環境省
Ministry of the Environment

Key Points for Chemical Safety Assessment in REACH (Draft)

This document was prepared by the Chemicals Evaluation and Research Institute, Japan (CERI) as "Information Gathering / Reporting Tasks Regarding Chemical Safety Assessment in REACH in 2008" founded by the Ministry of the Environment

Introduction

The new European chemical regulation, REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals), was enforced on June 1, 2007, and thereafter, pre-registration for REACH took place during the period between June and December 2008. Upon registration for REACH, the registering companies themselves need to conduct hazard and exposure assessments and submit a set of documents, which show that the risks are adequately controlled, to ECHA (European Chemicals Agency) as part of the documents required for registration.

In REACH, "manufacturers" and "importers" of substances on their own or in preparation in Europe which are covered by REACH are required to register these substances. For the registration, they are required to conduct Chemical Safety Assessment (CSA). The "Downstream Users (DUs)," who are at the downstream, must inform the registering manufacturers or importers (M/I) about the use[1] / exposure information required for CSA. If the usage in DUs is not included in CSA conducted by the upstream M/I, DUs need to conduct CSA by themselves.

Although REACH is applied only to legal entities (including individuals) within Europe, Japanese companies should take this system into consideration as well since exporters (those who export chemical substances themselves and various materials which contain these substances to Europe from outside Europe) would need to provide European importers the information required by REACH regulation in their business. In addition, even those who do not export directly to Europe or those who provide substances, preparations or products indirectly or directly to exporters to Europe may also be required to submit information. The failure to submit the necessary information to the authority or to put it on the supply chain in Europe may affect the marketing of the substance or any products containing the substance in Europe. For this reason, all associated companies outside Europe, including Japanese companies, are required to pay attention and take necessary action to this system in their business.

With regard to preparation of registration documents for REACH, a large number of guidance documents have been prepared and published mainly by ECHA, however, these documents contain a large amount of highly specialized contents. Of all guidance documents for REACH registration, the guidance document associated with CSA[2] is considered the most important for safety assessment of the chemical substance to be registered. There are concise and detailed versions for the CSA guidance documents. Of these, the concise version is translated and released to the public by Ministry of the Environment of Japan[3].

This document was first prepared to provide additional information that would promote understanding of CSA in REACH for those involved in risk assessment / management-associated tasks to conduct CSA mainly based on CSA guidance documents. In addition, explanatory topics regarding terms and ideas specific to REACH are newly added to the content. This document however dose not cover the entire content described in the guidance document. Therefore, it is recommended to refer to the original guidance documents upon the actual conduct of CSA.

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[1] The term "use" is defined by the REACH as follows, "use: means any processing, formulation, consumption, storage, keeping, treatment, filling into containers, transfer from one container to another". (REACH article 3(24)). It is noted that transfer from a container to another, storage and keeping are also included into "use" in REACH.

[2] "Guidance on information requirements and chemical safety assessment"; published in May 2008.
This includes concise guidance (Part A - Part G) and in-depth guidance (R.2 - R.20).
The original document can be downloaded from the website below.
http://reach.jrc.it/docs/guidance_document/information_requirements_en.htm

[3] The Japanese translation of the guidance document can be downloaded from the website of Network for Strategic Response on International Chemical Management below.
http://www.chemical-net.info/regulation.html

Upon preparation of this document, a technical committee, which consists of the following members and the secretariat, was established, and the contents and structures of this document were discussed.

Technical Committee Member （Honorific titles are omitted）	
Name	Office
Yasunobu AOKI (Chair person)	Section Head, Health Risk Research Section Research Center for Environmental Risk National Institute for Environmental Studies
Toshiaki ICHIKAWA	Chief Engineer, Corporate Environmental Policy Division Hitachi, Ltd.
Katsuya SATO	Professor, Department of Science and Engineering CHUO UNIVERSITY
Fumiaki SHONO	Vice Secretary-General, REACH Task Force Japan Chemical Industry Association
Norihisa TATARAZAKO	Senior Researcher, Exposure Assessment Research Section Research Center for Environmental Risk National Institute for Environmental Studies
Secretariat	
Chisumi ETO Toshiki Nozaka Kazumi KAWAHARA	Chemicals Assessment and Research Center Chemicals Evaluation and Research Institute (CERI)

Contents

1. Chemical Safety Assessment (CSA), Chemical Safety Report (CSR), and Safety Data Sheet (SDS) in REACH

1.1 CSA, CSR and SDS in REACH

The goal of the chemical Safety Assessment (CSA) is not to establish whether or not there is a risk, but to identify and describe the conditions under which the risks are controlled.

Upon REACH registration, a Registration Dossier needs to be prepared for each substance. The Registration Dossier contains the following two documents.

- Technical Dossier: Required for all substances (more than 1 ton / year) which require REACH registration.
- CSR (Chemical Safety Report): Required for a substance of 10 tons / year. This is a document which contains the results of CSA and the safety assessment (where operational conditions under which risks are adequately controlled are described).

The Technical Dossier must be prepared by using a specific software called "IUCLID5 (International Uniform Chemical Information Database)"[4]. Alternatively, CSR is independent of the Technical Dossier, and there is no specific software required for the preparation of the document.

The purpose of safety assessment of a chemical substance in REACH registration is to establish safety conditions associated with the manufacturing and use of the substance at any stage of the lifecycle. The registrant who manufacturers or imports chemical substances more than 10 tons / year is to conduct CSA and submit a document, which includes the results of CSA and its evaluation, to European Chemicals Agency (ECHA) as CSR along with the Technical Dossier.

Usually, CSA is conducted by the registering manufacturer or importer (M/I), but the registrant is required to evaluate if the risks associated with not only their own manufacturing / use but also processing / use of the substance by DUs (Downstream Users) in the supply chain are appropriately controlled.

The use of the substance recognized by M/I and specified in CSR is called "Identified Use (IU)." The "IU" is defined as "use of a substance on its own or in a preparation, that is intended by an actor in the supply chain" in REACH (Article 3 (26)). An assessment should be made if the risks are appropriately controlled in the use of the substance or in a preparation, and the results of the assessment need to be documented in SDS (Safety Data Sheet) along with hazard information of the substance and communicated to DUs.

Besides this, there are other types of CSAs e.g. when DUs use a chemical substance other than IU, etc., or CSA which is associated with application for authorisation of a substance of very high concern. The procedures required in these cases are described in the CSA Concise Guidance Document Part A.4.

[4] The software IUCLID5, which is used to prepare the Technical Dossier can be downloaded from the website below: http://iuclid.echa.europa.eu/

1.2 An Overview of CSA

CSA is required for a substance manufactured or imported in a quantity of 10 tonnes or more per year in EU region and is normally proceeds in following steps.

