



PBT Assessment & Category Approach

Dr. Volker Koch, Clariant

Corporate Product Safety, Environmental Safety Assessment

PBT & vPvB – Definitions & Obligations under REACH

PBT & vPvB REACH Annex XIII Criteria and Screening criteria

PBT Screening

Detailed REACH PBT Assessment

Example for a Category Approach

Quantitative Risk Assessment of PBT Substances

Take away message

Backup slides

PBT & vPvB

Definitions & Obligations under REACH

■ Substances which are

- Persistent (P)
- Bioaccumulative (B) and
- Toxic (T)

PBT

■ Or

- very Persistent (vP) and
- very Bioaccumulative (vB)

vPvB

- Are subjected to close scrutiny in the EU as they may have long-term impact on the environment.
- In other countries like Australia, Canada, Japan and USA regulatory schemes for PBT substances are implemented as well using partly different Definitions and Criteria

- **REACH Article 14** – Chemical Safety Assessment (CSA) & Risk Reduction Measures
 - For substances with ≥ 10 tons/year a CSA is requested encompassing a
 - **PBT & vPvB Assessment**
- **REACH Article 23** – Specific Provisions for Phase-in Substances
 - For substances with ≥ 1000 tons/year manufactured / imported at least once after 1 June 2007 have to be registered
 - UNTIL 1 DECEMBER 2010**
 - Additionally
 - **CMR Cat. 1 or 2 Substances if ≥ 1 ton/year manufactured / imported at least once after 1 June 2007**
 - CMR = Carcinogenic, Mutagenic, Reprotoxic
 - **R50/53 Very toxic to Aquatic Organisms, may cause long-term adverse effects in the aquatic environment**

PBT & vPvB

REACH Annex XIII Criteria

and Screening criteria

REACH PBT & vPvB 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	

Data required for comparison with the PBT & vPvB Criteria are not available in most cases. The EU REACH Guidance on “PBT Assessment” recommends to use Screening criteria instead (see later).”

■ Persistence

	Result	Assignment
Readily biodegradable	Not ready biodegradable	P or vP
Enhanced ready biodegradation	Not ready biodegradable	P or vP
Inherent biodegradability		
Zahn-Wellens (OECD 302B)	70 % mineralisation (DOC removal) within 7 d; log phase no longer than 3d removal before degradation occurs below 15%; no pre-adapted inoculum	Not P
MITI II test (OECD 302C)	70% mineralisation (O2 uptake) within 14 days; log phase no longer than 3d; no pre-adapted inoculum	Not P
QSAR Models		
Biowin 2 (non-linear model prediction), or	Does not biodegrade fast (probability < 0.5), or	Not P
Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability < 0.5) and ultimate biodegradation time \geq months (value < 2.2)	Not P

Screening criteria for B & vB

■ Bioaccumulation

	Parameter	Assignment
Convincing evidence that a substance can biomagnify in the food chain (e.g. field data)	e.g. BMF > 1	B or vB, definitive assignment possible
Substance belongs to a class of chemicals or is structurally similar to substance(s) that are known to accumulate in living organisms	Structurally similar substance(s) fulfil(s) screening criteria	Potentially B or vB
Octanol-water partitioning coefficient (experimentally determined or estimated by QSAR)	Log Kow \geq 4.5	Potentially B or vB
Physicochemical indicators Molecular size Average maximum diameter (Dmax aver) and molecular weight (MW) Maximum molecular length (MML) Octanol-water partitioning coefficient Measured octanol solubility (OS, mg/l)	Dmax aver > 17.4 Å and MW > 1100 Dmax aver > 17.4 Å and MW > 700 MML > 43 Å log Kow > 10 OS (mg/l) < 0.002 × MW (without observed toxicity or other indicators of bioaccum.)	Not B Not vB Not B, not vB

Screening criteria for T

■ Toxicity

	Result	Assignment
Short-term aquatic toxicity (algae, daphnia, fish)	EC50 or LC50 < 0.1 mg/L	T
Short-term aquatic toxicity (algae, daphnia, fish)	EC50 or LC50 < 0.01 mg/L	T-criterion considered to be definitely fulfilled
Read across/ member of category	Structurally similar substance(s) fulfil(s) (screening) criterion	T
Avian toxicity (subchronic or chronic toxicity or toxic for reproduction)	NOEC < 30 mg/kg food	T
Mammalian Toxicity with classification	R 45,46, 48, 49, 60, 61, 62, 63, or 64	T

■ EXPERIENCE was gained from the EU PBT & vPvB Working Group

- Around 2.500 EU HPV Substances were screened for potential PBT & vPvB Properties
 - **125 Potential candidates** in **2002** ca. **5 % of the total 2.500 HPVs**
 - A large number of candidates could be removed from the list due to enhanced data
 - It can be assumed that around < 1% of the substances which require a PBT Assessment under REACH may be potential PBT or vPvB Substances
 - **This means > 99% of the REACH substances are most likely NO PBT or vPvB Substances**
- **The major challenge for Industry is to screen out effectively those substances which are not PBT or vPvB in order to have sufficient time to refine the data for the potential PBT or vPvB substances**

■ CLARIANT EXPERIENCE from the EU PBT & vPvB Working Group

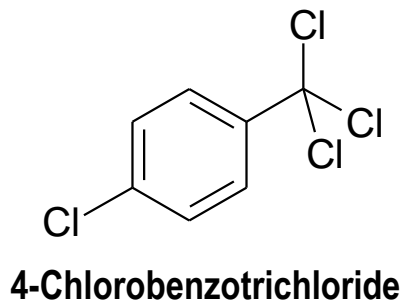
- Substances manufactured and used by Clariant on the 125 Candidate list
 - 21 Substance = 17 % of the 125 Potential PBT or vPvB Candidates
- After 4 Years discussion, assessment and testing
 - 20 Substances were delisted = 95 % of the 21 Potential Candidates
 - 1 Substance is assigned PBT (a **Borderline case**), an **Intermediate with emission control (very low emissions)**
- **OVERALL CONCLUSION**
 - It is relatively easy to conclude that a substance might be a Potential PBT or vPvB using e.g. QSARs because of lacking data
 - **It is very time consuming and resource demanding to prove the contrary** but the chances to be successful are not bad if the assessment is started **timely !**

PBT & vPvB

Screening

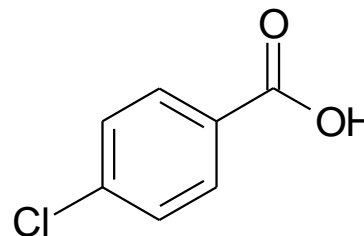
Screening for PBT & vPvB Substances Avoiding False Positive Results (1)

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



Hydrolysis

Half-life pH 4 = 2 min.



