Guidance for the preparation of an Annex XV dossier on the identification of substances of very high concern

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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 Guidance Document describes how the authorities (Member States Competent Authorities or the Agency) can prepare an Annex XV dossier to identify a substance of very high concern under REACH. 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) lead by the European Commission services, involving all stakeholders: 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/reach_en.html). Further guidance documents will be published on this website when they are finalised or updated.

The legal reference for the document is 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)

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1 INTRODUCTION

The REACH Regulation sets up a system under which the use of substances with properties of very high concern and their placing on the market can be made subject to an authorisation requirement. This authorisation requirement ensures that risks from the use of such substances are either adequately controlled or justified by socio-economic grounds, having taken into account the available information on alternative substances or processes.

The authorisation provisions require those using or placing on the market substances which are included into the system to apply for an authorisation for each use, regardless of the quantity of the substance used, within deadlines set by the Commission. The burden of proof is placed on the applicant to demonstrate that the risk from the use is adequately controlled or that the socio-economic benefits outweigh the risks.

The Agency, via its Committees for Risk Assessment and Socio-economic Analysis provides opinions on the applications, which the Commission will use when deciding on applications.

The Guidance on Annex XIV inclusion develops guidance on the process for inclusion of substances into Annex XIV (List of substances subject to authorisation) and on the prioritisation methods used in this process.

About this guidance

This document provides technical guidance to the Member States and the European Chemicals Agency in preparing an Annex XV dossier to propose and justify the identification of substances of very high concern in accordance with the procedure set out in article 59 of 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 (the REACH Regulation).

In this document the term 'Authority' is used to refer to the Agency or any Member State competent authority undertaking work on substance evaluation or developing an Annex XV dossier.

Where the term SVHC (Substance of Very High Concern) is used in this guidance, it includes all substances covered by article 57 (see section 0 below).

This guidance is intended for use by those within the Member State competent authorities and the Agency responsible for the production of Annex XV dossiers. In general, it assumes that the user has suitable experience for the part of the guidance they are using. However, the full range of Annex XV dossiers cover a wide range of subject areas and so some areas include more basic guidance.

The guidance is also relevant for registrants and others involved with a substance for following and participating in the process, understanding the basis of the Annex XV dossiers and the justification for any proposal.

2 LEGAL FRAMEWORK

Substances subject to authorisation (Art. 57)

Substances of very high concern which may be included in the Annex XIV, and for which thereby the authorisation requirement will be established, are substances with the following properties:

a) substances meeting the criteria for classification as carcinogenic category 1 or 2 in accordance with Directive 67/548/EEC;

b) substances meeting the criteria for classification as mutagenic category 1 or 2 in accordance with Directive 67/548/EEC;

c) substances meeting the criteria for classification as toxic for reproduction category 1 or 2 in accordance with Directive 67/548/EEC;

d) substances which are persistent, bioaccumulative and toxic in accordance with the criteria set out in Annex XIII of this Regulation;

e) substances which are very persistent and very bioaccumulative in accordance with the criteria set out in Annex XIII of this Regulation;

f) 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 fulfil the criteria of points (d) or (e) - 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 to those of other substances listed in points (a) to (e) and which are identified on a case-by-case basis in accordance with the procedure set out in Article 59.

Procedure to include substances into the authorisation system

The Guidance on Annex XIV inclusion is dealing with inclusion of substance in Annex XIV. This chapter will be updated once the project is finalised.

The procedure to include substances into the authorisation system consists of:

- the identification of substances of very high concern and their inclusion on the candidate list with an indication whether they are included in the Agency's work programme
- Agency's preparation of its recommendation of priority substances for inclusion in Annex XIV according to Article 58 (3);
- Comitology decision on which substances to include in Annex XIV.

Figure 1 gives an overview of these processes.

Identification of substances of very high concern (Art. 59)

All substances that will be included in Annex XIV, and by that be subject to the authorisation system, will need to be identified in a first step according to the procedure in Article 59 and will thus be included in the candidate list.

For this purpose the Authorities need to prepare an Annex XV dossier and detailed guidance on how to prepare such a dossier is given in section 3.

This identification procedure consists of the following steps:

1. A Member State or the Agency on request by the Commission, prepares a dossier in which it provides the argumentation why a substance has properties of very high concern. The dossier may be limited, if appropriate, to a reference to an entry in Annex I of Directive 67/548/EEC. This dossier needs to follow the format in Annex XV, and Member States need to send it to the Agency.

2. The Agency makes the dossier available to the other Member States within 30 days of receipt and publishes a notice and the non-confidential parts of an Annex XV dossier on its website, inviting interested parties to comment. In case of a dossier prepared by the Agency itself, the Agency distributes it to the Member States and publishes the notice and the non-confidential parts of the Annex XV dossier in the same way.

3. Within 60 days of the date of circulation the other Member States can send their comments on the identification of the substance in the dossier to the Agency; the Agency may also provide comments.

4. If no comments are received, the Agency shall include the substance in the candidate list for eventual inclusion in Annex XIV and may include the substance in its recommendations on priority substances to the Commission for inclusion into Annex XIV

5. If comments are received from Member States, third parties or the Agency itself, the Agency will forward the dossier to the Member States Committee within 15 days after expiry of the 60 days commenting period.

6. If the Member State Committee reaches unanimous agreement on the identification within 30 days after the dossier was referred to it, the Agency shall include the substance on the candidate list of substances for eventual inclusion in Annex XIV and may include the substance in its recommendations on priority substances to the Commission for inclusion into Annex XIV.

7. When the Member State Committee does not reach unanimous agreement on the identification within 30 days after the dossier was referred to it, it shall draft its opinion on the issue which will be sent to the Commission.

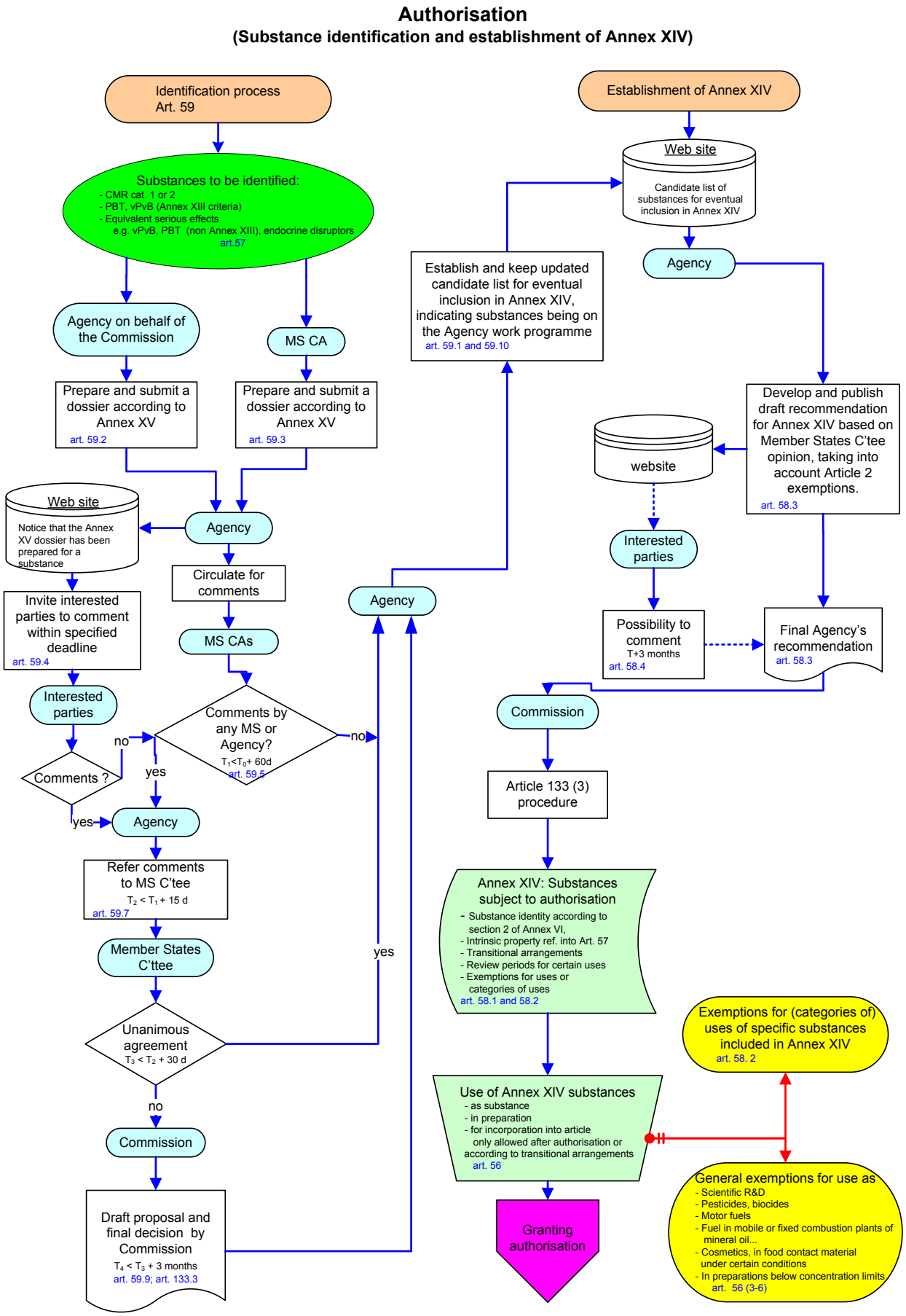
8. The Commission shall then prepare a draft proposal on the identification of the substance within 3 months after receiving the opinion from the Member State Committee and the final decision shall be taken in accordance with the comitology procedure.

All substances identified in this procedure will form the candidate list of substances from which the Agency will select priority substances for inclusion into the authorisation system.

Prioritisation of substances with identified properties of very high concern (Art. 58 (3) and (4)) for inclusion in Annex XIV

As the number of substances with identified defined properties of very high concern is expected to be relatively high, it is necessary to prioritise the progressive inclusion of identified substances into the system.

Figure 1 Substance identification and establishment of Annex XIV



3 PREPARATION OF AN ANNEX XV DOSSIER FOR THE IDENTIFICATION OF SUBSTANCES OF VERY HIGH CONCERN (ACCORDING TO ARTICLE 57)

Aim: The objective is to develop an Annex XV dossier proposing the identification of a substance as a CMR (cat 1 or 2) substance, a PBT substance, a vPvB substance or as a substance with probable serious effects which give rise to an equivalent level of concern.

Scope: The basic steps required are :

- Information collection.
- Information review.
- Completion of report sections.

The amount of work required for these steps will depend to some extent on the stage in the REACH process at which the substance is being considered, but the same general principles apply.

This section considers the preparation of an Annex XV dossier to propose substances to be identified for inclusion in the candidate list for eventual inclusion in Annex XIV. It provides guidance in relation to substances proposed to be identified as CMR substances under Article 57 (a) to (c), persistent, bioaccumulative and toxic (PBT) substances under Article 57 (d), very persistent and very bioaccumulative (vPvB) substances under Article 57 (e), and substances of equivalent concern under Article 57 (f).

Note that the legal text uses the phrase *'substances ... 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 to those of other substance listed in point (a) to (e) [of Article 57]'*. In this guidance, the phrase 'equivalent concern' is used as an abbreviated form of the legal text phrase, and should be considered as having the same meaning.

What is Annex XV

Annex XV of the REACH Regulation lays down general principles for preparing dossiers to propose and justify:

- harmonised classification and labelling of substances as carcinogenic, mutagenic and toxic to reproduction (CMR), as respiratory sensitisers and other effects (on a case-by-case basis where a justification demonstrating the need for action at Community level is provided).;
- the identification of a substance as a CMR Cat 1 or Cat 2, PBT, vPvB or a substance of equivalent concern (the term "substances of very high concern" (SVHC) is used) according to the procedure set up in Article 59;
- restrictions on the manufacture, placing on the market or use of substances within the Community.

Guidance on Annex XV for C&L and Guidance on Annex XV for restrictions are available on the website of the European Chemicals Agency (http://echa.europa.eu/reach_en.html).

Agreement (within the Agency or by Commission comitology decision) on the identification of a SVHC means that it is to be included in the candidate list of substances for eventual inclusion in Annex XIV, and through such inclusion be made subject to authorisation (Article 59). Substances

with PBT or vPvB properties, wide dispersive use or high volumes will be priority substances for inclusion in Annex XIV.

The Annex XV dossier consists of two parts, in parallel to the registration dossiers for substances manufactured or imported in quantities of ten tonnes or more per year, which consist of a technical dossier and a Chemical Safety Report (CSR). The two parts of the Annex XV dossier are:

1. The Annex XV report. For consistency between all the documentation produced under REACH, the format of the parts of the Annex XV report relating to the hazard and risk assessment of the substance follows closely that for (evaluation and of) the CSR. The basic format has been adapted to the specific requirements of the individual Annex XV dossiers in some cases. The formats for the three types of Annex XV report are included as Appendices to the guidance. The report will be produced and attached to the technical dossier in IUCLID.

