Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

PBT beoordeling

Screening and ultimate criteria

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12 December 2011

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Ministerie van Volksgezondheid, Welzijn en Sport

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PBT criteria in EU legislation

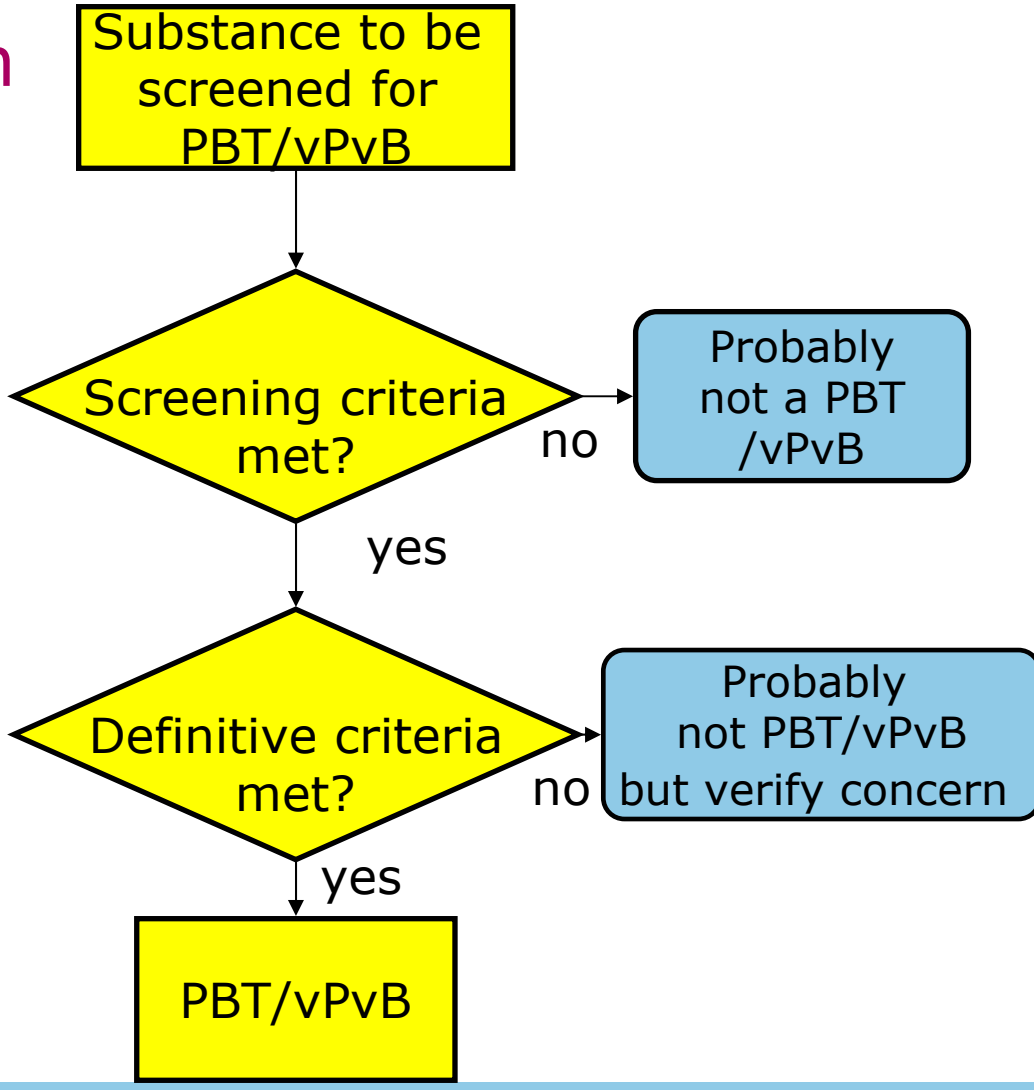
REACH UNEP Stockholm Convention UNECE POP protocol (LRTAP) Biocides Plant protection products	Humane geneesmiddelen Diergeneesmiddelen IMO OSPAR

REACH: Annex XIII sets out the criteria for the identification of persistent, bioaccumulative and toxic (PBT) substances, and very persistent and very bioaccumulative (vPvB) substances; it does not apply to inorganic substances.