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

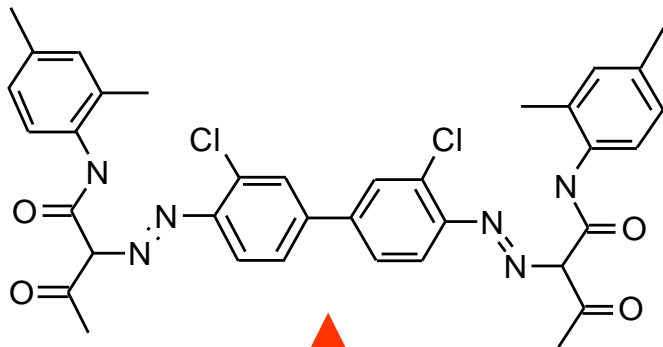
PERSISTENCE: ready biodeg (OECD 301) – not P

Result for Metabolite: not PBT, not vPvB

Check carefully QSAR estimates. Apply your knowledge about your substances to avoid wrong results.

Screening for PBT & vPvB Substances Avoiding False Positive Results (2)

■ Pigment Yellow 13, CAS No. 5102-83-0



QSAR Estimations & Available data

PERSISTENCE: recal. (BIOWIN) - vP
BIOACCUMULATION: $K_{ow} = 8.11$ (KOWWIN) - vB
TOXICITY: acute aquat. tox - not T

Screening result based on QSAR: vPvB

Measured Data for Bioaccumulation Assessment

Solubility

- Octanol 22 µg/L
- Water 0.8 µg/L

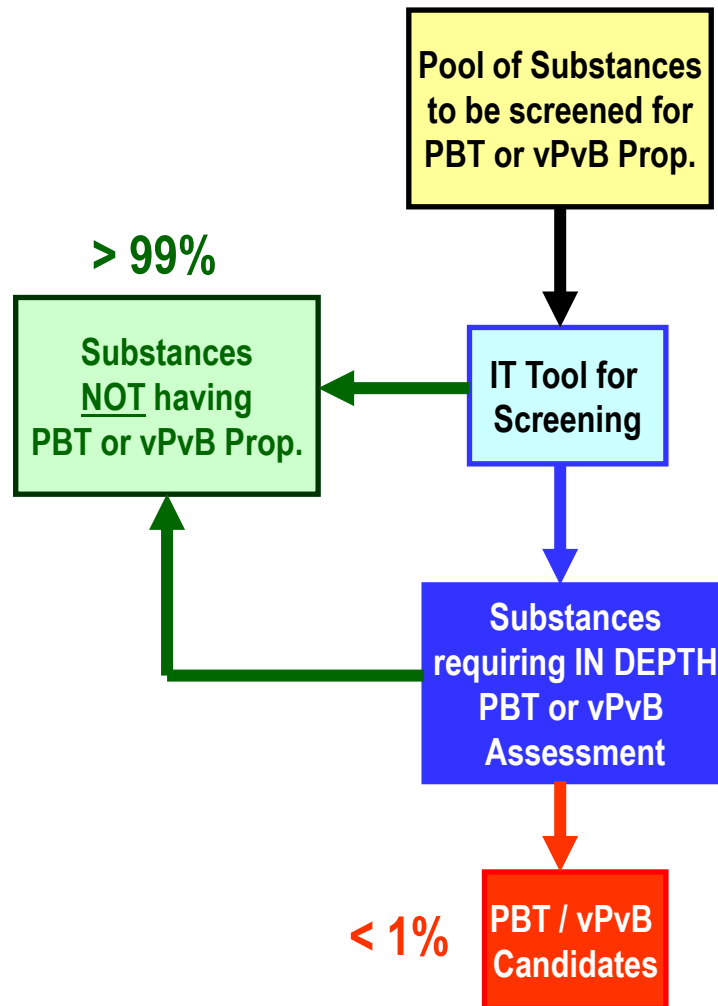
Partitioning Log Octanol /water 1.1 not B
not vB

Result based on measured data: not vPvB

Check carefully QSAR estimates. Apply your knowledge about your substances to avoid wrong results.

Proposed Strategy for a PBT & vPvB Screening

- A comprehensive Guidance on the REACH PBT Assessment as well as Endpoint Specific Guidance is available on the EChA Web site (http://reach.jrc.it/docs/guidance_document/information_requirements_en.htm)
- It cannot be recommended to use this complex guidance on PBT Assessment upfront but start with a Screening on PBT & vPvB properties using the Screening criteria shown before
- An IT Tool can support the screening process efficiently
- If a substance is identified as a potential PBT or vPvB an assessment using refined substance data is warranted and described later. This refinement can be multi-step process taking into account also exposure data



Clariant Screening Tool for the REACH PBT & vPvB Assessment

- As the **PBT & vPvB Assessment is complex** and allows different approaches. **Non-experts may struggle** how to proceed with the assessment.
- An **IT Screening Tool** which covers the elements of the PBT & vPvB Assessment
 - **May support and guide an user (pick lists, intermediate results, workflow etc.)**
 - **Data from Standard test, higher Tier tests, QSAR or Read across can be used**
 - **Will deliver screening results which take into account the different levels of data (e.g. measured data take precedence over QSARs)**
 - **Allows a proper documentation of the Assessment by generating a report**
 - **Supports a standardization of the PBT &vPvB Assessment**
- This **IT Screening Tool** can be used for **Organic chemicals only, not for Inorganics, not for Organometallics, not for Polymers, not for Perfluorinated subst. and not for mixtures**

Screening Tool for PBT & vPvB Assessment Substance ID & Solubility Data

Screening Tool for the PBT & vPvB Assessment including Equivalent Level of Concern

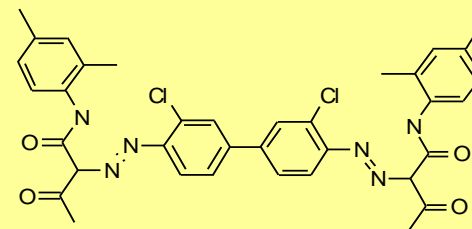
RESET INPUT DATA

In order to CLEAR ALL PREVIOUS INPUT DATA in pale yellow data input cells start an RESET INPUT MACRO pressing SHIFT+CTRL+R

SUBSTANCE DATA

Name:	Pigment Yellow 13
CAS No.:	5102-83-0
Mol weight (g/Mol):	686
Molecular size Dmax(Angstrom)	
Water solubility (mg/L)	0.022
Octanol solubility (mg/L)	0.0008
Clariant Division	PA
Clariant Divisional Substance Code	
REACH Range:	1

STRUCTURE



Light Yellow Fields
Allow Data Input

SUBSTANCE REMARK

Empty text area for substance remarks.