Step-1： Collection and generation of available and required information on intrinsic properties（See CSA Concise Guidance Document Part A）

Step-2： Human health hazard assessment; including classification and derivation of derived no effect levels（DNELs） (where that is not possible other indications of the potency of the substance) (See CSA Concise Guidance Document Part B.7.1 and CSA in-depth Guidance Document R.8)

Step-3： Physicochemical hazard assessment; including classification (see CSA In-depth Guidance Document R.9)

Step-4： Environmental hazard assessment; including classification and derivation of predicted no effect concentration (PNECs) (See CSA Concise Guidance Document B.7.2 and CSA In-depth Guidance Document R.10)

Step-5： PBT（Persistent, Bioaccumulative and Toxic） and vPvB（Very Persistent and Very Bioaccumulative） Assessment (See CSA Concise Guidance Document Part C, CSA In-depth Guidance Document R.11）

If, as a result of the hazard assessment, it is found that a substance meets the criteria for classification as dangerous according to the criteria of Directive 67/548/EEC[5] or 1999/45/EC, or is a PBT or vPvB substances, then exposure assessment and subsequent risk characterisation is required (See Figure 1-1). If a substance does not meet the criteria for classification as hazardous substances or is not a PBT and vPvB substance following steps are not required.

Step-6： Exposure assessment (covering development of exposure scenarios and exposure estimation (See CSA Concise Guidance Document Part D)

Step-7： Risk Characterization (See Concise Guidance Document Part E)

CSA iterations may be needed depending on a result of the risk characterisation.

Step-8： Potential CSA iteration (See Concise Guidance Document Part A)

Figure 1-1 shows an overview of CSA.

[5] Directive 67/548/EEC can be found at ECB's (ECB：European Chemical Bureau） web site below. It should be noted that this Directive will be repealed and replaced with GHS （Globally Harmonised System of Classification and Labelling of Chemicals） by 2015.
http://ecb.jrc.ec.europa.eu/classification-labelling/

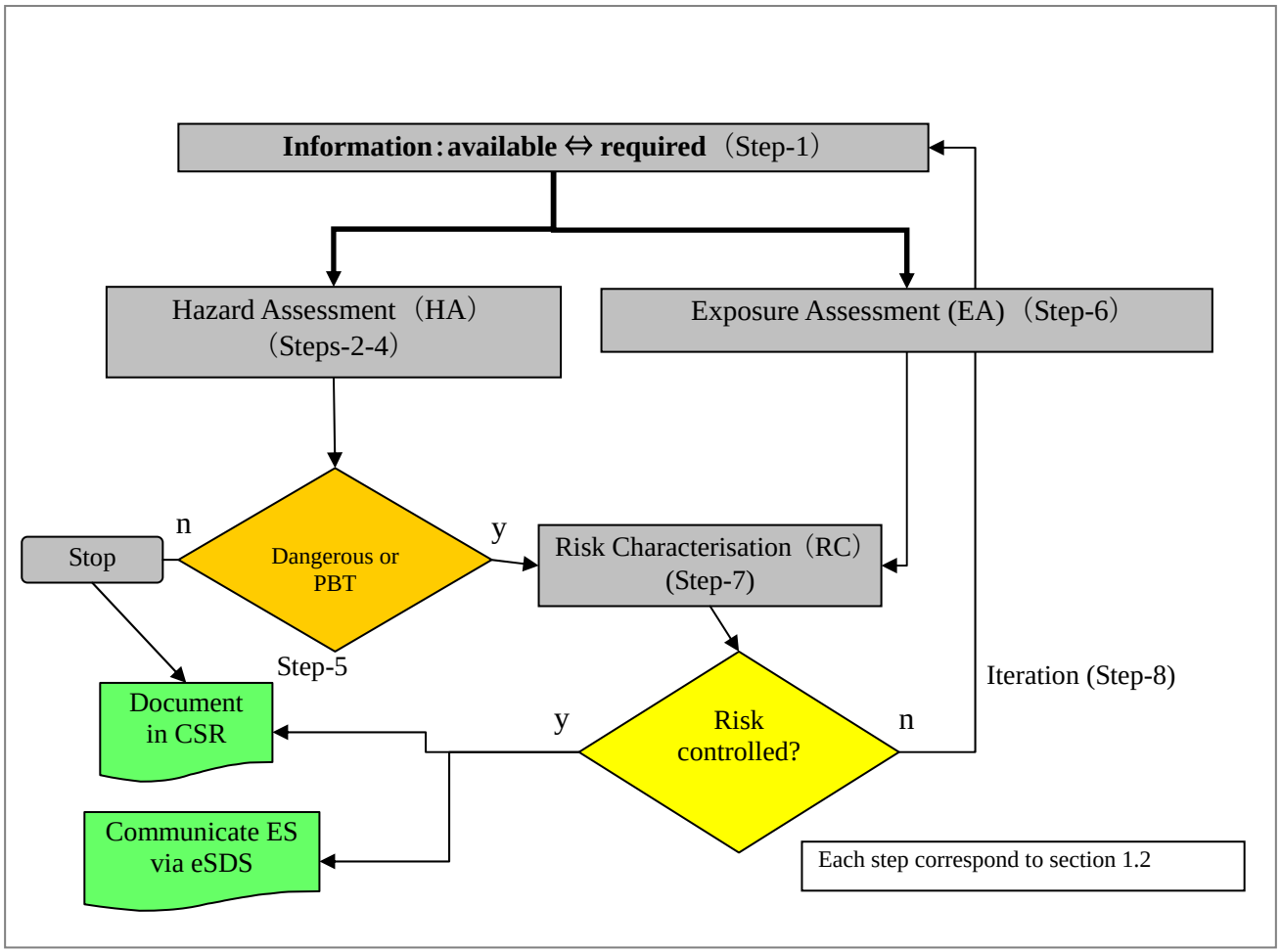

Figure 1-1 Overview of CSA

1.3 Items Required for Registration

The items required for REACH registration are described below.

Technical Dossier

- Identity of the registrant
- Identify the substance
- Information on manufacturing and use of the substance
- Hazard classification and labelling
- Guidance on its safe use
- (Robust) Summary of substance specific hazards
- Study plan (if necessary)
- Information regarding exposure

CSR

- Hazard, PBT, vPvB assessment

If it is dangerous (classified) or PBT, vPvB substance, the following are added.

- Exposure Scenario (ES)
- Estimation of the amount of exposure
- Risk characterisation

1.4 Output of CSA

Normally following outputs are required in CSA.

1) Available information for the hazard assessment, classification and labelling, PBT/vPvB assessment and the derivation of the hazard threshold levels for human health and the environment
2) Where the assessment shows that the substance meets the classification criteria or PBT/vPvB criteria,

identification the conditions under which the risks can be adequately controlled; i.e. exposure scenarios (ES)

3) Assessment results (described in CSR）
4) When ES are developed, the company and downstream users shall implement the conditions of use where risks adequately controlled. The information on the identified use is not only described in CSR but also its summary is attached in the extended safety data sheet (eSDS)[6] and is communicated further downstream users via the supply chain (See Chapter 8: Safety Data Sheet, p39, and CSA Concise Guidance Document Part G).