A screening approach is outlined as well with criteria in the guidance.

Evaluation of information

- The PBT assessment is initiated by an evaluation of all available information.
- Data on ready biodegradability, (log Kow) and tox are available that give an indication of the P, B and T properties of a substance.
- A screening assessment is done as a 'first pass'.
- If potential PB(T)/vPvB -> definitive assessment of the P, B and T criteria
- This can involve generation of additional information (in REACH: above minimum requirements)



Information in Annexes relevant for PBT assessment

	Type of information	Criterion
Annex VII (≥ 1 Tonnes)	• Ready biodegradability; hydrolysis) • Log K_{ow} • Acute toxicity to daphnia and algae • Mutagenicity	P / vP B / vB T T
Annex VIII (≥ 10 Tonnes)	• Acute toxicity to fish • Reproductive toxicity • Repeated dose toxicity	T
Annex IX (≥ 100 Tonnes)	• Degradation simulation tests • Bioaccumulation • Chronic aquatic toxicity • Reproductive toxicity	P / vP B / vB T T
Annex X (≥ 1000 Tonnes)	• Carcinogenicity	

Test strategy

- In order to avoid unnecessary studies:
  - where the screening assessment indicates a possible P, B, or T property, or a vP or vB property, additional information or additional testing is required to conclude its PBT and vPvB assessment
- Tiered approach:
  - (Q)SARs > experimental screening > experimental confirmation
  - e.g. P: BIODEG > ready > enhanced ready > marine simulation

    e.g. B: log Kow > BCF

- General sequence confirmatory steps
  - first P
  - second B (if necessary)
  - finally T (if necessary)

Screening criteria Persistence

Type of data	Criterion	
Readily biodegradable	Ready biodegradable	Not P
Enhanced ready biodegradation	Ready biodegradable	Not P
Hydrolysis	Substance hydrolyse and no metabolites > 10% are persistent	Not P
Marine biodegradability	60% (ThOD, CO_2 evolution) or ultimate70% ultimate biodegradability (DOC removal)	Not P
inherent biodegradability Zahn-Wellens (OECD 302B) MITI II test (OECD 302C)	≥ 70 % mineralisation (DOC removal) within 7/14 d; log phase longer than 3d;	Not P Not P
QSAR Biowin 2 , 3, 6	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation time ≥ months (value < 2.2)	P P

