Data requirements for active substances and formulations and tier 1 effects assessment

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Introduction to (eco) data requirements for Regulation 1107/2009

For a.s. approval

Commission Regulation (EU) 283/2013

For PPP approval

Commission Regulation (EU) 284/2013

Data in support of RISK assessment for non-target organisms (i.e. toxicity and exposure)

This GD concerns the aquatic ecotoxicity effects assessment and how to link exposure and effect assessment

Tier 1 tests

	Acute tox fish	Acute tox Daphnia	Tox to algae	Acute tox additional invertebrate	Tox to other (non-green) alga (e.g. diatom)	Tox to Lemna	Tox to other macrophyte (e.g. Myriophyllum or Glyceria)	Chronic tox Fish ELS	Chronic Tox Daphnia (or most sensitive of 2 arthropods)
Every a.s.	X	X	X						
a.s.with insecticidal MoA				X					
a.s.with herbicidal MoA or PGR					X	X			
a.s. with herbicidal MoA for which *Lemna* is not sensitive or there is expected uptake by the roots of submerged macrophytes							X		
Where exposure of surface water is possible and the substance does not hydrolyse instantly ($DegT_{90}$>1d)								X	X

Chironomus recommended if *Americamysis* data not available

If indication of higher toxicity to monocots (e.g. for grass herbicides) or to dicots (e.g. broad leaf herbicides, auxin inhibitors)

unless Fish Full Life Cycle available

Tier 1 tests

	Chronic spiked tox test on Chironomus or Lumbriculus	Fish short-term reproductive assay, 21d fish assay or fish sexual development test	Fish full life cycle test
Accumulation of the a.s. in sediment indicated or predicted from fate studies	*Chironomus* for insecticides, *Lumbriculus* for fungicides → X		
a.s. suspected to interfere with moulting hormones (e.g. IGR)	*Chironomus* data preferred → X		
a.s.identified as an EAS where the known MoA may be expected to impact fish sexual development and/or reproduction		X	
a.s. exhibiting endocrine activity in 21d fish screening assay or fish sexual development test			X

Standard tests

Limit tests

- 100 mg/L where rangefinders indicate no likely effects
- Threshold approach for acute toxicity limit tests in fish (OECD 2010*)
- Compound properties
- Needs for RA

Ionisable substances – pH for testing

Benchmark concentrations - ECx

*OECD (2010) Short Guidance on the Threshold approach for Acute Fish Toxicity, Series on Testing and Assessment No 126, ENV/JM/TG(2010)/7.

Benchmark endpoints

Value of x?

- appropriate to protection goals
- appropriate x for variability of endpoint

Use of EC_x

- quality of estimate (CIs) in RA
- Considerations in using alternatives (incl. NOEC)
- Harmonization across regulations

Fish

One tier 1 species *(Rainbow trout)*

Chronic tox when expect stability in water via hydrolysis *($DegT_{90}$ >24h)*

- ELS unless FFLC available

FFLC when

- BCF > 1000
- elimination in 14d depuration phase < 95%
- stable in water/sediment ($DegT_{90}$ > 100d)
- other reasons for long term exposure

