REACH

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What is REACH ?

- REGULATION of European Parliament and Council (EC) no. 1907/2006 of 18 December 2006
- In force in EU member states as of 1 June 2007 (no approval by the National Parliaments needed)
- In case of non-compliance with current national legislation, that national legislation should be changed

What is REACH ?

New requirements for

the introduction

of chemicals on EU market

What is REACH ?

R egistration

E valuation

A uthorization

CH emicals

MAIN FEATURES OF REACH

- **Registration**: coherent system designed to provide basic hazard and risk information on **new** and **existing** chemical substances **manufactured** in or **imported** into the EU

- **Evaluation**: in hands of the **authorities** to check the completeness of the registration dossiers and to ensure that risks raised by chemicals are safely controlled

- **Authorisation**: procedure for the most hazardous substances with the aim to gradually squeeze them out of the market and consequently **substitute** them by safer substances, providing they are economically and technologically equivalent;

- **Ch**emicals **Restriction** process in parallel

Why REACH ?

- The purpose of this Regulation is to ensure
  - a **high level of protection** of human health and the environment,
  - including the **promotion of alternative methods** for assessment of hazards of substances,
  - as well as the **free circulation of substances** on the internal market
  - while **enhancing competitiveness and innovation**

OBJECTIVES OF REACH

- Previous system for chemicals management in the EU was inefficient
- Difficult to identify and to address risks:
  - Lack of information about substances on the market produced before 1981
  - No efficient instrument to deal with problematic substances
  - Burden of proof on public authorities!

OBJECTIVES OF REACH

- EU distinguishes between so called „old“ chemicals entering the market before 1981 (ca. 102.000, listed in EINECS) and „new“ chemicals (> 3.200) after 1981
- General lack of knowledge about the properties of old chemical substances because up to 1981 it was possible to market the chemicals without any formal authorisation (and insufficient evaluation)
- Vast majority of existing chemicals (around 105.000) with unknown or not sufficiently known properties. So far, only about 9.000 (= 8%) chemicals are sufficiently investigated with respect to the human´s health and the natural environment

REACH REQUIREMENTS

Reversal of burden of proof from authorities to

- industry
- manufacturer,
- importer,
- supplier,
- downstream users

for testing and risk assessment of chemicals.

Shift of responsibility

from authorities to industry

DOWNSTREAM USERS (DU)

- Manufacturer/importer registration to cover all uses identified by downstream users
- DU must
  - implement supplier's risk reduction measures for identified uses
- DU need to:
  - enter into dialogue with their suppliers
  - consider consortia building and/or cost sharing
- DU may need to apply for authorisation

REACH – KEY TIMETABLE

MAIN CHARACTERISTICS OF REACH

- Registration is submitted to European Chemicals Agency
- All substances > 1 t/year/manufacturer or importer must be registered. **Non-registered substances shall not be manufactured or placed on EU market**
- „No data – no market“
  Registration implies ensuring appropriate information
- Downstream users are involved in the system

Hazard identification

Data adequacy

Data must be evaluated on the base of their reliability and relevance

Data reliability can be evaluated by means of the Klimisch code of reliability (Klimisch et al. 1997)

- 1: reliable without restriction
  - according to valid or internationally accepted guidelines (preferably GLP)
- 2: reliable with restrictions
  - not entirely according to accepted guidelines (often not GLP), but well documented
- 3: not reliable
  - Not accepted method, irrelevant exposure, species etc.
- 4: Not assignable
  - Do not give sufficient experimental details

REACH: REGISTRATION

- Registration not required for
  - substances for use in research activities
  - polymers
  - radioactive substances
  - substances in drugs or nutrient, additives, pesticides
  - REACH appendix IV (e.g. water, natural oils)
  - REACH appendix V (e.g. minerals, coal)

  -Information required will be proportional to production volumes and risk potentials

REGISTRATION DOSSIER

Technical Dossier including:

(i) the identity of the manufacturer(s) or importer(s)

(ii) the identity of the substance

(iii) information on the manufacture and identified use(s) of the substance

(iv) the classification and labelling of the substance

(v) guidance on safe use of the substance

(vi) study summaries (physicochemical, toxicological and ecotoxicological data)

INTRODUCTION TO CSA/CSR

- What is Chemical Safety Assessment/Chemical Safety Report:
  - The CSA is a Risk Assessment exercise that must be carried out by the registrant for the production step and the uses of a substance along the supply chain.
  - The CSA is documented in the CSR in accordance with the format reported in Annex I.
- When CSA is needed:
  - For all substances subjected to Registration and manufactured/imported at > 10 tonnes/year.
  - For all substances subjected to Authorisation (CMR class 1 and 2, PBT, vPvB or substances of "equivalent level of concern")
- Why CSA is needed:
  - To ensure the safe use of the substance by identifying and applying the "appropriate measures to adequately control the risks identified"

CSA/CSR OVERVIEW - CSA PROCESS

- **Hazard identification and assessment**

  a) Human health hazard assessment

  b) Physicochemical hazard assessment

  c) Environmental hazard assessment

  d) Persistent, bioaccumulative and toxic (PBT) and very persistent very bioaccumulative (vPvB) assessment

If the substance is classified as dangerous (in accordance to 67/548/EEC) or meets PBT or vPvB criteria, then:

- **Exposure assessment**, including:
  - Generation of the Exposure Scenarios (ES)
  - Exposure estimation
- **Risk characterisation** (human health, environment)

