not apply to a specific group/gender