OPPORTUNITIES AND LIMITATIONS OF USING ALTERNATIVE METHODS AND NON TESTING STRATEGIES IN REACH REGISTRATION DOSSIERS

Geneviève Deviller, Virginie Burosse, Corinne Dubourg, Matthieu Duchemin, Cyril Durou, Pauline Frizet, Blandine Journel, Aurélie Sevestre, Paul Thomas

CEHTRA, Consultancy for Environmental and Human Toxicology and Risk Assessment

www.cehtra.com

Introduction

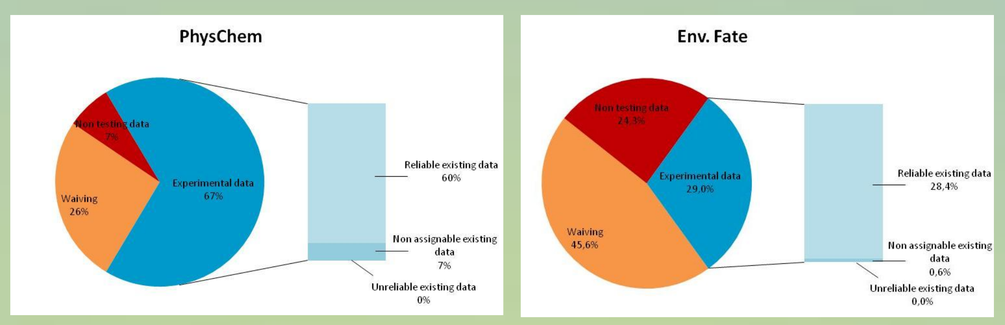
By 1 December 2010, substances manufactured or imported ≥ 1000 Tons/Year (T/Y) as well as Carcinogenic, Mutagenic or Reprotoxic substances category 1 and 2 manufactured or imported ≥ 1 T/Y, or substances classified as dangerous for the aquatic environment with R50/53 and manufactured or imported ≥ 100 T/Y have been registered under REACH. The lack of data on the hazardous properties of chemicals was the driving force behind the development of a new chemicals policy in the EU nevertheless one of the objectives of REACH is to promote alternative methods for the assessment of hazards of substances both to reduce animal testing and to reduce the costs. CEHTRA helped the industry sector to comply with their regulatory obligations providing input on more than one hundred REACH substance dossiers. The aim of this poster is to illustrate at which extend non testing data's and methods have been used to perform the environmental risk assessment of the first registration dossiers and to identify the most reliable approaches and the limitations in using non-testing strategies under REACH.

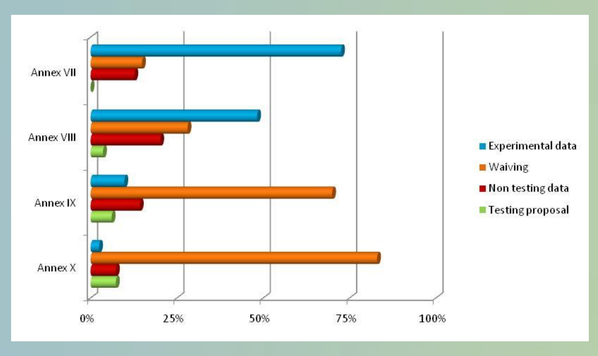
Materials and Methods

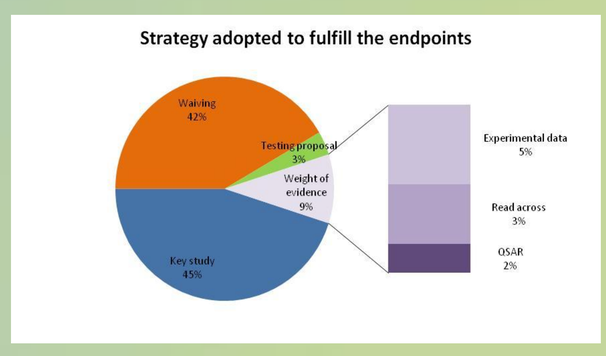
A selection of thirty dossiers including organic/inorganic substances and mono/multi constituents have been used in this study. Both the tonnage and the objectives of information requirements have been taken into account. The relevant information was extracted from the IUCLID dossiers in order to address the existing data coverage, the reasoning for waiving tests, the use and adequacy of alternative data's (QSAR modeling, in vitro and read-across) and methods (weight-of-evidence approach) and the experimental testing strategies. The dataset includes the complete Environmental fate & pathways and Ecotoxicological information sections as well as the data's from the endpoints of the Physical/ Chemical properties (Kow, Water solubility, Melting point/freezing point, Boiling point, Vapour pressure, Surface tension, Dissociation constant) and Toxicological information (Repeated dose toxicity: Oral, Toxicity to reproduction, Developmental toxicity / teratogenicity) relevant for the environmental risk assessment.

