This policy brief summarizes HBM4EU’s results on mercury, the adverse human health effects of mercury, the main exposure pathways for humans, and how human biomonitoring of mercury could be of value in the development of EU policy.

Mercury (chemical symbol Hg) is a naturally occurring heavy metal in the earth's crust (abundance in the Earth's crust is 0.03 parts per million/mg per kg) and can exist in three main forms: elemental (metallic), inorganic, and organic. Mercury is ubiquitous in the global environment and its sources of release to the environment can be both natural (e.g. weathering of rocks, volcanic eruptions) and anthropogenic (e.g. from industrial/commercial uses and combustion of fossil fuels and waste).

**KEY MESSAGES**

- Human biomonitoring of European pregnant women in the frame of the HBM4EU-MOM study, contributed to improved understanding of how prenatal exposure to mercury may be controlled to prevent lifelong impacts from mercury exposure.
- Results from the HBM4EU-MOM study confirmed that the European pregnant women, whose diet includes specific fish and seafood, remain exposed to mercury and in some cases, their exposure exceeds EFSA’s health-based guidance value. However, fish is an important component of a healthy diet, and exposure can be controlled through suitable consumption. It is very important to communicate fish consumption advice to vulnerable populations.
- The HBM4EU-MOM study showed that the provision of dietary advice through healthcare providers of vulnerable populations is important and that suitable communication tools for these professionals are necessary.
- Long-term institutionalised EU-wide human biomonitoring activities are required to provide regular assessment of the risks posed by pollutants, such as mercury, to our health and well-being.
- Based on engagements with citizens in the frame of Eurobarometer surveys and HBM4EU Facebook live events, focus groups and citizen surveys, there is significant public concern in Europe, with regards to the risk posed by mercury in the environment.
- EU-policy in relation to the control of mercury use and release to the environment is well developed. However, because of mercury's persistence in the environment and ongoing global emissions, the risks are unlikely to decrease for many decades. Further policy measures aimed specifically at reducing human exposure to mercury in Europe could be beneficial.
- A new analytical method using Dry Blood Spots (DBS) in new-borns was developed by the HBM4EU project and can be systematically applied to assess and control mercury exposure.
- HBM4EU developed a framework to provide a comprehensive mechanism to determine the impact of mercury exposure on the European population, including the development of harmonised assessment methods and HBM-based guidance values for mercury for the general population. This framework can be exploited for monitoring time-trends, in support of evaluations of the effectiveness of policy actions at the European and global level.
**BACKGROUND: HBM4EU**

The European Human Biomonitoring Initiative, HBM4EU, running from 2017 to June 2022, is a joint effort of 28 countries, the European Environment Agency and the European Commission, and co-funded under Horizon 2020. The main aim of the initiative is to coordinate and advance human biomonitoring in Europe. HBM4EU has provided a wealth of improved evidence of the actual exposure of citizens to chemicals and their possible health effects. Human biomonitoring allows us to measure our exposure to chemicals by measuring either the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can be linked to data on sources and epidemiological surveys to inform research, prevention, and policy with the objective of addressing knowledge gaps and promoting innovative approaches. If you would like to read more about the project itself, please visit the HBM4EU website.

**HBM4EU RESULTS**

In order to further support current and future HBM studies, HBM4EU has produced a variety of publicly available groundwork materials for a harmonised approach to study planning and conduct in Europe.

Data on total mercury exposure from different countries across Europe are available. The HBM4EU-MOM study (Methylmercury-contrOl in expectant Mothers through suitable dietary advice for pregnancy) assessed mercury exposure of pregnant women in five coastal European countries (Cyprus, Greece, Spain, Portugal and Iceland). However, several countries lack recent data, data on vulnerable populations, such as children, adolescents, women of reproductive age and pregnant women; and association with specific sources of exposure (e.g. specific species of fish).

Under HBM4EU, research protocols aimed at estimating internal Hg levels by using non-invasive matrices and factors affecting the predictive potential in the European population were developed. The objective was to evaluate the current exposure of European residents to organic and inorganic Hg on a geographic and time scale. And if possible, verify the effectiveness of policies different countries/regions are taking, and to evaluate the percentage of population currently exceeding the known health-based values.

