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Management-Team

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SIEF, Data Sharing and Cost Effective Strategies for REACH Registration

Dr. Michael Cleuvers
Head of Business Unit
Industrial Chemicals – REACH

Member of HELSINKI REACH CENTRE HRC

REACH Ready Approved Supplier

REACh NET

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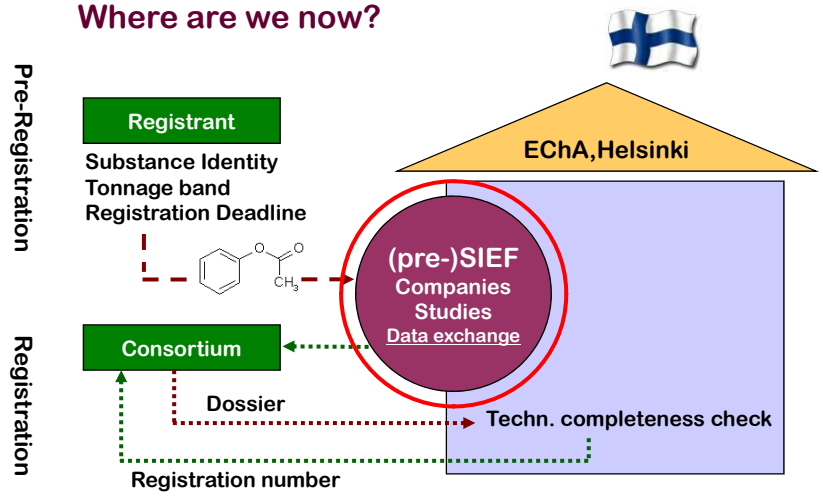
Where are we now?



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From pre-registration to pre-SIEF to SIEF

REACH-IT brings companies that pre-registered the "same" substance together in a "pre-SIEF" webpage

Pre-registrations: 2.750.000

Companies: 65.000

Substances: 146.000

If pre-SIEF members agree on sameness definition, e.g. using a „"Substance Identification Profile (SIP)" the pre-SIEF moves to the SIEF-status

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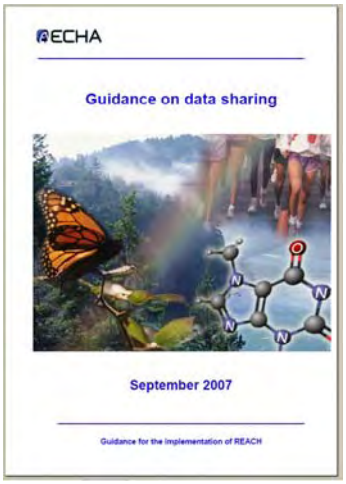

4.3 Obligations of SIEF Participants

All SIEF Participants shall:
- React to requests for information from other participants
- Provide other participants with existing studies upon request

Potential Registrants shall:
- Request missing information from other SIEF participants
- Collectively identify needs for further studies to comply with registration requirements
- Make arrangements to perform the studies
- Agree on classification and labelling

Communication within SIEF - SIEF Formation Facilitator (SFF)

Exchange of information within a SIEF will be greatly facilitated if one participant agrees to play the role of a coordinator and initiate the acting together.

It would be helpful if the "Lead Registrant to be" or another participant would take the initiative already at the SIEF formation stage.

Acting as a SIEF Formation Facilitator is voluntary and does not entail any specific obligation. It simply means that the company/companies volunteering are those expected to take the initiative to contact the others within the pre-SIEF;

Next step for the facilitator or designated Lead Registrant:
to make proposals related to any or all of the possible following steps:

The form of co-operation (consortium?) between the parties and possible internal rules

Who could perform the necessary technical work (either the Potential Registrants themselves or a contracting Third Party or a combination of both)

Scope of the co-operation: whether the co-operation should be limited to the SIEF obligations (data sharing and classification and labelling) or whether it should be extended to cover other objectives

Organization of the exchange of data

Designation of a Lead Registrant (unless this has already been done)

Data sharing

Step 1 Individual gathering of information available to Potential Registrants

Step 2 Agreement on the form of cooperation/cost sharing mechanism

Step 3 Collection and inventory of information available to Potential Registrants

