European Commission
Enterprise and Industry Directorate-General

REACH and alternative testing: the REACH information requirements and the perspectives to use alternatives to animal experimentation

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WHY REACH?

Existing Chemicals Legislation

- Data gaps: 86% of HPVCs have less than base set data
- The process takes (too much) time
- Burden of proof on public authorities
- Administrative burden for new chemicals (low volume) prevents innovation

REACH: Main features

- New registration requirements for old substances to ensure safe use of chemicals.
- Burden on industry to generate information about substances and adopt risk management measures
- Data sharing as a general principle.

REACH: Main features

Registration dossier

- **For** Chemical Safety Assessment
- **For** Classification and Labeling **of chemicals (C&L)**
- **For the identification of** Persistent, Bioaccumulative and Toxic **(PBT) and** very Persistent very Bioaccumulative **(vPvB) substances**

REACH Context

- Article 1.1: ..purpose of REACH is to ensure a high level of protection on HH and ENV as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation..
- Article 25.1:.. Testing on vertebrate animals for the purpose of REACH shall be undertaken only as a last resort… necessary to take measures limiting duplication of other tests..

Standard information requirements under REACH

- Guidance note on fulfulling the requirements of Annexes (explained in Annex VI)
- Standard information requirements are listed in Annex VII to X:
  - Minimum information in Technical Dossier depends on volume:

≥ 1 tonne/y:	Annex VII	(~20,000 subst)
≥ 10 tonnes/y:	Annex VIII	
≥ 100 tonnes/y:	Annex IX	
≥ 1000 tonnes/y:	Annex X	(2,500 subst)

Information on intrinsic properties of a chemical to be provided

- Phys-chem properties (e.g. solubility, vapour pressure)
- Toxicity properties (e.g. acute toxicity, irritation, mutagenicity, carcinogenicity)
- Fate properties (e.g. (bio)degradation, partition coefficients)
- Ecotoxicity properties (e.g. toxicity to aquatic or terrestrial organisms)

Adaptation of information requirements under REACH

- Information requirements, not data requirements
- Standard information is no tick-list

and

- Extensive possibilities of adaptation of information requirements

Adaptation of information requirements under REACH

- Specific adaptations for individual endpoints (Annexes VII – X, column 2)

- General adaptations (Annex XI)
  - Testing is not scientifically necessary
  - Testing is technically not possible
  - Substance-tailored exposure-driven testing

Annex IX REACH

COLUMN 1 STANDARD INFORMATION REQUIRED	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
8.6.2. Sub-chronic toxicity study (90-day), one species, rodent, male and female, most appropriate route of administration, having regard to the likely route of human exposure.	8.6.2.The sub-chronic toxicity study (90 days) does not need to be conducted if: – a reliable short-term toxicity study (28 days) is available showing severe toxicity effects according to the criteria for classifying the substance as R48, for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure; or – a reliable chronic toxicity study is available, provided that an appropriate species and route of administration were used; or – a substance undergoes immediate disintegration and there are sufficient data on the cleavage products (both for systemic effects and effects at the site of uptake); or – the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day "limit test", particularly if such a pattern is coupled with limited human exposure.

Process for obtaining information

Generate new data / propose testing strategy:

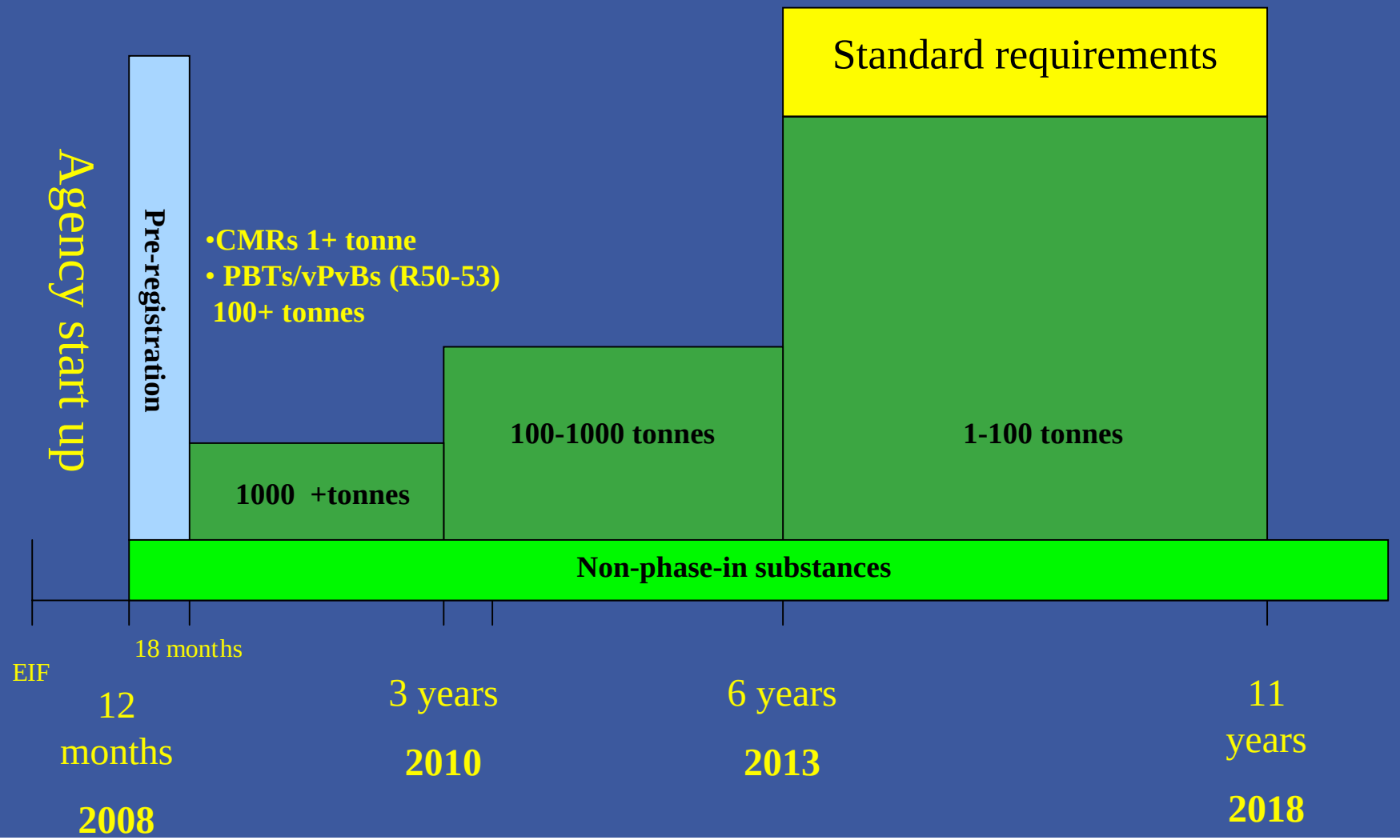
- **Endpoints in Annexes VII and VIII**
  - **Not requiring use of vertebrate animals,**
    → conduct test
  - **Requiring use of vertebrate animals, assess whether a suitable *in vitro* test method is available and, if possible,**
    → conduct *in vitro* test
  - **Requiring use of vertebrate animals but no suitable *in vitro* test method is available,**
    → conduct *in vivo* test