An effort has been made to identify new biomarkers of mercury-associated effects by reviewing epidemiological studies. This was done assuming that health effects of mercury exposure could be linked with epigenetic changes (Couderq et al. 2022, submitted).

HBM4EU explored genetic aspects of susceptibility to mercury toxicity across Europe by investigating the frequencies of relevant genetic variations in different European regions and whether they could explain variability in Hg exposure.

Regarding HBM4EU work on risk assessment, an update of the organic mercury risk assessment (methyl mercury-MeHg RA) has been carried out integrating data from human biomonitoring surveys conducted in European general population from 2012, specifically in children/adolescents from 3 to 17 years old and women of childbearing age in the range of 18-50 years.

HBM4EU also laid the foundations for a European HBM Network to monitor human exposure to priority chemicals, including mercury.

**EXPOSURE AND HEALTH EFFECTS**

The main source of mercury (a highly toxic heavy metal that poses a significant global threat to human health and the environment) emissions in Europe is the combustion of fossil fuels. However, from a human health perspective, inhalation is not a significant exposure route. Mercury deposited from the air into our oceans is converted to methylmercury which is a form of mercury that presents a significant risk to human health. The primary exposure route for the general population is through seafood and in particular the consumption of larger predatory fish.

As a result of different consumption patterns of seafood across Europe, there is a geographical variation in exposure to mercury.

Trans-placental exposure, from mother to child, is a significant exposure route since mercury crosses the placenta and results in foetal exposure. Maternal exposure to mercury can damage the neurodevelopment of the foetus, with noticeable effects on behaviour, cognition, motor skills and the immune and reproductive systems later in life. Mercury and its compounds are well known reproductive toxins and are suspected to promote carcinogenic risk.
INPUT TO POLICY PROCESSES
AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability, the Zero-Pollution Action Plan, as well as the Secretariat of the UN Minamata Convention on Mercury. These are available in the HBM4EU Science to Policy section.

The effects of mercury on the environment (for example impacts on animal reproductive cycles) and on humans have been recognised for some time and the EU has a well-developed suite of policies to reduce emissions and impacts of mercury, including:

- The EU is a party to the global Minamata Convention on Mercury and has implemented EU mercury regulations which go beyond the obligations defined under the Convention;
- The permitted intentional uses of mercury are now very limited as a result of regulatory measures, with the production, use and sale of mercury being restricted under the REACH Regulation;
- The Industrial Emissions Directive sets maximum emission rates for mercury from coal burning combustion activities such as power generation and cement production;
- Use of mercury in cosmetics, toys, electrical products, batteries and medical equipment are controlled under various EU legislation;
- Mercury is designated as a priority hazardous substance under the Water Framework Directive and limits on the mercury content of drinking water are also in place;
- The mercury content of fish and other foods for human consumption is also controlled under EU food safety legislation.
POLICY QUESTIONS

1 How effective are policy actions to reduce human exposure to mercury in Europe?

HBM4EU results confirm that Europeans who consume fish and seafood remain exposed to mercury. The findings of the HBM4EU-MOM study confirm that there is potential to significantly reduce prenatal exposure to mercury through the provision of timely advice and guidance to women planning to have children, pregnant women and parents of young children. Healthcare providers of pregnant women are important stakeholders for awareness-raising and educational actions. Harmonized, quality assured HBM results can support the evaluation of the effectiveness of policy actions at the European and international levels.

2 How can harmonised, validated and comparable information be collected and transferred to support and evaluate current policies?

HBM4EU has produced a variety of support materials to provide the basis for a harmonised approach to study planning and conduct in Europe. This includes a data platform with information on existing, ongoing and planned general and occupational HBM studies, manuals/guidelines for study planning and conduct, standard Operating Procedures for qualified recruitment of participants, fieldwork, sampling and exchange of samples.

3 What biomonitoring and exposure data on mercury (and its species), relevant to the European population, are currently available and what new data are needed to address policy-related questions?