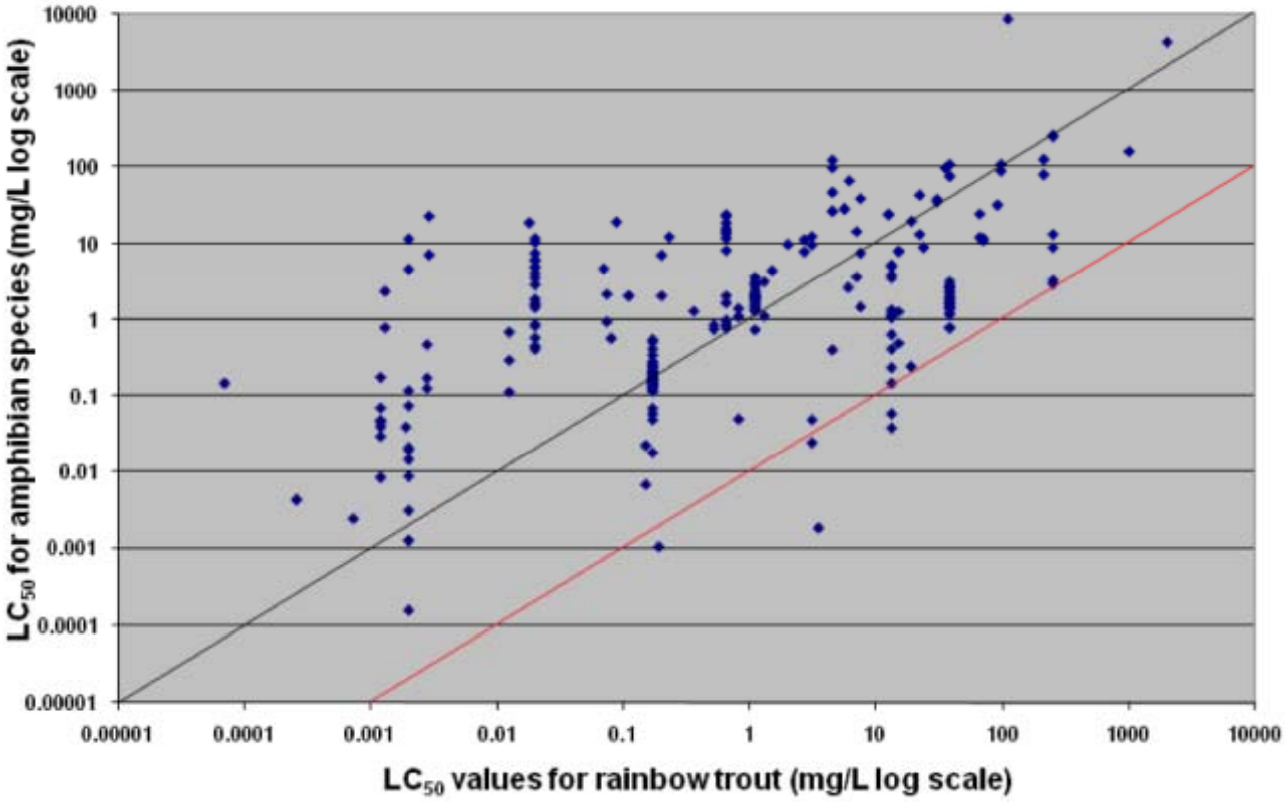
e.g. leaching from drain pipes (if properties indicate relevance)

- Endocrine activity in screening assays or other evidence

Amphibians

Amphibians to be included in RA but no tests specified

- use available relevant data
- Terrestrial amphibian RA in future guidance
- Aquatic Tier 1 RA assumes Rainbow trout protective



Invertebrates

Second arthropod acute test if
- a.s. has insecticidal mode of action

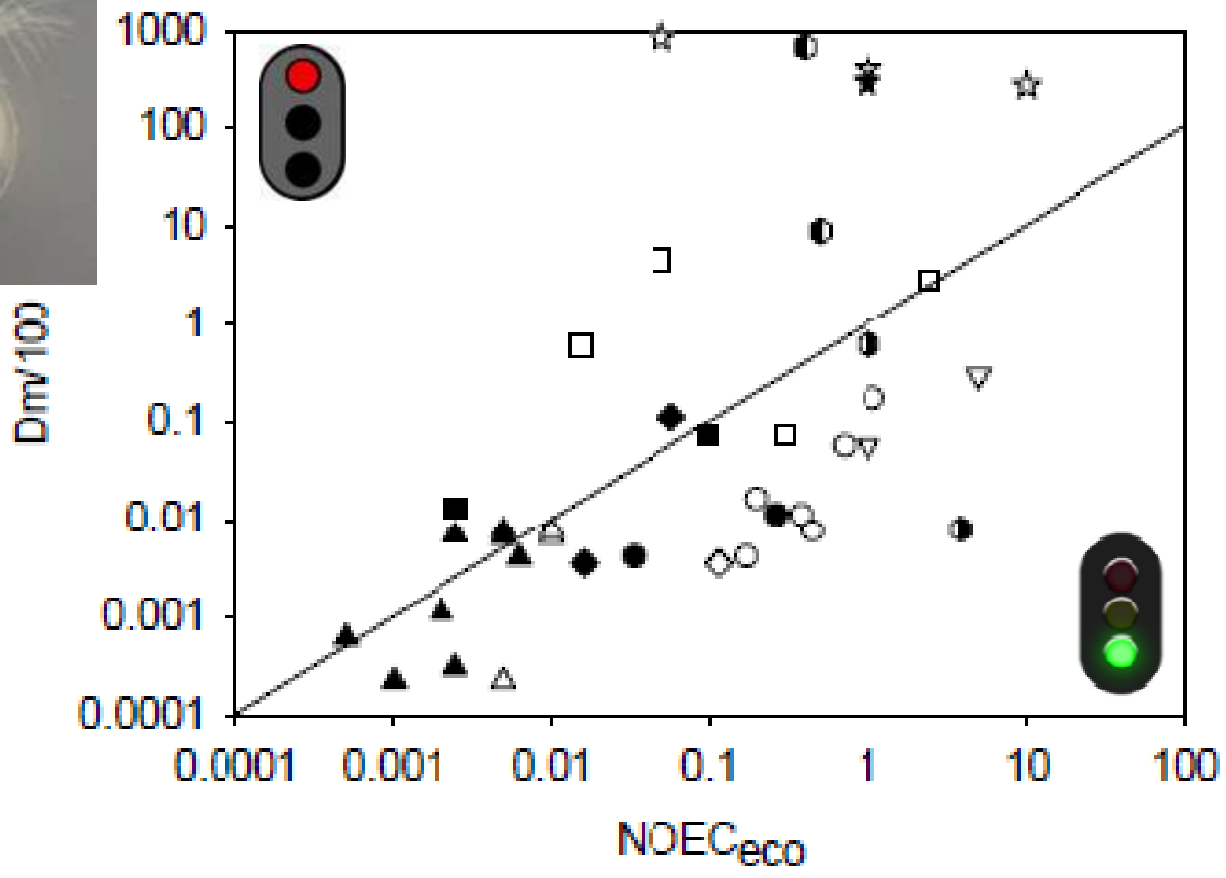
- *Daphnia* > 1 order magnitude more sensitive than fish or algae