Testing proposal

- **Endpoints in Annex IX and X:**
  - **Not requiring use of vertebrate animals, → testing proposal**
  - **Requiring use of vertebrate animals, when a suitable *in vitro* test method is available → testing proposal for *in vitro* test**
  - **Requiring use of vertebrate animals but no suitable *in vitro* test method is available**

    → testing proposal for *in vivo* test

When dossiers



Timing of testing proposals

- **Endpoints in Annex X (>1000 tonnes):**
  - **Testing proposal to be submitted in spring 2010**
  - **Agency to evaluate testing proposals by spring 2012**
- **Endpoints in Annex IX (>100 tonnes):**
  - **Testing proposal to be submitted in spring 2013**
  - **Agency to evaluate testing proposals by spring 2016**

⇨ **This time can be used to develop alternative testing**

Annex XI: general rules for adaptation

→ Testing not scientifically necessary

- Use of existing data (not GLP/ non standard tests)
- Historical Human data
- Weight of evidence
- (Q)SAR
- *In vitro* methods
- Grouping of substances and read-across approach

→ Testing technically not possible

→ Testing not necessary because of limited exposure

Promotion of non-animal testing throughout REACH

- **REACH article13.1 ((Q)SAR, grouping)**
- **Guidance note of Annex VI (the 4 steps in information gathering**
- **Annex VII-X (column 2 adaptations)**
- **Annex XI (general rules for adaptation)**

But:

Alternative information needs to be adequate for C&L and/or RA

Further measures to reduce animal testing

→ **Data sharing**

→ **Develop alternative methods (ECVAM, RTD)**

→ **Revision of Test methods regulations based on 3-Rs principle:**

Testing according to COM Regulation (replacing current Annex V to 67/548/EC), which shall be revised as appropriate in particular to refine, reduce or replace animal testing

→ **Review of the Annexes**

Basic principles of data-sharing

1. OSOR (One Substance, One Registration): Vertebrate testing information must be shared, new tests only once, SIEF mechanism
2. Right to access prior studies.
3. Data and cost sharing.

Ongoing RESEARCH via the Commission

ERP currently allocates nearly €30 million to three Integrated Projects involving over 90 public and industrial laboratories.

The A-Cute-Tox (2005-2010) initiative: Acute systemic toxicity to replace present in vivo procedures in this field. The work involves reviewing existing technologies, identifying error factors, developing new tools and, finally, designing a global strategy amenable for robotic testing and linked to a computer forecasting model.

ReProTect (2004-2008) project is concerned with reproductive toxicity. Specific working groups for, e.g. masculine or feminine fertility, embryo implantation, pre- or post-natal development, and transverse techniques. in vitro tests, computer models and sensors are being examined, developed if necessary, and then incorporated in a global strategy for the analysis of chemical products.

Sens-it-iv (2006-2010) is looking at the question of the hypersensitivity of the lungs and skin to certain products.

Aim:to develop a global strategy for in vitro analyses.

The methods developed will pass to the ECVAM for validation before coming before the European regulators (ECB) and the OECD .

CONCLUSION

- REACH requires industry to prove that chemicals can be used safely
- Animal tests are still needed as part of methods to generate information
- However, REACH is flexible and encourages the use of existing information and alternative methods
- All forces should work together to actively develop output of alternative methods