Using alternative methods and non testing data's for environmental risk assessment in REACH 2013 dossiers: how far can we go?

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Introduction

According to REACH regulation, 31 May 2013 is the deadline for industry to register all phase-in substances manufactured or imported in the EU between 100 and 1000 tonnes a year. One of the objectives of the directive was to promote alternative methods for the risk assessment of substances to reduce animal testing. Since the first tonnage band, less availability of experimental data was expected and several lines of guidance and tools had been developed for further use of these methodologies, especially on QSAR and read-across (ECHA, ECETOC...). Solvay as a specialty chemical company applied for the registration of more than one hundred substances. The aim of this poster is to illustrate how these strategies were used for the environmental risk assessment of the second tonnage band registration based on our experience of the most reliable approaches used to assess the different properties of the substance. Further, their impact on the reduction of testing on animals is presented.

Material & Methods

Thirty five dossiers for 100-1000 t/y registration (Solvay as lead registrant) were included in the study dataset containing a total of 830 endpoint study records. They covered different types of substance origin (23 organics, 12 inorganics) and composition (22 mono-constituents, 6 multi-constituents and 7 UVCBs) and different registration status (9 intermediates and 26 full dossiers).

The relevant information was directly extracted from IUCLID to determine the extending of non-experimental data (QSAR and calculated values) and the use of alternative methods (waiving, read-across, weight of evidence) for the different annexes, sections and endpoints required to perform the environmental risk assessment in compliance with REACH. In-vitro data were not taken into account since they were not represented in any of the dossiers. We have also estimated the number of spared vertebrates using non-testing strategies (waiving, estimated values, read-across) to fulfill the fish toxicity and bioaccumulation information requirements by comparison with the required animals numbers in commonly used standard tests (OECD).

Results

The experimental data's were the main source to cover the Annex VII and VIII data gaps and the waiving of data's was the main strategy to fulfill the Annex IX (**Fig.1**). Non-testing data's were used for all annex coverage with a maximum in Annex VIII and testing proposal were only marginally used in Annex IX.

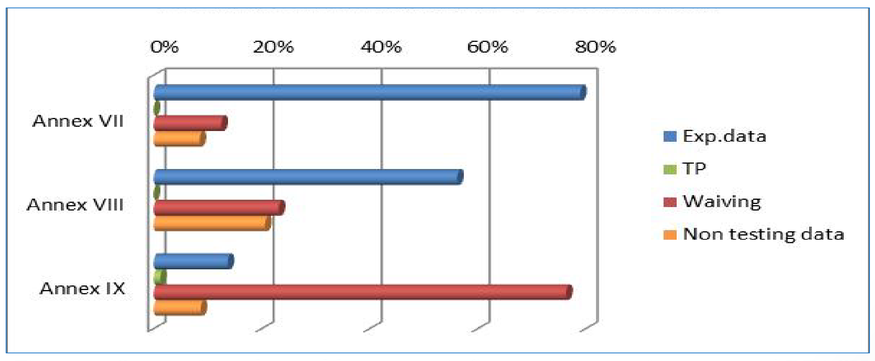

Figure 1. Strategies adopted by annex information requirements of REACH

Experimental data's, available or generated for the registration, were significantly submitted in a large majority of endpoints when only few testing proposals were made for long term testing on aquatic organisms (**Fig.3**). For some endpoints, full use of the adaptation options had been followed (e.g. partition coefficient, biodegradability in water, adsorption/desorption, long term toxicity to aquatic invertebrates) while for some higher-tiers endpoints only waiving of testing was proposed (biodegradation in soils and terrestrial macro-organisms).

