How to bring your registration dossier in compliance with REACH – Tips and Hints

Part 1

Hints and Tips on Physico-chemical, environmental and human health related endpoints

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Environmental endpoints

Aquatic Toxicity

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Environmental endpoints

Aquatic Toxicity – information requirements (1/4)

REACH Annex	Column 1	Column 2
Annex VII	9.1.1. Short-term toxicity testing on invertebrates (preferred species *Daphnia)* The registrant may consider long-term toxicity testing instead of short- term.	9.1.1. The study does not need to be conducted if: — there are **mitigating factors indicating that aquatic toxicity is unlikely to occur**, for instance if **the substance is highly insoluble in water or the substance is unlikely to cross biological membranes**, or — a long-term aquatic toxicity study on invertebrates is available, or — adequate information for environmental classification and labelling is available. The **long-term aquatic toxicity study** on *Daphnia* (Annex IX, section 9.1.5) **shall be considered if the substance is poorly water soluble**.

Aquatic Toxicity – information requirements (2/4)

REACH Annex	Column 1	Column 2
Annex VII	9.1.2. Growth inhibition study aquatic plants (algae preferred)	9.1.2. The study does not need to be conducted if there are **mitigating factors indicating that aquatic toxicity is unlikely to occur** for instance if **the substance is highly insoluble in water or the substance is unlikely to cross biological membranes**.

Aquatic Toxicity – information requirements (3/4)

REACH Annex	Column 1	Column 2
Annex VIII	9.1.3. Short-term toxicity testing on fish: the registrant may consider long-term toxicity testing instead of short- term.	9.1.3. The study does not need to be conducted if: — there are **mitigating factors indicating that aquatic toxicity is unlikely to occur**, for instance if **the substance is highly insoluble in water or the substance is unlikely to cross biological membranes**, or — a long-term aquatic toxicity study on fish is available. Long-term aquatic toxicity testing as described in Annex IX shall be considered if the chemical safety assessment according to Annex I indicates the need to investigate further effects on aquatic organisms. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment. The **long-term aquatic toxicity study** on fish (Annex IX, Section 9.1.6) shall be considered if the substance is poorly water soluble.

Aquatic Toxicity – information requirements (4/4)

REACH Annex	Column 1	Column 2
Annex IX	9.1. Aquatic toxicity	9.1. Long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment according to Annex I indicates the need to investigate further the effects on aquatic organisms. The choice of the appropriate test(s) depends on the results of the chemical safety assessment.
	9.1.5. Long-term toxicity testing on invertebrates…	
	9.1.6. Long term toxicity testing on fish…	

Aquatic Toxicity

The following IUCLID fields are relevant:

- 6.1.1 short-term toxicity to fish,
- 6.1.2 long-term toxicity to fish,
- 6.1.3 short-term toxicity to aquatic invertebrates,
- 6.1.4 long-term toxicity to aquatic invertebrates,
- 6.1.5 toxicity to aquatic algae and cyano bacteria,
- 6.1.6 toxicity to aquatic plants other than algae,
- 6.1.7 toxicity to microorganisms
- 6.1.8 toxicity to other aquatic organisms

Testing vs. Adaptations:

- Adaptation of the standard testing regime is possible but needs to be justified with a well built justification
- Registrant needs to demonstrate safe use of substance according to REACH Annex I and show that proper Risk Management Measures (RMM) are in place
- Adaptations according to:
  - Column 2 of REACH Annexes (VII – IX)
  - REACH Annex XI

Adaptations according to Column 2 (Annex VII and VIII)

- The study does not need to be conducted if there are mitigating factors indicating that **aquatic toxicity is unlikely to occur**, for instance if the substance is **highly insoluble in water** or the substance is **unlikely to cross biological membranes**

- Registrant needs to demonstrate that aquatic toxicity is unlikely to occur

- The water solubility endpoint needs to be available

- If adequate information **for ENV classification is available** – no need to test on invertebrates – however testing on algae (according to Annex VII) and fish (according to Annex VIII) is necessary

Substances highly insoluble in water

- Information on water solubility needs to confirm no concerns regarding aquatic toxicity
- Justification on why aquatic toxicity is unlikely to occur needs to be well developed
- Examples of alternative approaches to support column 2 adaptation:
  - Use the transformation/dissolution protocol for inorganic substances
  - Use the Water Accommodated Fraction technique for organic substances

Transformation/dissolution protocol (1/3)

- OECD Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media (OECD, 2001)
- Developed for of metals and sparingly soluble metal compounds for C&L and risk assessment
- Determine the production in the lab of soluble available ionic and other metal-bearing species in aqueous media under conditions representative of those generally occurring in the environment.
- Can be applied to sparingly soluble inorganic substances, including UVCB, determining the release of components, elements and ions and other chemical species.
- Can be used to justify that aquatic toxicity is unlikely to occur due to high insolubility in water (Column 2 adaptation)
- Can also be used for the safety assessment of poorly soluble metals and metal compounds (Annex XI adaptation)

Transformation/dissolution protocol (2/3)

- Column 2 adaptation:
  - Justification that aquatic toxicity is unlikely to occur shall include **all** components/elements/ions potentially solubilised under environmentally relevant conditions

EXAMPLES of column 2 adaptation justifications:

- No release of any component or element is observed in the study, with limits of detection below the PNEC (or the toxicity divided by the AF) for the component/element/ions

- Release of components or elements is observed in the study, but all released components/elements/ions are of very low toxicity (e.g. non hazardous for the aquatic environment according to the CLP)

Transformation/dissolution protocol (3/3)

- Annex XI adaptation:

Justification that the study is not needed (e.g. study scientifically unjustified):

- the substance is a poorly water soluble inorganic, **and**
- the risk of all released components/elements/ions is adequately controlled

EXAMPLES of Annex XI adaptation justifications:

- The release of components/elements/ions is measured in a T/D study, and the analytical determination, cover all potentially relevant components/elements/ions, and the measured levels are below the respective PNECs in all cases.