Why?

Calibration of Tier 1 RAC based on *D. magna*

vs mesocosm-derived $NOEC_{eco}$

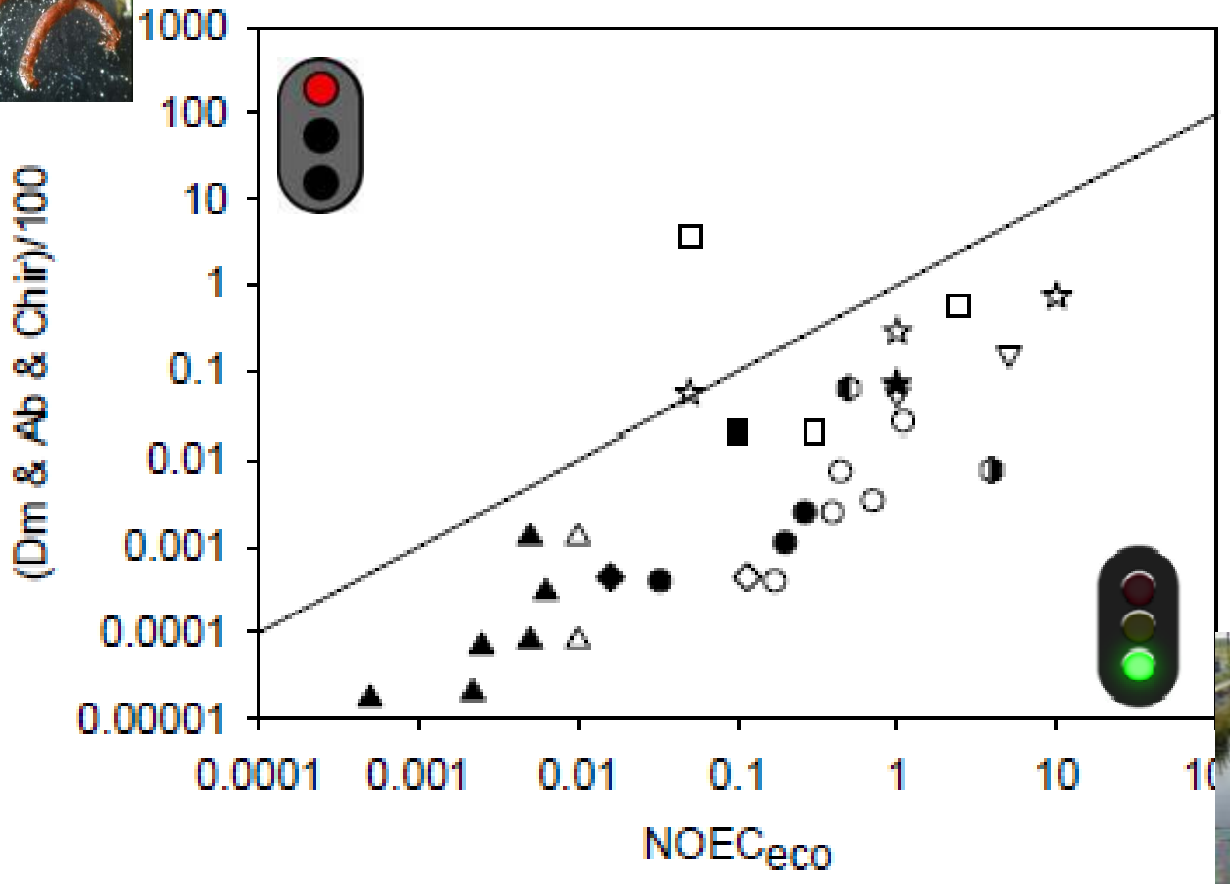
Additional invertebrate test



In 14 out of 38 cases the tier-1 RAC for *D. magna* was not protective in micro-/mesocosms

