

How to bring your registration dossier in compliance with REACH – Tips and Hints Part 2

Long-term aquatic toxicity

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Overview

1. REACH requirements
2. IUCLID sections for long-term aquatic toxicity tests
3. Long-term aquatic invertebrates test: guidelines
4. Long-term fish test: guidelines
5. PNEC/AF
6. QSAR
7. Weight of evidence/read-across



REACH requirements for long-term aquatic toxicity tests

Annex IX and beyond		
9.1.5	Long-term toxicity on invertebrates	
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

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IUCLID sections

IUCLID sections relevant for long-term aquatic toxicity:

- 6.1.2 long-term toxicity to fish,
- 6.1.4 long-term toxicity to aquatic invertebrates,

Further IUCLID sections also considered for deriving PNEC and AF:

- 6.1.5 toxicity to aquatic algae and cyanobacteria,
- 6.1.6 toxicity to aquatic plants other than algae,
- 6.1.8 toxicity to other aquatic organisms

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Long-term aquatic toxicity on invertebrates

- Guidelines for long-term aquatic toxicity test on invertebrates :
 - OECD Guideline 211/ EU Method C.20 (Daphnia magna Reproduction Test)
 - OECD 202 part 2, performed before 1998
 - EPA OPPTS 850.1300, EPA OTS 797.1330 (Daphnid Chronic Toxicity Test),
 - EPA OPP 72-4 (Fish Early Life-Stage and Aquatic Invertebrate Life-Cycle Studies),
 - EPA OPPTS 850.1350, EPA OTS 797.1950 (Mysid Chronic Toxicity Test),
- In some cases the use of non standard guidelines (mesocosms studies) can also be accepted with thorough justification and documentation
- Guidelines for short-term aquatic toxicity test on invertebrates :
 - OECD 202, part 1 or performed from 1998
 - EU Method C.2 (Acute Toxicity for Daphnia)
- These guidelines cannot be used as long-term toxicity testing

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Long-term toxicity fish

- Guidelines for long-term toxicity test on fish:
 - OECD Guideline 210/ EPA OPPTS 850.1400/ EPA OTS 797.1000 (Fish Early-life Stage Toxicity Test)
 - OECD Guideline 212/ EU Method C.15 (Fish, Short-term Toxicity Test on Embryo and Sac-Fry Stages)
 - OECD Guideline 215/ EU Method C.14 (Fish, Juvenile Growth Test)
 - EPA OPP 72-4 (Fish Early Life-Stage and Aquatic Invertebrate Life-Cycle Studies)
 - EPA OPPTS 850.1500, EPA OPP 72-5 (Fish Life Cycle Toxicity)
- In some cases the use of non standard guidelines (mesocosms studies) can also be accepted with thorough justification and documentation
- Guidelines for short-term toxicity test fish:
 - OECD Guideline 204 (Fish, Prolonged Toxicity Test: 14-day Study)
 - ASTM 729-88a
 - ISO 10229-1
 - EPA/600/490/027...
- These guidelines cannot be used as long-term toxicity testing

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Derivation of PNEC/AF

Define a correct Assessment Factor (AF) estimation before derivation of PNEC aqua

Acceptable PNEC derivation

- With AF used > 100

If three aquatic toxicity short-term study results (algae, invertebrates, fish) provided only, or

If three aquatic toxicity short-term study results provided with non recognised long-term test for fish or invertebrates

Non acceptable PNEC derivation

- If AF between 1 and 10 whereas the long-term aquatic toxicity endpoints are issued from non-recognised guidelines or/and not properly justified
- If AF too low, when using Annex XI adaptations (QSAR, WoE)

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QSAR

A single QSAR prediction can rarely be used instead of an experimental study:

- ➔ It is more typically used as a **supporting study** or as part of a **weight of evidence (WoE)**.

QSARs are valuable only if conditions listed in REACH Annex XI-1.3 are fulfilled and documented by the registrant:

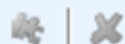
- ➔ The registrant should demonstrate that the substance falls within the **applicability domain** (fragments, descriptors)
- ➔ Each QSAR prediction must be **fully documented** in the IUCLID endpoint study record **alike any experimental study**.