Screening Tool for PBT & vPvB Assessment P Assessment

User can select from List of Values (Drop down list) Light yellow fields allow data input, other fields are protected

WORKFLOW					
	A	B	C	D	F
1	Screening Tool for the PBT & vPvB Assessment including Equivalent Level of Concern				
2					
3	PERSISTENCY				
4	BIODEGRADATION				
5	READY TESTS	TEST DURATION	TEST CRITERIA ACHIEVEMENT	TEST RESULT	P' RESULT BASED ON TEST
6					REPORT REFERENCE
7					
8	SEAWATER TEST	TEST DURATION	TEST CRITERIA ACHIEVEMENT	TEST RESULT	P' RESULT BASED ON TEST
9					REPORT REFERENCE
10					
11	INHERENT TESTS	TEST DURATION	TEST CRITERIA ACHIEVEMENT	TEST RESULT	P' RESULT BASED ON TEST
12	OECD 302 B 'Zahn-Wellens Test'	28d	DOC: < 70% after 7d	degrades not fast	persistent
13					
14	SIMULATION TESTS	TEST DURATION	HALF-LIFE CRITERIA ACHIEVEMENT	TEST RESULT	P' RESULT BASED ON TEST
15					REPORT REFERENCE
16					
17	QSAR		QSAR CRITERIA ACHIEVEMENT	RESULT	P' RESULT BASED ON QSAR
18	US EPA BioWin		Prediction: no ready biodeg.	QSAR: Not readily biodegrad.	persistent
19					
20	READ ACROSS	CAS NO. / NAME OF READ ACROSS SUBSTANCE		RESULT FROM READ ACROSS	P' RESULT BASED ON READ ACROSS
21					REPORT REFERENCE
22	ABIOTIC DEGRADATION				
23	HYDROLYSIS		HALF-LIFE CRITERIA ACHIEVEMENT	RESULT FROM HYDROLYSIS	P' RESULT BASED ON TEST
24	OECD 111				REPORT REFERENCE
25					
26	OVERALL P Assessment Result	Persistent		based on measured data	

Screening Tool for PBT & vPvB Assessment B Assessment

User can select from List of Values (Drop down list)
Is calculated from input data

Light yellow fields allow data input, other fields are protected
White and light green fields are calculated

	A	B	C	D	E	F
1	Screening Tool for the PBT & vPvB Assessment including Equivalent Level of Concern					
2						
3	BIOACCUMULATION					
4	MEASURED BCF	TEST DURATION	BCF (L/kg)	B' CRITERIA ASSOCIATED	B' RESULT BASED ON TEST	REPORT REFERENCE
5						
6						
7	MEASURED Log Kow		MEASURED Log Kow	B' CRITERIA ASSOCIATED	B' RESULT BASED ON TEST	REPORT REFERENCE
8		n.a.				
9						
10	MEASURED Log Coctanol/Cwater		Log Coct./Cwater	B' CRITERIA ASSOCIATED	B' RESULT BASED ON TEST	REPORT REFERENCE
11	see SUBSTANCE SHEET	n.a.	1.4	BCF <= 2000	not bioaccumulative (not B)	
12						
13	CALCULATED Log Kow		CALCULATED Log Kow	B' CRITERIA ASSOCIATED	B' RESULT BASED ON TEST	REPORT REFERENCE
14	US EPA QSAR KowWIN	n.a.	8.1	BCF > 5000	very bioaccumulative (vB)	
15						
16	QUALITATIVE INDICATORS FOR BIOACCUMULATION					
17						
18	Critical Body Burden (CBB) (mg/L)	Octanol solub. (mg/L)	Coctanol < CBB	REDUCED BIOACCUMULATION	B' RESULT BASED ON CBB	REPORT REFERENCE
19	1.372	0.0008	yes	yes	not bioaccumulative (not B)	
20						
21	Molecular size & MW Criteria		Criteria fulfilled	REDUCED BIOACCUMULATION	B' RESULT BASED ON MW & SIZE	REPORT REFERENCE
22	If data available see SUBSTANCE	n.a.				
23						
24	Bioaccumulation data from Mammalian studies		Limited or NO Uptake observed	REDUCED BIOACCUMULATION	B' RESULT BASED ON CBB	REPORT REFERENCE
25	Check appropriate studies.	n.a.	yes	yes	not bioaccumulative (not B)	
26						
27	OVERALL B Assessment Result	not B		based on measured data		

Screening Tool for PBT & vPvB Assessment T Assessment

User can select from List of Values (Drop down list)

Light yellow fields allow data input, other fields are protected
White and light green fields are calculated

Is calculated from input data

	A	B	C	D	E	F
1	Screening Tool for the PBT & vPvB Assessment including Equivalent Level of Concern					
2						
3	TOXICITY					
4	ACUTE ECOTOXICITY	TEST DURATION	TEST RESULT L(E)C50 (mg/L)	T' CRITERIA ASSOCIATED	T' RESULT BASED ON TEST	REPORT REFERENCE
5	OECD 203 'Acute Fish'	96h	110	> 0.1 mg/L	not toxic	
6						
7	CHRONIC ECOTOXICITY	TEST DURATION	TEST RESULT NOEC (mg/L)	T' CRITERIA ASSOCIATED	T' RESULT BASED ON TEST	REPORT REFERENCE
8						
9						
10	HUMAN TOXICITY CRITERIA (R PHRASES)		R PHRASES MEETING CRITERIA	CRITERIA FULFILLED	T' RESULT BASED ON R PHRASE(S)	REPORT REFERENCE
11	R 40 (C o. M cat. 3), R 45, 46, 48, 60,61, 62, 63, 64		no such classification	no	not toxic	
12						
13	QUALITATIVE INDICATORS FOR TOXICITY					
14	ENDOCRINE DISRUPTOR (proven or suspected, similarity)	LIST NO. OR CAS NO./NAME OF SIMILAR SUBSTANCE		CRITERIA FULFILLED	T' RESULT BASED ON READ ACROSS	REPORT REFERENCE
15	EU Strategy COM(2001)262 final			no	not toxic	
16	Critical Body Burden (CBB) (mg/l.)	Octanol solub. (mg/l.)	Coctanol < CBB	LIMITED TOXICITY	T' RESULT BASED ON CBB	
17	1.372	0.0008	yes	yes	not toxic	
18						
19	OVERALL T Assessment Result	not toxic		based on measured ecotoxicity data		