Step 4 Evaluation of available information

Step 5 Consideration of information needs

Step 6 Identification of data gaps and collection of other available information

Step 7 Generation of new information/testing proposal

Step 8 Data and cost sharing

Step 9 Joint submission of data

Cost Effective Strategies for REACH Registration:

Be prepared for cost sharing issues

Avoid new animal testing whenever possible and justifiable

REACH in Practice: Cost Sharing

As data gathering induces costs, data sharing implies some form of cost sharing. As required under the REACH Regulation, parties sharing data must make "every effort to ensure that the costs of sharing the information are determined in a fair, transparent and non-discriminatory way" (Article 27(3) and 30.1).

Agreement on cost sharing usually requires parties to agree on:
(1) the reliability, relevance and adequacy of the data ("Data Quality")
(2) the economic value of the data ("Data Valuation"), and
(3) how the agreed value is shared among parties ("Cost Allocation / Compensation")

The current value of all study reports should be determined in accordance with the respective guidelines.
This serves as the measurement base for subsequent cost allocation and compensation and determines also the costs for the Letter of Access (LOA)

REACH in Practice: Cost Sharing

In the absence of specific rules, Potential Registrants are free to select any cost allocation and compensation mechanism that they perceive to be fair, transparent and non-discriminatory. Possible mechanisms include:

- Sharing data equally, based on the number of parties involved
- Proportionality, based on production or sales volume
- Alternative mechanisms using part of the models in different mode

The REACH Regulation refers to equal sharing as a default mechanism in some cases and this will be an important element. However, parties are free to agree on any model

REACH in Practice: Cost Sharing

Pursuant to Art. 30(1), registrants are only required to share the costs of information that they are required to submit to satisfy their registration requirement.

Therefore, companies cannot be forced to pay for studies that they do not need and they also cannot be forced to pay before they actually need them in their respective tonnage band.

However whenever the (potential) registrant requests data earlier, he has to pay on receipt of the data.

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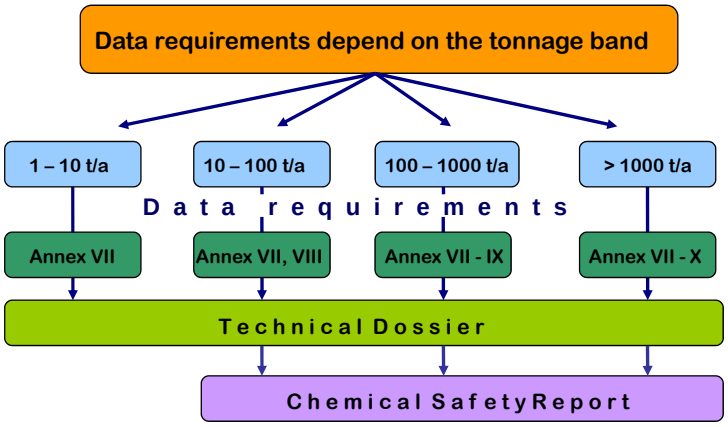
Data requirements



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Data requirements

Phys.-chem.	Toxicology	Ecotoxicology
Density Melting / Boiling point Water solubility Vapour pressure Partition coefficient Flashpoint (Self-)Ignition temperature Explosivity Surface tension Oxidising properties Granulometry	Acute toxicity (oral) Skin irritation (in-vitro) Eye irritation (in-vitro) Skin sensitisation Mutagenicity (Ames-Test)	Acute Daphna toxicity Toxicity to algae Biodegradation
Stability in org. solvents Identity of metabolites Dissociation constant Viskosity	Skin irritation (in-vivo) Eye irritation (in-vivo) In-vitro-cytogenicity tests In-vitro-gene mutation test Acute toxicity (dermal/inhalativ) Assessment of toxicokinetic behaviour Short-term-toxicity (28 d-Test) Reproduction-/developmental toxicity (Screening-test)	Short-term-toxicity to fish Activated Sludge Abiotic degradationt Adsorption-/Desorption
	Subchronic toxicity (90 d-Test) Reproduction toxicity Prenatal developmental toxicity 2-Generation-reproduction toxicity	Daphnia-reproduction test Long-term-toxicity to fish Biodegradation in water Biodegradation in soil Biodegradation in sediment Identification of degradation products Bioaccumulation in fish Adsorption-/Desorption Acute toxicity to terr. invertebrates Soil microorganisms Short-term-toxicity to plants
	Developmental toxicity Carcinogenicity	Biodegradation Environmental fate Long-term-toxicity terr. invertebrates Long-term-toxicity sediment organisms Long-term-toxicity to birds