Topic-1

Viewpoints of risk assessment in REACH

"Risk assessment" is a concept which appears in REACH text, but its definition is not provided there. The "risk" is generally expressed by the product of hazardous properties intrinsic to the substance, and the amount of exposure to humans or living organisms determined by the amount manufactured or the condition of use. However, in REACH, the concepts of "risk characterisation" and "control of risk" which are the main concepts in CSA, are clearly described rather than giving a general definition of "risk." Although the hazardous properties are inherent in each substance, risks can be reduced by changing the condition of use consisting of the operation conditions or Risk Management Measure (RMMs), including the use patterns.

In CSA Guidance Document, it is defined that "the goal of the assessment is not to establish whether or not there is a risk, but identify and describe the conditions under which risks are controlled". The risk characterisation is a process to confirm such conditions and performed by 1) collecting hazard information and deriving the hazard descriptor (DNEL, PNEC, etc.) for the risk characterisation, 2) exposure assessment, and by 3) comparing the amount of exposure to the hazard descriptor. As a result, it is considered that "the risk is controlled" when the amount of exposure does not exceed the hazard descriptor.

Therefore, for a substance of which the level of the hazard descriptor is very small (highly hazardous substance), it may be required to take some measures to reduce the amount of exposure compared to a substance with high hazard descriptor level. In addition, for substances with high hazard descriptor level (low hazard substances), risk assessment can be discontinued at the point where the risk control is confirmed in comparison with the amount of exposure which is predictable in a worst case scenario, without performing detailed and complicated exposure assessment. Furthermore, a substance which is considered as low-hazard (unclassified) according to the results of hazard assessment and do not correspond to PBT / vPvB substance is judged as low risk, and quantitative exposure assessment or risk characterisation is not required regardless of the manufactured or imported volume.

For those substances having a property of carcinogenicity, mutagenicity and reproductive toxicity (CMR) or PBT/vPvB (See Chapter 4: PBT Assessment), or possibly having similar properties which are highly concern (e.g. endocrine disruption) is specified as Substances of Very High Concern (SVHCs) and is subject to the authorisation. The SVHCs in articles are required to notify all users of the substance. Some substances prioritised for the authorisation from the SVHCs shall be prohibited to use as substances themselves or substances in the mixture and to incorporated into articles unless the user of the substances or the suppliers for the user would submit the application for authorisation for such use(s) of the substance(s) and to be granted authorisation to such use(s) by ECHA. Detailed guidance document "Guidance for the preparation of an Annex XV dossier on the identification of substances of very high concern" is published by ECHA.

[6] Information on identified use, operational conditions and risk management measures (RMMs) under which risks are adequately controlled is described in usual MSDS and is used to communicate to downstream users. This MSDS is called as extended SDS (eSDS) in REACH.

2. An Overview of Guidance Document on Information Requirements and Chemical Safety Assessment

European Chemicals Agency (ECHA) has prepared and published a document including the following contents as guidance on information requirements and CSA (hereinafter referred to as CSA Guidance Document).

- Collection of information regarding intrinsic properties of a substance to be registered under REACH
- Evaluation of information required in REACH
- Identification of data gap (lack of data required for registration)
- Acquisition of additional information to fulfil the data gap

This CSA Guidance Document is prepared to support registrants to conduct CSA appropriately and to record the assessment results in CSR. The CSA Guidance Document consists of the Concise Guidance Document (Part A – Part G) and the In-depth Guidance Document (R.2 – R.20) (Figure 2-1).

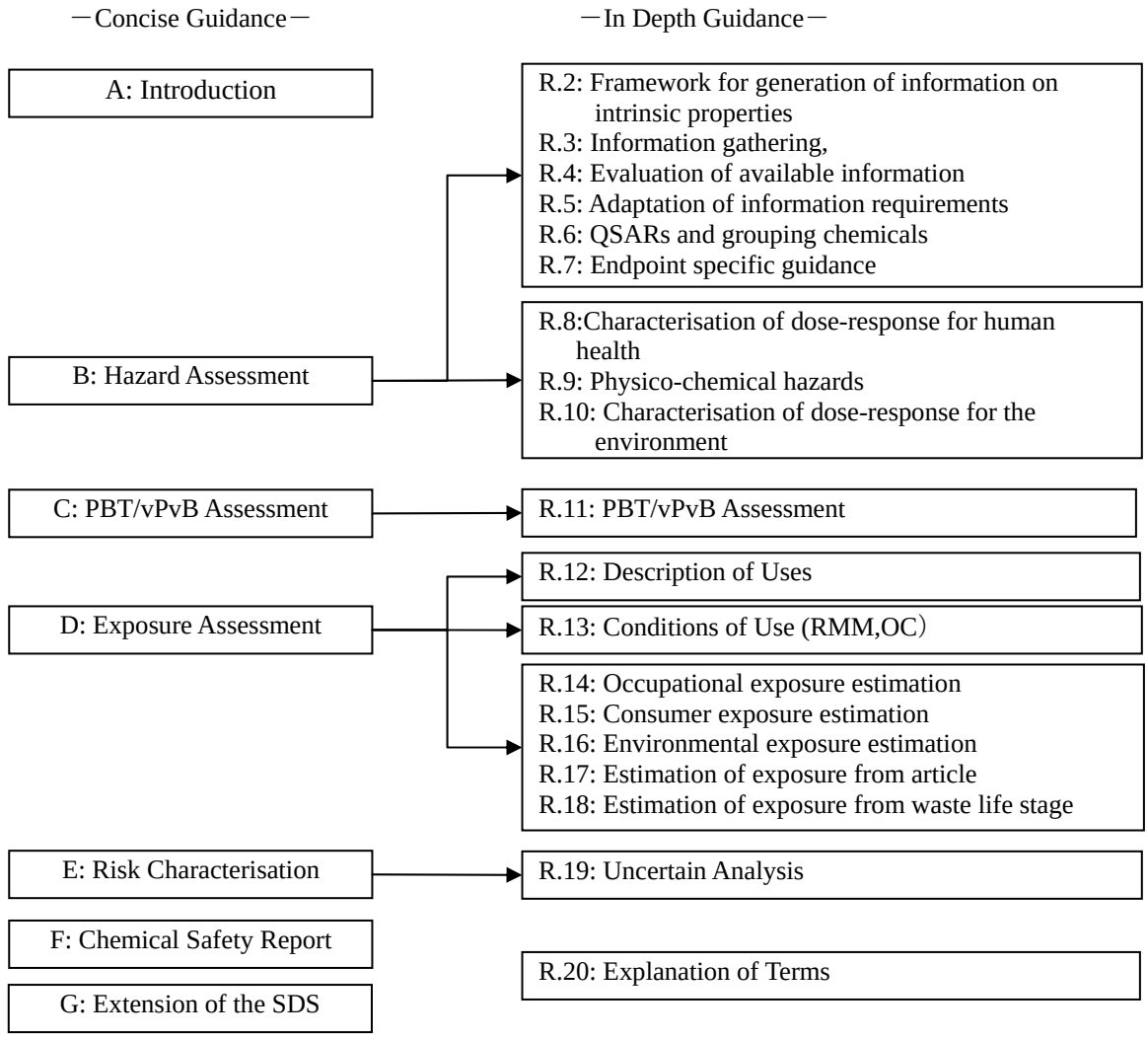

Figure 2-1 Structure of the Guidance Document

Main contents in the concise guidance documents are shown in table 2-1.

