



HBM4EU

POLICY BRIEF

JUNE 2022



European Human Biomonitoring Initiative

Acrylamide

This policy brief summarizes the adverse human health effects of acrylamide, their main exposure pathways for humans, and how human biomonitoring (HBM) of acrylamide could be of value in the development of EU policies.

Acrylamide is a highly water-soluble and non-persistent organic compound used in the chemical industry and research. Its primary use is to manufacture polyacrylamides (used as flocculants) that produce dyes, organic chemicals, permanent-press fabrics, textiles, pulp, and paper products. However, it has also been identified to form in food unintentionally during everyday cooking, with further associated health risks.

KEY MESSAGES

- The most important source of exposure for the general population in Europe to acrylamide is the diet.
- Carcinogenic and neurotoxic effects are suspected, but further investigation is necessary to address health impacts in the general population.
- HBM4EU Aligned Studies¹ (2014-2021) have allowed for the collection of exposure data from four and six countries, covering Northern, Western and Southern Europe for children and adults respectively.
- They revealed an exceedance of a health-based guidance value in about 96% when compared to the biomonitoring equivalents (16µg/g crt). However, when compared to HBM Orientation Values (321.7 µg/L and 291.4µg/L), only 2% of children and 7% of adults had acrylamide values higher than HBM Orientation Values (321.7 µg/L and 291.4 µg/L). However, the data are not yet representative for the whole EU.
- Children seem to be the most vulnerable to the adverse effects of acrylamide.
- Gestational acrylamide during pregnancy is associated with adverse effect on the foetal growth.
- Mitigation measures were not visible until 2017 but there is an indication of a first effect of the 2017 EU regulation on internal exposure of adults.
- Societal concern is mainly related to the discovery that acrylamide is produced in processed foods rich in carbohydrates like chips, making acrylamide exposure widespread.
- Strengthening the existing regulations is encouraged in order to reduce acrylamide in food and implement a strategy to increase awareness of the general population and especially in certain groups at high risk, such as children and pregnant women.

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](#).

¹ The HBM4EU Aligned Studies are a survey aimed at collecting HBM samples and data as harmonised as possible from (national) studies to derive current internal exposure data representative for the European population/citizens across a geographic spread.

HBM4EU RESULTS

The main outputs from HBM4EU to date include an overview of available HBM data regarding acrylamide from European studies, as well as an overview of available health-based guidance values. Estimation of the current exposure to acrylamide in the European population was also performed as well as an evaluation of the effectiveness of the policy measures adopted to reduce acrylamide in food products by assessing whether the levels of acrylamide in the European population have been decreasing and whether these trends are equally observed in all European countries.

Studies were reviewed to identify the association between acrylamide and the risk of cancer, as well as neurological alterations. HBM4EU also measured acrylamide biomarkers of exposure in children and adults across Europe.

HBM4EU laid the foundations for a European HBM platform to monitor human exposure to priority chemicals (including acrylamide) and related health effects in a harmonised and quality-controlled way. A Quality Assurance/Quality Control Programme was implemented in order to establish a [HBM European Platform](#) of laboratories that are equally qualified for exposure biomarker analysis.

HBM4EU has produced a variety of [publicly available](#) groundwork material for a harmonised approach to study planning and conduct in Europe in order to further support current and future HBM studies.

