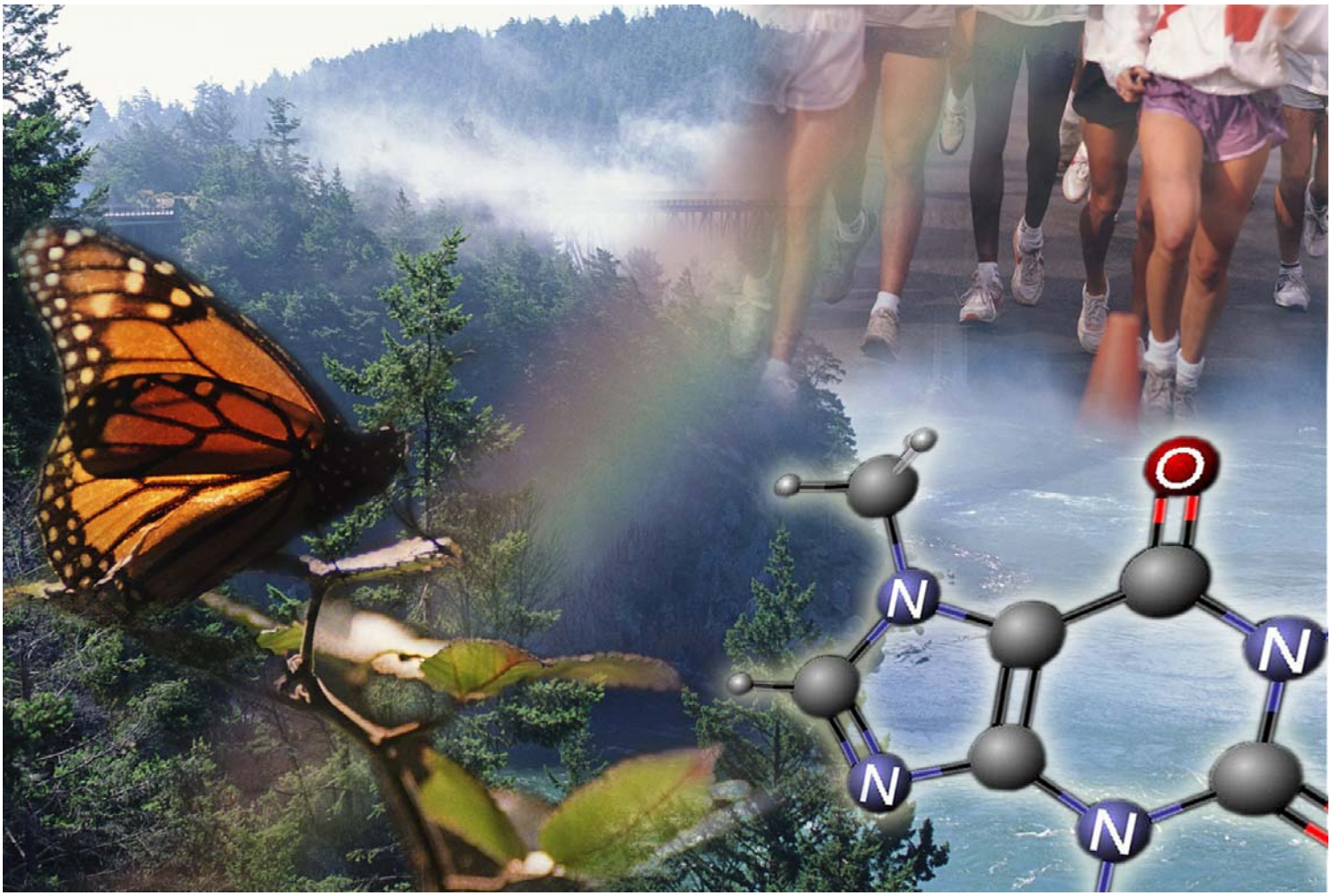
Guidance on information requirements and chemical safety assessment

Part C: PBT Assessment



May 2008

Guidance for the implementation of REACH

LEGAL NOTICE

This document contains guidance on REACH explaining the REACH obligations and how to fulfil them. However, users are reminded that the text of the REACH regulation is the only authentic legal reference and that the information in this document does not constitute legal advice. The European Chemicals Agency does not accept any liability with regard to the contents of this document.