Table 2-1 Overview of the Concise Guidance

Structure	Summary
Part A Introduction	Overview and summary of the CSA and concise guidance documents Part B to Part G.
Part B Hazard Assessment	Part B contains concise guidance on the hazard assessment. Part B covers the information requirements under REACH, including information gathering, non-testing approaches and the so-called 'integrated testing strategies' for generating the relevant and required information on each endpoint. It also provides concise guidance on how to characterise hazards, including where possible derivation of DNELs and PNECs. Each sections in Part B corresponds to the more in-depth guidance contained in Chapters R.2 to R.10.
Part C PBT Assessment	Part C contains the concise guidance on how to assess whether or not a substance is PBT or vPvB substance. In-depth guidance on the PBT and vPvB assessment is covered in Chapter R.11.
Part D Exposure Scenario Building	Part D details how to develop exposure scenarios and related exposure estimation. Part D contains in-depth workflows on how to identify uses in the supply chain, how to develop exposure scenarios and finalise them based on the iterations necessary for controlling risks. Part D provides in particular how to describe uses, how to collect information on operational conditions and risk management measures, and how to carry out exposure estimates. In-depth guidance on the exposure scenario is described in in-depth guidance R.12 to R.18.
Part E Risk Characterisation	Part E contains the guidance on the risk characterisation. In the risk characterisation, information on hazard and exposure is combined in the risk characterisation ratio (RCR) or in qualitative risk characterisation. The uncertain analysis is further in-depth in in-depth guidance R.19.
Part F CSR and its Template	Part F details the format and requirements for preparing the chemical safety report, which documents the results of the entire chemical safety assessment. Part F details subsections to the main headlines and provides guidance on how to present the outcome of the CSA. It also explains how to use the CSR template.
Part G Extending the SDS	Part G contains the guidance on preparing the extensions to the safety data sheet (SDS). This contains information on how the exposure scenario is communicated and implemented in the supply chain. In an appendix to Part G it is exemplified how DUs may scale exposure scenarios according to their conditions of use. It also includes a number of approaches how to process at DUs level information received with the extended safety data sheets and how to communicate to further down.

3. Hazard Assessment

3.1 The Basic Method of Hazard Assessment

The procedures for hazard assessment in REACH are described in the following four steps in the CSA Concise Guidance Document.

Step-1: Gather and share existing information (See CSA Concise Guidance Document Part b.4 to B.6)

The registrant must collect all physicochemical, toxicological, ecotoxicological and exposure information that is relevant and available regardless at the specific tonnage level. Animal testing data shall share with registrants of the same substance and other information as well. For phase-in substances, Substance Information Exchange Forum (SIEF) will play as such role.

Step-2: Consider information needs (See CSA in-depth Guidance Document R.2, R.5, R.7, REACH Article Annexes VII to X)

The registrant needs to identify the standard information requirements according to tonnage manufactures or imports. In this stage waving of the information requirements and additionally required information should also be confirmed.

Step-3: Identify information gaps（See CSA In-depth Guidance Document R.7）

In step-3, the registrant compares the information needs for the substance identified in step 2 with the reliable and relevant information already available as identified in step 1. Where the REACH regulatory requirements cannot be fulfilled with relevant and available information, data should be obtained in accordance with the procedures of step 4.

Step 4: Generate new information or propose a testing strategy (See Concise Guidance Document B.6, CSA in-depth Guidance Document R.7)

When a data gap has been identified in step 3 for information requirements, the registrant needs to develop a testing proposal and include it in the registration dossier. While waiting for the results of this testing, the registrant should apply interim safety operational conditions (OCs) and risk management measures (RMM) to own manufacture or use, and communicate such information to down stream users.

3.2 Exemption from or Addition to the Information Requirements

Although information requirements are determined in REACH according to the manufactured or imported volume of the substance, it is also mentioned that an additional study is not necessarily required if the conditions described below are fulfilled. However, if information is available, it has to be reported in the Registration Dossier regardless of the following conditions. Moreover, information which is not included in the requirements may be requested according to the exposure condition. Contrary testing may possibly be exempted depending on the exposure conditions (See CSA In-depth Guidance Document R-5 for details).

1) Testing does not appear scientifically necessary

Existing data, Weight of Evidence approach (See Topic-2), non-testing methods and *in vitro* methods may provide information that may be judged to be valid, reliable and adequate for the identified purpose (classification and labelling, PBT assessment, and/or risk assessment).

2) Testing is technically not possible

It is described in REACH that testing for a specific endpoint may be omitted if it is technically not possible to conduct the study as a consequence of the properties of a substance, e.g. volatile, low water solubility, reactivity. However, justifiable such reasons should be stated in the registration dossier.

3) Substance-tailored exposure driven waiving or testing

In certain situations, the exposure pattern of the substance to be registered may justify adaptation of the testing strategy leading to omission, triggering, replacement or modification of the studies required for compliance with REACH. For example, in case a specific exposure route (oral, inhalation, dermal, etc) is not expected at an ES, and adding testing data of such administration route does not affect the risk characterisation, it may be decided that conducting the study is not necessary.

Topic-2

What is Weight of Evidence?

（See CSA Concise Guidance Document Part B.4 for details）

In recent years, the term “Weight of Evidence” has been seen in documents not limiting in guidance documents on REACH but also other documents. Although the term “Weight of Evidence” is not defined strictly, it can be generally considered as the following.

If multiple study data are available in the same endpoint and the level of hazard varies, one data has priority over the others to be used in the risk assessment according to the applicability, reliability, and validity, etc. of the data. In order to judge this, “Weight of Evidence” is used. In other case that all data indicate the same direction but none of which is in itself sufficient to draw a conclusion, then only together they give enough weight to allow a conclusion.

The criteria to judge heaviness or lightness of evidence include the following.

1) Applicability: The types or the results of the study agree with the purpose of assessment (it can be thought that the longer study (administration) period, the higher the applicability of the data in the assessment for chronic effects).
2) Reliability: The criteria to judge reliability include the following conditions: the study must have been conducted in accordance with international study methods, such as OECD Test Guideline, etc., as well as GLP criteria, and the results of the study should be relatively consistent. In addition, Klimisch Code, which is described in Topic-6, is often used as quantitative criteria to judge reliability.
3) Validity: The equivalence is usefulness of data. For instance, usefulness is considered higher with *in vivo* study data than with *in vitro* study data.

The weight of evidence of available data is evaluated based on the above mentioned points, but this requires experts’ judgement.