EXPOSURE & HEALTH EFFECTS

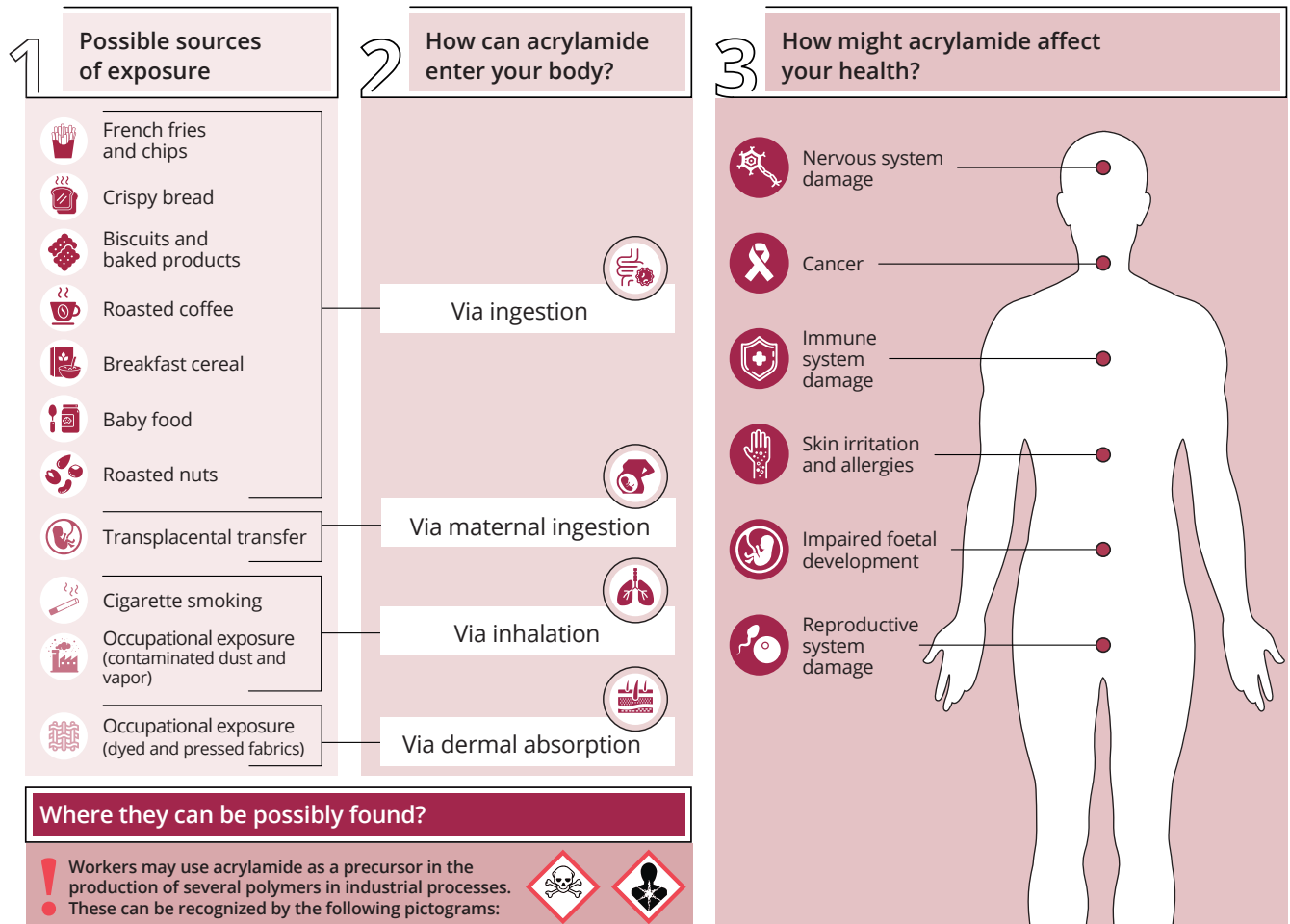
Based on the data examined within HBM4EU the main source of exposure being diet.

Once ingested, acrylamide does not bioaccumulate - it is metabolised. There is limited evidence available concerning human health impacts caused by dietary acrylamide. In particular, EU-wide HBM data to map population-level exposure to acrylamide is very scarce.

In addition, workers on industrial sites and in manufacturing are vulnerable target groups as they undergo prolonged and repeated exposure over time.

An overview of main sources of exposure (environmental, occupational, consumer), exposure pathways (oral, inhalation, dermal) and health effects is provided in Figure 1.

Figure 1. Overview of exposure sources, pathways and health effects associated with acrylamide



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. These are available in the [HBM4EU Science to Policy section](#).

Several policy measures have already been introduced at European Union level to address potential human exposure to acrylamide. In general, the existing EU policies cover i) regulations on chemicals; ii) consumer products; iii), the environment and iv) occupational exposure.

Acrylamide is registered under REACH ([Regulation \(EC\) No 1907/2006](#)) and included in the candidate list of substances of very high concern. Acrylamide is part of the registration list in Annex XVII and should not be placed on the market or used as a substance or constituent of a mixture in concentration equal or greater than 0.1 % by weight for grouting applications.

It is subject to EU-harmonised classification and labelling under

[CLP](#) (Directive on the Classification, Labelling and Packaging of Substances and Mixtures) ([Regulation \(EC\) No 1272/2008](#)).

In terms of food, [Regulation \(EU\) 2017/2158](#) provides mitigation measures and benchmark levels in food (e.g., roast coffee 400 µg/kg). Acrylamide is banned in plastic material and articles intended to come in contact with food as required under [Regulation \(EU\) No 10/2011](#). Regarding cosmetics, acrylamide is subject to [Regulation \(EC\) No 1223/2009](#) on cosmetic products. Its use in products is prohibited under Annex II.

In terms of the environment, the [Drinking Water Directive \(98/83/EC\)](#) limits the concentration of acrylamide in water for human consumption to 0.10 µg/L.