2. A technical dossier supporting the Annex XV report and stored in IUCLID. This can include robust study summaries imported from registration dossiers available in IUCLID. These reference study records may be annotated by the Authority. Robust study summaries or study summaries can also be created by the Authority in the case of additional data being available (see the Guidance on registration).

The term Annex XV dossier is used to refer to the package of the Annex XV report and the technical dossier. The guidance on reporting the results relates to the preparation of the Annex XV report.

3.1 Process of the preparation of the dossier

The overall process leading to the Annex XV dossier will start when an Authority considers that a substance meets the criteria for identification as a PBT or vPvB substance, or that it has properties which make it of equivalent concern, or when an Authority wishes to initiate the inclusion of a CMR (cat 1 or 2) substance in the candidate list.

There may be different reasons why an Authority may wish to initiate the process leading to the production of an Annex XV dossier for CMR, PBT, vPvB or substances of equivalent concern. For a substance with PBT properties the simplest case would be where a registration dossier(s) has already identified that the substance meets the Annex XIII criteria. A more complex case would arise where the registration identifies that the substance has PBT properties, but at least some of the evidence does not relate directly to the Annex XIII criteria; in this case a justification for an equivalent level of concern, including scientific evidence of probable serious effects to human health or the environment will be needed. For a CMR substance the simplest case would be where there is a harmonised classification and labelling established under Article 115.

In other cases the Authority may not agree with the interpretation of some of the data in the registration dossier or new data not considered in the CSR may have become available[2]. There may also be information not directly related to the specific criteria for PBT or vPvB which is considered to demonstrate scientific evidence for probable serious effects for human health or the environment and therefore that the substance exhibits behaviour giving rise to an equivalent level of concern. Such information is considered in more detail in Section 3.3.3 in relation to the concept of equivalent concern.

[2] In such cases where new information has become available since the submission of a registration, the registrant should also consider this and revise the Chemical Safety Report if appropriate.

When the Authority considers the need for developing an Annex XV dossier for the identification of SVHC, the first step is to check via REACH-IT the 'registry of intentions' whether another Member State or the Agency is already preparing such an Annex XV dossier on the same substance. The Agency's registry of intentions includes also information on the intentions of Authorities to prepare an Annex XV dossier for harmonised classification and labelling and for restriction proposals. It is recommended that the Authority checks also the stage of any such work on the same substance. If the Authority decides to proceed with the preparation of an Annex XV dossier for the identification of SVHC although another Annex XV dossier for harmonised C&L or a restriction proposal is under preparation, it is recommended that he contacts the other Authorities working on the substance to ensure that work is not duplicated. The registry is accessible for the Agency, the Commission the Member States and interested parties.

The Agency will recommend priority substances to be included in the Annex XIV. The priority shall normally be given to substances with PBT or vPvB properties, wide dispersive use or high volumes (Art 58(3)). The Guidance on Annex XIV inclusion includes guidance on priority setting. It is recommended that the Authorities consider the same prioritisation principles when deciding for which substances they prepare Annex XV dossiers.

The next steps will be to obtain the relevant available information and review it. If the available data are considered by the Authority to be sufficient for making the proposal then the Annex XV dossier can be prepared. In cases where the data are not sufficient for making the proposal, but where there are still concerns that the substance may meet the criteria for identification and Community wide action is needed, a substance evaluation could be initiated in order to generate information to clarify the concerns.

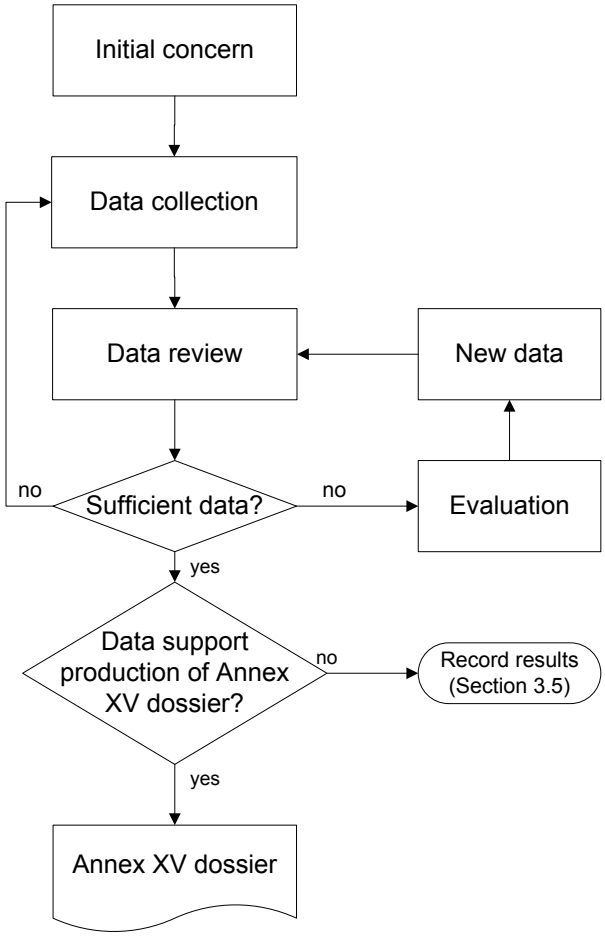
3.1.1 Link with dossier and substance evaluation

The use of substance evaluation as a way to increase the data available for the Annex XV dossier is considered here as a part of the process. Sufficient information has to be obtained before the formal submission of the Annex XV dossier. It should be noted that development of parts of this dossier (or at least material for parts of the dossier) may take place both before, during and after substance evaluation. The specific requirements for substance evaluation, in terms of identifying the required information and providing justification, are not included here, but are developed in the Guidance on evaluation.

The normal procedure during the initial development of the Annex XV dossier would be that the readily available sources such as registration dossiers and results from previous evaluation(s) are obtained and reviewed. Following the review of these sources it may be that there are gaps in the information available. If such information should have been in the registration dossier according to the information requirements, this information could be required by the Agency through dossier evaluation. Information could also be requested through substance evaluation performed by a Member State. Other possibilities could include more specific searching for information, or consideration of other substances for read-across. It is likely that an iterative process between information gathering and review may be useful in some cases. The aim is to ensure that, once the substance evaluation process is complete, there are sufficient data available with which to prepare the Annex XV dossier.

The basic process for Annex XV dossiers is set out in Figure 2.

Figure 2 Basic process for Annex XV dossier production



Note: Sufficient data – are there sufficient data to make a decision on whether the substance is a substance of very high concern

3.1.2 Identification of CMRs for eventual inclusion into Annex XIV

For dossiers identifying CMR substances for inclusion in the candidate list for eventual inclusion on Annex XIV, the dossier may be limited, if appropriate, to a reference to an entry in Annex I of Directive 67/548/EEC. This reference may be sufficient to include the substance in the candidate list. Having only a reference to Annex I to Directive 67/548/EEC may not be enough for the purpose of priority setting. Therefore, it is recommended that the Authority includes in the Annex XV dossier available information on exposures, alternative substances and risks. [The [Link=Guidance on Annex XIV inclusion#file=annex_XIV_en]] will further develop methods for prioritising substances for inclusion in Annex XIV.

Nonetheless, it is recommended to propose and achieve an entry for a harmonised classification in Annex I to Directive 67/548/EEC before a CMR substance is proposed to be identified for inclusion in the candidate list for authorisation. In that case, the identification of a CMR substance for inclusion in the candidate list might also be more easily agreed.

3.1.3 What to do when an Annex XV dossier is not appropriate

This guidance on the compilation of the Annex XV report largely considers the situation where the substance is identified as a SVHC. There may be cases where the Authority carries out work towards an Annex XV dossier but concludes at some point that there is in fact no need for a dossier,

if the investigation for the preparation of the dossier shows that the substance does not meet the criteria as a CMR (cat 1 or 2) or the criteria for PBT or vPvB, or an equivalent level of concern. In all cases, it is important that the work that has already been undertaken is not lost but is made available for future work. In such cases, the Authority is encouraged to record the results of the work they have carried out in the form of an Annex XV dossier, as described in this guidance. The Authority can add an appropriate conclusion instead of a proposal in the first part of the report. This will allow their work to be submitted to the Agency and stored within REACH-IT, and provide a starting point in the event of a change in circumstances or new data.

This level of work may not be required in all cases; for some situations a simple statement of the reasons why it was decided not to proceed may be more appropriate. It is up to the Authority to decide how much of the work they have done needs to be documented, and this will be on a case-by-case basis. The key outcome must be that the work undertaken by one Authority should be known and available to the Agency and other Authorities so that the process works efficiently and without undue duplication of effort.

3.1.4 Informal consultation in the preparation of an Annex XV dossier

Although Annex XV includes no specific requirement for Authorities to engage in consultation, stakeholder involvement in the process is important. Consultation of industry and other stakeholders may be an important way for the Authority to obtain additional information although stakeholders have no legal obligation to provide information on the basis of informal consultation during the development of an Annex XV dossier. It should be noted that the term consultation is used throughout this document to refer to contacts with stakeholders aiming at voluntary submission of information and should not be confused with the formal invitation for commenting and providing information which will follow the submission of a finalised dossier to the Agency (such as under Articles 59(4) and 69(6) of the REACH Regulation).

The Authority preparing the dossier should decide upon the need for consultation and the resources and time to be allocated to consultation activities. However, Authorities are encouraged to engage stakeholders and other interested parties in the development of the dossier as early in the process as possible. This will facilitate the timely collection of the necessary information and will contribute to the transparency and representativeness of the dossier. Authorities should consider informing the identified interested parties that work related to a possible identification of substance of very high concern dossier has been initiated.

3.2 Information collection

Aim: To identify sources of the information required to assess whether the substance meets the criteria in Articles 57 (d-f)[3].

Output: Identified data sources to be reviewed.

The main source of information on substances under REACH is the registration dossier. A registration dossier will be produced by each manufacturer or importer registering the substance. These will be stored within IUCLID in the REACH-IT system. The registration dossier consists of a technical dossier and, in some cases, a CSR.

[3] For information collection related to CMR effects (Articles 57 (a-c)), see the Guidance on Annex XV for C&L.

A technical dossier is submitted for all substances manufactured or imported in quantities of one tonne or more per year. The technical dossier contains study summaries and robust study summaries as well as registrant's classification and labelling. The information required to be included in this technical dossier is all the relevant physicochemical, toxicological and ecotoxicological information available to the registrant; the minimum required depends on the quantity manufactured or imported, with thresholds of 1, 10, 100 and 1,000 tonnes/year leading to increased data requirements. The requirements are also modified by the expected classification and the use pattern. In the case of multiple registrants for one substance, most parts of the technical dossier will be submitted in a joint dossier, including these study summaries unless companies demonstrate that they have reasons to submit parts individually. The time by which the registration is required to be submitted also depends on the quantity and the classification of the substance. Details of the information requirements are set out in Annexes VII to X of the REACH Regulation.

For substances manufactured or imported in annual quantities of ten tonnes or more per year, a CSR is required to accompany the technical dossier. This includes a hazard assessment (human health and environment) and a PBT/vPvB assessment for the substance. If this hazard assessment shows that the substance meets the criteria for classification according to Directive 67/548/EEC, or the substance is assessed as a PBT or vPvB, then an exposure assessment and risk characterisation must also be carried out. The results of the CSA are documented in the CSR.

A further source of information under REACH is through dossier or substance evaluation. Under compliance check (part of the dossier evaluation) registrants may be required to submit any information needed to bring the registration(s) in compliance with the REACH requirements. Following examination of testing proposals (another part of dossier evaluation) more information will have to be generated and submitted. Substance evaluation is the procedure by which further information (such as testing or exposure and use information) may be requested to clarify potential risks from substances. After the generation of any requested information, conclusions will be drawn and documented.

The amount of information available to an Authority when beginning the preparation of an Annex XV dossier will, therefore, depend on the status of the substance in REACH, and this may have an influence on the development of the dossier. Possible scenarios of data availability through REACH are:

- Substance is not registered because
    - it is exempt from registration
    - the timeline for registration has not yet been reached.
- Substance has been registered but no CSR exists (i.e. the substance is produced at quantities starting at 1 but below 10 t/a).
- Substance has been registered and a CSR exists.
- Substance has been registered and has undergone substance evaluation.

There could also be situations where more than one of these applies, in particular where some manufacturers or importers dealing with higher tonnages have registered the substance, but the timetable for other registrations at lower tonnages is still to be completed, or where an already registered substance is imported or manufactured by a new manufacturer/importer, resulting in a new registration.

For the second and third cases listed above, the primary information source will be the registration dossier. For the third and fourth cases listed, the CSR will document how the registrant reached the

reported conclusions on the classification and labelling and will include an assessment of whether the substance meets the PBT or vPvB criteria based on the information in the technical dossier.

For some substances, as noted above, the CSR will include an exposure assessment and a risk characterisation, which will be of direct relevance to the preparation of a restrictions dossier, and will also be a source of information to be used in the prioritisation process for Annex XIV following agreement on the SVHC dossiers.