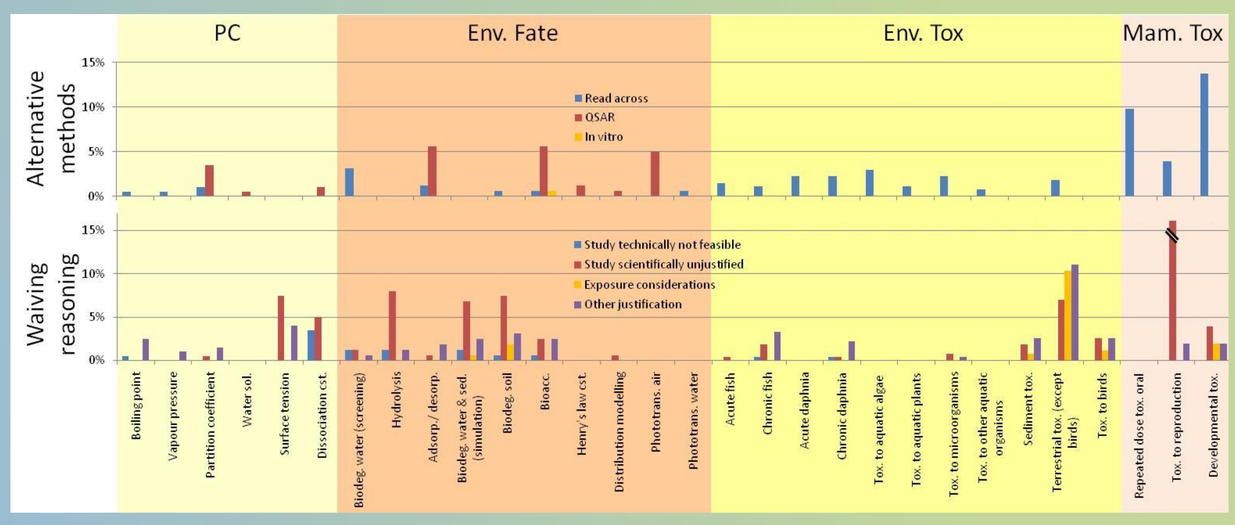
Results

Experimental data: Graph. 1 demonstrated that studies were available for about 70% of the physico-chemical endpoints and around 30% of the environmental, ecotoxicological and toxicological endpoints. Almost all of these studies were assess as reliable (corresponding to a Klimish score 1 or 2) and few of them were assess as non assignable (Klimish score 4) and even less as unreliable (Klimish score 3) . When experimental data's were not available, non testing data's were used mainly for the environmental and toxicological sections followed by the ecotoxicological and the phychem sections. Finally data waiving was use in almost half of the endpoints of the environmental and ecotoxicological sections and to a lower extent in the toxicological (35%) and phys-chem (25%) sections. The experimental data's were the main resource to cover the so-called "base dataset" (Annex VII) and the Annex VIII information requirements and the waiving of data's to fulfill the Annex IX and X requirements (Graph. 2). Non testing data's were use for all the annex coverage with a maximum in Annex VIII and a minimum in Annex X. Testing proposal was the last resort strategy and increased with the Annex increasing.









Non testing versus testing strategies: Graph.3 indicates that on the global dossier, reliable experimental data's were used to cover almost half of the endpoints by a key study approach and the non testing strategy of waiving was almost used as the same level. The weight of evidence approach was much less employed with a use in the same proportions of non assignable experimental data's and non testing data's (read across and QSAR). Finally the testing proposal was the least used because it was envisaged only as a last resort.

Data generated by alternative methods: Graph. 4 gives the use of alternative methods to cover specific endpoints. QSAR models were used only to calculate specific physchem and environmental data's. Read across data's were used in all sections but more systematically in "eco-toxicology" sections and frequently in toxicology. In-vitro data's was scarcely used for one specific endpoint (bioaccumulation).

Waiving reasoning: among the reasons not to present data, the absence of scientific justification was the main used argument followed by other justifications (Graph.4). These waiving were mainly based on the column 2 specific rules described in the REACH directive and some scientific evidence available in the literature. At a lower level the justification for technical unfeasibility and exposure considerations were employed according to the chemical properties and the results of the risk characterization (tier 1).

Discussion/ Conclusion

For the first registration's deadline, the results illustrate that almost **half of the endpoints were fulfilled by experimental data's and the other half by waiving strategy**. This situation is expected to be different for the second and third registration deadlines because less experimental data's will be available. As recommended by REACH, testing proposal were envisaged as a latest resort but unexpectivelly the alternative methods were poorly used. The main difficulties encounter in using QSAR appeared to be their validation according to the OECD rules and their public accessibility. The read-across approach have been mainly justify by scientific evidence according to the ECHA guidances. The improvement of the QSAR toolbox should increase their use in the next dossiers. In-vitro tests were only performed to resolve some specific issues and the limited set of validated test should maintained this situation in the near future.

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