PROJECT

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1) Project title
Risk assessment of combined chemical exposures
2)Abstract (max 500 words)
The project is included in a larger Horizon Europe project that will deal, among others, with combined exposures to chemicals and their risk assessment. Risk assessment will be performed using lower and higher tier risk estimates, including the Hazard Index approach, mode of action and adverse outcome pathway (AOP). A comparison between observed real-life mixtures and mixture risk assessment predicted by regulatory accepted models will be studied in case studies. It expected to contribute to the development of AOP to better define endocrine disrupting chemicals (EDC). This is based on the fact that in the long run, hazard based management of these compounds will be applied in all fields in EU. Conservative application of EDC definition of compounds based on in silico/in vitro data might lead to the ban of a large number of compounds. This can have adverse social, economic, technological consequences with little, if any, benefit for public health. Hence, careful evaluation of such AOPs is needed. Similarly, (developmental) neurotoxicity might be addressed. In addition, substances that will be identified based on real-life exposure data will be grouped based on Mode of Action and AOPs following e.g. European Food Safety Authority (EFSA) opinions and building on experience from previous Horizon 2020 projects (EuroMix, HBM4EU). A fundamental step for the risk assessment of combined exposures is the derivation Relative Potency Factors (RPFs) for each component of the mixture in relation to a reference compound, called Index Compound (IC). RPFs can be derived from in-silico, in-vitro and/or in-vivo point of departures (PoDs). This needs careful interpretation of the PoDs obtained from the experimental work available from the literature or provided by partners in the project. The applicability of using RPFs from different type of data will be explored. This will include analysis of the uncertainty associated with an estimation of the under or overestimation of the risk. Attention will be paid to exposure duration (acute, sub-acute, chronic) of both the experimental data and the expected human exposure in order to derive the appropriate RPF. Also, internal vs external exposure estimates, based on available human biomonitoring data and human biological guidance values (HBGV) will be compared. Moreover, human biomonitoring (HB) data will be

compared with biological effective doses estimated from dose-response curves obtained from cell test systems. On these bases to need to derive internal mixture HBGV might be developed.

Based on a proposal from the EU Commission, an analysis of the usefulness, acceptability and applicability of the proposed MAF (Mixture Assessment Factor) will be carried out. This will be done on case study(ies) with data rich compounds (e.g. pesticides, biocides, well-studied pollutants) conducting "classical" mixture Risk Assessment and apply MAFs at different levels of data acquisition, for both toxicology and exposure. The outcome of this studies will help in developing criteria for the application (or waiving) of MAF.