Prioritised substance group: Arsenic

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Short overview of results of the activities carried out within HBM4EU in 2020 to answer the policy questions with reference to corresponding deliverables

Policy Question	Short Summary of Results
1. What is the current exposure of the EU population to arsenic?	When reviewing the literature on exposure to inorganic arsenic, recent review data indicate existing drinking water pollution in Europe and possible exposure to iAs. There are several such regions in Europe where the arsenic content of water is between 7 and 90,000 mcg/l [Medunic et al 2020]. In addition to drinking water, the European population is exposed to arsenic through the consumption of food products containing, in addition to organic arsenic, inorganic arsenic. Within the framework of WP 7 activities, the identification of studies related to biological monitoring of exposure to As. A protocol has been developed under the activities of WP 10 (Task 10.4) on the possibility of using available studies related to the As exposure. From the available data (IPCHEM), 24 projects (studies) on the adult, adolescent, child and pregnant women populations were found. Arsenic was analysed in different matrices (cord blood, blood, urine, breast milk), as total arsenic and/or chemical forms. A thorough exposure assessment should be carried out based on the data made available by stakeholders (WP 10) and as part of the compensatory studies carried out for the activities of WP 8 (Task 8.1). Classification (QA/QC) of laboratories carrying out analyses of arsenic and chemical forms in urine (WP 9) has been carried out as this form of exposure assessment was considered the most appropriate. A list of approved laboratories is currently available and includes 3 laboratories. The results obtained from standardised testing will also enable European Reference Values (ERVs) to be obtained under task 10.3.
2. What biomonitoring and exposure (environmental and occupational) data on arsenic, relevant to the European population, are currently available.	The activities carried out in WP 7 and WP 10 provide highly differentiated data based on the IPCHEM database for the European adult, child, adolescent and pregnant women population. Compensatory research (WP 8) offers the possibility of obtaining analytically homogeneous (single matrix, most favourable biomarker) data on the population of children, adults and adolescents
3. What is the geographic spread of the current exposure and how does it relate to different exposure sources	In Europe there are several regions of so-called hotspots where there is significant exposure to inorganic arsenic with drinking water (e.g. Romania, Hungary, Slovakia). In Poland, the population exposed to iAs (air, soil) occurs as a result of industrial activities. General population in Finland,Greece, Italy, Czech Republic is also exposed to arsenic compounds. In other European countries, where the