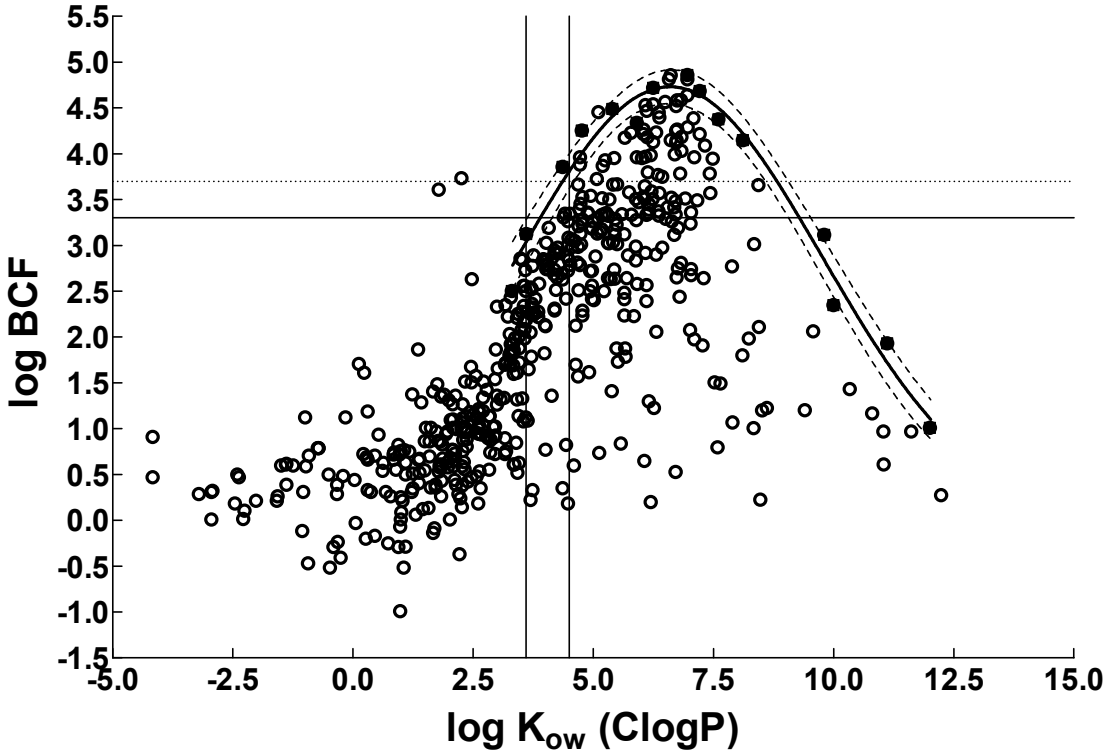
Screening criterion bioaccumulation

Criteria B and vB are not met if

- log K_{ow} < 4.5
  - QSAR Veith et al 1979: BCF(log K_{ow} = 4.5) = 1334 L/kg
  - Reach R.11 ⇒

- If convincing field evidence shows biomagnification:
  - B or vB

- Log Kow pitfalls:
  - Need reliable method
  - Hydrophobicity ≠ lipophilicity (etc.)



Screening criteria toxicity

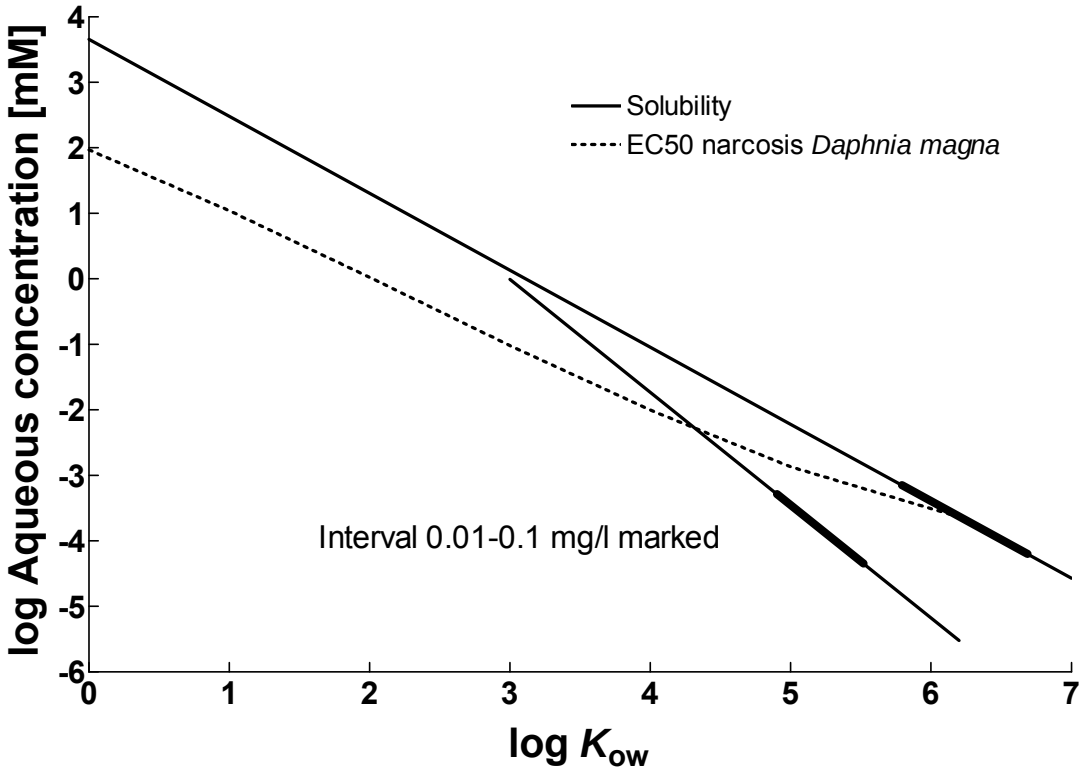
- Criteria T is presumably not met if acute aquatic EC50 > 0.1 mg/l
- Criteria T is possibly met if acute aquatic EC50 < 0.1 mg/l
- Criteria T is probably met if NOEC for birds < 30 mg/kg food
- Criteria T is definitely met if acute aquatic EC50 < 0.01 mg/l

- Is a definitive conclusion “not T” possible based on screening data or not?