PREFACE

This document describes the information requirements under REACH with regard to substance properties, exposure, use and risk management measures, and the chemical safety assessment. It is part of a series of guidance documents that are aimed to help all stakeholders with their preparation for fulfilling their obligations under the REACH regulation. These documents cover detailed guidance for a range of essential REACH processes as well as for some specific scientific and/or technical methods that industry or authorities need to make use of under REACH.

The guidance documents were drafted and discussed within the REACH Implementation Projects (RIPs) led by the European Commission services, involving stakeholders from Member States, industry and non-governmental organisations. These guidance documents can be obtained via the website of the European Chemicals Agency (http://echa.europa.eu/about/reach_en.asp). Further guidance documents will be published on this website when they are finalised or updated.

This document relates to the REACH Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006[1]

1 Corrigendum to Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006); amended by Council Regulation (EC) No 1354/2007 of 15 November 2007 adapting Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) by reason of the accession of Bulgaria and Romania (OJ L 304, 22.11.2007, p. 1).

Convention for citing the REACH regulation

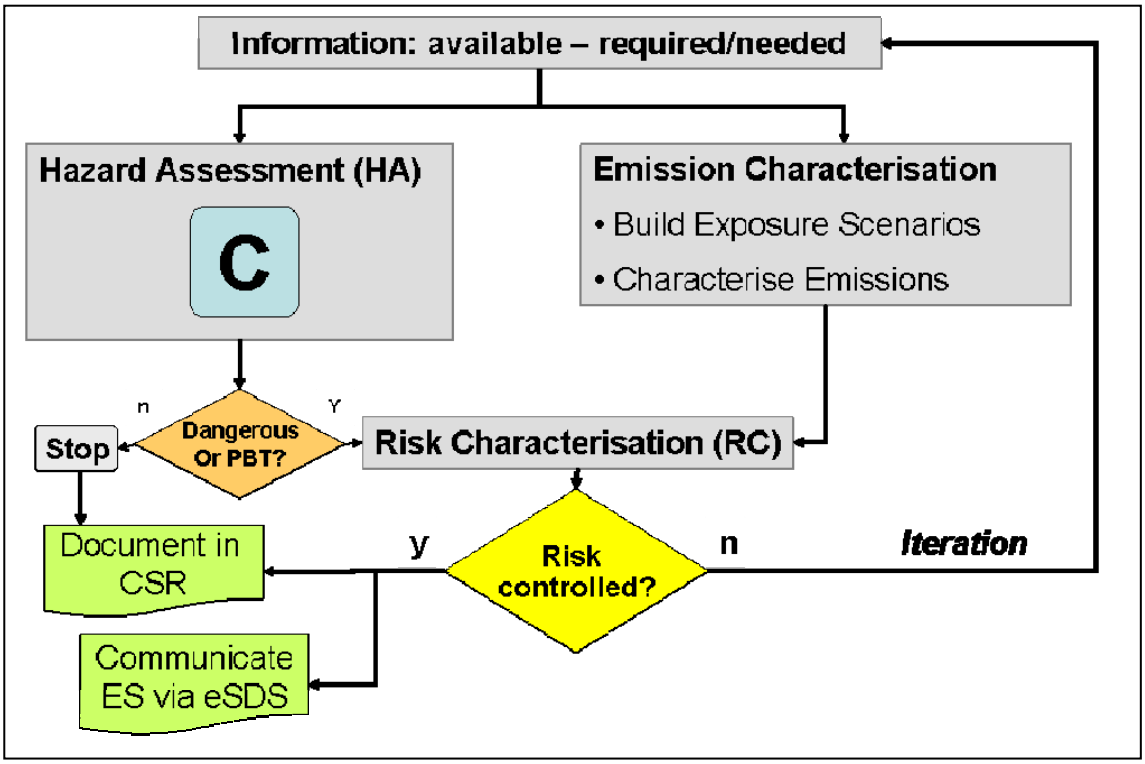
Where the REACH regulation is cited literally, this is indicated by text in italics between quotes.

Table of Terms and Abbreviations

See Chapter R.20

Pathfinder

The figure below indicates the location of part C within the Guidance Document.



CONTENTS

TABLES

C.1 PBT AND vPvB ASSESSMENT

A PBT/vPvB assessment is required for all substances for which a chemical safety assessment (CSA) must be conducted. These are in general all substances manufactured or imported in amounts of 10 or more tonnes per year that are not exempted from registration under REACH. However, some further exemptions apply, e.g. substances present in a preparation if the concentration is less than 0.1 % weight by weight (Article 14(2)), for on-site isolated (Art. 17) or transported intermediates (Art. 18), and for Product and Process Oriented Research and Development (Art. 9) (see *Guidance on Registration*, Section 1.8.1, for further information).