Acrylamide is subject to [Directive \(EC\) 2004/37](#) on the protection of workers from the risks related to exposure to carcinogens or mutagens at work.

POLICY QUESTIONS

1 What is the current exposure of the EU population to Acrylamide?

The answers to the policy questions below are summarised. For more details, please see the Substance Reports available on the [substance specific page](#) of the HBM4EU website.

New data for two acrylamide biomarkers (AAMA and GAMA) is available from the HBM4EU Aligned Studies in children (6-11 years) and adults (20-39 years).

Despite the studies not being representative, the Aligned Studies in children collected data between 2014-2021 across four sampling sites in Europe (Norway, Italy, Germany and France) representing 1,198 individuals.

In adults, it collected data between 2014-2021 across five sampling sites in Europe (Iceland, Portugal, France, Germany and Luxembourg) representing 1,180 individuals.

P50 of urinary AAMA concentrations are in the range of 51.44 -83.88 µg/g crt across studies in children and 28.78 - 91.70 µg/g crt across studies in adults. P95 of urinary AAMA concentrations are in the range of 126.39-220.50 µg/g crt across studies in children and 90.82 -503.92 µg/g crt across studies in adults. P50 of urinary GAMA concentrations are in the range of 8.32 - 30.74 µg/g crt across studies in children and 7.13 - 25.01 µg/g crt across studies in adults. P95 of urinary GAMA concentrations are in the range of 17.72 - 65.16 µg/g crt across studies in children and 13.51 - 48.82 µg/g crt across studies in adults.

For AAMA the share of individuals with exposure levels exceeding the BE-value of 16 µg/g crt ranges from 98.33%-100% for children and 90.20%-100% for adults. However, compared to the HBM orientation values (OV) calculated according to EFSA BMDL10 value of 0.43 mg/kg b.w. per day for peripheral neuropathy in rats - 7% of adults (France and Portugal) had acrylamide values higher than the HBM-OV (291.4 µg/L for adults with a body weight of 70 kg) and 2% of children had acrylamide values higher than the HBM-OV (321.7 µg/L for children).

2 Does the exposure to acrylamide differ significantly between countries and population groups? Are the main reasons for these differences related to different dietary habits or to other factors?

The exposure to acrylamide investigated in the HBM4EU Aligned Studies shows that the levels of acrylamide exposure measured in urine are higher in the participating studies from Southern Europe when compared to Northern and Western Europe in both children and adults. The reasons for these differences are still unclear and were not fully uncovered under HBM4EU.

3 Which population groups are more at risk? Are there other sources of exposure of acrylamide that need to be examined (e.g. smoking habits or other food sources)?

Children have slightly higher levels of exposure than adults. These results are in line with previous studies investigating values in children. In both children and adults, sex does not seem to be a determinant of exposure levels. Smoking was confirmed to be a strong determinant of acrylamide exposure in all the participating studies. In adults, acrylamide levels were higher in relation to high consumption of fried potatoes and coffee but lower in relation to an increase in body mass index, intake of fruit/vegetables and cereals. These results may indicate a strategy to reduce acrylamide in certain foods as well as to make the citizens more aware of healthy choices. In children, higher levels of acrylamide were found in relation to low socioeconomic factors and living in cities, but lower levels were found in relation to increasing age. These results might indicate that the awareness of acrylamide, and healthy lifestyle/choices in general, among certain groups of low socioeconomic status and groups living in cities (where the access to fast food might be easy and of easy choice) is still low. Also, these results suggest that urinary biomarkers of acrylamide, reflecting short-term exposure, may not capture the dietary exposure of acrylamide in these population of children as well as the other biomarkers measured in blood known to reflect longer dietary exposure.

We also found an association between higher levels of acrylamide with increasing sampling year (2014-2017) in children, suggesting that the typical food eaten by children is still high in acrylamide (2014-2017). These results are also confirmed by the time-trend analysis, underlining that acrylamide exposure is a relevant problem in current times.

Overall, our results may suggest an urgent need to implement a strategy to reduce acrylamide in certain foods and to make certain groups more aware of the problem with acrylamide exposure, or healthy choices in general.

4 Is there an impact from the mitigation for the production in food processing and manufacturing and REACH restrictions on the distribution of acrylamide exposure? Do we need to implement other restrictions to decrease the level of exposure of acrylamide?