Where a substance has not yet been registered or is exempted from registration, there will be no information within the REACH-IT system at the time, apart from the classification and labelling inventory entries, and so other sources of information will then need to be considered. Reviews may have been produced by other fora such as the OECD, IPCS, IARC, national reviews by Member States etc., and if so it will be useful to use these to identify the information that is available. There may also be new studies published in the literature or new research reports. A more detailed search of the literature could potentially help to identify relevant information where there are significant gaps in any available reviews, or where there are no reviews. It should nevertheless be carefully evaluated whether sufficient information is available to scientifically support the identification of the substance as being of very high concern.

Given the possible importance of the outcome, it is recommended that the primary sources of data, for example the full study reports, where available to the Authority, should be reviewed for the Annex XV dossier, particularly for the key studies. Information from secondary sources should not generally be used as the basis for the proposal unless there is a high confidence in the robustness of the approach used to review the data for the secondary source (for example where it is documented that the secondary source had recently reviewed the original full study report against known and acceptable criteria).

The information needed for the dossier depends on whether the Annex XV dossier is being developed for a CMR, a PBT, a vPvB or a substance of equivalent concern. The criteria to be used for identification of a substance as a PBT or a vPvB substance are outlined in Annex XIII of the REACH Regulation (see Appendix II). In order for a substance to be designated a PBT or a vPvB substance, all of the relevant criteria have to be demonstrated to be fulfilled for the substance based on measured or experimental data. There are no specific criteria for identifying a substance as being of equivalent concern and the important considerations are outlined in Section 3.3.3. The information requirements here are less specific, but can be of a similar nature to those for PBT and/or vPvB.

The potentially relevant parts of the technical dossiers and CSRs are shown in Table 1.

Table 1 Technical dossier (in IUCLID) and CSR sections relevant for SVHC dossier

Topic	Sections in IUCLID	Sections in CSR (all in Part B)
Identification of the substance and physical and chemical properties	Section 1, Section 3	Section 1
Classification and labelling	Section 1.5	Section 3
Environmental fate properties	Section 4	Section 4
Human health hazard assessment	Section 6	Section 5
Environmental hazard assessment	Section 5	Section 7
PBT. vPvB assessment		Section 8
Exposure assessment	Section 2	Section 9

In the case where the substance has been the subject of a substance evaluation, there will also be an evaluation report(see the Guidance on evaluation). Depending on which types of substance(s) and the reasons for considering that the substance presents a risk and leading to the substance evaluation, this evaluation report may have considered the relevant endpoints already.

Where a substance has not (yet) been registered or is exempted from registration, whether it should be a priority for resources depends on the reasons (e.g. high priority according to Article 58(3)) for considering the need for proposing the substance as a SVHC and whether and in what tonnage bands the substance is pre-registered. As the Authority will have some suspicions concerning the substance, they may discuss with Industry whether they would be prepared to register the substance earlier (where relevant), so that all the relevant information can be made available.

As well as information which is related directly to the specific criteria for PBT or vPvB as set out in Annex XIII, information on other areas will be of use, for example physico-chemical data relevant to the interpretation of other test results. The need to consider other information will depend on the specific case.

Information on other related substances and other supporting information should be reviewed in a similar way using the relevant sections of the Guidance on information requirements and the Guidance on the Chemical Safety Report as appropriate. When making use of information on related substances, the Authority will need to explain how these relate to the substance being assessed, and how this justifies the use of the information. The amount of information needed for related substances used to support the proposal is likely to vary case-by-case, depending for example on whether or not there was an agreed classification for the similar substance or not. Guidance on the use of a category approach will also be part of the Guidance on information requirements (section 6.2). This may be of relevance here.

The REACH Regulation also requires that the available information on use, exposure, risks and on alternative substances and techniques be included in the dossier for the identification of SVHC . Such information might be useful for priority setting purposes. Such information on alternatives is most likely to come from the registration dossiers for other substances in the REACH-IT system. Section 5.5 of the Guidance on Annex XV for restrictions considers alternatives in the case of restrictions, and the early parts of this guidance on the identification of alternatives may be useful here, recognising that the purpose of this information is priority setting for inclusion in Annex XIV and, therefore, the level of detail required for the SVHC dossier is lower.

Confidential information

A registrant may identify certain information in their registration as commercially sensitive. If the justification with regard to information listed in Article 119 (2) is accepted as valid by the Agency, then this information will be marked as commercially sensitive in REACH–IT. Such information can be used in the preparation of an Annex XV dossier for discussion with the Agency and Member States, as such discussions can be confidential. However, such information must not be included in any documents to be used for public consultation. The Authority therefore has to consider this when preparing an Annex XV dossier. It is recommended to include or mark confidential information in such a way (e.g. in separate annexes) that it can easily be left out when the Agency publishes a notice and the non-confidential parts of an Annex XV dossier for commenting in accordance with Art 59(4).

Authorities need to pay attention also to information listed in Article 118 (2). Information to which access cannot be granted under Article 118 must not be published on the internet because the Agency would already have to deny access to such information on request in a single case on the basis of Regulation 1049/2001.

The general provisions on access to information are twofold:

- Some pieces of information will be made available over the internet in accordance with Article 119 (1).
- Access to other pieces of information will be granted by the Agency on request on a case by case basis in accordance with Regulation 1049/2001, as per Article 118 (1). Regulation 1049/2001 defines cases in which access to information has to be denied e.g. for reasons related to the protection of commercial interests which are further explained in Article 118 (2). It also requires the Agency to check with companies that have submitted information to it whether the company claims that the information asked for is confidential. The Agency then has to take a decision.

3.3 Information review

Aim: To review the information sources identified in the previous stage and select the data to support the proposed identification as a CMR (cat 1 or 2), a PBT, a vPvB substance or as a substance giving rise to an equivalent level of concern[4].

Output: Information to be included in the Annex XV dossier.

The Guidance on information requirements and the Guidance on the Chemical Safety Report will contain detailed guidance on the interpretation of studies in relation to the individual criteria. The present guidance therefore does not discuss technical issues in relation to such studies. This section provides some comments on possible situations which might arise in using the REACH-related data sources for PBT and vPvB. It also discusses the issues to be considered in the identification of a substance as of equivalent concern.

3.3.1 Identification of the substance for which the dossier is prepared

The identity of the substance for which a dossier is prepared should be clearly described. Substances can either be of well defined composition (mono-constituent, multi-constituent) or of Unknown or Variable composition, Complex reaction products or Biological materials (UVCB). Guidance for identification and naming of substances in REACH is available in the Guidance on substance identification.

For CMRs (cat 1 and 2), the classification criteria (guidance will be developed in the Guidance on Classification, Labelling and Packaging) are used to classify a substance taking into account the classification of its constituent(s).

Guidance on the assessment of the PBT or vPvB properties is given in the Guidance on information requirements and the Guidance on CSR. It is stressed in particular that for multi-constituent substances, in cases where the composition of the substance is well defined, or the major constituents are defined, it is necessary to consider the PBT or vPvB properties of the constituents of the substance.

The PBT and vPvB properties of a multi-constituent substance depend on the respective properties of its constituents and of its degradation and transformation products. The same applies for substances giving rise to an equivalent level of concern.

[4] For information review related to CMR effects, see the Guidance on Annex XV for C&L.

Terminology to be sued for substance containing PBTs and vPvBs

Rules are proposed for the naming of such substances in the Table below. It is proposed to distinguish, in terms of naming, in:

- substances having a constituent with PBT, vPvB or equivalent concern properties which is present at a concentration of 80% or more will be called: PBT, vPvB or substance of equivalent concern;
- substances having one or more constituents with PBT, vPvB or equivalent concern properties in individual amounts of 0.1% or more, but less than 80%, will be called: substance containing maximum x% (or [x% - y%]) of PBT, vPvB constituents/impurities or constituents/impurities of equivalent concern;

This naming rule applies as well for UVCB substances.

"Type of substance"	Composition of the substance in terms of PBT, vPvB or equivalent concern	Terminology
Mono or multi constituent substance	One constituent with PBT-, vPvB- or properties giving rise to an equivalent level of concern is ≥80%	The substance is PBT vPvB or gives rise to an equivalent level of concern
	One or more constituents/impurity in individual amounts ≥ 0.1 % but <80 % have PBT-, vPvB- or properties giving rise to an equivalent level of concern	The substance contains PBT, vPvB constituents/impurities or constituents/impurities giving rise to an equivalent level of concern
	No constituent or impurity present in an amount of 0.1% or more has PBT-, vPvB- or properties giving rise to an equivalent level of concern	Substance is not a PBT, vPvB or a substance giving rise to an equivalent level of concern

Furthermore, if a substance or any of its constituents or impurities degrades, or is transformed into substances which have PBT or vPvB properties or properties of equivalent concern and if these are present in individual amounts equal or above 0.1% (of the weight of the initial substance), then the substance will be called a substance forming PBTs, vPvBs or substances of equivalent concern.

Substances for which an authority may prepare an Annex XV dossier

If a substance contains a constituent or an impurity at or above 0.1% which has PBT, vPvB or equivalent concern properties, the Authority may prepare an Annex XV dossier to propose the substance to be identified as being a PBT, vPvB or substance of equivalent concern. The same applies to a substance that degrades or is transformed into substances which have PBT or vPvB properties or properties of equivalent concern and if these are present in individual amounts at or above 0.1% (of the weight of the initial substance).

When the dossier is prepared for a substance, all necessary information on the identity of the substance needs to be given. In particular the identification of the constituents and/or impurities that have properties of very high concern and their concentrations or concentration ranges shall be included in the description of the composition of the substance. When the dossier is prepared to identify a substance as a SVHC because it degrades or is transformed into PBT, vPvB or substance of equivalent concern, both the identity of the substance and the identity of the relevant degradation/transformation product need to be recorded with the related concentrations or concentration ranges. It is recommended to use the naming rules described above in the dossier.

An Annex XV dossier can be prepared

- for a given substance, or
- for several substances containing a given constituent having properties of very high concern.

When the dossier is prepared on the basis that there is a constituent or impurity of one or more substances that is identified as having PBT or vPvB properties or properties of equivalent concern, the Authority may propose to identify the substances that contain this constituent or impurity. These substances will be included in the candidate list in accordance with the procedure set out in Art 59 for eventual inclusion in Annex XIV.

In the case the Authority considers preparing a dossier on the basis that there is a constituent or impurity having PBT or vPvB properties or properties of equivalent concern, if a substance evaluation is felt necessary in order to clarify its PBT or vPvB properties or properties of equivalent concern, the Agency may consider to include all substances containing such a constituent on the Community Rolling Action Plan (CRAP, see the Guidance on evaluation).

Any substance containing a constituent or an impurity at or above 0.1% which has PBT, vPvB or equivalent concern properties, may be identified as a SVHC and by that included in the candidate list. It is advised that the volume of the substance and the percentage of PBT, vPvB or equivalent concern constituents are considered in the process of priority setting of substances for inclusion in Annex XIV. It is recommended that the Authorities use these same prioritisation principles when deciding for which substances they prepare Annex XV dossiers.

3.3.2 PBT/vPvB

The information gathered should be reviewed against the Annex XIII criteria for PBT or vPvB.

Guidance on the assessment of PBT, vPvB properties will be developed in Guidance on information requirements and the Guidance on the Chemical Safety Report..

Where a substance evaluation has been completed that addressed the hazards relevant for PBTs and vPvBs, then the results of the evaluation should be considered in addition to the information contained in the registration dossiers. In such cases there may be little or no need for further data review, and the Annex XV dossier can be produced directly.

There may be registration dossiers which contain different results or different interpretations of data. Where these are relevant for the endpoints being considered, the justifications for any differences in the interpretation of the same data should be considered and the overall conclusions reviewed. This may have already been done as part of dossier or substance evaluation.

The studies which are considered to be the key ones for each endpoint should have been identified within the registration dossier. Comments on the studies included in the technical dossiers from registrations can be added to them as annotations. All (robust) study summaries necessary to support the Annex XV dossier should be copied from registration dossiers into a new Annex XV technical dossier produced by the Authority. It is important to highlight where studies are interpreted in a different way, and to develop justifications for these differences.

(Robust) study summaries of any new data to be included in the Annex XV dossier should be recorded in the technical dossier for the Annex XV dossier.

Information on other related substances and other supporting information should be reviewed in a similar way using the relevant sections of the the Guidance on information requirements and the Guidance on CSR as appropriate. When making use of information on related substances, the Authority will need to explain how these relate to the substance being assessed, and how this justifies the use of the information. Guidance on the use of a category approach has been developed by the OECD under the HPV programme (OECD, 2005) and will also be part of the Guidance on information requirements and this is of relevance here.

It may be the case that the substance is undergoing testing. Any such testing should be considered in case it might be of relevance to the proposal. If the testing is relevant, then it should be considered very carefully whether to proceed or to await the result of the testing.

3.3.2.1 Examples of possible situations

This section considers a number of possible situations which may be found after the collection of the information or following an initial brief review. These are presented as examples and are not intended as an exhaustive list to cover all possible situations.