C.1.1 Aim and procedure

The objective of the PBT/vPvB assessment is to determine in a stepwise procedure:

1. Whether the substance fulfils the criteria given in Annex XIII (comparision with the criteria) .

   If it is concluded that the substance is not a PBT/vPvB substance, the PBT/vPvB assessment stops after comparison with the criteria. An exposure and risk assessment as for a non-PBT/vPvB substance could however be required if the substances is dangerous in accordance with the classification criteria of Council Directive 67/548/EEC.

2. If a substance is confirmed to be a PBT/vPvB substance, the registrant needs in a second step (emission characterisation; see Sections C.1.6 and R.11.2 for further guidance) to estimate the amounts of the substance released to the different environmental compartments during all activities carried out by the registrant and all identified uses. In addition, it is necessary to identify the likely routes by which humans and the environment are exposed to the substance.

3. The registrant shall use the information obtained during the emission characterisation step, for implementing on his site, and recommending to downstream users, risk management measures (RMM) which minimise emissions and subsequent exposures of humans and the environment throughout the lifecycle of the substance that results from manufacture or identified uses.

C.1.2 PBT and vPvB criteria

A substance that fulfils all three of the criteria for persistence, bioaccumulation and toxicity described in Table C.1-1 is a PBT substance.

It should however be noted that, even where a criterion is marginally not fulfilled, the overall evidence can be sufficient to justify the conclusion that a substance fulfils the Annex XIII criteria. This includes for example substances that do not fulfil the persistence criteria but bioaccumulate significantly and are measured in increasing levels over time in biota distant from anthropogenic sources (see Section R.11.1.5 for further guidance).

C.1.3 Comparison with the PBT and vPvB criteria

The PBT and vPvB assessment of a substance shall be based on all the relevant information available, which is normally the information that shall be submitted as part of the technical dossier, including the physicochemical, hazard and exposure information generated in the context of the CSA. If the technical dossier, for one or more endpoints, contains only the information as required in Annexes VII and VIII, the registrant shall, based on screening criteria or other information available, consider whether further information needs to be generated to fulfil the objective of the PBT and vPvB assessment, i.e. to assess whether the substance fulfils the criteria. Hence, it is task of the registrant to assess if the information that is available and/or produced is sufficient to conclude whether the substance is a PBT or a vPvB substance or not. In many cases further information as detailed in Annexes IX and X of the Regulation may need to be generated before it can be judged whether the substance fulfils the Annex XIII criteria. Generally, before generating information detailed in Annexes IX and X, a testing proposal needs to be submitted to and authorised by the ECHA.

The PBT assessment is initiated by an evaluation of all available information. For substances below a volume of 100 t/y normally data on ready biodegradability, octanol-water partitioning coefficient (log Kow) and environmental toxicity are available that give an indication on the P, B and T properties of a substance.

Table C.1-2 gives an overview of information that can be used for a screening assessment and provides criteria to decide whether an in depth assessment on the PBT or vPvB properties is necessary.

When the screening criteria do not clearly indicate that there is no concern that the substance could meet the Annex XIII criteria (Table C.1-1), a stepwise approach is followed for the definitive assessment of the P, B and T criteria, which is further outlined below.

Table C.1-1: PBT and vPvB criteria according to Annex XIII of the REACH Regulation

Property	PBT-criteria	vPvB-criteria
Persistence[1]	- $T_{1/2}$ > 60 days in marine water, or - $T_{1/2}$ > 40 days in fresh- or estuarine water, or - $T_{1/2}$ > 180 days in marine sediment, or - $T_{1/2}$ > 120 days in fresh- or estuarine sediment, or - $T_{1/2}$ > 120 days in soil.	- $T_{1/2}$ > 60 days in marine, fresh- or estuarine water, or - $T_{1/2}$ > 180 days in marine, fresh- or estuarine sediment, or - $T_{1/2}$ > 180 days in soil.
Bioaccumulation[2]	BCF > 2000 L/kg	BCF > 5000 L/kg
Toxicity	- NOEC < 0.01 mg/L for marine or freshwater organisms, or - substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic for reproduction (category 1, 2 or 3), or - there is other evidence of chronic toxicity, as identified by the classifications: T, R48, or Xn, R48 according to Directive 67/548/EEC.	-