3.3 Human Health Hazard Assessment

3.3.1 Hazard data for human health

For human health hazard assessment, the following effects need to be considered.

- Toxicokinetics, absorption, distribution, metabolism and excretion
- Acute effects (acute toxicity, irritation and corrosivity）
- Sensitisation
- Repeated dose toxicity, and
- CMR effects （carcinogenicity, mutagenicity and reproductive toxicity）

In REACH, hazard assessment for humans requires calculation of Derived Non-Effect Level (DNEL), and for this, No Observed Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL) needs to be obtained from the study data.

Furthermore, data on exposure characteristics (See Chapter 5 Exposure Assessment in this document) and physiochemical properties of the chemical substance need to be collected as well (See CSA Concise Guidance Document B.7).

3.3.2 Calculation of Derived No-Effect Level (DNEL)

In hazard assessment for humans in REACH, DNEL needs to be calculated for each route of exposure caused by the identified use (IU). Therefore, when more than one route of exposure has been identified, DNEL and DNEL of combined exposures need to be calculated by using a dose descriptor[7] for each route of exposure (See Topic-3).

In order to address differences between animal testing data and real human exposure situations, it is proposed to use assessment factors (AF) considering following uncertainties.

- The uncertainty arising from the variability in the experimental data and from intra- and inter-species variation
- The nature and severity of the effect;
- The uncertainty arising from the variability of the frequency of the exposure and variation of the exposed concentration.

Taking into account the above factors, unusually DNEL can be derived from NOAEL using several AFs.

$$DNEL = \frac{NOAEL}{AF1 \times AF2 \times \cdots AFn} = \frac{NOAEL}{OverallAF}$$

See CAS In-depth Guidance Document R-8 for the actual AF values and the method of calculation to obtain DENL.

Figure 3-1 shows the workflow of the deviation of DNEL and the risk characterisation for human health.

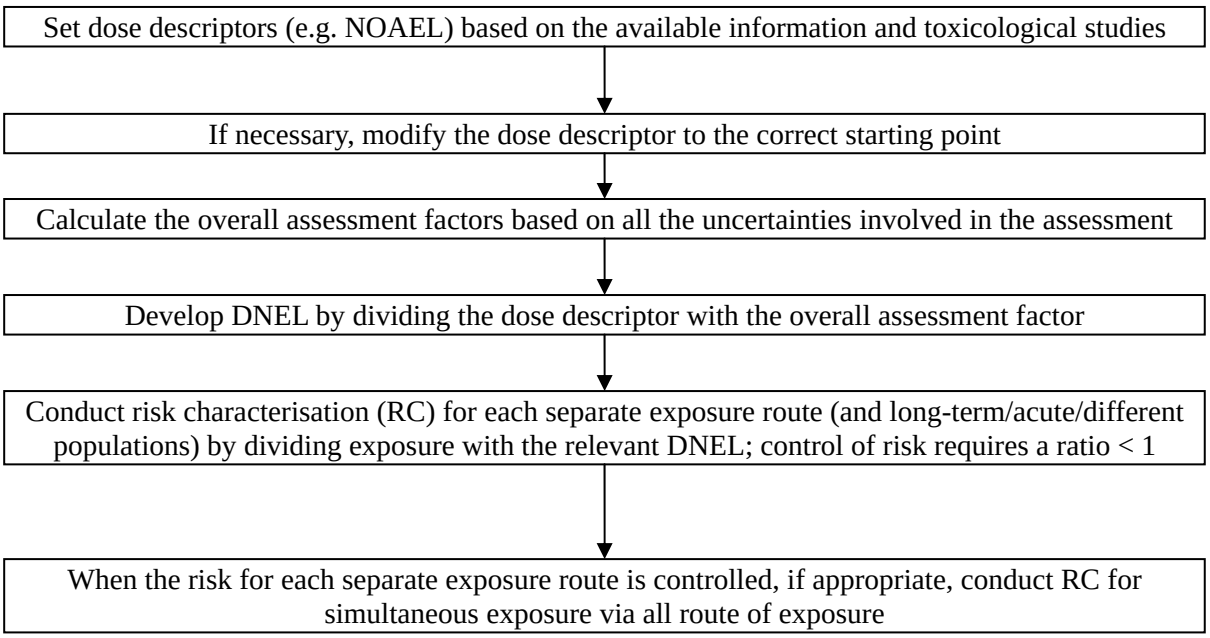

Figure 3-1 Overview of the human health risk assessment for threshold endpoints

[7] Dose descriptor: This is an indicator for toxicity obtained from a toxicity / Eco-toxicity study or other related data and is usually a dose required to induce specific adverse effects (e.g., lethal dose 50) or the maximum concentration which do not induce adverse effects (e.g., NOAEL). The dose descriptor becomes a basis to determine / set DNEL or PNEC.
（http://guidance.echa.europa.eu/public-2/glossary.htm?lang=en#D_Dose descriptor)

Topic-3

Derived Non-Effect Level (DNEL) and Predicted Non-Effect Concentration (PNEC) in REACH

(See CSA In-depth Guidance Document R.9 and R.10 for details)

In CSA in REACH, "Derived Non-Effect Level (DNEL)" and "Predicted Non-Effect Concentration (PNEC)" are used as dose descriptors for human health hazard assessment and for the environmental hazard assessment, respectively.

The following are the methods commonly used for the above.

1) Available hazard data (including laboratory study, monitoring data, non-testing method) for the corresponding tonnage level specified in REACH are collected and evaluated. Key studies (generally, NOAEL, NOEC, etc.) are selected for the calculation of DNEL and PNEC.
2) Uncertainty Analysis: Assessment Factor (AF) is selected from administration routes, animal species, difference of populations to be assessed (workers, consumers, aqueous organisms, soil organisms, etc.), duration of administration, and other uncertainties.

Under REACH, all endpoints are considered for whether they can deliver a DNEL but normally the risk characterisation is only performed for the lowest DNEL or DMEL. The results of a laboratory study are divided by an appropriate assessment factor, or several assessment factors get together result in an overall assessment factor. When data which do not reflect the actual exposure situation (oral, dermal route or duration of exposure) are used for the assessment, it is decided that the uncertainty is high and therefore bigger value of the AF should be applied. For the risk characterisation of long term or continuous exposure, AF for the results of a long-term study is smaller than that for the results of a short-term study.

DNEL and PNEC should be calculated by using an appropriate AF for each of the subjects to be assessed target population (workers, consumers, aqueous organisms, benthos, etc.), the route of exposure (oral, inhalation, dermal), local or systemic effects.

3.3.3 When DNEL cannot be derived

It is generally considered that the risk cannot be excluded for a substance which induces effects by a mode mechanism with no threshold, such as a genotoxic carcinogenic substance, even if the amount of exposure is extremely low. For such a substance, an acceptable amount of exposure called Derived Minimal Effect Level (DMEL) can be used instead since DNEL cannot be obtained. DMEL is often calculated by using additional AF, which is used upon extrapolation of effects from the dose associated with lifetime cancer risk, which is commonly used in the risk assessment, or the high dose to the low dose. Special knowledge is required in the calculation of DMEL, and an overview of the methodology is described in the CSA In-depth Guidance Document R-8 (see Topic-4).