- The substance is identified in the CSR(s) as a PBT or vPvB. In this case the information and discussion in the registration dossier(s) will support the proposal, and only a brief review may be needed to identify what to include in the dossier.
- The substance is registered, and the CSR(s) conclude that it is not a PBT or a vPvB. The Authority may need to focus on the key studies on which the conclusions are based. They will need to examine the underlying data and the way in which the conclusions were reached in the CSRs. There may be other information not included in the CSRs which the Authority considers as demonstrating that the criteria is met. Here the review needs to explain why the new information should overturn the conclusions in the CSRs.
- If there are differences in the conclusions in different CSRs for persistence, bioaccumulation or toxicity, so that some of the CSRs consider the criteria to be met and others do not, then the reasons for the differences in interpretation of the data should be investigated and the arguments presented in the CSRs should be examined carefully. Each of the three areas (persistence, bioaccumulation and toxicity) should be reviewed to identify if the Annex XIII criteria are met in these areas. Where the criteria are met, a justification has to be included in the Annex XV dossier of why the substance is concluded to be a PBT or vPvB.
- The CSR(s) conclude that the substance is a possible PBT or vPvB but no testing strategy is proposed in the CSR to refine this assessment as it is technically difficult (or impossible) to carry out the necessary testing (for example a bioconcentration factor (BCF) test for a substance of very high log P and very low water solubility)[5]. Here it may not be possible to show unambiguously that the substance meets the strict PBT or vPvB criteria of Annex XIII and so the substance should be considered under the concept of equivalent concern if sufficient evidence about the PBT properties exists. In the particular case mentioned above, further accumulation testing using a more relevant route of exposure (for example a fish feeding study) may be possible and this will provide useful information on the accumulation potential in relation to equivalent concern (see Section 3.3.3).
- The CSR(s) conclude that the substance is a possible PBT or vPvB but no testing strategy is proposed in the CSR to refine this assessment, as the registrant decided to implement and recommend sufficient RMMs and operational conditions. As sufficient RMMs should be implemented it might be considered whether an Annex XV dossier is needed.
- No registration available at the time of preparing the Annex XV dossier. In this case the Authority will need to review the information gathered against the criteria using the guidance developed for the production of the CSR. Here also it should be carefully considered whether

[5] In this situation the Authority may wish to consider the technical difficulties and offer proposals for testing if appropriate, including the identification of other information which might be useful in drawing a conclusion. This could be addressed under dossier or substance evaluation.

sufficient information is available to scientifically support the identification of the substance as being of very high concern.

3.3.3 Equivalent level of concern

The REACH Regulation describes substances of equivalent concern in Article 57 (f):

> *(f) 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 fulfil the criteria of points (d) or (e) - 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 to those of other substances listed in points (a) to (e) and which are identified on a case-by-case basis in accordance with the procedure set out in Article 59.*

Thus the equivalence is with the levels of concern for substances covered by points (a) to (e) from the same article.

A key part of the definition of equivalent concern relates to there being scientific evidence of probable serious effects to humans or the environment. This can be taken to mean that any effects, should exposure occur, will be at least equivalent to those that could occur from substances included under points (a) to (e), and this will need to be demonstrated. An additional aspect to be considered is the uncertainty of standard risk assessment for substances with such effects and the consequences of the risk assessment being wrong. For substances giving rise to an equivalent level of concern, this is discussed in detail in relation to specific cases in the following sections.

This guidance has been left open in some areas to allow for future, as yet unknown, problematic properties to be considered under the concept of equivalent concern. As a result, this part of the guidance is different from other parts of the guidance in that it outlines factors for consideration rather than indicating specific criteria for when a substance is of equivalent concern. It should also be recognised that science in this area is constantly developing and there are likely to be other factors not included in the guidance that may need to be considered.

3.3.3.1 Equivalent level of concern in relation to PBT or vPvB properties

When considering the concept of equivalent concern in relation to PBT or vPvB properties it is useful to consider the protection goals behind the PBT concept. For substances with persistence, bioaccumulation and toxicity properties, the risks are difficult to estimate using traditional risk assessment methodologies, but they potentially do lead to effects and risks of concern from which ecosystems should be protected.

For example these additional concerns include the following:

a) Hazardous substances may accumulate in parts of the environment, including the marine environment and remote areas and

   – the effects of such accumulation are unpredictable in the long-term and

   – such accumulation would be difficult to reverse.

b) Remote areas should be protected from further contamination by hazardous substances resulting from human activity, and the intrinsic value of pristine environments should be protected.

A key part of this concern is that if, ultimately, harmful effects on man or ecosystems are observed, then such effects will be difficult to reverse by control at that stage. Thus, it is the dual potential of uncertainty in being able to say with confidence at what level the substance may be considered safe, along with the serious consequences that could arise from this, that dictate a different approach to risk assessment for these substances.

These additional concerns arise particularly for substances that can be shown to persist for long periods and bioaccumulate in biota, and can give rise to toxic effects after a greater time, and over a wider geographical distribution, than substances without these properties. The PBT and vPvB[6] criteria in Annex XIII are designed to identify the substances for which these additional concerns arise. However, the PBT/vPvB criteria are defined in a specific way, and it is possible that such additional concerns may also be associated with substances that do not precisely meet all the PBT/vPvB criteria in Annex XIII. These substances may be considered as being of equivalent concern to a PBT or a vPvB substance. The following guidance outlines situations that could be considered as being of equivalent concern.

Elaborating the PBT and vPvB criteria and concepts

There are two basic circumstances which could arise here.

1 Where the available data are not those described in Annex XIII, but based on a scientific assessment, it can be demonstrated that the data are relevant and the criteria would, in high probability, be met. Thus, for example, a substance may be persistent and toxic (meeting the criteria). No measured BCF value is available; the predicted BCF from QSAR is below the threshold value. However, there is evidence from either field measurements or laboratory studies for significant bioaccumulation in organisms at or near the top of the food chain, or of high bioconcentration from structurally similar compounds. Hence here other data are used to substitute for data directly related to the Annex XIII criteria which are unavailable.

2 Where the available data cannot be shown to meet the Annex XIII criteria but the particular properties of the substance do lead to an equivalent level of concern. An example would be a substance which has been demonstrated not to be persistent in one or more environmental media but there is scientific evidence that it may be persistent in other media through analysis of available monitoring data. Here additional data are used in place of data directly related to the Annex XIII criteria as these additional data are considered more relevant for the substance.

A further example of a substance that could be considered as being of equivalent concern is where one of the PBT or vPvB criteria is marginally not fulfilled but the other criteria are exceeded

[6] Although the vPvB criteria do not include a measure of toxicity there is an underlying assumption that substances with vPvB properties could accumulate in the environment and eventually reach concentrations that are toxic, regardless of the inherent toxicity of the substance.

considerably, and there is other evidence to suggest that the substance gives rise to an equivalent level of concern such as a potential for long-range transport.

Additional data relevant for showing an equivalent level of concern

The following sections present some considerations relevant to the P (vP), B (vB) and T criteria in turn. These considerations could help in the justification for identifying the substance as being of equivalent concern on a case by case basis. It should be remembered that all three parts for PBT or both parts for vPvB have to be addressed here.

Additional considerations specifically relevant to the P or vP criterion

The persistence-criterion is used to reflect the potential for long-term exposure of organisms, and also the potential for the substance to reach the marine environment and to be transported to remote regions. Data that could also be used to demonstrate or support persistence include the following (note that further guidance on the interpretation of data in relation to persistence is being developed in the Guidance on information requirements and the Guidance on the Chemical Safety Report).

- Lack of degradation in a ready biodegradation test[7] or inherent biodegradation tests indicates the substance is potentially P or vP. A positive result in a ready biodegradation test can be used to show the substance is not persistent (not P), although a positive result in an inherent biodegradation test cannot always be used to show the substance is not P. This would need to be considered on a case-by-case basis, taking into account any factors such as relatively low overall mineralization (which may indicate the formation of persistent degradation products), and pre-exposure or acclimation of the microorganisms to the substance, lag phases etc. (which may mean the results from the test cannot be extrapolated to the likely degradation in a relatively pristine environment). Further information on the use of ready and inherent biodegradation tests for determining if a substance is potentially persistent in a screening assessment is given in the Guidance on information requirements and the Guidance on CSR.
- Biodegradation estimation models (e.g. BIOWIN). Evidence from such models can be used if the Authority considers it to be sufficiently reliable to demonstrate persistence.
- Information from field studies (e.g. environmental monitoring data). Time trend studies showing increasing levels would be potentially indicative of accumulation in the environment and hence persistence, although this could also result from increasing levels of use or changes in use leading to higher emissions (and so consideration of use pattern data would be important in the interpretation). The presence of the substance at locations where it was previously released but where emissions ceased a significant time ago could also indicate persistence. The quality of the monitoring data is an important consideration and this is considered further in relation to the B or vB criteria.
- Modelling studies. For example these could be used to estimate the levels or distribution that would be expected on the basis of the known properties of the substances, including its degradability. The results from such modelling could be compared to what is found in the environment (where suitable measured levels data are available). It also has to be considered that it can be difficult to obtain precise estimates of releases and so predictions have to be considered to include a level of uncertainty. An indication of different behaviour might be the occurrence of the substance in parts of the environment where modelling would predict very little, but the limitations of the modelling would also need to be considered. Another use of

[7] This is one of the screening criteria or methods for identifying a potential PBT or vPvB substance. Further guidance on this is given in the Guidance on CSR.

modelling could be to estimate the actual half-lives in various environmental media or the overall environmental persistence.

In terms of assessing whether the substance has an environmental persistence that is equivalent to the P-criterion, a weight of evidence approach should be taken, drawing together the available data. Part of this assessment could include consideration of the degree the substance fails the actual P or vP criteria based on the available studies and on the quality of the underlying data.

Additional considerations specifically relevant to the B or vB criterion

With respect to the bioaccumulation criterion, the BCF in aquatic organisms is used as an indicator of the bioaccumulation potential of the substance. Data that could also be used to demonstrate or support a high bioaccumulation potential in relation to equivalent concern include the following (note that further guidance on the interpretation of data in relation to bioaccumulation is being developed in the Guidance on information requirements and the Guidance on CSR):

- Log Kow. A value of around 4.5[7] or greater is generally accepted as indicating a high potential for bioaccumulation.
- Modelled BCF data.
- Results from laboratory feeding studies on accumulation through food for fish. It may be possible to combine these data with BCF data to show that the overall bioaccumulation (i.e. taking into account exposure via both water and food) is high. For example a substance with a BCF close to, but just below the B-criterion cut-off, that also demonstrates uptake from food could be considered to be equivalent to meeting the B-criterion when the combined uptake from both routes is taken into account, provided that both are relevant under realistic exposure conditions.
- Uptake and metabolism data from laboratory studies on other species, including mammalian species
- Evidence from field studies that the substance shows a high bioaccumulation potential.

For substances with a log Kow < 6 bioconcentration models are generally linear with log Kow and so an assessment based on log Kow or modelled BCF is similar. For log Kow > 6 experimentally derived BCFs tend to decrease with increasing log Kow, and different models may lead to different (and possibly conflicting) results. Therefore the potential for bioaccumulation for these substances needs to be assessed by expert judgement on the basis of the log Kow value and the estimated BCF using the available and relevant BCF methods. Attention should be paid, in particular, to the domain of applicability of any BCF estimation method used (in terms of both the log Kow range to which it applies and the chemical types to which it applies).

It should also be borne in mind that some substances can accumulate in organisms by processes other than fat partitioning (e.g. accumulation in bone or active transport into the body) and so log Kow may not always be a good descriptor for the accumulation potential for this type of substance. If a substance is demonstrated to accumulate significantly in such a way (expert judgement may be required to determine this), it could be deemed to be of equivalent concern for bioaccumulation as a substance that meets the defined B-criterion. Direct accumulation testing would identify this provided that a suitable species was tested (in this case it is possible that such testing may show that the substance meets the actual B- or vB criterion in Annex XIII and so would be considered a PBT or vPvB substance rather than a substance of equivalent concern), or consideration of data for a range of species may be necessary (for example it may be that aquatic organisms do not exhibit such an alternative accumulation process).

Particular attention should be paid to the use of monitoring data from field studies. Measured data in biota provide a clear indicator that the substance is taken up by an organism. However the analytical detection of substances in organisms is not in itself always an indicator that significant bioconcentration or bioaccumulation has occurred or is occurring that would lead to effects in biota. The interpretation of such data in terms of actual bioaccumulation or biomagnification factors can be especially difficult when the sources and levels of the exposure (for example through water as well as food) are not known or cannot be estimated reasonably. Useful in this respect are data representing different trophic levels within a single food chain, where relative differences in concentration between the various levels can often provide useful information on the bioaccumulation potential.

In this respect, monitoring data for biota in remote regions is particularly useful as it provides indications that the substance is both transported long-distances (and so is relatively persistent) and is taken up by organisms (although this again is not sufficient to say the substance has a high bioaccumulation potential). Time trend data can also provide very useful information in terms of whether the levels of the substance is building up over time in the environment, although again the interpretation of such data may not always be straightforward (for example increasing concentrations in the environment may reflect increasing use rather than a high persistence/accumulation potential).