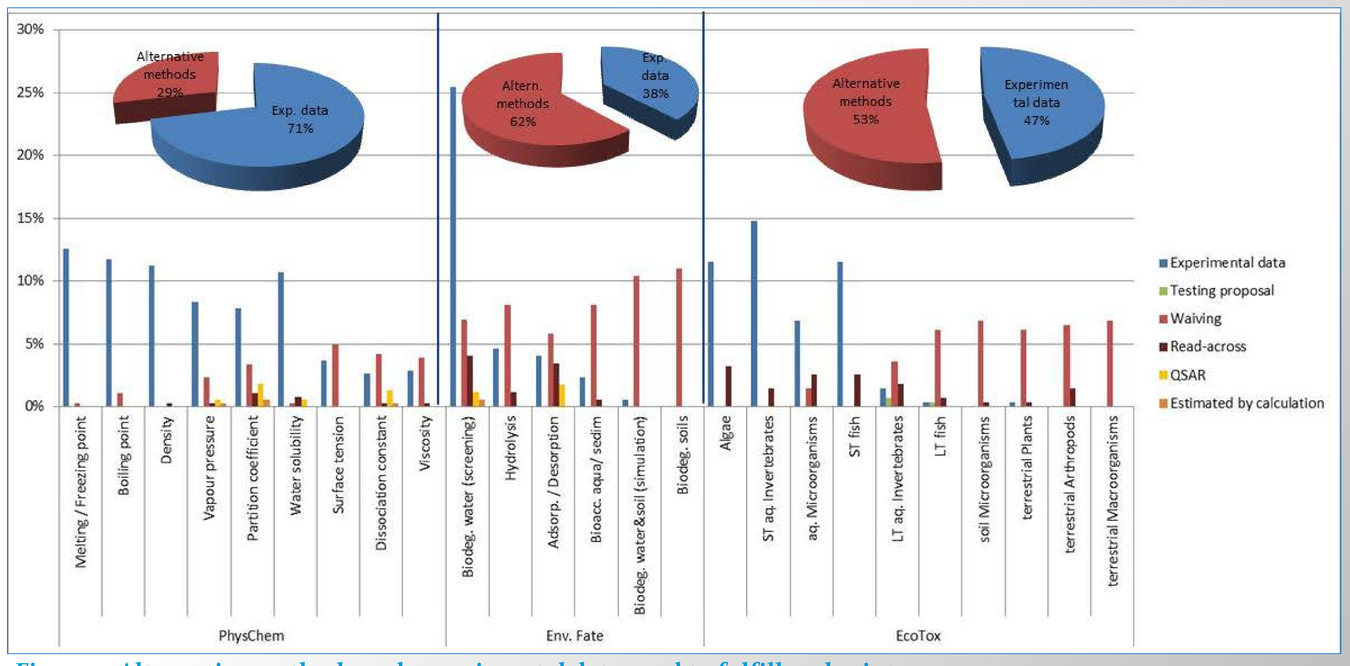

Figure 3. Alternative methods and experimental data used to fulfill endpoints

Among the adopted strategies (**Fig.2**), the approach based on key studies (KS) with or without supportive studies (SS) is dominant in both the Phys-Chem (PC) and Ecotoxicological (Ecotox) sections. Waiving is the main strategy adopted for the Environmental fate and pathways (Env Fate) section, followed by the Ecotox and the PC sections, respectively. The main justifications to waive information requirements were explained in "other justification" and were often based on the adaptation possibilities according to the column 2 of Annex VII to IX. The weight of evidence approach (WoE) is poorly represented with a maximum percentage for PC endpoints. It was built using a majority of experimental data's on the registered substance or on analogue substance by read-across (RA) and estimating value by QSAR or calculation except, for the latest, for the Ecotox endpoints.