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Data requirements

Article 13 (1) of REACH states that *information on the intrinsic properties of substances may also be generated by means other than tests..... In particular for human toxicity, information shall be generated* ***whenever possible*** *by means other than vertebrate animal tests, through the use of alternative methods, for example, in vitro methods or qualitative or quantitative structure-activity relationship models* ***or from information from structurally related substances (grouping or read-across)*****.**

Consequentially, within the 847 pages of the REACH regulation the term „*study requirement*" does not occur. Not once.

Instead of that, „*information requirements*" have to be fulfilled.

Annex VII – X:

„Before new tests are carried out to determine the properties listed in this Annex, all available in vitro data, in vivo data, historical human data, data from valid (Q)SARs and data from structurally related substances (read-across approach) shall be assessed first"

ECHA

Guidance on information requirements and chemical safety assessment

Chapter R.2: Requirements and generation of information on intrinsic properties

May 2008

„To achieve a high level of protection of human health and the environment **while limiting the need for additional testing**, all available data on the intrinsic properties of a substance **must first be evaluated**. Where available data are not adequate to meet the requirements of the REACH Regulation, additional testing may need to be generated. However, **before embarking on animal testing, use of alternative methods and all other options must be considered**".

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ANNEX VI
INFORMATION REQUIREMENTS REFERRED TO IN ARTICLE 10
GUIDANCE NOTE
ON FULFILLING THE REQUIREMENTS OF ANNEXES VI TO XI

STEP 1 — GATHER AND SHARE EXISTING INFORMATION
gather all existing available test data on the substance to be registered, this would include a literature search for relevant information on the substance

STEP 2 — CONSIDER INFORMATION NEEDS
identify what information is required for the registration. In particular, information on exposure, use and risk management measures shall be considered at this stage

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ANNEX VI
INFORMATION REQUIREMENTS REFERRED TO IN ARTICLE 10
GUIDANCE NOTE
ON FULFILLING THE REQUIREMENTS OF ANNEXES VI TO XI

STEP 3 — IDENTIFY INFORMATION GAPS
The registrant shall then compare the information needs for the substance with the information already available and identify where there are gaps.

STEP 4 — GENERATE NEW DATA/PROPOSE TESTING STRATEGY
In some cases it will not be necessary to generate new data. However, where there is an information gap that needs to be filled, new data shall be generated.

ANNEX XI
GENERAL RULES FOR ADAPTATION OF THE STANDARD TESTING REGIME SET OUT IN ANNEXES VII TO X

1.TESTING DOES NOT APPEAR SCIENTIFICALLY NECESSARY

a) Use of existing data

- Data on physical-chemical properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3)
- Data on human health and environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3)
- Historical human data

ANNEX XI
GENERAL RULES FOR ADAPTATION OF THE STANDARD TESTING REGIME SET OUT IN ANNEXES VII TO X

1. TESTING DOES NOT APPEAR SCIENTIFICALLY NECESSARY

b) Weight of evidence
c) Qualitative or Quantitative structure-activity relationship ((Q)SAR)
d) In vitro methods
e) Grouping of substances and read-across approach

2. TESTING IS TECHNICALLY NOT POSSIBLE

3. SUBSTANCE-TAILORED EXPOSURE-DRIVEN TESTING

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First conclusion:

REACH offers possibilities to avoid unnecessary testing in the regulation itself:

- Use of all available data: in-house data, Literature/database searches
- QSAR-Modelling (Quantitative Structure Activity Relationships)
- Grouping (Category approach)
- Bridging (Read-across)
- Exposure-based Waiving (EBW)

No data gaps, but no unnecessary testing!