An important factor to take into account with regard to monitoring data is the quality of the data. Many substances with PBT-type properties are difficult to analyse at low concentrations and the use of poor quality data may lead to erroneous conclusions being drawn. The Arctic Monitoring and Assessment Programme (AMAP, 2001) has published recommendations with regard to assessing the quality of monitoring data for use in determining spatial and temporal trends and other types of data interpretations. These are summarised in Appendix 3**Error! Reference source not found.**.

Another factor to take into account when considering the available data (from both certain laboratory studies and field data) is that the accumulation seen in any given situation can depend to a large extent on the lipid content of the species in question. Therefore differences in lipid contents may need to be considered, particularly when comparing the concentrations found in one species with another in relation to bioaccumulation processes.

In terms of assessing whether the substance has a bioaccumulation potential that is equivalent to the B-criterion, a weight of evidence approach should be taken, drawing together the available data. Part of this assessment could include consideration of the degree to which the substance fails to meet the actual B or vB criteria if BCF data are available. It should be stressed that the equivalence of concern here is in relation to bioaccumulation potential and not solely occurrence in biota.

Additional considerations specifically relevant to the T criterion

For persistent and bioaccumulative substances, long-term exposure of organisms in the environment can be anticipated that may cover the whole life-time of an organism, or even multiple generations. Therefore chronic or long-term ecotoxicity data, ideally covering the reproductive stages, or indications of severe chronic mammalian toxicity (e.g. CMR or R48), are used to define the T-criterion. Some discussion relating to chronic toxicity is included in Section 3.3.3.2.

Other information that can be used, in a weight of evidence approach, to demonstrate a high toxicity potential in relation to equivalent concern for this endpoint include, for example, the following.

- Substances classified as carcinogenic, category 3, or mutagenic, category 3. For these substances a case-by-case assessment should be carried out to decide whether the evidence is

sufficient for the substance to be considered as toxic in terms of the PBT assessment, or whether further information is needed to clarify this point[8].

- Substantial evidence of long-term adverse effects. Such evidence may include endocrine disrupting effects for example (see also Section 3.3.3.3) in cases where they cannot be assessed with conventional hazard assessment methodology. This should be considered on a case-by-case basis.
- In the absence of suitable long-term NOEC data for aquatic organisms, an acute $L(E)C_{50}$ of <0.1 mg/l[7] can be used as an indicator that the substance may have a high long-term toxicity. In most cases it would usually be necessary to carry out testing to obtain a long-term NOEC in order to determine if the actual T-criterion is met, but there may be instances where this is not technically possible and so could be considered in relation to equivalent concern.
- In the absence of suitable repeated dose studies for mammals the results of acute toxicity studies can be considered. In particular, for a substance classified as very toxic or toxic after oral dosing (i.e. LD_{50} <200 mg/kg bw/day[9]) and where the toxicity is expected to be the result of systemic effects[7], the probability that the subacute (28 days) or the chronic NOAEL (90 days) after repeated dosing will be lower than the trigger value for serious/severe effects for R48 (150 or 50 mg/kg/bw/day) will be high, and so the substance might be considered as demonstrating an equivalent level of concern for the T-criterion.
- Quantitative structure-activity relationships (QSARs) can be used to estimate the chronic toxicity for some aquatic endpoints[10]. Attention should be paid, in particular, to the domain of applicability of any QSAR method used (in terms of both descriptor variable range to which it applies and the chemical types to which it applies). Guidance on QSAR is developed within the Guidance on information requirements section 6.1.
- Toxicity data for soil or sediment organisms. This is particularly relevant for substances that do not fulfil the T-criterion based on data for pelagic organisms. For example, if the NOEC based on the aquatic toxicity data is close to, but above, the T-criterion, but the substance shows toxicity to sediment or soil organisms that is significantly higher than expected based on equilibrium partitioning considerations, then this could be considered as being equivalent to the T-criterion. Similar considerations could also be used in cases where the substance shows no aquatic toxicity at concentrations up to its limit of solubility in water, but shows a significantly higher toxicity to sediment or soil organisms than would be expected based on equilibrium partitioning considerations based on the water solubility limit.
- Demonstrated toxicity in the environment. Expert judgement would be needed here to relate the observed effects to exposure to the substance, and to consider the severity of the effects. An example would be the effects of tributyltin on dog whelks and other marine shellfish.

In terms of assessing whether the substance has a toxicity potential that is equivalent to the T-criterion, a weight of evidence approach should be taken, drawing together the available data.

[8] It might be considered that, as category 3 for mutagenicity or carcinogenicity are not included in the T criteria, then on their own they are not sufficient to be considered equivalent, and that other information (e.g. on potency) would be required.

[9] NB under GHS i.e. LD_{50} <300 mg/kg bw/day

[10] QSARs for other ecotoxicity and toxicity endpoints may be developed in the future. Similar considerations are likely to be important for the use of these approaches.

Part of this assessment could include consideration of the degree to which the substance fails to meet the actual T-criterion based on the toxicity data available.

Other examples of equivalent concern in relation to PBT and vPvB criteria

In addition to the elaborations of PBT and vPvB properties and related considerations described above, there are some other particular situations and circumstances that could lead to a consideration of an equivalent level of concern:

- Substances that are not themselves persistent but have degradation products or metabolites that have PBT or vPvB properties.
- Substances for which it is technically difficult (or impossible) to carry out the necessary testing to confirm whether or not the PBT or vPvB criteria as given in Annex XIII are met but there are indications from other data (e.g. screening data) that they are of equivalent concern.
- Read-across of data for a structurally similar substance with known PBT, vPvB properties, or properties of an equivalent level of concern.
- The PBT concept is linked closely to other similar concepts in other international fora, such as the Stockholm Convention on Persistent Organic Pollutants (Stockholm Convention, 2001) and The United Nations Economic Committee for Europe (UNECE) Protocol (UNECE, 1998). Substances already identified as POPs under the Stockholm Convention are not subject to Authorisation under REACH as their production and use are already banned (with only a few exceptions). However the criteria developed under the Convention can be used to identify substances with similar properties, and these could be considered when preparing an Annex XV dossier in combination with some of the other considerations discussed earlier in this section. The criteria used under the Stockholm Convention for identifying potential for long-range environmental transport are summarised in Appendix 5.

PBT or vPvB substances based on screening data alone

Situations may arise where registrant(s) agrees that the substance is most likely to meet the PBT or vPvB criteria based on screening data and do not consider it necessary to carry out the further testing to prove that the substance does meet the actual criteria in Annex XIII. The Authority would need to consider on a case-by-case whether preparation of an Annex XV dossier is warranted, particularly in cases where control measures are already in place. In such cases where the Authority decides to prepare an Annex XV dossier based on screening data alone, they should provide sufficient justification for considering the substance to be of equivalent concern to a PBT or vPvB substance.

3.3.3.2 Equivalent level of concern in relation to CMR

The concerns for substances which exhibit carcinogenicity, mutagenicity and reproductive toxicity arise from a number of factors – the seriousness of the effects, the often irreversible nature of the effects, the consequences for society and the difficulty in performing concentration-based risk assessments (except for reproductive effects) among them. Hence these factors should be taken into account when considering whether a substance shows an equivalent level of concern to CMR (cat 1 or 2) substances.

Other effects that are serious could be considered in relation to an equivalent level of concern to CMR, especially if the effects may also be irreversible. Examples of other effects that can be considered to be serious and irreversible in humans are included in the box.

- Substance-related deaths.
- Major permanent functional changes in the central or peripheral nervous system, including sight, hearing and the sense of smell.
- Severe organ damage or major permanent functional changes in other organ systems (for example the lungs).
- Consistent changes in clinical biochemistry, haematology or urinalysis parameters which indicate severe and permanent organ dysfunction.

However, as noted above, indications or confirmation of these serious effects alone are not sufficient for deciding whether the substance is considered to be of equivalent concern and all contributing factors to the observed serious effect(s) need to be considered. Another consideration is whether the risks from the serious effects seen can be adequately addressed by a normal risk assessment or not. If the answer to this is yes, then the substance could probably be managed through other REACH procedures, primarily registration. For example, although e.g. lethality is a serious effect, an equivalent concern should not be generated on the basis of acute lethality alone, as this can usually be adequately addressed by a normal risk assessment methodology. If an Authority has suspicion or concerns that such a substance poses an unacceptable risk, it could be considered to address these through the restrictions procedure. If the answer to the question above is that a normal risk assessment methodology is not adequate, and there is sufficient scientific evidence to conclude that serious effects are probable and that exposure of humans to the chemical is likely to occur under normal conditions of use, then the substance should be considered as being of equivalent concern.

3.3.3.3 Endocrine disrupting properties

An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently can cause adverse health effects in an intact organism, or its progeny, or (sub)populations (Community strategy for endocrine disrupters)

The substances can exert their action through a number of different mechanisms:

- They may mimic the biological activity of a hormone by binding to a cellular receptor, leading to an unwarranted response by initiating the cell's normal response to the naturally occurring hormone at the wrong time or to an excessive extent (**agonistic effect**).
- They may bind to the receptor but not activate it. Instead the presence of the chemical on the receptor will prevent binding of the natural hormone (**antagonistic effect**).
- They may **bind to transport proteins** in the blood, thus altering the amounts of natural hormones that are present in the circulation.
- They **may interfere with the metabolic processes** in the body, affecting the synthesis or breakdown rates of the natural hormones.

Substances that can exert their action through the above mechanisms are “endocrine active substances” or “chemicals with endocrine active properties”. The specific mechanisms by which substances impact the endocrine systems are very complex and not yet fully understood. Although endocrine disruption is not a toxic endpoint *per se*, but rather a mechanism by which toxicity can be exerted, the consequences that may result from endocrine disruption can be both serious and irreversible and so endocrine disruptive effects should be considered as being of equivalent concern.

Substances displaying endocrine active properties can result in changes in growth, development, reproduction or behaviour in the organism or in future generations. Some substances can act on the endocrine system to disturb the homeostatic mechanisms of the body or to initiate processes at abnormal times in the life cycle.

There is currently much effort focused on the development and the validation of both *in vivo* and *in vitro* screening and test methods for identifying endocrine active substances and confirm those that have endocrine disrupting properties, notably under the OECD Test Guidelines programme, and in the United States and Japan. However there are currently no internationally agreed methodologies or criteria available for the evaluation and confirmation of endocrine effects. Therefore the decision on whether or not this mechanism of action is a relevant consideration for a given chemical will need to be taken on a case-by-case basis taking into account the following:

- the available information and evidence for the substance in question,
- the available evidence for structurally related substances.

A candidate list of possible endocrine disrupting substances for further investigation was drawn up in 2000 and 2002 (European Commission, 2000, 2002), and further work on the identification of potential endocrine disrupting substances is on-going internationally.

Given the complexities of the possible mechanisms and effects of endocrine active substances it is unlikely that the results from isolated screening assays will be sufficient to confirm that the substance has potential to cause endocrine disrupting effects in humans or wildlife. Therefore a weight of evidence approach is needed. This should consider the following factors when evaluating the available data.

- The balance of positive and negative responses observed in both *in vitro* and *in vivo* assays.
- The nature and range of the biological effects observed in assays intended to identify and characterize hazards. Again, does a potential estrogenic substance lead to the observation of a pattern of consistent changes in estrogen related target tissues and developmental endpoints
- The shape of the dose-response curves when available. For example, does the dose response in the in vivo screen for an endocrine mechanism show a correspondence to the dose response of those endocrine related changes?
- The severity and magnitude of effects induced. For example, potent estrogens halt the estrous cycle and potent antiandrogens cause malformations of the male reproductive tract. Both are examples where fertility and reproduction are impaired
- The presence or absence of responses in multiple taxa. Endocrine systems are conserved, and a substance acting via an endocrine mechanism is expected to cause endocrine related effects in most or all taxa having those endocrine pathways. For example, estrogenic, androgenic, and thyroid effects would be typically expected to occur in several vertebrate classes for a substance truly acting via a relevant endocrine mechanism

The OECD, through its Endocrine Disrupters Testing and Assessment (EDTA) Task Force, has developed a conceptual framework for the testing and assessment of potential endocrine disrupters and this is outlined in Appendix 4 and further details can be obtained from the OECD website[11]. The framework is not intended to be a testing scheme but rather a tool box into which the various tests that can contribute information for the detection of the hazards of endocrine disrupting

[11] http://www.oecd.org/document/58/0,2340,en_2649_34377_2348794_1_1_1_1,00.html

substances are placed. The framework is divided into five levels, each level corresponding to a different level of biological complexity for both toxicological and ecotoxicological areas. The conceptual framework is subject to further elaboration and discussion as the state of knowledge with regards to endocrine disruptors increases.

Many of the effects on human health that have been linked to exposure to endocrine disrupting substances, for example cancer or effects on fertility and reproduction, may themselves result in the classification and labelling of the substance for carcinogenicity (e.g. category 1 or category 2) or as toxic for reproduction (category 1 or category 2). Substances with these classifications already qualify for inclusion in the candidate list of substances for inclusion in Annex XIV (and a classification and labelling dossier should be produced if a harmonised classification does not already exist).