Screening assessment

The screening criteria (Table C.1-2) should always be considered in conjunction for P, B and T to decide whether the substance has to be regarded as a potential PBT/vPvB. It has to be kept in mind that the fact that a substance does not meet the T criterion is not enough to stop the evaluation of the remaining endpoints in the PBT/vPvB screening step. Similarly, conflicting evidence arising from further information, e.g. monitoring data indicating potential P or B properties, needs to be considered in the assessment and the overall conclusion on the PBT or vPvB properties (see Section R.11.1.5 for further guidance).

Table C.1-2: Screening criteria for Persistency, Bioaccumulation, and Toxicity[2]

Type of data	Criterion	Screening assignment
Persistence		
Ready biodegradability test	Readily biodegradable	Not P and not vP
Enhanced ready biodegradability test	Readily biodegradable	Not P and not vP
Specified tests on 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
Biowin 2 (non-linear model prediction) and Biowin 3 (ultimate biodegradation time) **or** Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability <0.5), and ultimate biodegradation timeframe prediction: ≥months (value < 2.2) **or** Does not biodegrade fast (probability <0.5) and ultimate biodegradation timeframe prediction: ≥months (value < 2.2)	P P
Bioaccumulation		
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
Octanol-water partitioning coefficient (experimentally determined or estimated by QSAR)	Log Kow ≤ 4.5	not B and not vB
Toxicity		
Short-term aquatic toxicity	EC50 or LC50 < 0.01 mg/L	T, criterion considered to be definitely fulfilled
Short-term aquatic toxicity	EC50 or LC50 < 0.1 mg/L	T
Avian toxicity (subchronic or chronic toxicity or toxic for reproduction)	NOEC < 30 mg/kg food	T

[2] For further description of the tests and guidance on their interpretation see Chapter R.11 of the Guidance Document for Preparing the Chemical Safety Assessment.

Definitive assessment

If, on the basis of the screening assessment, a substance is considered to potentially fulfil the criteria for P, B and T or for vP and vB, the registrant may choose to treat the substance as a PBT/vPvB-substance and report accordingly in the chemical safety report without further evaluation of the properties.

If the registrant decides to further evaluate the properties of a substance that based on the screening assessment potentially fulfils the PBT or vPvB criteria, a definitive assessment of P/vP should be conducted first. Definitive assessment of P/vP should normally be based on half-life data collected under adequate conditions for the relevant compartment(s) of exposure (see Section C.1.4.1).

If the substance is considered to fulfil the P and/or vP criterion, the PBT/vPvB assessment is continued by evaluation of the B/vB criterion. Definitive assessment of B/vB should normally be based on measured data on bioconcentration in aquatic species (see Section C.1.4.2).

If the substance is not identified as vPvB but considered to fulfil the P and B criteria, the PBT assessment is continued by evaluation of the T criterion. Definitive assessment of T should be based on evaluation of the data for classification of the substance for human health hazards and/or on no-observed effect concentration(s)(NOECs) from long-term toxicity tests with aquatic organisms (see Section C.1.4.3).

However, for substances for which persistency testing is difficult or practically impossible, like e.g. for certain multi-constituent or very poorly water soluble substances, it may sometimes be more reasonable to start the PBT/vPvB assessment by evaluating the B criterion (see Section R.11.1.3.2 for further guidance).

C.1.4 Test strategies

C.1.4.1 Persistency

The detailed testing strategy on degradation for PBT/vPvB assessment is set out in Section R.11.1.3.1 and Figure R.11-1. It is based on a weight of evidence approach starting with the review of all available screening test data and non-test data ((Q)SAR model predictions, read across, and chemical categorisation). The criteria for the screening methods are given in Table C.1-2. In some cases, the performance of an enhanced ready biodegradation test may deliver sufficient information to draw the conclusion that the substance can be considered as "not P".

If persistency cannot be excluded, it should be determined which compartments are likely to be exposed, and hence which simulation tests need to be conducted. This determination of the compartments(s) for simulation testing should take account of the intrinsic properties of the substance (e.g. water solubility, vapour pressure, log Kow, Kp, Koa, half-life in air) that are significantly influencing the environmental fate of the substance. Multi-media modelling (e.g. Mackay level 3 models) may also be used in order to determine the environmental compartment(s) of primary concern.

