How to bring your registration dossier in compliance with REACH – Tips and Hints (Part 3)

Long-term Aquatic Toxicity

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REACH information requirements

Long-term aquatic toxicity

Annex IX	COLUMN 1 STANDARD INFORMATION REQUIREMENT	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
9.1.5.	Long-term toxicity on invertebrates	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.
9.1.6.	Long-term toxicity on fish	
9.1.6.1.	Fish Early Life Stage (FELS)	
9.1.6.2.	Fish short-term toxicity on embryo and sac-fry stages	
9.1.6.3.	Fish, Juvenile growth test	

- Column 1 shows the standard information requirement for substances registered in 100-1 000 tonnes and above (see also next slide).
- Column 2 gives further clarification on when the studies in Column 1 could be possibly waived, and on which test/tests to choose.

REACH information requirements

Short-term aquatic toxicity

Annex	COLUMN 1 STANDARD INFORMATION REQUIREMENT	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
VII 9.1.1.	Short-term toxicity on invertebrates	The long-term aquatic toxicity study on *Daphnia* (Annex IX, section 9.1.5.) shall be considered **if the substance is poorly water soluble***
VIII 9.1.3.	Short-term toxicity on fish	The long-term toxicity study on fish (Annex IX, section 9.1.6.) shall be considered **if the substance is poorly water soluble***

- Even for lower tonnages long-term testing should be considered if the substance is poorly water soluble

*Poorly water soluble if water solubility is:

- below 1 mg/L, or
- below the detection limit of the analytical method of the test substance (ECHA Guidance R.7b section R.7.8.5)

REACH information requirements Annex I

Long-term aquatic testing may also be needed to cover the information requirements of REACH Annex I:

Annex I	
Section 3	ENVIRONMENTAL HAZARD ASSESSMENT
Section 3.2	Step 2: Classification and Labelling
Section 3.3	Step 3: Identification of the PNEC
Section 4	PBT AND VPVB ASSESSMENT

ECHA Guidance (1)

Chapter R7b: Aquatic pelagic toxicity (p.31→)

- The need to conduct further testing may be triggered by (e.g.):
  - Quantitative assessment: PEC/PNEC>1, risks occur.
  - Qualitative assessment: no toxicity shown in short-term studies due to low water solubility of a substance, long-term tests are needed to confirm or reject a possible risk.
  - Information on a specific mode of action and unexpected sensitivity of a group of organisms to the substance under investigation.
  - Monitoring data showing occurrence of a substance in the aquatic compartment.

Chapter R10: Characterisation of dose/concentration-response for environment (p.20)

- A long-term test has to be carried out for substances showing no toxicity in short-term tests
  - if the log K_{ow} > 3 (or BCF > 100) and
  - if the PEClocal/regional is > 1/100th of the water solubility.

ECHA Guidance (2) Possibilities for adaptation

- Chapter R7B: Column 2 adaptation may be possible:
  - if exposure assessment and consequent quantitative/qualitative risk characterisation has shown that there is no risk to the aquatic compartment, for example PEC/PNEC<1, no risk.
  - If there are mitigating factors indicating that aquatic toxicity is unlikely studies may be waived, detailed justification needs to be provided

(see slide 8 also)

ECHA Guidance (3)

Weight of evidence (WoE)

- To assess different pieces of available information
  - *weight of evidence* has to be chosen as the *purpose flag* in IUCLID for each *endpoint study record* used for reaching the conclusion.
- If both WoE and data waiving apply
  - separate IUCLID *endpoint study records* have to be created for both/all.

- QSAR
- When using QSAR predictions, conditions in REACH Annex XI 1.3 have to be fulfilled.
  - The (Q)SAR model must be scientifically valid.
  - The registrant should demonstrate that the substance falls within the applicability domain of the model.
  - The results must be adequate for classification and labelling, and risk assessment.
  - Each QSAR prediction must be fully documented in the IUCLID endpoint study record like any experimental study.
- QSAR predictions typically used as supporting studies or as part of a weight of evidence (WoE).

Adaptation – examples (1) Exposure based adaptation

Adaptation based on exposure considerations needs to fulfil the criteria set in Annex XI section 3

- ”adequate justification and documentation shall be provided”, and
- ”the justification shall be based on a thorough and rigorous exposure assessment”.

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Justification given in a registration dossier for waiving long-term aquatic tests is based on exposure considerations, but:

- no exposure assessment is submitted as part of the CSR, and
- information in IUCLID section 3.5 indicates e.g. wide dispersive consumer use
  - exposure of aquatic environment cannot be excluded and no adequate justification/documentation is given
  - the given adaptation is therefore **unacceptable** and long-term studies are requested

X

Adaptation – examples (2)

Adaptation based on low water solubility of substance

X

The justification given in a registration dossier for waiving long-term aquatic tests is based on the poor water solubility of the substance.

- According to column 2 of Annex VII 9.1.1. and of Annex VIII section 9.1.3., long-term toxicity testing shall be considered for substances that are poorly water soluble.

    - The given adaptation is therefore **unacceptable** and long-term studies are requested.

Adaptation – examples (3)

Adaptation based on absence of toxicity in short-term tests, for low water soluble substance

X

The justification given in a registration dossier for waiving the long-term aquatic tests for a poorly water soluble substance is the absence of toxicity in short-term tests.

- According to ECHA Guidance Chapter R.7b, the need for long-term testing may be triggered by e.g. no observed toxicity in short-term studies, specifically for substances with low water solubility.
    - The given adaptation is therefore **unacceptable** and long-term studies are requested.

REACH information requirements –

Long-term aquatic toxicity Guidance

Guidance on information requirements and chemical safety assessment

- Chapter R.7b: Endpoint specific guidance
- Chapter R.10: Characterisation of dose [concentration] – response for environment

Practical Guides:

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

Specifically, Practical Guide 4: How to report data waiving

Guidance on the Application of CLP Criteria:

http://www.echa.europa.eu/guidance-document/guidance-on-clp

http://www.echa.europa.eu/documents/10162/13628/04_webinar20130128_aquatox_tips_en.pdf

Thank you