Prioritised substance group: Anilines

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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 occupational exposure to aniline and different aniline derivatives (including diamine forming diisocyanates) in the EU?	The available data on the occupational exposure to relevant aniline compounds have been collected under WP7.1 and summarised under AD8.1 (Report on access to occupational data). According to this analysis, the data are scattered and its coverage is limited. Many aniline compounds are nowadays restricted, which limits occupational exposure to them. Use of MOCA and technical MDA is authorised under REACH and exposure to them is rather limited in terms of number of workers. Occupational exposure to aniline itself is mostly related in its use in chemical manufacturing. Occupational exposure to anilines formed from diisocyanates, MDA/TDA as markers for diisocyanate exposure and effects for regulatory measures on the exposure to these substances, especially in small and medium sized companies, needs further data. Although some studies exist, the data is still limited. There are also some data on the occupational exposure to specific anilines (carcinogen o-toluidine and sensitiser PDA) through e.g. hair dyes but the biomonitoring data on these exposures, which may concern large number of workers, is still limited. In WP16, suspect screening is done from hairdresser's samples. This can provide additional information on the possible occupational exposure to these anilines. Results are expected during 2020-2021.
2. What is the exposure to paracetamol (aniline metabolite) among the general population?	There are single studies in Germany and Denmark on the exposure of general population to paracetamol. These has been described in aniline scoping document (D4.2 Scoping documents for 2018). To get a better overview of the paracetamol exposure, inclusion of paracetamol in the studies conducted under WP8 in general population would be needed. This is not, however, currently planned.
3. What are the risks related to these exposures?	WP5.3 deliverable report D5.1 (Human Biomonitoring in risk assessment: analysis of the current practice and 1st examples on the use of HBM in risk assessments of HBM4EU priority chemicals) describes the recent risk assessment of MOCA under REACH, which serves as a good example on the use of biomonitoring in risk assessment. In 2018 a risk assessment utilising HBM data was performed for o-toluidine under WP5, included in the Deliverable Report D5.5 (Human Biomonitoring in risk assessment: 2nd set of examples on the use of HBM in risk assessments of HBM4EU priority chemicals). In summary, a one-compartment model-based approach was used to estimate the urinary levels corresponding to the external intake levels of o-toluidine or vice versa. This allowed the comparison between available HBM data and existing binding occupational exposure level (OEL) and established cancer risk estimates. The results suggested that the workers exposed to o-toluidine have a cancer risk of 1:20 000 in the worst-case exposure scenario (0.5

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	mg/L in urine). The exposure levels calculated based on HBM data were below the binding occupational exposure level set under the EU Carcinogens and Mutagens Directive (BOELV, 0.44 mg/m3 corresponding to 2.2 mg/L as urinary total o-toluidine). However, the result includes several uncertainties, related especially to the limited amount of HBM data available, and therefore the RA should be seen as an example. In addition, further data on the toxicokinetics of o-toluidine in occupational settings, focusing especially to the correlations between external intake and urinary levels, would strengthen the assessment. If o-toluidine will become authorised under REACH, HBM is recommended to be used to support exposure assessment, as regardless of the uncertainties, it is the only method able to provide information on the total internal exposure via all routes of exposure. To strengthen risk assessment of o-toluidine, PBPK modelling to calculate external intake on the basis of the urinary o-toluidine levels were performed under WP12. The results of this modelling are comparable to those obtained earlier by using urinary mass balance-based calculation approach. These results were used to calculate RCRs and were reported in D12.5. AOPs for anilines have been developed under WP13 to support human health risk assessment.
4. What is the possible impact of REACH on the exposure and risks?	WP5.3 deliverable report D5.1 (Human Biomonitoring in risk assessment: analysis of the current practice and 1st examples on the use of HBM in risk assessments of HBM4EU priority chemicals) describes the current situation with MOCA and MDA which are authorised under REACH. Because of the authorisation there are only limited number of exposed workers in EU. Occupational biomonitoring data collected under WP7.1 and summarised under AD8.1 (Report on access to occupational data) describes a decline in the exposure to MOCA observed in UK and in Finland. Therefore, MOCA was not considered as a good candidate for further research under HBM4EU although laboratories performing biomonitoring of MOCA are still needed in EU as long as it is used. Laboratories performing analysis of different aniline compounds have been listed in D9.3 (Database of candidate laboratories for the 1st prioritisation round of substances) and ICI/EQUAS for aromatic amines started in June 2019 and the results are finalised in mid-2020. Regarding MDA, AD8.1 describes the potential exposure to MDA (and similar diamine TDA) via the production and use of diisocyanates. A study to collect new data on diisocyanate and corresponding amine exposures is under preparation and samplings are planned in the end of 2020 and beginning of 2021. This new study will bring us information to study the impact of the planned REACH restriction/EU OEL for diisocyanates.