- The measured levels in the T/D protocol are used to estimate the PECs for each relevant component/element/ion using the OC and RMM, and the RCR are below 1 for all released components/elements/ions

NOTE: If no information on any components/elements/ions is available, a Testing Proposal on the component/element/ion should be considered

EXAMPLES INORGANIC SUBSTANCES

Example 1	Example 2
Metal, metal compound or well characterised substances	Slugs, ashes, substances with unknown impurities, etc.
• The metal/elements/ions to be measured in the T/D study can be determined	• Consider a wide coverage of analytical measurements in the T/D study, not just the main element
• Toxicity information (or indication of lack of hazard) is needed	• The limit of detection should be based on the toxicity information

Water Accommodated Fraction (WAF) technique (1/3)

- Defined in: OECD Guidance document on aquatic toxicity testing of difficult substances and mixtures (ENV/JM/MONO(2000)6)

- An aqueous fraction containing the dissolved and/or suspended and/or emulsified fraction of a multi-component substances (multi-constituent, UVCB) or a mixture.

- WAF contains only the fraction of the multi-component substance that is dissolved and/or present as a stable dispersion or emulsion.

- Test data obtained with WAFs apply to the multi-component substances as an entity.

Water Accommodated Fraction technique (2/3)

- Column 2 adaptation:

Justification that aquatic toxicity is unlikely to occur shall include all components dissolved and/or present as a stable dispersion or emulsion.

EXAMPLES of column 2 adaptation justifications:

- No components dissolved and/or present as a stable dispersion or emulsion observed in the study, with limits of detection below the PNEC (or the toxicity divided by the AF) for all components.

- Release of components is observed in the study, but all released components are of very low toxicity (e.g. non hazardous for the aquatic environment according to the CLP)

Water Accommodated Fraction technique (3/3)

- Annex XI adaptation:

Justification that the study is not needed (e.g. study scientifically unjustified):

- the substance is a poorly water soluble multi-constituent or UVCB organic, and
- the risk of all components dissolved and/or present as a stable dispersion or emulsion is adequately controlled

EXAMPLES of Annex XI adaptation justifications:

- The relevant components are identified in a WAF study **and** the analytical determination covers all potentially relevant components **and** the registrant has sufficient aquatic toxicity information on all components to demonstrate a safe use.

NOTE: If no information on any components/elements/ions is available, a Testing Proposal on the component/element/ion should be considered

Substances unlikely to cross biological membranes

- Registrant needs to demonstrate that **aquatic toxicity is unlikely to occur**
- Registrant needs to prove that physico-chemical properties as well as the chemical structure is suggesting that the substance is unlikely to cross biological membranes
- No evidence of toxicity should be observed in any available test (tox. and ecotox.)
- Supporting evidence is needed, e.g. toxicokinetics or additional *in vitro* tests

Poorly water soluble substances

- If registrant is unable to demonstrate that the aquatic toxicity is unlikely to occur - testing can not be waived based on Column 2:
  - The substance should be considered as **poorly water soluble instead of highly insoluble in water**

NOTE: The **long-term aquatic toxicity study** instead of short term aquatic toxicity study **shall be considered if the substance is poorly water soluble**.

Rapidly hydrolysing substances: adaptations

- The hydrolysis endpoint needs to be covered and provide information on rate and hydrolysis products (at least qualitative)

- Adaptation according to Column 2 must justify that aquatic toxicity is unlikely to occur:
  - e.g. extremely rapid hydrolysis into products of very low toxicity (i.e. non hazardous for the aquatic environment according to the CLP)

- Adaptation according Annex XI is also possible, e.g. Testing does not appear scientifically necessary
  - Registrant has information on the degradation products and can demonstrate low risk and safe use
  - Other concerns, such as change in pH, should be also addressed

Rapidly hydrolysing substances: Testing

- The hydrolysis kinetics and use patterns (Operational Conditions (OCs) and RMMs) need to be considered for selecting the likelihood of exposure to the parent and or the degradation products
- Testing on the degradation products instead of on the registered substance should be considered in some cases
- See OECD Guidance document on aquatic toxicity testing of difficult substances and mixtures (ENV/JM/MONO(2000)6), to consider testing on:
  1. Parent substance or
  2. Parent substance and degradation products or
  3. Degradation products
- Registrant needs to demonstrate safe use

Substances reacting with water and other substances for which aquatic testing is not technically feasible

- Adaptation according to Column 2 must justify that aquatic toxicity is unlikely to occur:

  e.g. reaction products are of very low toxicity (e.g. non hazardous for the aquatic environment according to the CLP)

- Adaptation according to Annex XI:

  e.g. Testing is not technically feasible - should also indicate how the concerns related to the degradation products have been address and indicate the appropriate RMM

- Adaptation according to Annex XI:

  e.g. Testing does not appear scientifically necessary - is also possible in case registrant has information on the degradation products and can demonstrate low risk and safe use

- Testing on relevant degradation products should be considered if needed

Aquatic toxicity - Guidance

- Guidance on information requirements and chemical safety assessment:
  - Chapter R.7b: Endpoint specific guidance for environment
- Practical Guides:

http://echa.europa.eu/web/guest/practical-guides

- Especially:
  - Practical guide 4: How to report data waiving
- Guidance on the Application of the CLP Criteria:
  - http://www.echa.europa.eu/web/guest/guidance-documents/guidance-on-clp
  - Annex IV.2.1 Interpretation of aquatic toxicity data