Problem substances: neonicotinoids and IGRs

Additional invertebrate test



In 1 out of 30 insecticide cases the acute tier-1 RAC using 2 invertebrate species is not protective in micro-/mesocosms

Invertebrates cntd

Chronic invertebrate toxicity if expect

- a.s. stable in water: use most sensitive species where acute test differ by >10x

- suspect IGR MOA (*Chironomus*)

- accumulation in sediment (*Chironomus* or *Lumbriculus*) or appropriate alternative if guideline available

Scientific Opinion on effects assessment in sediment dwelling orgs in preparation

Algae

Algal tests are short term but provide chronic endpoints

Use growth rate inhibition (E_rC_{50}) not yield (E_bC_{50})

- Biomass endpoint not appropriate in exponential growth conditions (ECHA 2008)

- Growth rate less dependent on test conditions

Where only E_bC_{50} reported
- re-analyse raw data (if available) to generate E_rC_{50}
- use E_bC_{50} (tends to be more sensitive: conservative)

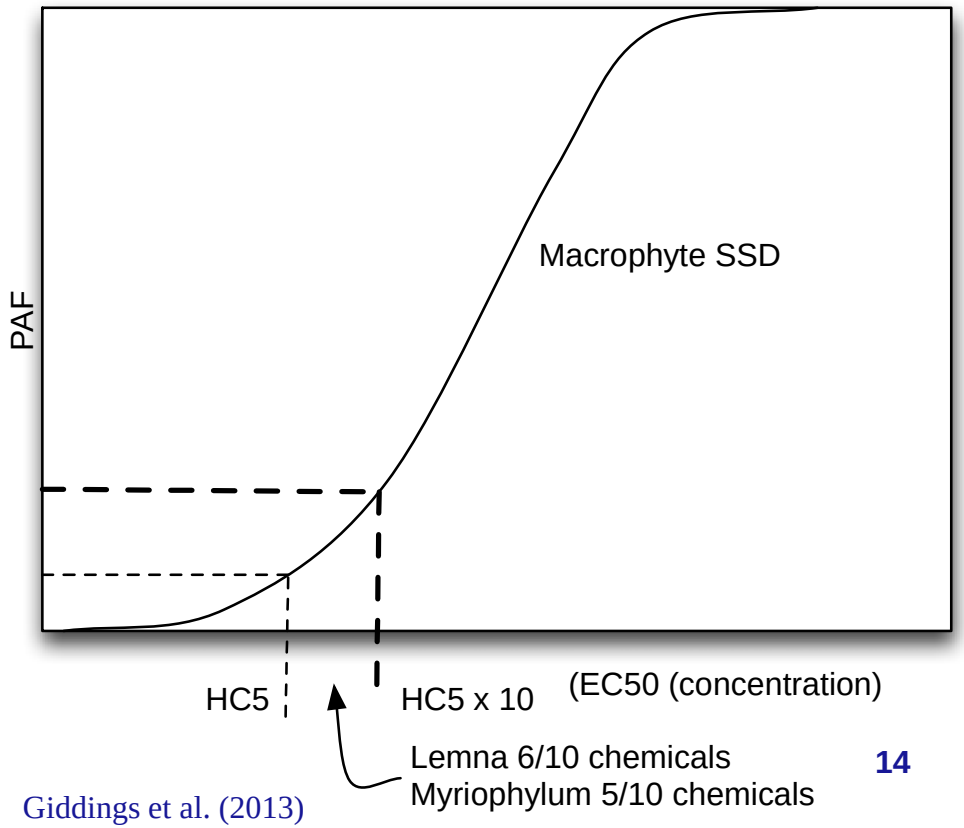
OECD 201 – guidance on growth endpoint
yield only if to meet specific regulatory requirement

Macrophytes

Lemna test if herbicidal or plant growth regulator activity

- Frond number plus one other endpoint (total frond area, wet weight, dry weight)
- Growth rate inhibition (E_rC_{50}) on most sensitive endpoint
- yield only if to meet specific regulatory requirements

Additional macrophyte spp (monocots/dicots) depending on MOA



Giddings et al. (2013)