Results indicate an overall increase of acrylamide exposure between the year 2000 and 2017 in non-smokers based on the analysis performed with published data and data from the HBM4EU Aligned Studies. Such a trend is also visible in individual data and yearly means of single studies based on children. HBM4EU Aligned Studies focusing on adults with samples collected after 2018 do not show increasing exposure anymore nor yet declining values. Regional differences appear to affect absolute values, but not the overall time-trend of exposure. In 2018, benchmark levels for acrylamide content in food were adopted in Europe, and therefore HBM4EU results may only show slight effects of these measures, although only for adults as similar data are still missing for children. Further biomonitoring studies with samples taken after 2018, in both children and adults, are necessary to check the effect of these measures on the European population.

5 Is the exposure to acrylamide associated to cancer, neurological alterations and foetal growth in humans? Is the health risk dependent on long-term or intermittent exposure to low quantity of acrylamide?

Acrylamide has been clearly shown to be carcinogenic in experimental studies, but the association with cancer in humans is still unclear. Results from our risk assessment, based on extrapolations from current HBM data, indicate that average acrylamide cancer risk for humans is approximately 1:500, meaning one extra cancer in population of five hundred. However, these results have several limitations. Results from our meta-analysis, based on 31 epidemiological studies, showed that high dietary intake of acrylamide was not associated with an increased risk of any of the several specific cancers investigated including oral cavity, oesophageal, gastric, colon-rectal, pancreatic, prostate, bladder, lung and melanoma.

As a novel finding, we found that the potential shape of the association between different levels of dietary acrylamide and the risk of any of the specific cancers considered, if present, would be linear. Considering studies performed in Western geographical areas, a borderline increased risk of lymphoma was observed in relation to high intake of dietary acrylamide. In general, findings did not differ by smoking status except for lung cancer in smokers and melanoma for never-smokers. In another meta-analysis of epidemiological studies on dietary acrylamide intake and gynecological cancer risk, an association between acrylamide intake and an increased risk of endometrial and ovarian cancer risk, particularly in never-smoking women, and an increased risk of premenopausal breast cancer risk were found. Most of the epidemiological studies on acrylamide and cancer were performed using dietary assessment of acrylamide. There is a lack of epidemiological studies investigating the risk of acrylamide in relation to cancer using HBM studies. This observation is of importance since it may explain the reason why epidemiological studies have failed to show an increased risk of cancer with acrylamide exposure. We encourage further high-quality epidemiological studies using biomarkers of acrylamide to understand better whether acrylamide is associated with cancer in humans.

Health-based guidance values are available, to which the newly generated HBM data in the HBM4EU Aligned Studies can be compared. The critical endpoints are nerve damage or peripheral neuropathy in rats.

There are no studies on neurodevelopmental functional effects in the general population exposed to acrylamide. Moreover, evidence from animal studies indicates that acrylamide exposure during neural development has the potential to affect key events known to lead to cognitive impairment in children.

The lowest "low observed adverse effect level" (LOAEL) reported for neurodevelopmental toxicity in rats was 0.5 mg/kg bw/day after maternal exposure of acrylamide in drinking water up to 3.0 mg/kg bw/day [starting at GD6 until 2 years of age]. However, in most cases the neurodevelopmental NOAEL was below the dose levels of acrylamide tested in the studies and therefore unknown. It is thus currently not established a NOAEL for developmental neurotoxicity of acrylamide.

Furthermore, most in vitro studies were performed using concentrations far above the levels estimated from the daily dietary intake in the general population. Thus, there is an urgent need for further research to examine whether pre- and perinatal acrylamide exposure might impair neurodevelopment in humans.

Acrylamide may cross the placenta and lead to exposure of the unborn child. Based on a meta-analysis of epidemiological studies, we found that high maternal acrylamide exposure during pregnancy is associated with reduced birth weight, birth length and head circumference indicating an adverse effect of gestational acrylamide exposure on fetal growth. The results were based on exposure assessed either through dietary acrylamide estimated via dietary questionnaire or biomarkers measured in blood. If results will be confirmed, these findings suggest that dietary intake of acrylamide should be reduced especially among pregnant women.

Although a toxic effect of acrylamide on the neurological system is known in animals and occupationally-exposed humans, there are no studies on neurodevelopmental functional effects of acrylamide exposure in the general population. Moreover, evidence from animal studies indicates that acrylamide exposure during neural development has the potential to affect key events known to lead to cognitive impairment in children.

KNOWLEDGE GAPS

HBM4EU has developed quality research in support of the policy questions. However, certain knowledge gaps still remain. We strongly encourage policies aimed at reducing the levels of acrylamide exposure through targeted public health education and awareness. There is a need to 1) generate more HBM data linking to cancer risk in the general population; 2)

investigate the European HBM exposure values and understand geographical differences better; 3) explore the mechanism behind the possible adverse effect on foetal growth; and 4) generate more data on the possible neurological alterations in the exposed general population and especially in children.

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