If a substance is identified as having endocrine disrupting effects, it should be confirmed that a traditional hazard assessment approach could not be used or would be insufficiently protective of such effects. Such considerations would need to take into account the mechanism(s) of action, the severity of the effects, and the uncertainties over whether such effects could occur at (very) low doses and whether the assessment factors used account sufficiently for the uncertainties in these.

3.3.3.4 Future equivalent concerns

It is important that as yet unidentified substance properties can be captured under the consideration of equivalent concern, where there is scientific evidence (relating to probable serious effects) that these properties give rise to an equivalent level of concern to those of CMR cat 1 and 2, PBT and vPvB substances. It might be that other as yet unidentified aspects of a chemical's behaviour in the environment or its impacts on organisms will lead to a change in the current paradigm for chemical hazard and risk assessment. Authorities are encouraged to employ the underlying principles behind the preceding sections in considering such aspects and properties in the future.

3.3.4 Information for prioritisation for inclusion in Annex XIV

Certain types of information, including exposure-related information, are needed for the later process used to prioritise the substances for inclusion on Annex XIV, once the dossier has been accepted. Annex XV requires to include the available information on exposures, alternative substances and risks in the Annex XV dossier for PBT, vPvB and substances giving rise to an equivalent level of concern in order to facilitate the later decision making processes. The methods to be used in the prioritisation are still under development and this section will need to be revisited in the future once more details of the prioritisation methods and related information requirements are available.

In terms of the needs of the dossier, it is likely that the most important exposure-related information will be that the main uses of the substance and sources of emissions or exposure are identified. This could include the following elements.

- Production or import volumes as tonnage bands.
- Information on the uses of the substance.
- Qualitative or quantitative information related to the emissions and exposure, particularly whether the use of the substance leads to a possibility of widespread exposure of humans or widespread emissions to the environment. This may include:

Identifying whether the emission is to air, water and/or soil. This may also be relevant for exposure of man via the environment.

  - Estimates for the percentage of the total use that is emitted to air, water and/or soil.
  - Actual or estimated emission figures for the daily release from example sites.
  - Estimates of the continental or regional emission or other similar data such as a country-wide emission.
  - Measurements or estimates of exposure of humans (e.g. occupational exposure, consumer exposure, number of people exposed) resulting from use of the substance.
  - Estimates of the final distribution of the substance in the environment after release.

- Potency considerations.

The aim of the summary of the use, emission and exposure data should be to identify (and if possible) quantify the steps of the lifecycle of the chemical that can lead to significant exposure of man or the environment. Information related to exposure of the marine environment, or related to the reasons why the substance is considered a PBT, vPvB or substance of equivalent concern, may be particularly useful in this respect.

If a CSR is available and includes an exposure assessment then this can be used to develop a summary of the emissions from the manufacture and use(s) of the substance. This should reflect the overall picture if there are several CSRs for the same substance. Similarly if the substance has been registered, but has no CSR available (or the CSR does not include an exposure assessment), then the technical dossier(s) will identify the main uses of the substances, and also possibly sources of emission.

Where the substance is not registered at all, the Authority is encouraged to characterise the potential for emission and exposure from the manufacture and use of the substance (which can include emission estimates if desired) based on the information available to them. Consultation with manufacturers or users, where they can be identified, would be useful in such cases. The sections on exposure estimation in the Guidance on the Chemical Safety Report and in the Guidance on Annex XV for restrictions may be useful in this area.

Information on DNELs and PNECs could also be included and could be taken from the available CSRs. If no CSR is available then the guidance on deriving such values in the Guidance on CSR should be followed. It may also be useful if possible to relate the DNELs to the same endpoints to which the T-criterion or the equivalent concern relates.

The information for prioritisation for inclusion on Annex XIV should be based on (easily) available information.

When documenting the available information on alternatives, guidance can be found in section 5.5 of the Guidance on Annex XV for restrictions and the Guidance on Socio Economic Analysis may be useful as well.

Available information on risks may include

- Information on risks related to the substance in question, especially related to endpoints other than those resulting in a proposal of identification as a SVHC.
- Information on risks related to alternative substances.

3.4 Preparing the report

Aim: To include the selected information in the relevant sections of the Annex XV report.

Output: The completed Annex XV report with proposal for identification of the substance as a CMR, PBT, vPvB or of an equivalent level of concern.

As noted in Section 0, the Annex XV dossier consists of two parts. This section of the guidance considers the preparation of the Annex XV report. Preparation of the technical dossier is not addressed here, the Guidance on registration should be followed along with the Guidance on IUCLID.

A CMR, PBT, vPvB or equivalent concern Annex XV report consists of four parts: (1) proposal; (2) justification; (3) information on use, exposure, alternatives and risks; and (4) other information. The approach to completing the report is similar for all types of endpoints. The format for the Annex XV report is given in Appendix 1.

For clarity, references to sections of the report are written in italics thus: *Section 1.1*, in order to differentiate them from the sections in this guidance.

3.4.1 Proposal

The first part of the Annex XV report contains a summary of the proposal for identification of the substance as a CMR substance, a PBT substance, a vPvB substance or a substance of equivalent concern. This should contain the main identifier of the identity of the substance.

The summary of the proposal should also contain a summary of the properties of very high concern of the substance. This should include one of the following statements[12].

- It is proposed to identify the substance as a CMR (cat 1 or 2) according to Article 57 (a), (b) and/or (c).
- It is proposed to identify the substance as a PBT according to Article 57 (d).
- It is proposed to identify the substance as a vPvB according to Article 57 (e).
- It is proposed to identify the substance as a substance of equivalent concern according to Article 57 (f).

This should be followed by a short paragraph outlining the main reasons for the proposal. It is also important to indicate in this part of the Annex XV report if the proposal is based on the presence of a constituent or an impurity with PBT properties in the substance(s) rather than the PBT properties of the substance itself.

If the dossier is prepared for a registered substance, the registration numbers need to be included. When the dossier is prepared for substances containing a constituent or impurity which is identified as having properties of very high concern, then the registration numbers of those substances need to be included.

[12] If the Authority has concluded that the substance is not a PBT etc, then a negative statement could be included here.

3.4.2 Justification

The second part of the Annex XV report contains the detailed technical and scientific justification for the proposal. The format of this section of the Annex XV report follows Part B of the format of the CSR. The objective of having compatible formats for different types of reports within REACH (for registration, for evaluation, for Annex XV) is to facilitate the use of already available data within the system. Details of the reviewed relevant information and discussions should be entered into the relevant sections of the format. The headings outlined in the format should be used in all cases, but it is recognised that some of the headings will not be relevant in all cases. Therefore information need only be entered under the relevant headings, and wording along the lines of 'not relevant for this dossier' should be entered under the other headings not used. In addition, a short explanation on why the information under a specific heading is not relevant for the case in concern is recommended to be included.

In order to be considered as a PBT or vPvB substance, the substance has to meet each of the relevant criteria. Therefore the dossiers (both the technical dossier and the Annex XV report) for these endpoints will need to contain information on each of the relevant areas as a minimum. The information required for an equivalent concern dossier may vary on a case-by-case basis.

For a CMR substance, if a relevant harmonised classification is already included in Annex I then a reference to this classification will be sufficient in this part of the Annex XV report (in *Section 3*). If there is no relevant classification in Annex I, then the Guidance on Annex XV for C&L should be followed for *Sections 1 - 7* of the *Justification*. The following guidance relates to reports for PBT and vPvB substances and substances of an equivalent level of concern.

The format for the technical and scientific justification of the Annex XV report is broken down into a number of sections. The guidance below outlines the types of information that could be included in each section for each type of dossier. In addition to the information indicated, any differences in interpretation of the key data between the source of the information (such as the technical dossier(s) or CSR(s) submitted by registrant(s), but also where other data sources are used) and the Authority should be outlined. The level of detail required will vary from substance to substance but the aim should be to include sufficient detail in the report in order to allow the reader to put the data into context and come to their own conclusion as to the relevance to the proposal. In this respect, areas where there are interpretational issues (for example over degradation half-lives) may need more detail than others.

- *Section 1*. This outlines the identity of the substance and includes a summary table of the physico-chemical properties. This information could be extracted from IUCLID. The substance identification to be reported in the Annex XV dossier should be in accordance with the Guidance on substance identification (section 8 describes how to report the information in IUCLID).
  Section 1.1 should be used to describe the identity of the substance for which the dossier is prepared. *Section 1.2* should detail the composition of the substance. All constituents should be identified (with their name, structure, molecular weight) and their proportion in the substance given. The same should apply for the impurities and additives that impact the outcome of the dossier. *Section 1.3* should contain the physico-chemical properties. It is not necessary to complete the table for all of the properties. The most useful physico-chemical properties in relation to PBT considerations are likely to be melting point, boiling point, vapour pressure, water solubility, n-octanol/water partition coefficient and dissociation constant (if relevant) and it is recommended that at least these data be included.

- *Section 2*. This section is not needed for a PBT, vPvB or equivalent concern report. Information on the uses of the substance may be useful for priority setting for Annex XIV inclusion but this

information should be reported in the section on the information on exposure and use of the report.

- *Section 3*. This outlines details of the current classification. For the needs of the PBT assessment, the most relevant classifications relate to the human health classification, particularly if the substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), toxic for reproduction (category 1, 2 or 3), T, R48 or Xn, R48. Therefore it is useful to include the current classification in this Section. The classification should be reported in *Section 3.1* if it is listed in Annex I of Directive 67/548/EEC, in S*ection 3.2* if is according to GHS and in *Section 3.3* for the classification(s) given in the publicly available classification and labelling inventory. Guidance on classification and labelling will be developed within the Guidance on Classification, Labelling and Packaging.

- *Section 4*. This outlines the environmental fate properties of the substance. Guidance on how to assess environmental fate properties is available in the Guidance on the Chemical Safety Report. *Section 4.1* should summarise all of the relevant abiotic and biotic degradation data for the substance. The amount of information that needs to be reported here will depend on whether the report is for a PBT or vPvB substance or a substance of equivalent concern. For a PBT or vPvB substance, the information reported should be focussed on demonstrating that the half-life in the environment is longer than the half-lives given in Annex XIII for the environmental media relevant to the substance i.e. the media to which the substance is expected to distribute to in the environment. The most relevant information here is likely to be information from simulation studies. A summary of the key studies should be included in *Section 4.1.1* (in the case of abiotic studies) or *Section 4.1.2* (in the case of biotic studies). A key part of this section is the summary and discussion of persistence (*Section 4.1.3*). Here the available data should be discussed and the actual derived half-life or half-lives of the substance in the various environmental media considered should be summarised. In the case of equivalent concern, a summary of the main discussions related to persistence should be given if appropriate.

  Section 4.2 is concerned with the environmental distribution. This section is of relevance to a PBT or vPvB report as information on the environmental distribution can be useful for identifying the relevant environmental compartment(s) for consideration of the persistence of the substance. In addition considerations of environmental distribution may also be relevant for equivalent concern, particularly in relation to transportation over long distances (for example consideration of the adsorptive properties and/or volatility of the substance may be relevant). In these cases a summary of the relevant information should be added to the appropriate section.

  Section 4.3 is concerned with the bioaccumulative properties of the substance. For a PBT or vPvB report the most relevant data are likely to be the results from actual bioconcentration studies with aquatic organisms and so most attention should be focused on including a summary of the key study (or studies) under *Section 4.3.1.2* (Measured bioaccumulation data). In this case, screening data (for example log Kow values or predicted BCFs) or monitoring data are likely to be used only as supporting information (if at all) and so only a very brief summary of these data would generally be needed in *Section 4.3.1.1*, and in some cases there will be no need to complete this section at all. The summary and discussion of bioaccumulation data (*Section 4.3.3*) should clearly outline the key findings and values for the bioconcentration or bioaccumulation factors if relevant.

  Section 4.4 concerns any information relevant to potential for secondary poisoning. Here any relevant information on accumulation through the food chain could be summarised. This type of information is likely to be most useful in relation to equivalent concern.

In relation to equivalent concern, a wider range of information may be required, ranging from screening information (e.g. log Kow or predicted BCFs), to uptake and accumulation studies with non-aquatic species, to other supporting data such as monitoring data. Therefore it may be that more information may be needed in *Section 4.3* and *Section 4.4* than may be required for a PBT or a vPvB report. This information should be added to the appropriate subsection(s) of the report.

- *Section 5*. This outlines the mammalian toxicity data and needs mainly to be filled when the substance is identified as PBT or as a substance of equivalent concern. The criterion for T in Annex XIII is based on the classification and labelling of the substance. In cases where an agreed appropriate classification exists there is no need to report the underlying toxicity data that leads to the classification in this section. However, in some cases it may be necessary to complete at least some of this section in detail for a PBT assessment, for example where there is no CSR or technical dossier or if there is a disagreement over the actual classification and labelling presented in the CSR or technical dossier. The aim should be to demonstrate that the substance meets the relevant classification criterion and hence the T criterion for PBT. Evidence of uptake in mammals from toxicity studies may also be useful in relation to the B or vB criterion. Guidance on how to evaluate the data for PBT assessment is available in the Guidance on information requirements and the Guidance on the Chemical Safety Report.