Soil/sediment simulation degradation testing is warranted if the screening data indicate potential persistency and direct or indirect exposure of these compartments is likely. This includes cases where a substance is released to surface water but due to high sorption

partitions to sediment or sewage sludge, which may be spread on soil, or where a substance is volatilised from water to air and deposited to soil.

The Kp (sediment) may be used as an indicator of whether testing in a water-sediment system may be warranted. For example, it may be considered to conduct an aquatic sediment simulation test in addition to a pelagic simulation test for substances with Kp (sediment) > 2000.

C.1.4.2 Bioaccumulation

A detailed test strategy for bioaccumulation testing for PBT/vPvB assessment is set out in Section R.11.1.3.2 and Figure R.11-2. In general, all existing information on the bioaccumulation potential of a substance should be collected and evaluated first before a decision on the necessity to conduct further testing is drawn. The existing data may include laboratory bioconcentration tests (aquatic, terrestrial and benthic) and field studies on biomagnification or bioaccumulation. Such available information might be sufficient to conclude whether the substance is vB, B, or not B (see Section R.11.1.3.2).

If the above mentioned information is not available for a substance produced or imported at a level of less than 100 t/y and the substance has a log Kow ≤ 4.5 and no specific uptake mechanism apart from lipophilic partitioning is known or suspected, then the substance can be considered as not B and not vB and further evaluation of the B and vB criteria is not necessary.

However, for a substance produced or imported at a level of 100 t/y or more, information on bioconcentration in aquatic species has to be made available by the registrant and to be considered in the assessment, unless this information can be waived according to column 2 of Annex IX or according to Annex XI(3) (e.g. low bioaccumulation potential, no exposure, testing technically not possible).

In other cases, where:

- no direct data on bioconcentration are available and the substance has a log Kow > 4.5, or the partitioning process into aquatic organisms is not driven by lipophilicity ;
- direct data on bioconcentration are available but these data are not reliable and/or consistent to a degree sufficient to conclude whether the B or vB criteria are met;

the B and vB properties should be evaluated in more detail.

In this further evaluation, non-testing data should be used as indicators for limited bioaccumulation in a weight of evidence assessment together with supplementary information to examine whether the substance potentially meets the B and vB criteria. Because the indicators for limited bioaccumulation (e.g. molecular weight and size of the molecule, octanol solubility or log Kow) are on their own considered to be insufficient to abstain from confirmatory testing, the availability of other reliable information indicating a low bioaccumulation potential is essential. This supplementary information may comprise data showing no toxicity in a chronic toxicity study with mammals, no uptake in a toxicokinetic study, or it could be a bioconcentration study with invertebrates or reliable read-across from a structurally similar compound. Evidence of significant uptake of a substance in fish or mammals after prolonged exposure is a contraindication to using the above indicators of limited bioconcentration.

C.1.4.3 Toxicity

A detailed test strategy for toxicity testing for PBT/vPvB assessment is set out in Section R.11.1.3.3 and Figure R.11-3. The strategy starts with the evaluation of the classification of the substance. If any classification criterion leading to the assignment of the R-phrases R45, R46, R48, R49, R60 – R63 is met, the substance fulfils the T criterion[3] and there is no need to perform any further aquatic studies for T assessment.

When no such classification is assigned, data on aquatic toxicity should be evaluated. When no chronic toxicity data are available, a substance is considered to meet the T-criterion when an acute L/EC50 value from a standard toxicity (or reliable non-standard) test is < 0.01 mg/l. When the L/EC50 is < 0.1 mg/l, the substance is considered to meet potentially the T-criterion, and consequently the substance is referred to definitive T testing and chronic studies are required (regardless of the tonnage band). Note however that, due to animal welfare concerns, the general scheme of testing and confirming first P and B should be applied before further T-testing is considered. Also, vertebrate-animal testing should be minimised by first testing non-vertebrate species. Normally, the testing order for conclusion on T based on chronic data is Daphnia and then fish[4], unless there is evidence that fish are more sensitive than daphnia. If the T-criterion is fulfilled by the chronic algae or Daphnia data, a chronic fish test is not necessary. If however a long term test on Daphnia or algae provides a NOEC close to but above 0.01 mg/l, a long-term fish study is likely to be needed to confirm "not T".

