Screening and Prioritization of Chemicals for REACH: the Cumulative PBT Index Model in QSARINS

PAOLA GRAMATICA, ALESSANDRO SANGION,STEFANO CASSANI, ESTER PAPA

QSAR Research Unit in Environmental Chemistry and Ecotoxicology, DiSTA, University of Insubria, Via J.H.Dunant 3, 21100 Varese, Italy, paola.gramatica@uninsubria.it

The limited availability of comprehensive data for Persistence, Bioaccumulation and Toxicity (PBT) of chemicals is a serious hindrance in the assignment of any chemical to the category of PBTs or vPvB, chemicals that require an authorization in REACH for their use and additionally plans for safer alternatives.
In the context of screening and prioritization tools, the cumulative PBT Index model (PAPA & GRAMATICA 2010), implemented in QSARINS (QSAR-INSubria) (GRAMATICA et al. 2013, 2014), the new software for the development and validation of QSAR models, by Ordinary least Squares (OLS) method and Genetic Algorithm (GA) for variable selection, offers a new holistic approach for an early identification of chemicals with cumulative PBT properties, directly from their molecular structure.

The Insubria PBT Index was applied to screen and prioritize big datasets for a total of more than 4000 chemicals of environmental concern and with heterogeneous molecular structure. The results of this screening have been compared with those obtained by the on-line US-EPA PBT Profiler. A good agreement (higher than 76%) between the two approaches has been found, supporting the need of a consensus approach: a priority list containing 1313 compounds, identified as the most hazardous for their potential PBT behavior by both the methods, has been proposed (GRAMATICA et al. 2015)
In addition, some classes of chemicals of high concern as emerging pollutants, such as Flame Retardants (FRs) and Personal Care Products (PCPs), have been specifically screened in this comparative exercise. It is interesting to note that some FRs, already marketed as “safer alternatives” to banned FRs, have been identified as potential PBTs, starting from their molecular structure (GRAMATICA et al. 2015).

This structure-based approach is an early safety strategy which responds to two levels of action in relation to the management, according to REACH regulation, of chemicals of highest concern: a) the need for screening tools for identification and prioritization of PBTs, and b) the *a priori* design for the synthesis of safer alternatives, according to the green chemistry philosophy of “benign by design”.