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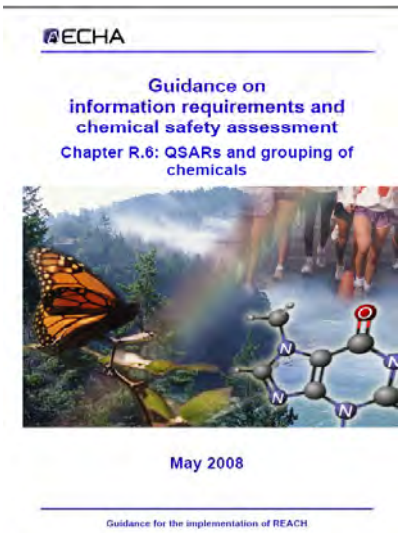
READ-ACROSS / CATEGORY APPROACH



Grouping (category approach) & read-across

Substances whose phys.-chem., tox and ecotox properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or 'category' of substances.

The similarities may be based on:

(1) a common functional group (e.g., aldehyde, epoxide, esters, specific metal ion);

(2) the common precursors and/or the likelihood of common breakdown products via physical and biological processes, which result in structurally similar chemicals; or

(3) a constant pattern in the changing of the potency of the properties across the category.

Benefits of the chemical category approach

- data from one or more chemicals can be interpolated or extrapolated to other chemicals, reducing the need to test for every endpoint for every chemical;
- the use of animal testing is reduced;
- the category evaluation is based on a greater body of data than on data on a single compound;
- the identification of compounds as members of a category provides an insight into the potential effects of the compounds that might otherwise be overlooked
- in most cases, category testing can be completed earlier than individual tests for each chemical that requires registration

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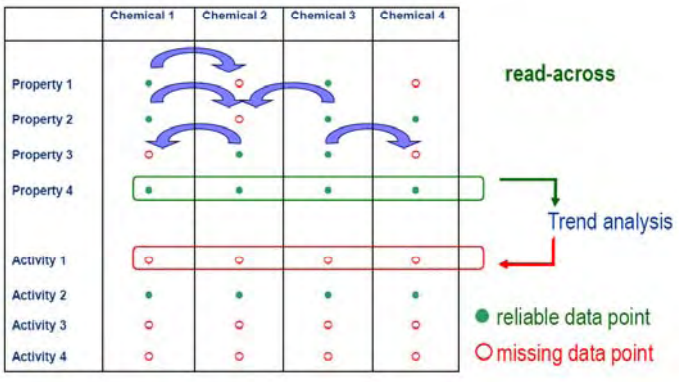
Category approach



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Example 1: Lithium salts with inert anions

Lithium salts of strong or medium acids will exert any biological effect by virtue of their lithium content. The following anions are stable in water and will have little effect on the disposition and physiological effects of the lithium cation:
Acetate, bromide, iodide, carbonate, chloride, meta-borate, phosphate, ortho-silicate, meta-silicate, sulphate, sulphite, and tetra borate.

Neither compound (nor any of their sodium analogues) is classified in Annex I of Directive 67/548/EEC. The aquatic ecotoxicity of Lithium compounds in general is considered to be low (WGK: 1, low hazardous to waters).

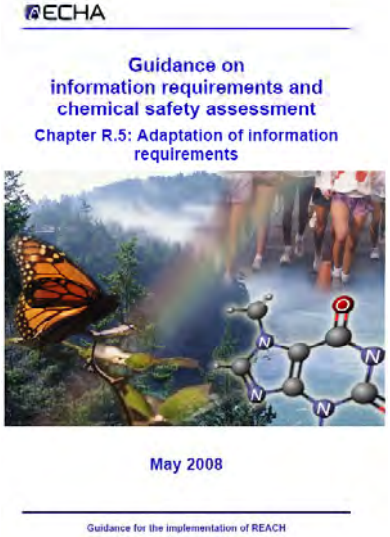
Example 2: Zinc salts

Zinc is labelled R50/53. The free zinc ion in solution is highly toxic to plants, invertebrates, and even vertebrate fish. The Free Ion Activity Model (FIAM) is well-established in the literature, and shows that just micromolar amounts of the free ion kills some organisms. A recent example showed 6 micromolar killing 93% of all Daphnia in water*.
Thus, for a lot of zinc compounds the aquatic ecotoxicity is predictable without additional testing.