T screening

- Criteria T is **presumably not** met if acute aquatic EC50 > 0.1 mg/l and **likely met** if acute aquatic EC50 < 0.1 mg/l ⇒

- Screening criterion of 0.1 mg/l is not very useful for narcotic compounds (data Verbruggen et al 2008)



PBT or vPvB if substance meets the final criteria

- REACH Annex XIII Criteria

		PBT Criteria	vPvB Criteria
PERSISTENCE	Medium	Half-life (Days)	Half-life (Days)
	Water (marine)	> 60	> 60
	Water (fresh/estuarine)	> 40	> 60
	Sediment (marine)	> 180	> 180
	Sediment (fresh/estuarine)	> 120	> 180
	Soil	> 120	> 180
BIOACCUMULATION	Parameter	Value	Value
	Bioconcentration factor (BCF)	> 2000	> 5000
TOXICITY	Exposure duration	Value (mg/L)	
ECOTOXICITY	Chronic NOEC	< 0.01	
	Endpoint	Category	
MAMMALIAN TOX	Carcinogenic, Mutagenic	1 or 2	
	Reprotoxic	1 or 2 or 3	

Confirmatory testing

- Further testing on
  - Degradation; simulation testing in relevant compartments.
  - Bioaccumulation; OECD TG 305 test, new addition for very hydrophobic substances: dietary exposure method
  - Toxicity; e.g. if chronic data for (very) hydrophobic substances are not available.

Indirect evidence that a substance may have PBT/vPvB properties

- The following additional information can be used:
  - Bioaccumulation in terrestrial species
  - Scientific analysis of human body fluids or tissues
  - Elevated levels in biota
  - Chronic toxicity study on animals
  - Toxicokinetic behaviour of the substance
  - Ability of the substance to biomagnify in the food chain
  - Scientific evidence of persistence in media through analysis of available env. monitoring data.

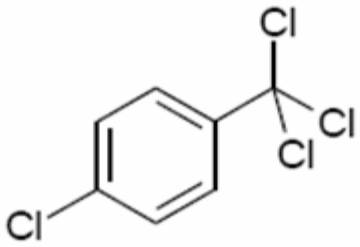
Substances with an equivalent level of concern

- Defined in EC 1907/2006, art. 57 (f) as:
  substances - such as those having endocrine disrupting properties or those having persistent, bioaccumulative and toxic properties or very persistent and very bioaccumulative properties, which do not fulfill the criteria of Annex XIII - for which

  "there is scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern [….] and which are identified on a case-by-case basis […].

Example

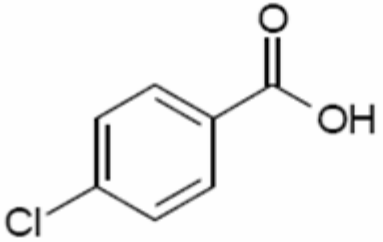
- 4-Chlorobenzotrichloride, CAS No. 5216-25-1



4-Chlorobenzotrichloride

Hydrolysis

Half-life pH 4 = 2 min.



4-Chlorobenzoic acid

QSAR Estimations & Available data

PERSISTENCE: not ready (BIOWIN) – P
BIOACCUMULATION: K_{ow} =4.54 (KOWWIN) – B
TOXICITY: Carc. Cat 2 (67/548/EEC) – T

Screening result based on QSAR: PBT

Result based on rapid Hydrolysis: no PBT
no vPvB

Measured Biodegradation Data

PERSISTENCE: ready biodeg (OECD 301) – not P

Result for Metabolite: not PBT, not vPvB

Conclusions

- A PBT/ vPvB assessment starts with the available information from (in principle) both the open literature and information from the registration/ notification file.

- A tiered, integrated test strategy may be needed to arrive at the final verdict on the PBT/ vPvB properties.

- A weight of evidence approach can be used to demonstrate whether the PBT/vPvB criteria are met.

Thank you for your attention!

Thanks to Dr. Koch (SETAC REACH workshop 2008) for the example