Topic-4

Quantitative/Qualitative approach in hazard assessment

（See CSA In-depth Guidance Document R.8 for details）

REACH Annex I describes that derivation of DNELs for the human health and PNECs for the environmental hazard assessment shall be conducted in order to demonstrate that risks are adequately controlled by comparison of these DNELs and PNECs with exposure levels. Therefore, conducting a quantitative assessment is considered as a standard approach of the chemicals safety assessment in REACH.

However, the Annex I also specifies that "….it was not possible to determine a DNEL or a PNEC, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out".

In the CSA concise guidance document Part B.7.1.2.2, it is described that in case a DNEL for the human health is cannot be derived, a qualitative approach shall be applied. Examples that a DNEL cannot be derived are described that; when test data are absent, non-threshold effect (e.g. non-threshold carcinogens), and for an endpoint having a threshold level but the level cannot be established from test data（e.g. irritation and sensitisation）. For a non-threshold effect, semi-quantitative approach by deriving a DMEL (Derived Minimal Effect Level) is explained as one of qualitative approaches. On the other hands, in CSA concise guidance document Part E.3 "Risk Characterisation for Human Health" it is described that the quantitative or semi-quantitative approach is carried out in advance by deriving a DNEL or DMEL. Furthermore, it is mentioned that in case a DNEL or DMEL cannot be derived (e.g. corrosion/irritation, sensitisation, acute toxicity, mutagenicity/carcinogenicity), a qualitative risk characterisation is conducted. For example, appropriate RMMs should be taken according to the yes/no answer and severity from the tests irritation/corrosion.

For the environmental hazard assessment, CSA concise guidance document part E.4.4 describes that, a qualitative risk characterisation should be conducted for remote marine areas or when either PEC or PNEC cannot be properly derived. It means that when a proper PNEC cannot be derived, for example, for those substances with a low water solubility and/or a high hydrophobicity (i.e. high bioaccumulative). For such substances an absence of short-term toxicity does not necessarily mean that a substance has no long-term toxicity. Consequently, it is recommended to conduct a qualitative risk assessment in order to decide if further long-term testing is required.

3.4 Environmental Hazard Assessment

3.4.1 Assessment of environmental hazard data

The environmental hazard assessment is implemented following two steps (See Topic-3)

- Step-1: Evaluation of the validity of all available data
- Step-2: Identification of the study or studies giving rise to the highest concern (key studies)

When it is considered valid for the assessment, the results of an *in vitro* study or a field study and a non-testing method (QSAR, SAR, or read-across) can be used in addition to a laboratory study.

3.4.2 Calculation of Predicted No Effect Concentration (PNEC)

In the environmental hazard assessment in REACH, a PNEC needs to be calculated for each environmental compartment (water, soil, etc.) which is assumed to be exposed. For the air compartment, normally only a qualitative assessment is possible. The PNEC for the aquatic compartment is preferably based on the No Observed Effect Concentration (NOEC) in a long-term toxicity study. If no long-term toxicity studies are available, the PNEC can be based on the outcome of a short-term toxicity study ($L(E)C_{50}$)[8], but in that case the assessment factor (AF) is higher (see the equation below). In many cases, only toxicity studies for the aquatic compartment are available. In those cases, the PNEC of other target environments (sediment, soil) can be estimated using the study results of aquatic organisms, using the equilibrium partitioning method that is described in more detail in the In-depth Guidance Documents R-10.

In order to estimate PNEC in the environmental hazard, the following formula can be used as well as the human health hazard by applying various AF.

$$PNEC_{comp} = \frac{Min(\text{NOEC}) \text{ or } L(E)C_{50}}{AF}$$

In the above formula, $PNEC_{comp}$ indicates the environmental compartment (water, soil, etc.) to be assessed, and *Min (NOEC)* or $L(E)C_{50}$ indicates the minimum NOEC or $L(E)C_{50}$ in the available study results.

See CAS In-depth Guidance Documents R-10 for the actual AF value and the method of calculation to estimate the PNEC.

3.5 Physicochemical Hazard Assessment

3.5.1 Endpoints for physicochemical hazard assessment

Under REACH, the potential effects to human health shall be assessed for at least the following physicochemical properties.

- explosivity
- flammability
- oxidising potential

Above information can be obtained from laboratory tests and investigations but it may also comprise via non-testing methods such as QSAR, SAR, read-across (See topic-5) (See CSA in-depth Guidance Document R.6).

[8] $L(E)C_{50}$: the test concentration at which 50% of the organisms is affected or at which 50% effect is measured for a specifically defined endpoint (e.g. growth rate effects on algae).

Topic-5

Category Approach

（See CSA In-depth Guidance Document R.6.2 for details）

Assessment of multiple chemical substances as a group, but not by the individual substance basis, is accepted in REACH for the information required according to the tonnage level of the substance. This method is called Category Approach. The category approach is a technical method to categorize substances, which are assessed at the same time, into a group, and the read-across is a method to fulfil the data gap (lack of required data) in the category approach. The chemical substances which are grouped by the category approach must have similar physicochemical properties, health effects to humans, and ecotoxicity or follow a consistent law determined by the structure of the chemical substances.

Generally, as increased number of category members, the reliability of read-across to fill the data gap is improved. When it is necessary to assess a large number of substances, the category approach is a very useful method. In addition, from an animal welfare point of view, it can avoid unnecessary animal testing.

Furthermore, when multiple substances are assessed simultaneously by the category approach, a toxicity mechanism which has been shown with a specific substance can be used to verify its applicability to the substances of interest that have no data. Ideally, the substance of interest lies in between substances for which the required information is available and that show similar toxicity profiles.

3.6 Reliability Assessment of Study Data

In hazard assessment, reliability of available data is evaluated, and the most reliable data are used. If a study has been conducted according to a method which is accepted internationally (OECD Test Guideline, etc.) and in accordance with the GLP (Good Laboratory Practice) standards, the results of the study (mainly laboratory study) are considered reliable (See Topic-6). The Klimisch Code is commonly used as an index for the reliability assessment of hazard data in REACH.

If the study has not been conducted according to a method accepted internationally, or it does not meet the GLP standards (or if such information is not available), the judgment of reliability is made on a case-by-case basis. It may be possible to consider the study reliable if appropriateness of conditions or results of the study have been verified in a document or if the identical data have been accepted in the database or assessment documents, etc.

The data obtained by a non-testing method (quantitative or qualitative structure activity relationship (QSAR, SAR), read-across from a similar substance, category assessment, etc.) can be accepted if reliability is adequately verified. In such a case, however, transparency of the approach being used and the results, clarification of application domain, and fulfilment of validation criteria must be assured (See CSA In-depth Guidance Document R-6).