*Muyssen, Brita, T. A.; De Schamphelaere, Karel A. C.; Janssen, Colin R. (2006). "Mechanisms of chronic waterborne Zn toxicity in Daphnia magna". Aquatic Toxicology 77 (4): 393–401.

- Within the analogue and category approaches, data gaps can be filled by read-across
- This avoids the need to test every substance for every endpoint
- Results should be adequate for classification and labelling and/or risk assessment
- Adequate and reliable documentation of the applied method shall be provided
- Strong expertise is indispensable

EXPOSURE BASED WAIVING (EBW)



„Waiving“ means
to prepare a sound justification for a non-submission of data

“In situations where human or environmental exposure is absent or so low that additional effects information will not lead to improvement of risk management, exposure-based waiving may be considered”.

“REACH allows that certain tests may be waived based on exposure scenario(s) or on absent, unlikely, not relevant or not significant exposure. These provisions were included to avoid unnecessary animal testing”.

Exposure-driven testing (Annex XI (3))

Testing according to Annex VIII (only sections 8.6 and 8.7), Annex IX and Annex X may be omitted, based on exposure scenario(s) and related exposure estimation in a CSA.

In all cases, adequate justification and documentation shall be provided. The justification shall be based on an exposure assessment in accordance with section 5 of Annex I

The conditions of use as specified in the ES must be communicated through the chemical supply chain via the SDS or otherwise if an SDS is not required (REACH Article 32).

Starting points for the justification of exposure-based waiving

Specific use or limited emissions, e.g.

- Certain uses are excluded, e.g. no identified consumer uses
- Emissions to certain environmental compartments are excluded (e.g., air emissions are limited because the substance is a solid and no significant dusts or fumes are formed).
- No significant exposure, due to e.g. low emissions/ exposure to the substance, for instance due to a combination of substance properties (low vapour pressure, solids etc.) and 'no significant emissions' due to low emission rates and/or tonnage, low frequency of use etc.

Starting points for the justification of exposure-based waiving

Specific operational conditions or use conditions, e.g.

- Use in strictly controlled conditions according to article 18(4), leading to no significant exposure that should be argued in a quantitative way.
- Use in strictly controlled conditions (according to REACH Article 18(4)) and where emission minimisation is already in place

Intensity of use (duration, frequency), e.g.

- Infrequent use due to the function of the substance leading to no significant exposure:

– specialty products for highly specific occupational situations with a low frequency and duration.

Examples:

Type of study to be waived
Repeated dose (dermal)

Substance properties or operational conditions.
The substance is corrosive

Argumentation
The necessary RMM are in place due to well known corrosive effects. Dermal exposure would be not significant and e.g. repeated dose dermal toxicity studies could be waived.

Type of study to be waived
Repeated dose (90d)

Substance properties or operational conditions.
The substance is only used in closed systems, and occasional exposure is limited to maintenance or sampling tasks.
A very small, well-defined and trained group of people is using strict risk management measures, and is exposed occasionally to low levels.

Argumentation
The use pattern of substance is such that long-term exposure can be excluded. Expert judgement is necessary to justify the case, for instance based on evaluation of the available acute toxicity and sub-acute toxicity indicating low toxicity.

Type of study to be waived
Repeated dose by inhalation

Substance properties or operational conditions.
The substance is a solid at room temperature and no or very little dust is formed for the intended uses.
The substance is a liquid with a very low vapour pressure, is used in closed systems and no aerosols are formed in the process.

Argumentation
Due to physicochemical properties inhalation is absent. The formation of dust/aerosols is not significant due to the specific operational conditions (supporting information/measurements).

Conclusion

REACH in general demands a lot of „data“ or „information“, but the decision how to deal and/or how to fill data-gaps is up to the registrant.
Registrants are encouraged to use non-testing approaches (as much as scientifically justifiable) before going for animal testing

There is good guidance available for these issues, but scientific expertise is necessary to prepare sound and justifiable approaches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