  For an equivalent concern report (and in some cases a PBT or vPvB report), there are a number of other areas that may need to be considered. For example, information on the toxicokinetics (*Section 5.1*) may be relevant to the discussion of the bioaccumulation potential of the substance. Similarly it may be necessary to consider the acute toxicity (*Section 5.2*), repeated dose toxicity (*Section 5.6*), mutagenicity (*Section 5.7*), carcinogenicity (*Section 5.8*) and toxicity to reproduction (*Section 5.9*). The other sub-sections are likely to be less relevant for an equivalent concern dossier and would generally not need to be completed. For each relevant endpoint, a summary of the key studies should be added under the appropriate heading, and an overall summary of the key findings should be completed at the end of each sub-section.

- *Section 6*. This section relates to the human health hazard assessment of physicochemical properties and is not relevant of this type of report. Guidance on how to assess physicochemical properties is available in the Guidance on the Chemical Safety Report.

- *Section 7*. This section considers the available ecotoxicity data for the substance. For a vPvB substance, this section need not be completed. For a PBT substance, the most relevant data are the long-term toxicity data with aquatic organisms. Guidance on how to assess environmental hazard properties is available in the Guidance on information requirements. Therefore details of the key studies should be added to the appropriate sections for fish (*Section 7.1.1.1*), aquatic invertebrates (*Section 7.1.1.2*) and algae (*Section 7.1.1.3*). Only those values used for demonstrating that the T-criterion is met need be added, and so it is possible that not all of these *Sections* will need to be completed. Summaries of the key studies can be taken directly from the registration dossier if available.

  For an equivalent concern report, it may be necessary to consider ecotoxicity data other than long-term toxicity data for aquatic organisms. Thus it is possible that information on the acute toxicity to fish (*Section 7.1.1.1*), aquatic invertebrates (*Section 7.1.1.2*) or algae (*Section 7.1.1.3*) may need to be considered, or indeed toxicity data on sediment organisms (*Section 7.1.1.4*), other aquatic organisms (e.g. amphibians (*Section 7.1.1.5*), terrestrial organisms (*Section 7.2.1*), the atmospheric compartment (*Section 7.3*) or birds (*Section 7.2.1.4*) may need to be considered. Again summaries of only the key studies relevant to the discussions over equivalent concern should be added to the relevant *Sections* (the other *Sections* need not be completed).

- *Section 8*. This concerns the PBT, vPvB and equivalent concern assessment. Guidance is available in the Guidance on information requirements and in the Guidance on the Chemical Safety Report. If a PBT or vPvB assessment has already been completed, for example, as part of the CSR, the key findings can be taken directly from the CSR and used as the basis for the assessment here.

  Section 8.1 relates to the PBT and vPvB assessment. This section should summarise why the substance is considered to meet the PBT or vPvB criteria. Thus it should take each criterion in turn and discuss, by reference to the available persistence, bioaccumulation and toxicity (in the case of a PBT report) data summarised elsewhere in the dossier, why each of the criteria is met. No new data should be introduced in this section. Any information used (either data relating directly to the criteria or supporting information) should be summarised in the appropriate part of the report. Thus this section should be seen as a summary section whereby all the findings related to persistence, bioaccumulation and toxicity (in the case of a PBT dossier) are drawn together. For a PBT or vPvB report there is no need to complete *Section 8.2*.

  For an equivalent concern report, *Section 8.1* should not be completed, and all the discussion should be added to *Section 8.2*. This section should summarise why the substance is considered to be a substance of equivalent concern. Again any information used should be summarised in the appropriate part of the report. The summary should clearly outline what the equivalent concern relates to, for example if it is related to a concern equivalent to CMR, a concern equivalent to PBT or vPvB and summarise the main data that lead to this conclusion.

  Section 8.3 shall cover an estimation of the amounts of the substance released to the different environmental compartments during all activities carried out by the manufacturer or importer and all identified uses, and an identification of the likely routes by which humans and the environment are exposed to the substance.

  The conclusion on the PBT, vPvB or equivalent level of concern assessment (*Section 8.4*) should clearly outline the conclusion from the evaluation, which will then be reported in the *Proposal* section.

3.4.3 Information on use, exposure, alternatives and risks

This part of the report is used to present other information which is required by the REACH Regulation, relating to exposure and alternatives, or which may be useful in subsequent priority setting for inclusion on Annex XIV. As a consequence, this part of the guidance will be updated once the Guidance on Annex XIV inclusion will be finalised. The information included should be readily available to the Authority, for example through the REACH IT system. It is not intended that the Authority carry out an extensive search for this information.

- *Section 1*. The available exposure-related information should be summarised in this section. The main purpose of the exposure-related information is to identify if significant exposure of man or the environment can occur from the use(s) of the substance. General information on the amounts used, along with a description of the uses of the substance could be given. For substances where multiple registrations exist these data from the individual registrations should be combined where possible.

- *Section 2*. Alternatives. This section is divided into two parts, one dealing with alternative substances and the other with alternative techniques. If there is no information relevant to one or either section then a note to say this should be included in the report.

- *Section 2.1*. This section deals with alternative substances. Registration dossiers will be a major source of information on alternative substances, although other readily available sources could be used where appropriate. The information to be included should show that the alternative substance(s) are less hazardous. Hence information on the classification and labelling, and PBT/vPvB characteristics of the alternative substance should be included, together with information on use and potential for exposure. It should be made clear as far as possible for which uses the alternative substance is a replacement for the substance which is subject of the proposal. If available, information on the functionality of any alternatives should also be included.

- Where the information on the alternative(s) is limited it can be presented in this section of the report. Where the Authority wants to present more extensive information on alternatives, it is suggested that they make use of the PBT report format to provide a suitable framework for this. Clearly not all sections will need to be completed, only those which are considered significant.

- *Section 2.2*. This section should be used for information on alternative techniques which could be applied to reduce or eliminate releases of the substance.

It is suggested that if the information on alternative substances is extensive it can be presented using the relevant parts of the same format as for the Annex XV report.

- *Section 3*. This section can be used for other information relating to risks of the substance and alternatives which may be useful for the prioritisation process. This could include DNEL and PNEC values.

3.4.4 Other information

This section of the report can be used for any other information that is considered to be relevant. An example of information that could be included here are details of any consultation which took place during the development of the dossier. This could indicate who was consulted and by what means, what comments (if any) were received and how these were dealt with. Other similar types of information could also be included here.

The sources of the information used in the report could also be indicated in this section (see examples). However, this section should not contain any new technical information. All technical information should be reported in the *Justification* in the Annex XV report.

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4 REFERENCES

AMAP (2001) Guidelines for the AMAP Phase 2 Assessments. Arctic Monitoring and Assessment Programme. AMAP Report 2001:1 (available from http://www.amap.no/).

Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife' Com (1999) 706 http://ec.europa.eu/environment/endocrine/definitions/endodis_en.htm

European Commission (2000) Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption – preparation of a candidate list of substances as a basis for priority setting. Final Report. BKH Consulting Engineers in association with TNO Nutrition and Food Research, produced for European Commission DG ENV (available from http://europa.eu.int/comm/environment/docum/01262_en.htm#bkh).

European Commission (2002) Endocrine disrupters: study on gathering information on 435 substances with insufficient data. Final report. BKH Consulting Engineers in association with DHI Water & Environment and Kiwa Water Research. (available from

http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm#report2)

OECD (2005) Manual for Investigation of HPV Chemicals. Chapter 3.2. Guidance on the Development and Use of Chemical Categories in the HPV Chemicals Programme. Organisation for Economic Co-Operation and Development (available from: http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html).

Stockholm Convention (2001) Stockholm Convention on Persistent Organic Pollutants. Stockholm, 22 May 2001 (available from http://www.pops.int/).

UNECE (1998). Convention on Long-Range Transboundary Air Pollution. The 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) United Nations Economic Committee for Europe (available from http://www.unece.org/env/lrtap/pops_h1.htm).

APPENDIX 1 FORMAT FOR CMR, PBT, VPVB OR EQUIVLENT CONCERN REPORT

Annex XV

Proposal for identification of a substance as a CMR cat 1 or 2, PBT, vPvB or a substance of an equivalent level of concern

Submitted by:

Version:

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1 OR 2, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance name:
EC number:
CAS number:

- *It is proposed to identify the substance as a CMR according to Article 57 (a), (b) and/or (c).*
- *It is proposed to identify the substance as a PBT according to Article 57 (d).*
- *It is proposed to identify the substance as a vPvB according to Article 57 (e).*
- *It is proposed to identify the substance as a substance of equivalent concern according to Article 57 (f).*

Summary of how the substance meets the CMR (Cat 1 or 2), PBT or vPvB criteria, or is considered to be a substance of an equivalent level of concern

Registration number(s) of the substance or of substances containing the substance:

JUSTIFICATION

1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifier of the substance

Chemical Name:
EC Number:
CAS Number:
IUPAC Name:

1.2 Composition of the substance

For each constituent/ impurity/ additive, fill in the following table (which should be repeated in case of more than one constituent). The information is particularly important for the main constituent(s) and for the constituents (or impurity) which influence the outcome of the dossier.

Chemical Name:
EC Number:
CAS Number:
IUPAC Name:
Molecular Formula:
Structural Formula:
Molecular Weight:
Typical proportion %

Real proportion (range) in %

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

REACH ref Annex, §	Property	Value	[enter comment/reference or delete column]
V, 5.1	Physical state at 20 C and 101.3 kPa		
V, 5.2	Melting / freezing point		
V, 5.3	Boiling point		
V, 5.5	Vapour pressure		
V, 5.7	Water solubility		
V, 5.8	Partition coefficient n-octanol/water (log value)		
VII, 5.19	Dissociation constant		
	[enter other property or delete row]		

2 MANUFACTURE AND USES

Not relevant for this type of dossier.

Information on uses may be useful for prioritisation for inclusion in Annex XIV but this should be summarised under Section 9.2.

3 CLASSIFICATION AND LABELLING

3.1 Classification in Annex I of Directive 67/548/EEC

3.2 Classification according to GHS

3.3 Self classification(s)

This should include the classification, the labelling and the specific concentrations limits. The reason and justification for no classification should be reported here.

It should be stated whether the classification is made according to Directive 67/548/EEC criteria or according to GHS criteria

4 ENVIRONMENTAL FATE PROPERTIES

4.1 Degradation

4.1.1 Stability

Corresponds to IUCLID 4.1

4.1.2 Biodegradation

4.1.2.1 Biodegradation estimation

4.1.2.2 Screening tests

4.1.2.3 Simulation tests

4.1.3 Summary and discussion of persistence

4.2 Environmental distribution

4.2.1 Adsorption/desorption

Corresponds to IUCLID 4.4.1

4.2.2 Volatilisation

Corresponds to IUCLID 4.4.2

4.2.3 Distribution modelling

4.3 Bioaccumulation

4.3.1 Aquatic bioaccumulation

4.3.1.1 Bioaccumulation estimation

e.g. use of Kow, predicted BCF

4.3.1.2 Measured bioaccumulation data

4.3.2 Terrestrial bioaccumulation

4.3.3 Summary and discussion of bioaccumulation

4.4 Secondary poisoning

Assessment of the potential for secondary poisoning

5 HUMAN HEALTH HAZARD ASSESSMENT

5.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

5.2 Acute toxicity

5.2.1 Acute toxicity: oral

5.2.2 Acute toxicity: inhalation

5.2.3 Acute toxicity: dermal

5.2.4 Acute toxicity: other routes

5.2.5 Summary and discussion of acute toxicity

C&L including weight-of-evidence considerations.

5.3 Irritation

Not relevant for this type of dossier.

5.4 Corrosivity

Not relevant for this type of dossier.

5.5 Sensitisation

Not relevant for this type of dossier.

5.6 Repeated dose toxicity

5.6.1 Repeated dose toxicity: oral

5.6.2 Repeated dose toxicity: inhalation

5.6.3 Repeated dose toxicity: dermal

5.6.4 Other relevant information

5.6.5 Summary and discussion of repeated dose toxicity

Classification &Labelling, dose-response estimation including weight-of-evidence considerations.

5.7 Mutagenicity

5.7.1 *In vitro* data

5.7.2 *In vivo* data

5.7.3 Human data

5.7.4 Other relevant information

5.7.5 Summary and discussion of mutagenicity

Classification &Labelling, dose-response estimation including weight-of-evidence considerations.

5.8 Carcinogenicity

5.8.1 Carcinogenicity: oral

5.8.2 Carcinogenicity: inhalation

5.8.3 Carcinogenicity: dermal

5.8.4 Carcinogenicity: human data

5.8.5 Other relevant information

5.8.6 Summary and discussion of carcinogenicity

Classification & Labelling, dose-response estimation including weight-of-evidence considerations.

5.9 Toxicity for reproduction

5.9.1 Effects on fertility

5.9.2 Developmental toxicity

5.9.3 Human data

5.9.4 Other relevant information

5.9.5 Summary and discussion of reproductive toxicity

Classification & Labelling, dose-response estimation including weight-of-evidence considerations.