Topic-6

What is Klimisch Code: An Index for Reliability Assessment of Hazard Data?

(See CSA In-depth Guidance Document R.4 for details)

It is recommended in REACH to use a method called Klimisch Code to assess reliability of study data. Generally, the data judged Score 1 or Score 2 is considered highly reliable, and an assessment is conducted using the data. If the data was judged Score 3 or Score 4, it is either not used directly for risk assessment purposes or handled as reference data.

Score 1 = Reliable without restrictions: studies or data generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline or in which all parameters described are closely related/comparable to a guideline method.

Score 2 = Reliable with restrictions: studies or data (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable."

Score 3 = Not reliable: studies or data in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g. unphysiological pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment.

Score 4 = Not assignable: studies or data which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.)."

Source: H. J. Klimisch, et. al., A Systematic Approach for Evaluating the Quality of Experimental Toxicology and Ecotoxicological Data. Regulatory Toxicology and Pharmacology 25, 1-5 (1997)

4. PBT Assessment

4.1 An Overview of PBT Assessment

Assessments of PBT/vPvB（Persistent, Bioaccumulative and Toxic / very Persistent and very Bioaccumulative (Substances)） is required for all substances which are manufactured and imported at quantities equal or more than 10 tons per year and are not exempted from REACH registration. Overviews of the criteria for PBT/vPvB assessment, the assessment methods including the screening evaluation and the instructions in CSA Guidance Documents regarding the required measures for substances judged as PBT/vPvB are described in this chapter.

4.2 Aim and Procedures of PBT Assessment

PBT/vPvB assessment is carried out following steps and objectives.

Step-0: A screening assessment of PBT/vPvB substance, which is shown in Table 4-1. According to the results of the screening, PBT/vPvB assessment can be discontinued if the substance does not meet PBT/vPvB.

Step-1: Whether the substance fulfils the criteria given in Annex XIII (See Table 4-2).
If it is concluded that the substance is not a PBT/vPvB substance, the PBT/vPvB assessment stops after comparison with the criteria. An exposure and risk assessment as for a non-PBT/ vPvB substance could however be required if the substance is dangerous in accordance with the classification criteria of Council Directive 67/548/EEC. Therefore PBT assessment is conducted independent of the normal hazard assessment.

Step-2: If a substance is confirmed to be a PBT/vPvB substance, the registrant needs in a second step to estimate the amounts of the substance related to the different environmental compartments during all activities carried out by the registrant and all identified uses (IUs). In addition, it is necessary to identify the likely routes by which humans and the environment are exposed to the substance, subsequently needs to estimate the all possible exposure routes, amount of exposure and duration through the life cycle of the substance.

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

4.3 Screening Assessment of PBT Substance

In the assessment of PBT/vPvB substance, persistency, bioaccumulative, and toxicity are evaluated in the screening assessment, and eventually, it can be judged if it corresponds to PBT/vPvB substance. The judgment criteria for the screening are shown in Table 4-1.

Generally, the substance is not considered persistent in PBT criteria if it is readily degraded in one of the Ready Biodegradability studies as described in the OECD301 guideline or inherently biodegraded in the OECD302A, OECD302B or OECD302C inherent biodegradability study. .Similarly, bioaccumulation potential is considered low if log Pow is 4.5 or less in the “OECD TG107 Octanol- Water Partition Coefficient Study.”

For toxicity to the environmental organisms, a substance is considered as PBT substance (for environmental organisms) if $L(E)C_{50}$ is 0.01 mg/L or less in an acute toxicity study of algae, crustacean and fish, regardless of the presence or absence of long-term study data. In a case where it is not clear if the substance meets the PBT/vPvB substance criteria in the screening assessment, a step-by-step approach, which is described in section 4.2 in this document, is used in order to make a final assessment of persistency, bioaccumulative, and toxicity criteria.

Table4-1: Screening criteria for PBT Assessment

Property	Type of data	Criteria	Screening assignment
Persistence	Ready biodegradability study（OECD TG301 etc）	Readily biodegradable	Not P and not vP
	Specified tests on inherent biodegradability（OECD 302B、C, etc）	Inherently biodegradability ≥ 70% mineralization within 7d (DOC removal), and within 14d (O2 uptake); no pre-adapted inoculum	Not P
Bioaccumulation	Convincing evidence that a substance can biomagnify in the food chain (e.g. field data）	e.g. BMF > 1	B or vB, definitive assignment possible
	Octanol-water partition coefficient (OECD TG 107 or estimated by reliable QSAR）	Log Kow ≤ 4.5	Not B and not vB
Toxicity	Short-term aquatic toxicity（e.g. OECD TG201、202、203）	EC50 or LC50 < 0.01 mg/L	T criterion considered to be definitely fulfilled
	Avian toxicity (subchronic or chronic toxicity or toxic for reproduction)（e.g. OECD TG 205、206）	NOEC < 30mg/kg（feed）	T

4.4 PBT and vPvB Criteria

The PBT/vPvB criteria in REACH are shown in Table 4-2. In terms of vPvB substance criteria, a substance which meets the persistency and potential of accumulation criteria, is subjected regardless of hazard.

Table 4-2: PBT and vPvB criteria according to Annex XIII of the REACH

Property	PBT Criteria	vPvB Criteria
Persistence	$T_{1/2}$ > 60 days in marine water, or $T_{1/2}$ > 40 days in fresh-estuarine water or $T_{1/2}$ > 180 days in marine sediment or $T_{1/2}$ > 120 days in soil	$T_{1/2}$ > 60 days in marine , fresh or estuarine water, or $T_{1/2}$ > 180 days in marine, fresh or estuarine sediment or $T_{1/2}$ > 180 days soil
Bioaccumulation	BCF > 2000 L/kg	BCF > 5000 L/kg
Toxicity	NOEC < 0.01 mg/L for marine or freshwater organisms, or Substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic to 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.[9]	-

[9] Council Directive 67/548/EEC for the classification of dangerous substance can be found at following web site. http://ecb.jrc.ec.europa.eu/classification-labelling/

4.5 Further Measures to be Taken When the Substance is Confirmed to be PBT or vPvB

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

Generally, if a substance contains one or more constituents with PBT/vPvB properties in individual amounts $\geq$ 0.1% (w/w) or if transformation/degradation products with the respective properties in amounts $\geq$ 0.1% are being generated, the substance must be subjected to PBT/vPvB specific emission characterisation and risk characterisation. However, for the sake of relevance of risk exerted by the amount of a PBT/vPvB substance manufactured/imported by a registrant, and hence with regard to the requirements for risk characterisation and nature of RMM to be implemented, it may be considered to use a threshold value of 10% (w/w) for the total of all constituents or transformation/degradation products having PBT or vPvB properties, if it is possible to estimate with sufficient certainty that the total manufacture/import or supply of PBT/vPvB constituents in that substance and the total amount of degradation/transformation products with PBT/vPvB properties generated by that substance do not exceed 1 t/y[10].