For certain lipophilic substances (with a log Kow >5) acute toxicity may not occur at the limit of the water solubility of the substance tested (or the highest concentration tested). In such situations, chronic toxicity with a NOEC <0.01 mg/l cannot be excluded even if available short-term toxicity data indicate L/EC50 values > 0.1 mg/l, because these substances may not have had sufficient time in the acute test to be significantly taken up by the test organisms and to reach equilibrium partitioning. (see Section R.11.1.3.3, ITS for T-testing, Figure R.11-3 and decision tree Steps 2, 5 & 6).

In the absence of definitive information on T, for substances with very high lipophilicity, a weight of evidence or group approach for long term toxicity may be used to predict whether long term effects are likely to occur. If convincing evidence is available that aquatic toxicity is not expected to occur at <0.01 mg/l, chronic testing may not be required. Such evidence could comprise reliable QSAR predictions, read-across or grouping approaches indicating narcotic mode of action together with measured low chronic fish toxicity data from a related compound. Supporting information could be chronic data on aquatic species such as, e.g., daphnids, algae or sediment dwelling species and/or low acute or chronic mammalian and avian toxicity. Any conclusions on the suitability of data and the T criterion should be based on expert judgement and weight of evidence. If data from this approach provide insufficient evidence that toxicity will not occur in a chronic test long-term T-testing must be considered.

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3 Note the obligation to check whether the criteria for assigning a respective classification are fulfilled. It is not enough to check whether any of the mentioned R-phrases has already been assigned to the substance.

4 Algae are not mentioned here because chronic algae data (i.e. 72h NOEC) normally will be available, as it can be easily obtained from the same 72h standard test from which the acute endpoint (72h EC50) is derived.

C.1.5 Conclusions on PBT or vPvB properties

A detailed analysis of the persistence, bioaccumulation and toxicity should be brought together into a clear conclusion on whether the substance should be treated as a PBT/vPvB substance. There are a number of conclusions from this comparison that call for different responses from a registrant (see Section R.11.1.5 for further guidance).

(i) The data show that the properties of the substance meet the specific criteria detailed in Annex XIII, or do not allow a direct comparison with all the criteria in Annex XIII, but nevertheless indicate that the substance would have these properties

In this case an emission and risk characterisation for PBT/vPvB substances in accordance with the stipulations of Annex I is required.

(ii) The data show that the properties of the substance do not meet the specific criteria detailed in Annex XIII or do not allow a direct comparison with all the criteria in Annex XIII but nevertheless indicate that the substance would not have these properties and the substance is not considered a PBT/vPvB

In this case the PBT/vPvB assessment stops at this point. An exposure assessment and risk characterisation as for a non-PBT/vPvB substance may however be required if the substance is dangerous in accordance with the classification criteria of Council Directive 67/548/EEC.

(iii) The data on the properties of the substance do not allow a direct comparison with all the criteria in Annex XIII and further information is needed

In this case a registrant has two options:

- The registrant generates the required information (depending on the information needed, the submission of a testing proposal may be required) and concludes on the PBT/vPvB properties of the substance concerned once the lacking data are available (i.e. conclusion (i) or (ii)); or
- The registrant refrains from generating further information and treats his substances as if it were a PBT/vPvB.

(iv) Further information would be needed to conclude on the PBT/vPvB properties of the substance. However, the registrant (for several reasons) has decided not to conduct confirmatory testing.

If a clear decision on the properties of a substance cannot be made, either because it is not possible to characterise a substance, or since it is technically not possible to conduct testing, this lack of a clear decision does not obviate the requirement on a registrant to propose appropriate and proportionate RMMs and OCs.

C.1.6 Further actions if a substance is identified as a PBT or a vPvB

If it is concluded that the substance is a PBT or vPvB substance, or that it should be treated as such, the registrant must conduct an emission characterisation and a risk characterisation for PBT/vPvB substances in accordance with Article 14 (4).

Generally, if a substance contains one or more constituents with PBT/vPvB properties in individual amounts ≥ 0.1 % (w/w) or if transformation/degradation products with the respective properties in amounts ≥ 0.1 % are being generated, the substance must be subjected

to PBT/vPvB specific emission characterisation and risk characterisation. However, for the sake of relevance of risk exerted by the amount of a PBT/vPvB substance manufactured/imported by a registrant, and hence with regard to the requirements for risk characterisation and nature of RMM to be implemented, it may be considered to use a threshold value of 10% (w/w) for the total of all constituents or transformation/degradation products having PBT or vPvB properties, if it is possible to estimate with sufficient certainty that the total manufacture/import or supply of PBT/vPvB constituents in that substance and the total amount of degradation/transformation products with PBT/vPvB properties generated by that substance do not exceed 1 t/y[5]. In the considerations as to whether application of this percentage trigger could be appropriate, the use pattern of the substance and the potential emissions of the constituents or transformation/degradation products having PBT or vPvB properties must be accounted for.