Hazard identification

Information requirements (depending on tonnage band)

1-10 tonnes/y Annex VII

- P/C properties
- Irritation assessment
- Sensitisation
- Acute oral toxicity
- in vitro mutagenicity
- Acute ecotoxicity (daphnia/algae)
- Biodegradation

10-100 tonnes/y Annex VIII

- Skin and eye irritation
- Acute toxicity (other route)
- in vitro mutagenicity
- in vivo mutagenicity
- 28-day repeated toxicity
- Developmental toxicity (screening)
- Acute ecotoxicity (fish)
- Microbial resp inhibition
- Hydrolysis
- Absorption/desorption

+ ANNEX VII

100-1000 tonnes/y Annex IX

- 90-day repeated toxicity
- Developmental toxicity
- Reproductive toxicity
- Long-term aquatic toxicity
- Further biodegradation studies
- Bioaccumulation
- further absorption/desorption
- Terrestrial organism toxicity

+ ANNEXES VII, VIII

> 1000 tonnes/y Annex X

- Chronic toxicity /carcinogenicity study
- Further developmental toxicity
- Further ecotoxicological data
- Further biodegradation study

+ ANNEXES VII, VIII, IX

Hazard identification

Possible waiving options

Testing not technically feasible

Due to inherent properties of the substance and technical limitations of the experimental procedures.

Some examples:

- Dermal toxicity generally not required for gasses
- Aquatic ecotoxicity not required for substances highly insoluble in water
- Log Kow not applicable for surfactants
- Biodegradability not applicable to inorganic substances

Hazard identification

Possible waiving options

Testing not scientifically necessary

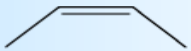
- **Existing data** – An acceptable (i.e. relevant and reliable) study is already existing
- **Human data** -Epidemiological studies, clinical data, occupational exposure data. Rather strict acceptability criteria
- **(Q)SAR** – provided that the method is scientifically valid and applicable to the substance
- ***In vitro* alternatives** – Validated methods must replace *in-vivo* studies. However, suitable non validated methods may be accepted for the **hazard identification** and eventually lead to study waiving
- **Category and Read across** – The properties of a substance can be predicted from reference substance(s) on the ground of chemical analogies, such as:
  - The presence of a common functional group
  - A common precursor and/or common breakdown products via physical or biochemical processes
  - A constant pattern in the changing of the properties across the category

Hazard identification

Possible waiving options

Example on grouping and read across

Source: Rila et al., 2006

	1-Butene	2-Butene	Isobutylene
			
Molecular weight	56.11	56.11	56.11
Melting point [°C]	-185.3	-138.9; -105.5	-140.4
Water solubility [mg/l]	222	265 to 700	263
Log Kow	2.40	2.31 to 2.33	2.31 to 2.33
Genotoxicity (*in vitro*)	Ames test: neg (+/- S9)	Ames test: neg (+/- S9); chromo. aberr.: neg	Ames test: neg; Mouse lymphoma: neg
Genotoxicity (*in vivo*)	Micronucleus: neg	No data	Micronucleus: neg

HAZARD IDENTIFICATION
POSSIBLE WAIVING OPTIONS

Exposure - driven testing (Exposure based waiving, EBW)

- Data generation can be avoided by showing that the toxicity of the substance occurs at (much) higher levels than the predictable exposure levels (Risk-based waiving)

For example:

A (sub)chronic toxicity (90-day) study could be not necessary if the NOAEL of the subacute (28-day) study is significantly higher than the predicted exposure levels.

But…

- Robust information on the exposure are needed to support this strategy

HAZARD ASSESSMENT – DNEL EXTRAPOLATION

The Derived No Effect Level (DNEL) is calculated from the most appropriate NOAEL available from repeated dose (subacute, subchronic or chronic) or reproductive toxicity studies

$$DNEL = \frac{NOAEL}{\text{Overall Assessment Factor}}$$

Default AF values

Interspecies	Toxicokinetics (differences in metabolic rates)	Rats 4 Mouse 7 Dog 2
	Toxicodynamics (other differences)	1-2.5
Intraspecies	Workers	5
	General population	10
Exposure duration	Subacute-to-chronic	6
	Subchronic-to-chronic	2
	LOAEL-to-NOAEL (severity of the effects and steepness of the dose-effect relationship)	3-10
Quality of the dataset	Completeness of the dataset/reliability of the alternative data	Case by case

HAZARD ASSESSMENT – DMEL EXTRAPOLATION

- A DMEL (derived minimal exposure level) shall be derived in the case no NOAEL can be defined (i.e. genotoxic carcinogens).

- The DMEL is a probabilistic parameter indicating the exposure level associated with an acceptable lifetime cancer risk ($1x10^{-4}$ – 10^{-6}, depending on the background incidence of the type of tumor)

- It is derived from a descriptor indicating the carcinogenic potency (T25, BMD10 or others) of the substance, divided by assessment and correction factors (similarly to DNEL).

CONCLUSIONS

- Toxicologists play a key and unique role in the preparation / support/development of technical dossiers and CSA/CSR which are foreseen by REACH.

- It is a fundamental role when future discussion with ECHA and/or Member States C.A. will occur.

- Hence there is a clear need for further developing a solid "Risk Assessor" professional expertise and function that can be used by various stakeholders such as industry, regulators (ECHA, C.A.) and Academia.

TOXICOLOGY LABORATORY