Screening Tool for PBT & vPvB Assessment Assessment Results and Recommendations

Screening Tool for the PBT & vPvB Assessment including Equivalent Level of Concern

RESULTS

P Assessment result | persistent

B Assessment result | not bioaccumulative

T Assessment result | not toxic

OVERALL SCREENING RESULT on PBT & vPvB | no vPvB Substance

ALERTS

Hydrolysis Alert

Endocrine Disrupter Alert

Alert Equal level of concern (P,T and B,T) | no

Near miss Alert on Criteria B and T |

BCF Alert | no

Kow Alert | no

Acute Toxicity Alert | no

Chronic Toxicity Alert |

Acute versus Chronic Tox Alert |

RECOMMENDATION related to PBT & vPvB | Assessment consistent, no further work for the time being

REMARK

Address Alerts if necessary and comment

■ **US PBT Profiler** (<http://www.pbtprofiler.net/>)

- Is Structure based, estimates substance properties from QSARs
- No refined data input possible
- Result is explained in detail

■ **CEFIC Long-range Research Initiative (LRI)**

– **AMBIT Computational Tool** (<http://ambit.acad.bg/>)

- The Clariant Screening Tool shown before will be implemented in this Open Source Software AMBIT. As AMBIT has built in various predictors and databases for substance properties, missing data for a PBT Assessment can be estimated and used for the PBT Assessment. AMBIT NEW VERSION will be available 1. Q to 2. Q 2009. A Workshop will be announced next year.

■ **The Clariant PBT Screening Tool itself is not available for use by third parties (Company policy)**

- **Hazard based Screening for PBT substances has been challenged recently by Arnot & Mackay**
 - **Arnot JA, Mackay D, 2008**. Policies for Chemical Hazard and Risk Priority Setting: Can Persistence, Bioaccumulation , Toxicity and Quantity Information Be Combined ?. **Environ Sci Technol 42:4648-4654**

- They propose a **Risk based scheme** as it takes into account also the used tonnage
 - Although a Risk based approach is reasonable it has to be ensured that the **uncertainty is minimized** and that
 - The Exposure models applied use reliable data especially with respect to partitioning data, half-lives and used amounts on a regional and local basis
 - Chronic Hazard data are available to address potential long-term effects

Detailed REACH

PBT Assessment

Detailed REACH PBT & vPvB Assessment

- If it has turned out after a Screening PBT & vPvB Assessment that refined data are required, detailed REACH Guidance is given the appropriate approach

 ECHA

Guidance on
information requirements and
chemical safety assessment

Chapter R.7a: Endpoint specific guidance



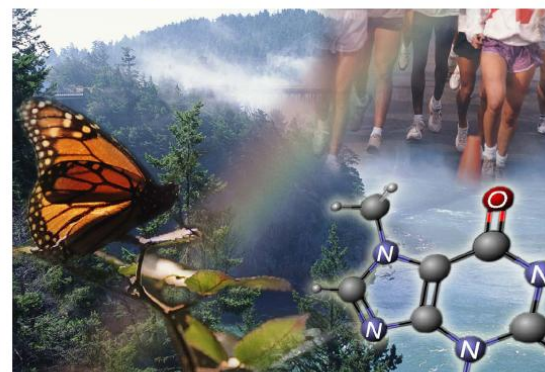
May 2008

Guidance for the implementation of REACH

 ECHA

Guidance on
information requirements and
chemical safety assessment

Chapter R.11: PBT Assessment



May 2008

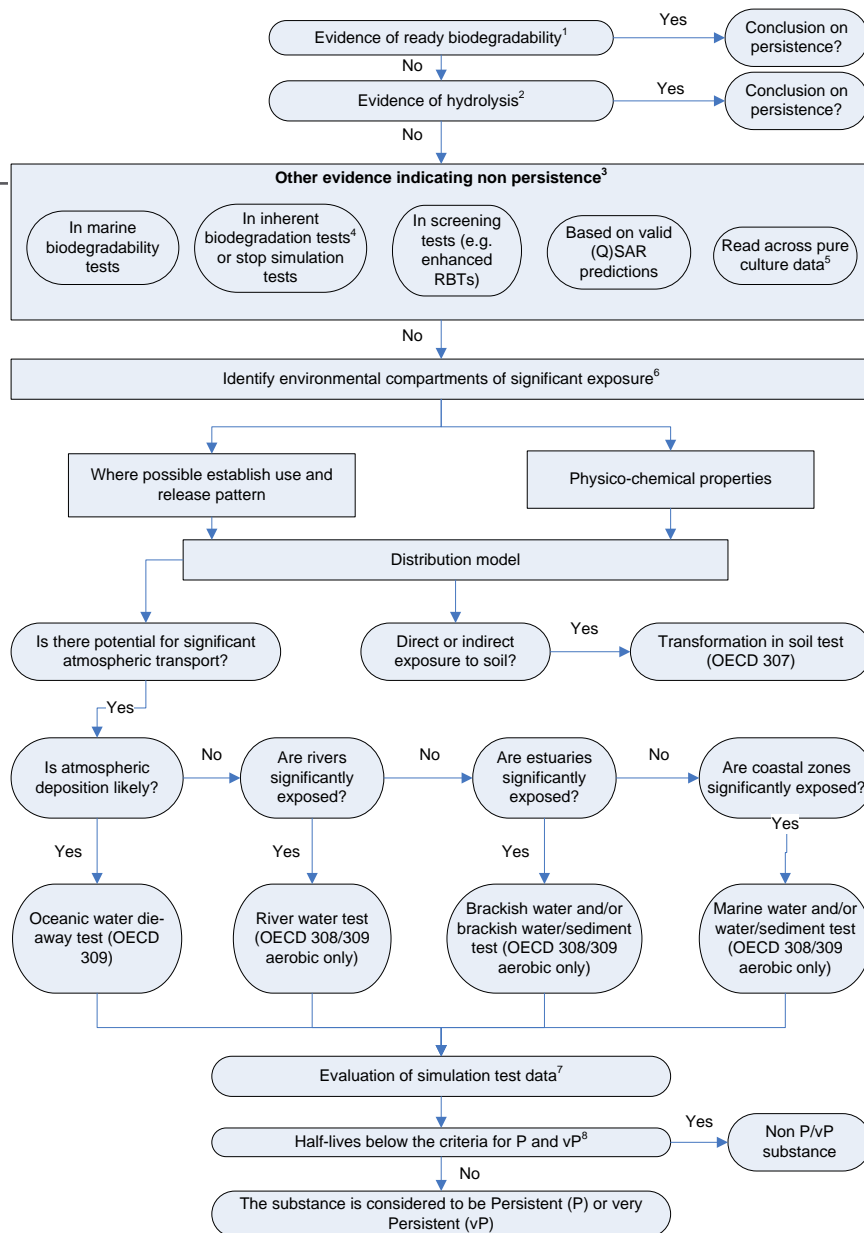
Guidance for the implementation of REACH