Summary statistics (percentiles) for mercury exposure data from existing HBM data collections are integrated in IPCHEM and the European HBM dashboard. Currently, there are 17 studies in total, 16 of which measure total Hg and one measuring MeHg, ranging from 2002 to 2017. New harmonized and quality-controlled data are needed covering vulnerable populations and collected at different time-points. This is important for the assessment of the effectiveness evaluation of policies. Existing data coming from previous studies, which were implemented without a harmonized frame, hinder the risk assessment process. The collection of data on exposure and fish consumption from pregnant women in five countries in the frame of the HBM4EU-MOM study, demonstrated the benefit of a harmonized approach, especially in association with the provision of fish consumption advice. Because of the need to communicate both the nutritional benefits of fish and risk from mercury in a balanced way, it is very relevant to follow up both with time and in different countries and to improve our understanding of the factors contributing to exposure (e.g. what fish, from what origin, frequency of consumption) and the impacts on health from dietary exposures, but also considering the nutritional benefits.

4 What is the geographic spread of the current exposure and how does it relate to different exposure sources (environmental; contaminated sites; dental amalgams; dietary, including different species of seafood)?

In the frame of the HBM4EU-MOM study, exposure of pregnant women varied according to the country of origin. The reason of the geographic differences was related to the different patterns of fish consumption in the different countries. People, whose fish consumption is not in line with suitable dietary advisories for mercury control, may exceed current health-based guidance values.

The answers below are summarised. For more details, please consult the substance report available on the dedicated substance page of the HBM4EU website.
How can the public be informed and how can public awareness and education be raised regarding the effects of mercury on health and the environment and management options?

The HBM4EU-MOM study has facilitated the generation of a range of educational materials to increase awareness of the risks posed by mercury. This included targeted information for pregnant women, factsheets and videos for non-technical audiences, Facebook live information sessions, citizen focus groups and surveys.

How does exposure relate to the manifestation of adverse health effects? What are possible health effects resulting from chronic low exposure to mercury and its organic compounds?

There is evidence that mercury exposure could have some effect in neuroendocrine disruption through biomarker NR3C1. (Appleton et al. 2017). Mercury has also been shown to disrupt placental amino acid transfer, oxygen consumption, enzyme activity, membrane fluidity and hormonal secretion (Gundacker and Hengstschläger 2012). A systematic review of all epidemiological studies published since 2012 on prenatal exposure to mercury and neurodevelopmental effects in the offspring was carried out to evaluate if current knowledge supports or contradicts EFSA’s Scientific Opinion on mercury. The findings since 2012 do not provide robust evidence for adversity at or above the current TWI.

Scoping reviews of the scientific literature for links of mercury to specific diseases suggested a possible association of mercury to Alzheimer’s disease, but further studies are necessary for confirmation. Evidence for association with attention deficit hyperactivity disorder (ADHD) is limited and mercury is only potentially linked to asthma.

A PBPK model that allows exposure reconstruction starting from available HBM data in all three available matrices (hair, urine and blood) has been developed for both methylmercury and inorganic mercury. Based on the available HBM data, median intake levels of methylmercury, are in the range of 0.1 μg/kgbw/d, while median intake levels of inorganic mercury, are in the range of 0.01 to 0.1 μg/kgbw/d.

KNOWLEDGE GAPS

The HBM4EU project has identified a number of knowledge gaps in relation to the impacts of mercury, including:

• The toxic effects of methylmercury at the levels of exposure found in the general population due to fish consumption are somewhat controversial since results in certain cohorts are not corroborated by others.
• Exposure to mercury has been linked with Alzheimer’s disease, but further research is required to confirm this.
• Mercury has endocrine disrupting effects which have raised public concern, but further investigation is required. Mercury is cytotoxic, nephrotoxic, immunotoxic, neurotoxic and teratogenic for humans. Further epidemiological investigations are required to fully understand the health implications of mercury exposure.
• Biomarkers of susceptibility in European populations need to be better understood.
• The exposure level at which health effects may develop needs to be revisited and studies on co-exposures are missing.
• More educational/awareness actions for vulnerable groups and health professionals are needed.
• A time-trend analysis in the EU population to map and follow mercury exposure should be developed.
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