Deriving RACs - Acute

Tax group		Test spp.	duration	endpoint	RAC
Fish		*Onchorynchus mykiss*	96h	LC50	LC50/100
Invertebrates	crustacean	*Daphnia* spp. (*magna* pref)	48h	EC50	EC50/100
additional	crustacean	*Americamysis bahia*	48h	EC50	EC50/100
additional	insect	*Chironomus* spp	48h	EC50	EC50/100

$RAC_{sw;ac}$ linked to $PEC_{sw;max}$

Deriving RACs - Chronic

Tax group		Species Test type	duration	endpoint	RAC
Fish		ELS		EC_{10}/NOEC	EC_{10}/10
		FFLC		EC_{10}/NOEC	EC_{10}/10
Inverts	crustacean	*Daphnia spp.*	21 d	EC_{10}/NOEC	EC_{10}/10
additional	insect	*Chironomus* spp	20-28 d	EC_{10}/NOEC	EC_{10}/10
	oligocheates	*Lumbriculus*	28 d	EC_{10}/NOEC	EC_{10}/10
algae	green	*P. subcapitata*	72 h	E_rC_{50}	E_rC_{50}/10
	diatom	*e.g. Navicula*	72 h	E_rC_{50}	E_rC_{50}/10
Macrophytes		*Lemna, Myriophyllum or Gylceria*	7-14 d	E_rC_{50}	E_rC_{50}/10

$RAC_{sw;ch}$ in first instance linked to $PEC_{sw;max}$,
and under certain conditions to $PEC_{sw;7d\text{-}twa}$

Additional testing

- to refine risk assessment
- address additional concerns (eg. endocrine disrupting properties)
- take into account existing data
- discuss with competent authorities

Additional species

Refined exposure

Experimental ecosystems

Formulated products - acute

Testing of formulation if

- cannot predict from a.s.
- intended use results in water exposure
- data on similar preparation not available

only most sensitive taxonomic group if difference of >10x for the a.s.

one Macrophyte required if expect effects on plants and can contaminate water

Test in all Tier 1 groups if most sensitive groups differ for two a.s. in one preparation

Formulated products - chronic

Testing only required if acute toxicity of formulation is > 10 x acute tox of the a.s., unless:

- no exposure expected
- increased formulation acute tox due to co-formulants expected to dissipate rapidly/no latency of effects

where toxicity of the a.s. and formulation differ, the PPP RA should be based on the most sensitive

(Regulation (EU) No 284/2013)

Bridging from similar formulations:

- Differences in a.s. content least critical
- Differences in toxicity > 3 x (GD on Equiv. Technical Materials)
- MOA (bridging within sensitive taxonomic groups)

Bioconcentration

Information required when

- Log P_{ow} >3
- Not rapidly degraded in water ($DegT_{90}$ hydrolysis >24h)
- Other indications of bioconcentration potential (structural alerts or monitoring data)

Fish bioconcentration study (OECD 305)

- Calculated or measured
- BCF_k growth-corrected and lipid normalized
- dietary exposure for substance with Log P_{ow} >6

Secondary Poisoning (when Log P_{ow} >3)

- Fish eating bird > 1kg
- Fish eating mammal >3kg
- GD Birds and Mammals (EFSA 2009)

Biomagnification

Old guidance required consideration of Biomag for compounds triggering FFLC

- food chain modelling or
- micro/mesocosm with (predatory) fish

both challenging

Revised GD recommends Tier 1 RA uses default Biomagnification factors

-TGD (EC 2003) Technical Guidance Document on risk assessment in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) No 1488/94 on risk assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market.

-EQS guidance (EC2011) Technical Guidance for Deriving Environmental Quality Standards, Guidance Document No: 27 under the Common Implementation Strategy for the Water Framework Directive (2000/60/EC). Technical Report 2011-055.

Deriving RAC for secondary poisoning (RAC_{SP})

Bioconcentration factor	Biomagnification factor
<2000 or log P_{ow}	1
2000-5000	2
>5000	10

AF for bird/mammal chronic RA	5

$$RAC_{SP} = \frac{NOAEL_{bird}}{5 \cdot 0.159 BCF_{fish} \cdot BMF} \text{ or } \frac{NOAEL_{mammal}}{5 \cdot 0.138 BCF_{fish} \cdot BMF}$$

Compare RAC_{SP} to 21-d TWA PEC_{sw}

Concluding remarks

Scientific justification of
tier 1 test species
measurement endpoints
AFs

are required for

- products with a novel mode of action
- primary producers, and macrophytes in particular