- In the following a brief Overview on the Testing and Assessment Strategy will be given together with examples & proposed improvements.

Detailed P Assessment

P Assessment Flow chart

from
REACH Guidance
CSA
PBT Assessment

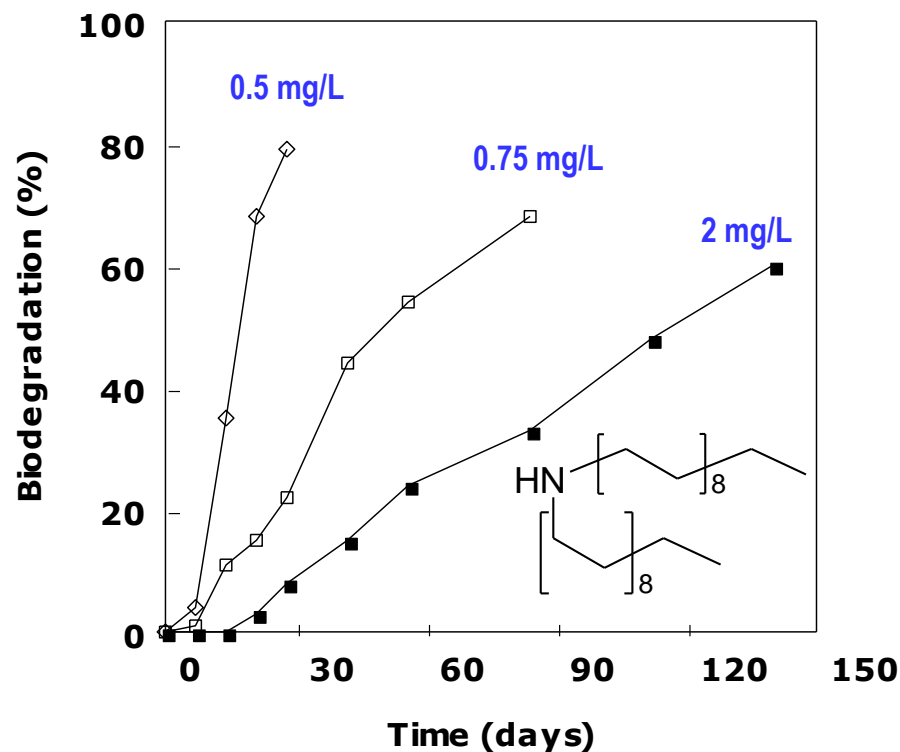


Refined P Assessment

Advanced Biodegradation Testing

- **Poorly water soluble, strongly sorbing substances often fail a classical Ready Biodegradation Test** although their structural elements are susceptible to transformation.
- The Biodegradation kinetic of such substances show a linear behaviour at higher conc.(see graph at 2 mg/L) instead of the logarithmic expected (see 0.75 & 0.5 mg/L). The reason is the reduced bioavailability of the substance. Lowering the substance concentration as well as enhancing the bioavailability e.g. by adding Silica may help to pass the ready criteria. These modifications are described in the EU REACH CSA Guidance on Endpoints

Closed Bottle Test Results for Dioctadecylamine at 3 different (nominal) concentrations



Refined P Assessment Inoculum in Biodegradation tests

- **The inoculum is the main source of variability in biodegradation tests**
- The stringency of Ready tests was demonstrated by showing that
 - The level of bacteria present in such tests varied by one to two orders of magnitude. Thouand (1995, 1999) has shown in a Sturm test (OECD 301B) setting that **4-Nitrophenol had a 20-80% chance of a false negative i.e. a biodegradable substance could be assigned as persistent**
- **Thouand** proposed at the ECETOC Workshop on ,Biodegradation & Persistence (2007) to
 - Check the probability of Biodegradation (probability concept)
 - Pre-evaluate the diversity of microorganisms
 - Use a standard array of microorganism for screening the biodegradability
- **Science issue**
 - Development of more advanced biodegradation tests
 - Refined predictors for biodegradation / metabolism