(environmental; dietary sources)?	concentration in drinking water is below the WHO recommended value of 10 mcg/l, we have to do with exposure related to the consumption of food containing inorganic arsenic. A recent investigation by EFSA (European Food Safety Authority) found that dietary exposure to inorganic arsenic in Europe is not as high as was previously assumed. There are currently no recommended maximum levels of inorganic arsenic in food at EU level, however, EU maximum limits for inorganic arsenic (particularly in rice and rice products) are being discussed. The analysis of exposure in the European population is ongoing. Once the required data from the available datasets will be acquired, the data will be compared statistically and visualised with respect to geographic regions (north, south, east, west), countries and the NUTS regions. In cases of individual data (which is the majority of the datasets), we'll be able to confound for the known and hypothetical determinants of As exposure (e.g. diets) to reveal the geographical and/or environmental pattern(s). This will also allow as to identify the main sources for possible exposure.
4. Which population groups are most at risk?	It is believed that risk groups for arsenic exposure are populations consuming high arsenic water and infants and children fed on rice-based foods. Long-term exposure to arsenic from drinking-water and food can cause cancer and skin lesions. It has also been associated with cardiovascular disease and diabetes. In utero and early childhood exposure has been linked to negative impacts on cognitive development and increased deaths in young adults. Children's metabolism of iAs differs from that in adults, which might explain the lack of data on arsenic metabolism as a susceptibility factor for arsenic toxicity in children. Children had higher arsenic methylation efficiency than adults, and there was no difference between boys and girls. Studies in vulnerable populations and studies for a better understanding of the health effects of inorganic arsenic in the population at exposure levels in EU are greatly needed. Aligned study under WP 8 should fill in the missing data, including for the most vulnerable population, namely children. The RV 95 for total arsenic in urine, according to the findings of the German HBM survey, is 15 µg/L for children and adults who did not eat fish during 48 hours prior to sample collection [Schulz et al., 2011]. The GM levels of total arsenic in European populations were from 0.5 µg/L to 1 µg/L in blood and from 4µg/g to 16 µg/g creatinine in urine. There was no obvious difference observed between children/adolescents and adults [WHO 2015].
5. What factors (genetic polymorphisms) make people more susceptible or not to the risk of health effects due to arsenic exposure? How are the best and more sensitive biomarkers for identification of reliable arsenic exposure and to link to potential adverse health-effect?	Many works indicate the relationship between the genetic polymorphism of arsenic-metabolising enzymes and the efficiency of methylation processes. The existence of such relationships is confirmed by the works of Gonzales-Martinez et al (2020) and Kazenifar et al (2020). There are several potential biomarkers for arsenic exposures. Preferred biomarkers are determination of As and its chemical forms in urine. Non-invasive, ease collection and because the majority of absorbed arsenic and its metabolites is eliminated via urine puts this type of markings in a privileged position. WP 13 (Task 13.2) and WP14 groups have coordinated the selection of biomarkers of effect according to their utility in human studies, the identification of needs for the implementation of both classical and novel biomarkers of effect and the decision criteria for their validation. As part of the assessment of potential effects of various chemical compounds, including arsenic, human health, a publication was prepared entitled "Arsenic and human health. "Scoping review - the association between asthma and environmental chemicals".
6. What are possible health effects resulting from chronic low exposure to	Low-level groundwater As contamination (≤50 µg/L) on public health by identifying the varied health effects, e.g., disorders of the skin, lungs, cardiovascular system, endocrine dysfunction, neuropsychological complications, aberrant pregnancy outcomes, liver and skin ailments, risk of carcinogenesis and mortality. In vitro and in vivo studies related with low-level As, depicted interplay of genomic

arsenic from food consumption?	variants, DNA damage and repair, aberrant methylation, inflammation, immune suppression and deregulation of signal transduction, which might have influenced health complications, including risk of carcinogenesis. In addition to the tasks carried out under WP 12 and WP 13, in search of the interdependencies between the exposure and health effects and new specific effect biomarkers, in task 12.3, parameterisation of the PBTK model was performed. The PBTK models are increasingly being used as an effective tool for designing toxicological experiments and for performing extrapolations necessary for risk assessment. Published human PBTK models have been reviewed, with particular emphasis on the values of pharmacokinetic parameters and methods used to estimate these values. In most of the models studied, the preferred approach to parameter value estimation was to use literature data based on experimental data (in vivo or in vitro). In the absence of experimental data, quantitative structure activity relationships (QSAR) were used for parameterisation. The work performed within this task was presented in "AD12.10 - Report on parameterisation of the second set of priority substance"
7. What are the best analytical methods should allow for differentiating species in urine?	The determination of arsenic in biological specimens requires sensitive analytical methods, performed under good quality control conditions. Due to the possibility of separating the different chemical forms that are relevant in the toxicity assessment, it was considered that the assessment of the different forms alongside total arsenic would be the most advantageous biomarker in the exposure assessment. The use of the ICP-MS technique in combination with separation techniques, e.g. HPLC, now appears to be the most advantageous analytical technique to use in the As exposure assessment. Under WP9 activities, laboratories invited to participate in proficiency testing were qualified on the basis of QA/QC checks carried out. Currently, the proficiency tests are completed, 3 laboratories that have successfully passed the controls are included in the list of laboratories performing the tests in the assessment of the second list of priority substances.
8. How can harmonised, validated and comparable information be collected to support and evaluate current policies?	Analysing the data on arsenic exposure in different age groups, one can see a lack of such data for a group of adolescents. The alignment study plans to assess exposure to different forms of arsenic (speciation) as the most reliable biomarkers.
9. How can HBM4EU results support European policy decisions?	The results of the project will identify stakeholder groups, prioritise the assessment of exposure to chemicals and meet the needs for biological monitoring research for stakeholders, starting with policy makers and researchers