5.10 Other effects

5.11 Derivation of DNEL(s) or other quantitative or qualitative measure for dose response

5.11.1 Overview of typical dose descriptors for all endpoints

5.11.2 Correction of dose descriptors if needed (for example route-to-route extrapolation)

5.11.3 Application of assessment factors

5.11.4 Selection / identification of the critical DNEL(s) / the leading health effect

6 HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES

Not relevant for this type of dossier.

7 ENVIRONMENTAL HAZARD ASSESSMENT

7.1 Aquatic compartment (including sediment)

7.1.1 Toxicity test results

7.1.1.1 Fish

Short-term toxicity to fish

Long-term toxicity to fish

7.1.1.2 Aquatic invertebrates

Short-term toxicity to aquatic invertebrates

Long-term toxicity to aquatic invertebrates

7.1.1.3 Algae and aquatic plants

7.1.1.4 Sediment organisms

7.1.1.5 Other aquatic organisms

7.1.2 Calculation of Predicted No Effect Concentration (PNEC)

7.1.2.1 PNEC water

7.1.2.2 PNEC sediment

7.2 Terrestrial compartment

7.2.1 Toxicity test results

7.2.1.1 Toxicity to soil macroorganisms

7.2.1.2 Toxicity to terrestrial plants

7.2.1.3 Toxicity to soil microorganisms

7.2.1.4 Toxicity to other terrestrial organisms

Toxicity to birds

Toxicity to other above ground organisms

7.2.2 Calculation of Predicted No Effect Concentration (PNEC_soil)

7.3 Atmospheric compartment

7.4 Microbiological activity in sewage treatment systems

7.4.1 Toxicity to aquatic microorganisms

7.4.2 PNEC for sewage treatment plant

7.5 Calculation of Predicted No Effect Concentration for secondary poisoning (PNEC oral)

7.6 Conclusion on the environmental classification and labelling

8 PBT, VPVB AND EQUIVALENT LEVEL OF CONCERN ASSESSMENT

8.1 Comparison with criteria from Annex XIII

8.2 Assessment of substances of an equivalent level of concern

8.3 Emission characterisation

8.4 Conclusion of PBT and vPvB or equivalent level of concern assessment

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

1 INFORMATION ON EXPOSURE

Exposure information may be useful for priority setting for Annex XIV inclusion.

2 INFORMATION ON ALTERNATIVES

The two sub-sections on alternatives should be used as appropriate

2.1 Alternative substances

2.2 Alternative techniques

3 RISK-RELATED INFORMATION

Information such as PNEC and DNEL values may be useful in priority setting for Annex XIV inclusion.

OTHER INFORMATION

(It is suggested to include here information on any consultation which took place during the development of the dossier. This could indicate who was consulted and by what means, what comments (if any) were received and how these were dealt with. The data sources (e.g. Technical Dossiers, CSRs, other published sources) used for the dossier could also be indicated here.)

APPENDIX 2 CRITERIA FOR THE IDENTIFICATION OF PERSISTENT, BIOACCUMULATIVE AND TOXIC SUBSTANCES, AND VERY PERSISTENT AND VERY BIOACCUMULATIVE SUBSTANCES (REACH REGULATION ANNEX XIII)

Annex XIII of the REACH Regulation lays down the criteria for the identification of:

i) persistent, bioaccumulative and toxic substances (PBT-substances), and

ii) very persistent and very bioaccumulative substances (vPvB-substances).

A substance is identified as a PBT substance if it fulfils the criteria in Sections 1.1, 1.2 and 1.3. A substance is identified as a vPvB substance if it fulfils the criteria in Sections 2.1 and 2.2. Annex XIII of the REACH Regulation shall not apply to inorganic substances, but shall apply to organo-metals.

1 PBT-SUBSTANCES

A substance that fulfils all three of the criteria of the sections below is a PBT substance.

1.1 Persistence

A substance *fulfils* the persistence criterion (P-) when:

- the half-life in marine water is higher than 60 days, or
- the half-life in fresh- or estuarine water is higher than 40 days, or
- the half-life in marine sediment is higher than 180 days, or
- the half-life in fresh- or estuarine water sediment is higher than 120 days, or
- the half-life in soil is higher than 120 days.

The assessment of the persistency in the environment shall be based on available half-life data collected under the adequate conditions, which shall be described by the registrant.

1.2 Bioaccumulation

A substance *fulfils* the bioaccumulation criterion (B-) when:

- the bioconcentration factor (BCF) is higher than 2000.

The assessment of bioaccumulation shall be based on measured data on bioconcentration in aquatic species. Data from freshwater as well as marine water species can be used.

1.3 Toxicity

A substance *fulfils* the toxicity criterion (T-) when:

- the long-term no-observed effect concentration (NOEC) for marine or freshwater organisms is less than 0.01 mg/l, or

- the 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.

2 VPVB – SUBSTANCES

A substance that fulfils the criteria of the sections below is a vPvB substance.

2.1 Persistence

A substance *fulfils* the very persistence criterion (vP-) when:

- the half-life in marine, fresh- or estuarine water is higher than 60 days, or
- the half-life in marine, fresh- or estuarine water sediment is higher than 180 days, or
- the half-life in soil is higher than 180.

2.2 Bioaccumulation

A substance *fulfils* the very bioaccumulative criterion (vB-) when:

- the bioconcentration factor is greater than 5000.

APPENDIX 3 ARCTIC MONITORING AND ASSESSMENT PROGRAMME GUIDELINES FOR QUALITY ASSURANCE OF MONITORING DATA

Quality assurance recommendations

The review of monitoring data should consider the following steps.

- Sampling design (site selection, spatial resolution, frequency of determination etc.).
- Field operations (sampling, field pre-treatment, field measurements).
- Sample shipments to laboratory (sample conservation and identification, time and method of delivery).
- Laboratory operations (laboratory pre-treatment, analysis, laboratory data verification, analytical quality control including intercalibration exercises).
- Data handling (data entry, storage, retrieval, presentation).
- Data analysis and evaluation.

The following four categories of data are proposed, based on quality assurance considerations.

A Evidence of certification or documented quality assurance on all stages of the data gathering process.

B Some parts of QA/QC process can be documented (but may not be fully described in e.g. published reports).

C No data available on QA/QC procedures, but results are consistent with other reports concerning the same sample types.

D No evidence of QA or of data compatibility with the certified data flux.

AMAP recommend that only data in categories A or B should be accepted for investigation of spatial and temporal trends or other types of basic data interpretations. Category C data can be used to show relative trends, assuming that they are internally consistent. Category D data should not be used in the assessment process.

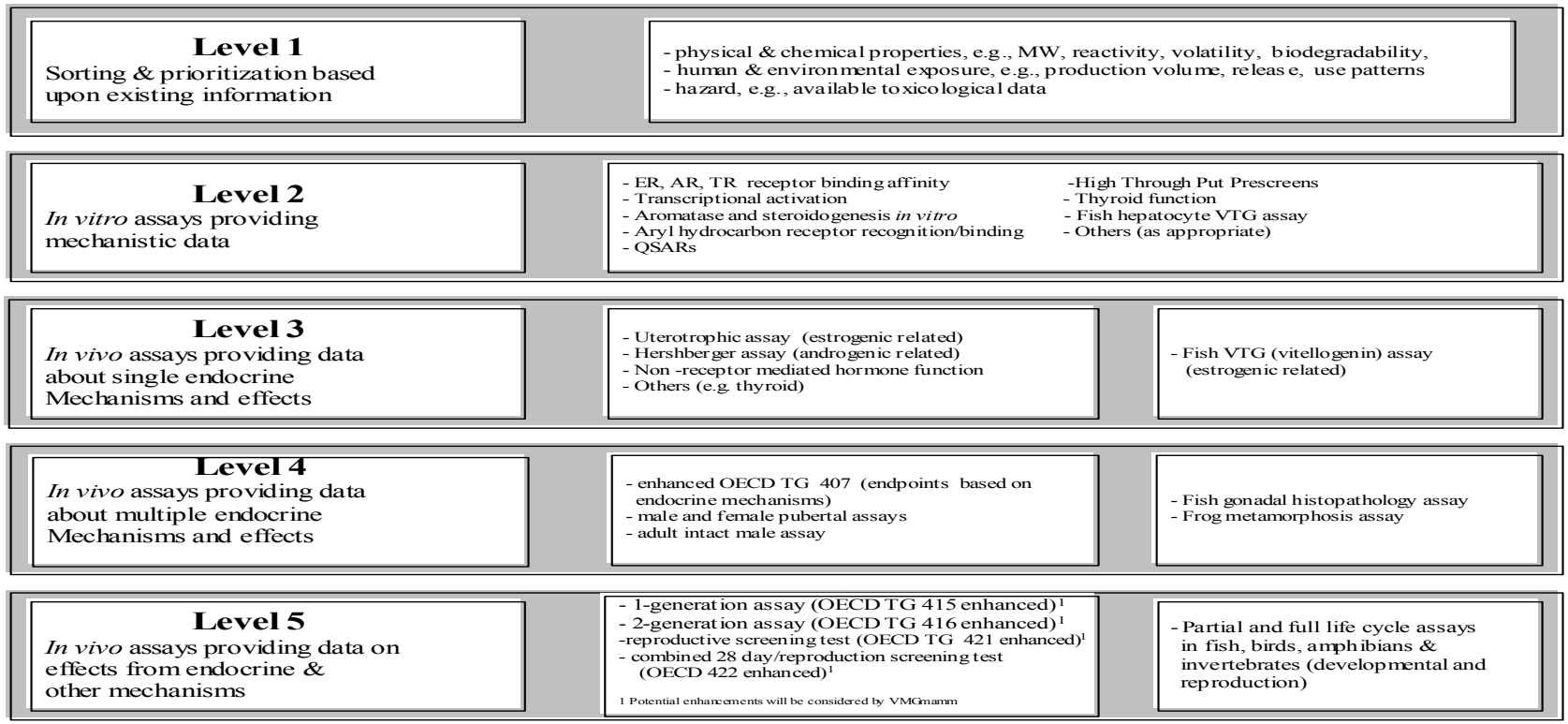
Reference

AMAP (2001) Guidelines for the AMAP Phase 2 Assessments. Arctic Monitoring and Assessment Programme. AMAP Report 2001:1 (available from http://www.amap.no/).

APPENDIX 4 THE OECD CONCEPTUAL FRAMEWORK FOR TESTING AND ASSESSMENT OF ENDOCRINE DISRUPTING CHEMICALS

Note: Document prepared by the Secretariat of the Test Guidelines Programme based on the agreement reached at the 6th Meeting of the EDTA Task Force

OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals



Notes to the Framework

Note 1: Entering at all levels and exiting at all levels is possible and depends upon the nature of existing information needs for hazard and risk assessment purposes

Note 2: In level 5, ecotoxicology should include endpoints that indicate mechanisms of adverse effects, and potential population damage

Note 3: When a multimodal model covers several of the single endpoint assays, that model would replace the use of those single endpoint assays

Note 4: The assessment of each chemical should be based on a case by case basis, taking into account all available information, bearing in mind the function of the framework levels.

Note 5: The framework should not be considered as all inclusive at the present time. At levels 3, 4 and 5 it includes assays that are either available or for which validation is under way. With respect to the latter, these are provisionally included. Once developed and validated, they will be formally added to the framework.

Note 6: Level 5 should not be considered as including definitive tests only. Tests included at that level are considered to contribute to general hazard and risk assessment.

APPENDIX 5 INFORMATION REQUIREMENTS AND SCREENING CRITERIA USED UNDER THE STOCKHOLM CONVENTION

(a) Chemical identity

(i) Names, including trade name or names, commercial name or names and synonyms, Chemical Abstracts Service (CAS) Registry number, International Union of Pure and Applied Chemistry (IUPAC) name; and

(ii) Structure, including specification of isomers, where applicable, and the structure of the chemical class.

(b) Persistence

(i) Evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months; or

(ii) Evidence that the chemical is otherwise sufficiently persistent to justify its consideration within the scope of this Convention.

(c) Bio-accumulation

(i) Evidence that the bio-concentration factor or bio-accumulation factor in aquatic species for the chemical is greater than 5,000 or, in the absence of such data, that the log Kow is greater than 5;

(ii) Evidence that a chemical presents other reasons for concern, such as high bio-accumulation in other species, high toxicity or ecotoxicity; or

(iii) Monitoring data in biota indicating that the bio-accumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention.

(d) Potential for long-range environmental transport

(i) Measured levels of the chemical in locations distant from the sources of its release that are of potential concern;

(ii) Monitoring data showing that long-range environmental transport of the chemical, with the potential for transfer to a receiving environment, may have occurred via air, water or migratory species; or

(iii) Environmental fate properties and/or model results that demonstrate that the chemical has a potential for long-range environmental transport through air, water or migratory species, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For a chemical that migrates significantly through the air, its half-life in air should be greater than two days.

(e) Adverse effects

(i) Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or

(ii) Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.