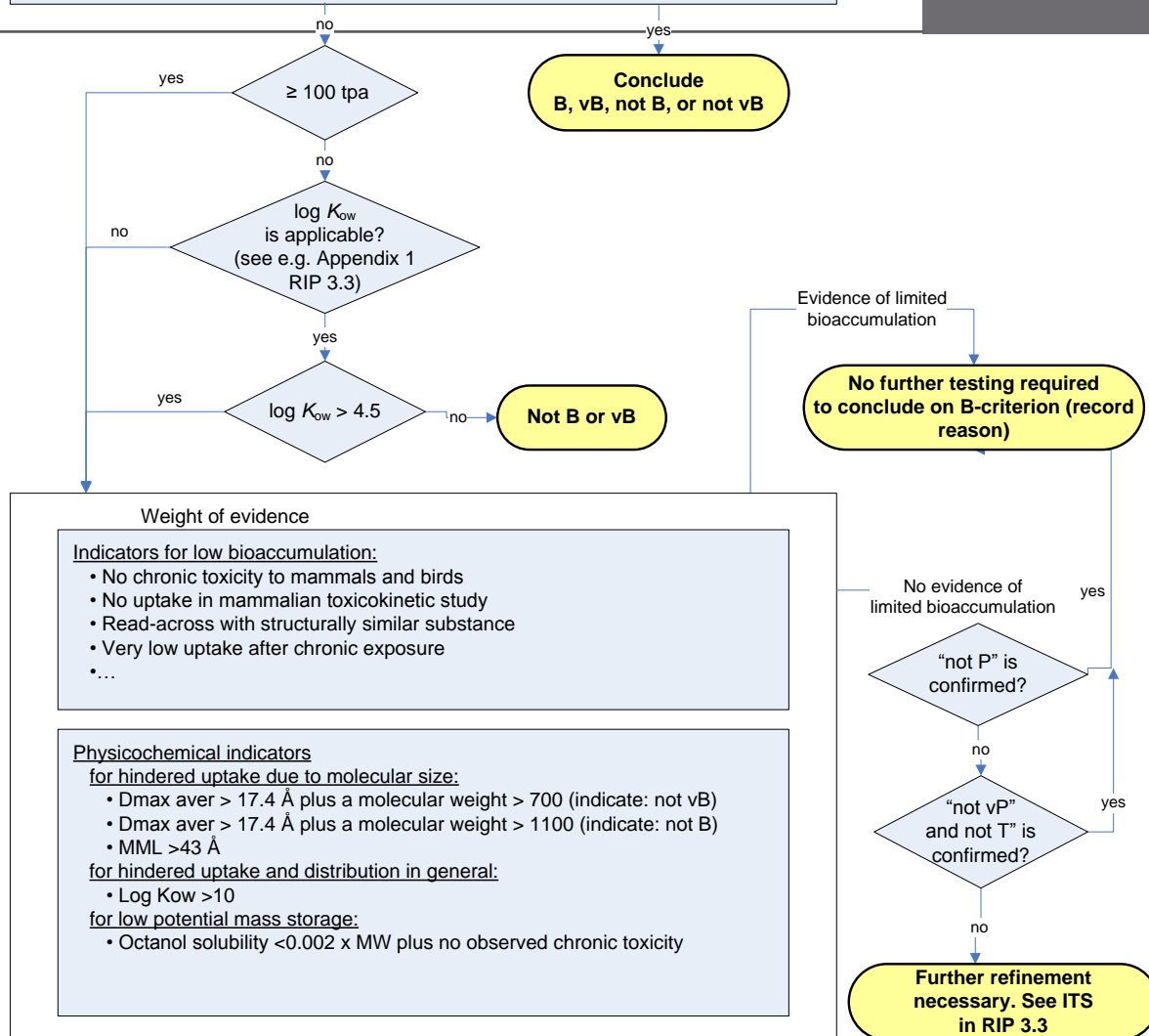
Detailed B Assessment

Using weight of evidence (See RIP 3.3), is there sufficient available information from

- aquatic BCF studies (fish, fish dietary, mussels)
- terrestrial and benthic accumulation studies
- field data concerning biomagnification and bioaccumulation to conclude on the B and vB assessment?

B Assessment Flow chart

from
REACH Guidance
CSA
PBT Assessment

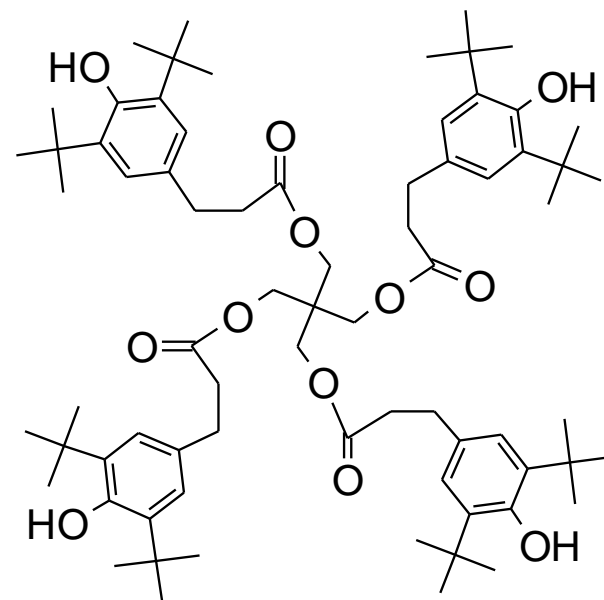


B Assessment

Indicators of Reduced Bioaccumulation

- **Molecular weight > 1100 g/Mol, Molecular size > 17 Angstrom and $K_{ow} > 10$** are indicators of reduced Bioaccumulation which can be used together with other indicators in a **Weight of Evidence Approach on Reduced Bioaccumulation**
- **The Antioxidant PETP has the following properties**
 - MW = 1178 g/Mol
 - Molecular size (D_{max}) = 17.9 Angstrom
 - K_{ow} = 19.6 (calc. KOWWIN)
 - **All three properties have values above the criteria for reduced bioaccumulation and a Weight of Evidence Approach for the B Assessment can be applied**

