Composition and health risk of chemical mixtures found in European adult and children populations

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INTRODUCTION

Human biomonitoring (HBM) data provide exposure information relating to different exposure pathways and sources. By harmonising and combining data from various geographical regions and substance groups, the HBM4EU project provides HBM data in aggregate form for 14 priority substance groups across 14 European countries. The dataset is available on the European Commission Information Platform for Chemical Monitoring (IPCHEM).

Addressing unintentional mixtures in legislation is a complex scientific and policy task, since such mixtures originate from various sources and their composition is often unknown and changes over time, making them difficult to regulate. One proposed approach is to introduce a mixture assessment factor (MAF) applicable to single substance risk assessment to account for possible combined effects. The EU Chemicals Strategy for Sustainability (October 2020) announced the implementation of an MAF under the REACH regulation. The objectives of this study were i) to derive generic mixtures that European adults and children are exposed to and ii) to quantify the combined risk informing an estimation of the range of a possible MAF for use under the REACH.

METHODOLOGY

We pooled aggregate data from all available data sets using simple filters to define the desired generic mixtures (e.g. sampling years, age categories, matrices). We then derived two co-exposure scenarios: (1) a median exposure to all chemicals at the 50th percentile (P50) and (2) a worst-case co-exposure to all chemicals at the 95th percentile (P95). The two resulting lists constitute the generic chemical mixtures (GCMs) for adults (>12) and children (<12). For these two mixtures, we estimated the health risk assuming additivity of all toxicities from the individual chemicals. We calculated the individual chemicals' risk quotients using Biomonitoring Equivalents (BEs) selected from the literature and added them up to derive the mixture Hazard Index (HI). We then calculated the maximum cumulative ratio (MCR), defined as the mixture HI divided by the risk quotient of the chemical contributing most to the overall risk. The MCR represents an estimation of a possible MAF.

RESULTS

HBM4EU aggregate data provided a solid basis for deriving realistic generic chemical mixtures (GCMs) combining data from 36 datasets for adults and 23 datasets for children. The mixtures comprised 115 biomarkers for adults and 106 for children, with a quantification level between 43 % (P50, adults) and 71 % (P95, children). Phthalates were the substance group with the most measurement data, followed by flame retardants, poly- and perfluoroalkyl substances (PFAS), pesticides (mostly organophosphates) and various metals. When considering all the biomarkers measured in both adults and children, concentrations in adults are on average a factor 1.4 (P50) and 2.1 (P95) higher than in children. Differences in concentrations, however, exist in both directions.

The mixture risk assessment based on BEs was possible for a fraction of the measured substances (16 for adults, 13 for children). Based on the assumption of concentration addition, the mixture hazard index ranged from 1.4 (P50, children) to 8.6 (P95, adults). In all scenarios, no more than six substances contribute to over 95 % of the total risk. The resulting MCR values point to an MAF ranging between 2.3 and 5.1.

DISCUSSION

Uncertainties associated with our assumptions could influence these values in both directions.

The contribution of chemicals not covered by the mixture calculations is unknown but probably significant, leading to a likely underestimation of the risk.

From a methodological point of view, the concentration addition concept applied to chemicals with diverse modes of action is a worst-case assumption. Our decision not to further subgroup leads to an overestimation of risk and MAF.

Assuming co-exposure to all measured chemicals, without knowing the actual co-exposure patterns in individuals, may be overly conservative especially for the worst-case (P95) scenario. A combination of realistic worst-case co-exposures is statistically unlikely for many substances in the same individual.

Other uncertainties are associated with the methodologies used to derive BEs, the analytical errors in HBM measurements across laboratories and the definition of population sub-groups.