The main objective of the emission characterisation is to estimate the amounts of the substance released to the different environmental compartments and to identify the likely routes by which humans and the environment are exposed to the substance. A registrant has only to take care of his own tonnage[6]. In co-operation with his downstream users he has to cover, where relevant, any manufacture in the EU he is responsible for, his own uses and all identified uses including all resulting lifecycle stages.

The principal tool to achieve this objective is exposure scenarios (ES(s)). Part D and Chapters R.12 to R.18 provide guidance on how to develop ESs for substances in general. Parts of the exposure assessment guidance are relevant also for PBT/vPvB substances (i.e. emission estimation and assessment of chemical fate and pathways). However, since the objectives are not the same the general scheme for exposure assessment needs to be adapted to the requirements of emission characterisation for PBT/vPvB substances. Below guidance is given on some issues where special considerations are needed for PBT/ vPvB substances. In the context of the emission characterisation, the registrant needs to develop ES(s) for all identified uses of his PBT/vPvB substance, unless he concludes to advise in his technical dossier (and SDS) against certain uses of his substance. In this latter case he does not need to perform an emission characterisation or other risk management work related to these uses.

As PBTs and vPvBs are substances of very high concern, the registrant shall pay special attention to the level of detail of his assessment and whether its accuracy and reliability is sufficient for a PBT/vPvB substance. Where generic scenarios and assumptions may be sufficient for exposure assessment of non PBT/vPvB-substances, specific scenarios and data will most likely be needed throughout an emission characterisation for PBT/vPvB-substances. All effort necessary should be made to acquire for manufacture and any identified use throughout the lifecycle, site- and product-specific information on emissions and likely routes by which humans and the environment are exposed to the substance. The emission

5 Please note that the proposed one tonne per year threshold for the total of compounds with PBT/vPvB properties in a substance consisting of more than one component (be it a preparation or a multi-constituent substance) is not an ‘allowable release’ threshold. It refers instead to the content in a substance that will need to have appropriate risk assessment and management justified in the chemical safety report. 1 t/y is the level at which the registration requirement under REACH normally begins to apply if a substance was supplied alone or in a preparation. 1 t/y is also the trigger for registration in an article. Therefore, this amount is considered to be a suitable threshold level for relevance and hence adaptation of required risk assessment efforts and, depending on the results of risk assessment, possibly risk management measures.

6 However, it can be useful to consider on a voluntary basis exposure resulting from emissions of the same substance manufactured or imported by other registrants (i.e., the overall estimated market volume), c.f. Part A.2.1.

characterisation shall in particular be specific in the use description and concerning RMMs, and shall furthermore contain an estimation of the release rate (e.g. kg/year) to the different environmental compartments during all activities carried out during manufacture or identified uses (see Section R.11.2.1 for further guidance).

The objective of a risk characterisation for substances satisfying the PBT or vPvB criteria is to use the information obtained in the emission characterisation step to implement on a registrant's site or to recommend to his downstream users RMMs which minimise exposures and emissions to humans and the environment throughout the lifecycle of the substance that results from manufacture or identified uses (Annex I (6.5)). To this end, the minimisation of exposures and emissions to humans and the environment needs to be considered throughout the development of ES(s). The need or a potential to (further) minimise emissions or exposure may therefore be recognised at any point in the development of an ES. In this way, the appropriateness and effectiveness of RMMs and OCs should be assessed in the development of the ES.

Suitable options and measures to minimise emissions of and exposure to a PBT/vPvB substance are, for instance, substitution of the substance or reduction of its use when technically possible, manufacture and use under strictly controlled conditions and handling of the substance by trained personal only (see Section R.11.2.2 for further guidance).

The final ES, or ES(s) in case of different uses, shall be presented under the relevant heading of the chemical safety report, and included in an annex to the SDS. It shall describe the required OCs and RMMs in a way that downstream users can check whether they have to implement any measures in order to minimise emissions or exposures of humans and the environment.