**Antioxidant PETP,
CAS No. 6683-19-8**



B Assessment

Sediment and Soil compartments

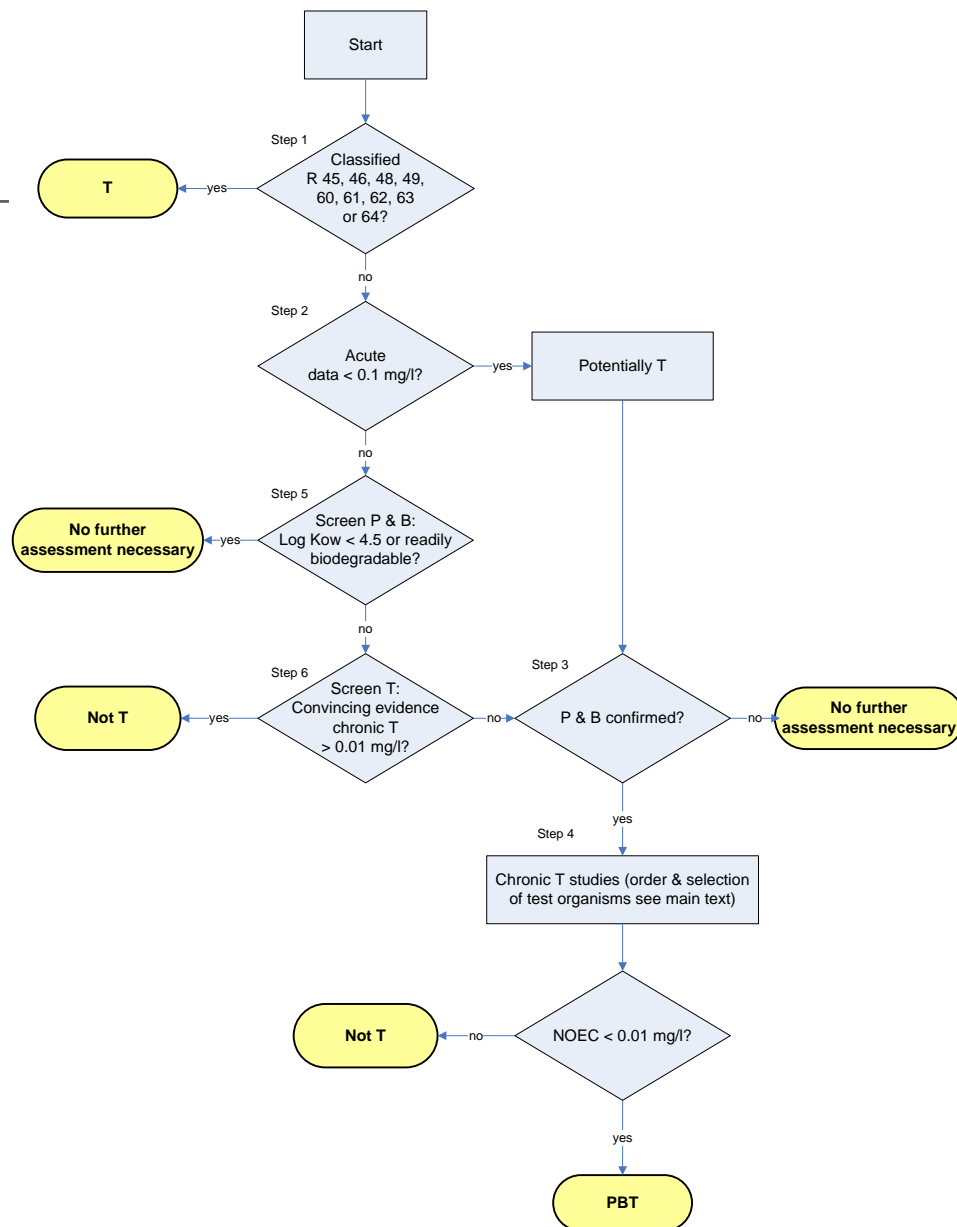
- **Organic Pigments** and certain **Antioxidants** have low water solubility and sorb strongly to solid phases.
 - The **target compartment of these substances are sediment or soil** and tests on fish bioconcentration can hardly be carried out.
 - Testing such substances in sediment and soil e.g. a Sediment Lumbriculus bioaccumulation test or a Soil Earthworm Soil bioaccumulation test would make sense in the framework of the PBT Assessment. But appropriate criteria for the bioaccumulation of these compartments are not yet defined

- **Science issue**
 - Development of a sound concept how to interpret
 - Bioaccumulation factors like BSAF in sediment & soil with respect to BCF of the Aquatic Compartment as well as Biomagnification in the Environment

T Assessment

**T Assessment
Flow chart**

from
**REACH Guidance
CSA
PBT Assessment**

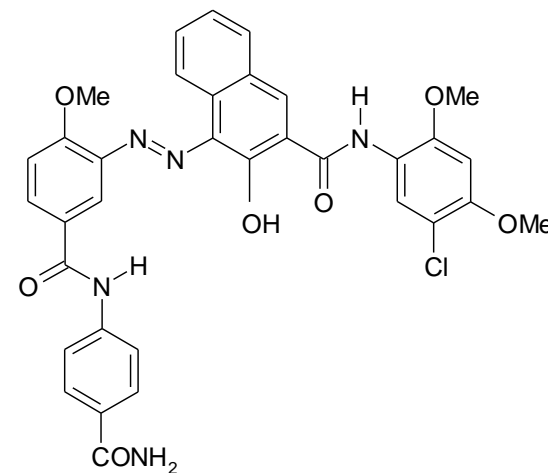


- **Organic Pigments** and certain **Antioxidants** have low water solubility and sorb strongly to solid phases.
 - The **target compartment of these substances are sediment or soil** and tests on aquatic ecotoxicity can hardly be carried out
 - Testing such substances in sediment and soil e.g. Chronic 28d Lumbriculus reprotoxcity test or Chronic 56d Earthworm reprotoxcity test would make sense in the framework of the PBT Assessment but appropriate criteria for ecotoxicity for these compartments are not yet defined

Pigment Red 187 CAS No. 59487-23-9

Acute ecotox: NOEC at water saturation 9 µg/L

Sediment: 28d Lumbriculus NOEC > 1000 mg/kg dw



■ Science issue

- Development of a sound concept how to interpret
 - Soil and sediment toxicity in the framework of the PBT Assessment

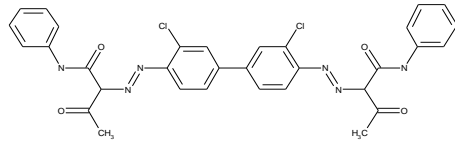
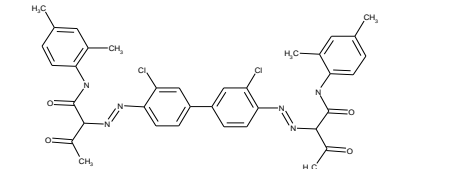
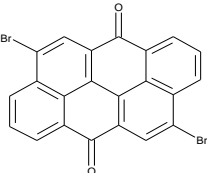
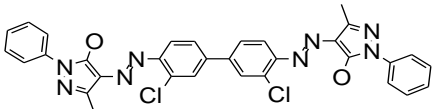
*Example for a
Category Approach*

Category Approach for Pigments to Check „B“ in the PBT Assessments (1)

- **Organic Pigments** very often have very low water and octanol solubility. These properties make a classical PBT Assessment Assessment very difficult to impossible especially th „B“ Assessment
 - **Measurement of a Kow** using OECD Methods is not possible due to analytical detection limits
 - **Using estimated Kow** for Pigments overestimate the true Kow by far in most cases
 - **Measuring the BCF for Organic Pigments** via a Fish Dietary Study would request ¹⁴C Pigment which is very difficult to synthesize in sufficient purity
- As the measurement of the Kow for Organic Pigments not possible the water and octanol solubility should be measured and instead of the log Kow the log $C_{\text{oct}}/C_{\text{water}}$ applied

Category Approach for Pigments to Check „B“ in the PBT Assessments (2)

Comparison of $\text{Log } C_{\text{octanol}}/C_{\text{water}}$ with estimated Log Kow (US EPA KOWWIN)