Test materials

Test material identity

Identifier	
EC number	204
CAS number	128
IUPAC name	2,6-
other: SMILES	<chem>CC1=CC=CC=CC1</chem>

Details on test material



SMILES to be indicated in one of these fields

SMILES: CC1=CC=CC=CC1

Any other information on results incl. tables

Rich text editor toolbar with icons for file operations, undo/redo, text formatting (bold, italic, underline), and alignment.

Discuss whether the substance falls in the applicability domain of the model.

Overall remarks, attachments

Attached background material

Attached document
QSAR Prediction Reporting Format.doc

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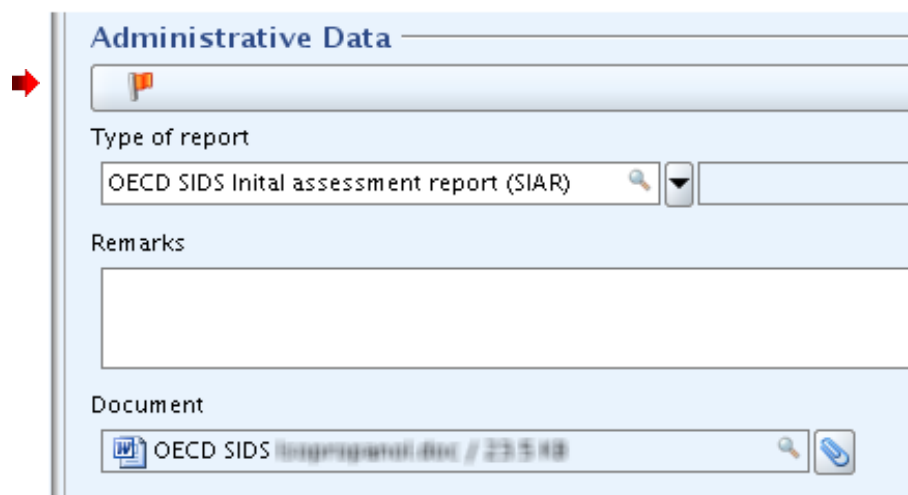


Weight of evidence

- **Experimental studies** which are part of a weight of evidence approach for long-term aquatic toxicity endpoints should be reported as **robust study summaries**.

- If all information, parts of the weight of evidence are of a low reliability (Klimisch score 3 or 4) : $AF \geq 100$

- References to **scientific papers** or to **assessment reports by other bodies** (e.g. in a report from OECD, WHO, IARC...) are not sufficient. Relevant studies have to be summarised in detail in a (robust) study summary.



A screenshot of a web-based administrative data form. The form is titled "Administrative Data" and contains several sections. A red arrow points to the top of the form. The sections are: "Type of report" with a dropdown menu showing "OECD SIDS Initial assessment report (SIAR)"; "Remarks" with a large empty text area; and "Document" with a file upload field showing "OECD SIDS Inispraganal.doc / 235 KB".

Read-across

Read-across adaptations

One of the requirements listed in **Section 1.5 of REACH Annex XI** stipulates that the test with the **source compounds** should provide **information about the property** to be read-across **as if it was tested in the standard test** prescribed by the REACH Regulation.

=> Same guidelines to be used than the ones listed previously.

Endpoints

- Guidance document on Endpoint specific guidance (R.7b)
: chapter R7.8, particularly table p.84-93 for aquatic toxicity testing

<http://echa.europa.eu/web/guest/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

- Guidance document on PNEC derivation: R.10, chapter R.10.2 and specifically R.10.3 for aquatic compartments, p17-34

http://echa.europa.eu/documents/10162/13632/information_requirements_r10_en.pdf

- Guidance document on QSARs and grouping (R.6)

http://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf

- Practical guides 1, 2, 3, 4, 5 and 6

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

 ECHA

Guidance on
information requirements and
chemical safety assessment
Chapter R.7b: Endpoint specific guidance



 **ECHA**
European Chemicals Agency

Practical guide 5:

How to report (Q)SARs

Thank you