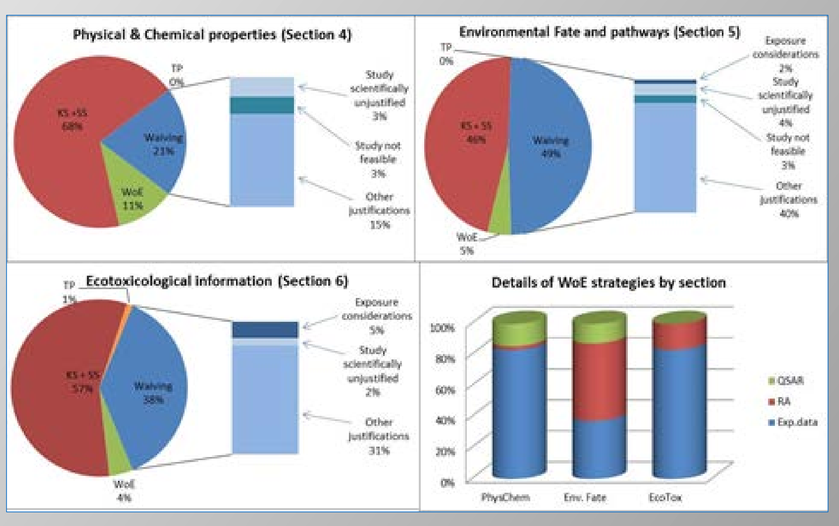

Figure 2. Strategies adopted by IUCLID sections (4, 5 and 6) detailing waiving and weight of evidence

The **table 1** shows that the highest number of spared animals was observed for the long term toxicity endpoint and the main strategy to reach it was by using the waiving (around 90% for bioaccumulation); on the opposite the read-across method was systematically used to avoid unnecessary animal testing for acute toxicity.

Endpoint	OCDE Guideline	Number of fishes used	Number of altern.meth.	Number of spared animals	
Bioaccumulation aquatic (Annex IX)	*305* "Bioaccumulation in Fish: Aqueous and Dietary Exposure" (2011)	*OECD 305* Min.= 40	15	600	Min.
		OECD 305 Max.= 230		3450	Max.
Long-term toxicity to fish (Annex IX)	*210* "Fish, Early-life Stage Toxicity Test" (2000)	*OECD 210* Mean= 300	19	5700	Mean
Short-term toxicity to fish (Annex VIII)	*203* "Fish, Acute Toxicity Test" (1992)	OECD *203* Min.= 14	7	98	Min.
		OECD 203 Max.= 42		294	Max.
				6398	Min. total
				9444	Max. total

Table 1. Number of spared animals

Discussion & Conclusion

For the second registration of REACH, more than half of the endpoints were fulfilled with experimental data's on the registered substance (57%) and the other endpoints by using alternative methods. This global strategy is comparable to the one adopted for REACH 2010 registration as presented by Deviller *et al.* (2011) with a slight increase of the experimental data coverage and an evolution of alternative methods with less testing proposal and waiving and more read-across. The testing proposal had only been submitted for higher tier studies in aquatic toxicology. We also noted that the justification flagged for the waiving has changed from mostly "study scientifically unjustified" to "other justifications". This might be due to the different interpretations that can be made of the possibilities of adaptation according to the Annex XI. Estimated data's by QSAR and other calculations have only been used to address a restricted number of Phys-Chem and Environmental fate properties. This might be explained by specific knowledge required in computational toxicology and the limited acceptability of these data's for some properties. The read-across was the most commonly used method to fulfill information gaps as already observed for REACH 2010 registration (ECHA, 2011). In the future, a larger use of the weight of evidence approach might be a way of improving the legitimacy and the acceptability of estimated data and read-across.

A minimum of 6400 fish has been spared thanks to the adaptation of the standard testing regime. Data waiving was the main strategy that allowed to avoid unnecessary testing on vertebrates. This result is encouraging and should be improved for the next registration tonnage band (2018) by using other alternative methods at a larger extend.

References

Deviller *et al.*, Opportunities and limitations of using alternatives methods and non testing strategies in REACH registration dossiers. SETAC Europe 21st Annual meeting, 2011.
ECHA. The use of alternatives to testing on animals for the REACH regulation, 2011.

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