CAS No.	CI Name	Structure	Coctanol (µg/L) at ambient temp	Cwater (µg/L) at ambient temp	Log Coct/Cwater	Log Kow (US EPA KowWin)
006358-85-6	Pigment Yellow 12		48.1	0.8	1.8	7.0
005102-83-0	Pigment Yellow 13		22.3	0.4	1.8	8.1
004378-61-4	Pigment Red 168		124	10.8	1.1	7.1
003520-72-7	Pigment Orange 13		67	4.5	1.2	9.6

Category Approach for Pigments to Check „B“ in the PBT Assessments (3)

■ BCF / BAF and Octanol solubility

- 1-Octanol is a reasonable surrogate for fish lipids and if a substance has a reduced solubility in octanol (and therefore by extrapolation in lipid) this may result in a reduced BCF / BAF (only if the substance partitions to lipids and not to proteins)

■ The **Critical Body Burden (CBB)** is the concentration in an Organism which would induce toxic effects

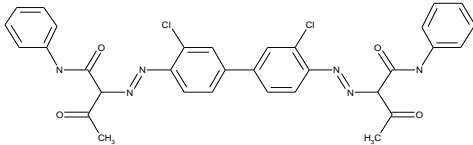
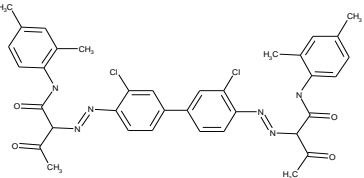
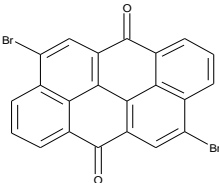
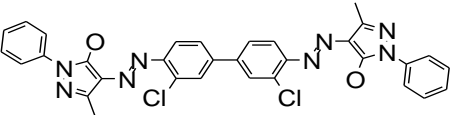
- Mostly acute and rarely chronic CBBs have been measured
- Based on published data and Safety factors applied the EU REACH Guidance on PBT Assessments recommends to use for the CBB

$$\text{CBB} = \text{Mol weight} * 2 \text{ } [\mu\text{g/L}]$$

- As Organic Pigments have a low octanol solubility one can compare this with the CBB. If the CBB is greater than Coctanol a reduced bioaccumulation and toxicity can be expected

Category Approach for Pigments to Check „B“ in the PBT Assessments (4)

Critical Body Burden Approach in comparison to the Octanol solubility

CAS No.	CI Name	Structure	Mol weight (g/Mol)	Coctanol (µg/L) at ambient temp	CBB 2* <i>MW</i> (µg/L)	Octanol solubility < CBB ?
006358-85-6	Pigment Yellow 12		629.51	48.1	1259	YES
005102-83-0	Pigment Yellow 13		685.62	22.3	1371	YES
004378-61-4	Pigment Red 168		464.12	124	928	YES
003520-72-7	Pigment Orange 13		623.51	66.6	1247	YES

Quantitative Risk Assessment of PBTs

- **Quantitative Risk Assessment** is a common methodology in the EU to address risks of a substance for Man and Environment
 - **Currently the EU states in the REACH CSA Guidance „PBT Assessment“**
 - Properties of PBT substances lead to an increased uncertainty in the estimation of risk to Human Health and the Environment when applying quantitative methodologies. **Safe concentrations in the environment cannot be established using methods currently available**
- **Industry is concerned** about this position and has asked EChA to establish a Working Group to address the uncertainty issue
- **Industry (ECETOC & CEFIC LRI) are currently planning several research projects** to enhance science in the context of PBTs and to reduce uncertainty in a quantitative risk assessment (e.g. establishing chronic body burdens)

Take away message

- Identify the substances under REACH which are NOT PBT or vPvB e.g. using an appropriate screening tool

- If potential PBT or vPvB substances were identified during the Screening establish a substance tailored testing approach considering the EU CSA Guidance „PBT Assessment“
 - Check if a Substance Category Approach can be used which helps in testing requirements (e.g. poorly water soluble and sorptive substances)
 - Check if the assessment issue is so difficult that an expert need to be involved
 - Do not hesitate to act immediately when further (complex) testing is necessary otherwise you may not meet the registration deadline

BACKUP SLIDES

PBT & vPvB Screening Criteria - Canada

- Ecological Categorisation Criteria can be found on the Web site

www.ec.gc.ca/substances/ece/eng/dsl/cat_criteria.cfm

PERSISTENCE	Medium	Half-life (Days)
	Air	≥ 2
	Water	≥ 182
	Sediment	≥ 365
	Soil	≥ 182
BIOACCUMULATION	Parameter	Value
	Bioaccumulation factor (BAF)	≥ 5000
	or Bioconcentration factor (BCF)	≥ 5000
	or log Kow	≥ 5
TOXICITY	Exposure duration	Value (mg/L)
	Acute L(E)C50	≤ 1
	Chronic NOEC	≤ 0.1

■ **The Japanese Chemical Control Law**

- **Gives no guidance on PBT Criteria**
- This is especially critical as the Japanese Ministry can do substance testing and evaluation on their own with little or no industry involvement. Can lead to a phase out decision on existing substances or a rejection of notification for new substances
 - An EU company had a recent case where they were forced to close a manufacturing for a substance which was classified as PBT. They even had to remove the substance from Japan. This was the only manufacturing site for the company for this substance worldwide and had severe consequences for their business
- **RECOMMENDATION FOR JAPAN**
 - Apply the PBT screening of Canada, EU and US before notifying in JAPAN

■ TSCA 5e Actions for New Substances

– Fed Reg 64, 60194-60204, 1999

	TSCA 5e ORDER pending Testing / SNUR (Exposure controls incl., Testing required)	TSCA 5e BAN pending Testing (Deny commercialization, testing results may justify removing from high risk concern)
PERSISTENCE	Half-life (days)	Half-life (days)
All media	> 60	> 180
BIOACCUMULATION	Value	Value
Bioaccumulation factor (BAF) or Bioconcentration factor (BCF)	>= 1000	>= 5000
or Log Kow	>= 4.2	>= 5
TOXICITY	TESTING STRATEGIES	Value (mg/L)
	Develop toxicity data (ecotox & mamalian) where necessary	
CUTOFF CRITERIA	If chemicals have a Mol weight > 1000 g/Mol and a cross-sectional diameter > 2 nm they are not considered to be 'B'	
TESTING STRATEGIES	A Testing strategy to overcome TSCA 5e Order or BAN has to take into account various factors including concerns for persistence, bioaccumulation, P-Chem properties and toxicity based on available data. The testing strategy is TIERED (see examples in Fed Reg 64, 60194-60204, 1999)	