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

The principle tool to achieve this objective is exposure scenarios (ESs). CSA Concise Guidance Document Part D and in-depth Guidance Document R.12 to R.18 provide guidance on how to develop ESs for substances in general. As PBTs and vPvB are substances of very high concern, the registrant shall pay special attention to the level of detail of his assessment and whether its accuracy and reliability is sufficient for a PBT/vPvB substance. Where generic scenarios and assumptions may be sufficient for exposure assessment of non PBT/vPvB substance, specific scenarios and data will most likely be needed throughout an emission characterisation for PBT/vPvB substances.

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

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

5 Exposure Assessment

5.1 An Overview of Exposure Assessment in REACH

The methods to develop Exposure Scenario (ES) and to conduct an exposure assessment, including estimation of the level of exposure, in CSA Guidance Document are illustrated in this document. Although the focus here is placed on how to develop ES, an overview regarding estimation of the level of exposure is also provided.

An ES is a set of information describing the conditions in which the risk associated with the identified use (IU) of a substance can be controlled. This includes Operational Conditions (OC) (e.g., the duration and frequency of use or the amount of used, the process temperature or the pH) and necessary RMM (Risk Management Measures) (e.g., local exhaust ventilation or some sort of gloves, waste water and gas treatment). If a manufacturer or importer fails to describe relevant and realistic measures that control risks for a substance in a certain use he can not cover this use in his exposure scenario. Otherwise he has to explicitly advice against that use in the safety data sheet. Exposure scenario building is likely to include dialogues (i) between manufacturer and downstream users (DUs and (ii) from downstream user to downstream users further down the supply chain.
The route of exposure to humans via the environment is shown in Figure 5-1 as examples of exposure routes.

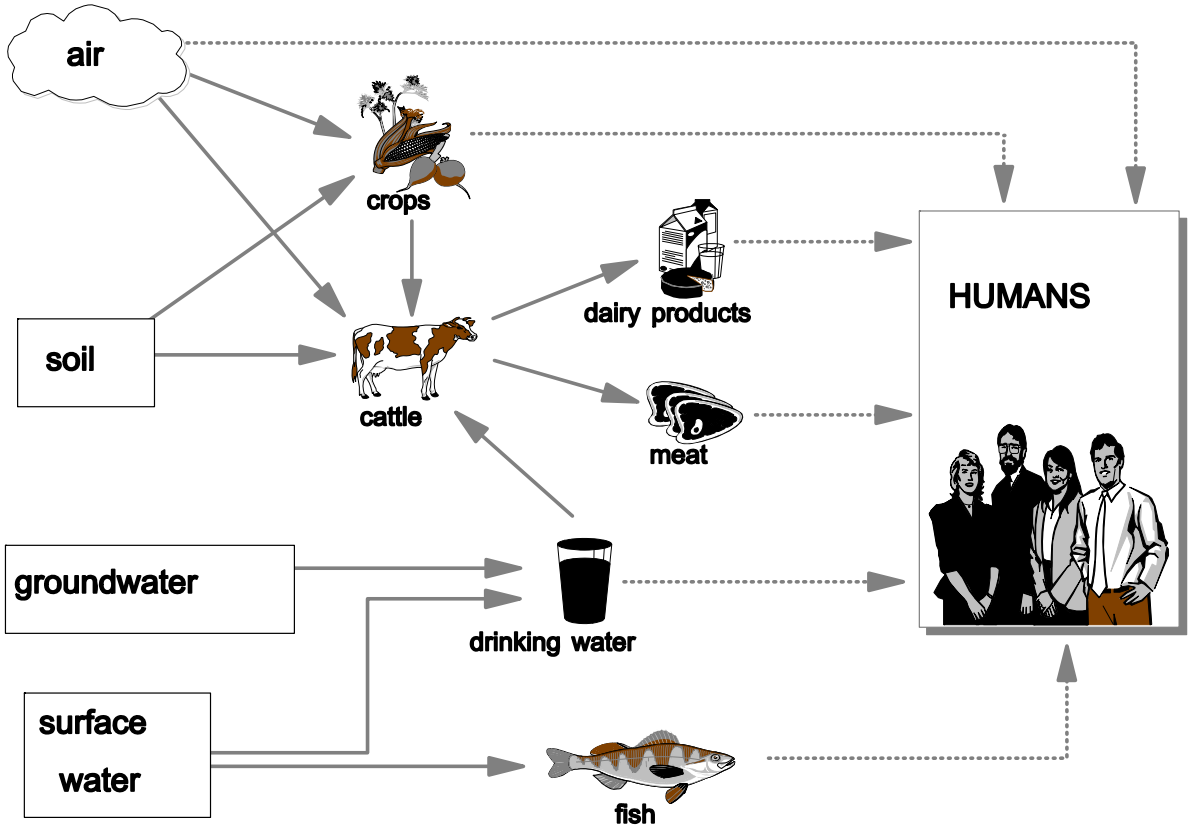

Figure 5-1 Human exposure routes via the environment

5.2 Actors in supply chain under REACH

Under REACH each actor of the supply chain is defined as follows (Article 3)

- Actors in the supply chain: means all manufacturers and/or importers and/or downstream users in a supply chain:
- Manufacturer: means any natural or legal person established within the Community who manufactures a substance within the Community.
- Importers: means any natural or legal person established within the Community who is responsible for import.
- Downstream user: means any natural or legal person established within the Community, other than the manufacturer or importer, who uses a substance, either on its own or in a preparation, in the course of his industrial or professional activities. A distributor or a consumer is not a downstream user.
- Distributor: means any natural or legal person established within the Community, including a retailer, who only stores and places on the market a substance, on its own or in a preparation, for third parties.

5.3 Determinants for Exposure Scenario Development

Parameters associated with several characteristics (the characteristics of the substance, processing / product, or surrounding environment), which are required to determine the substance release and exposure to the workers, consumers, and environment must be included in the Exposure Scenario (ES). These are called “the main parameters determining the release and exposure: *determinants*)” (See Table 5.1). These determinants are included in the ES as items which are further specified based on the Operational Conditions (OC) and the existing Risk Management Measures (RMM). For instance, processing / product features are subdivided into items such as the duration of the product use (durable years), the amount to be used, and RMM, and these are further subdivided into comprehensive parameters which determine the substance release and exposure.

The manufacturer and/or importer should develop the initial ES from the OC at the time of manufacturing, the existing RMM, the identified use (IU) as well as from appropriate and available information in the life cycles. In the initial ES, a scenario which can be assumed in the substance life cycle is established. It is also necessary at this stage to specify the determinants associated with biological exposure factors (dermal, oral, inhalation routes and environmental toxicity) and hazard information in accordance with ES.

The level of exposure is estimated in the ES, and a risk characterisation is performed. According to the results, RMM or several characteristics may be reviewed based on “the main parameters determining the release and exposure (the main parameters).” The integrated ES, which was established as above, is documented in a standard format, and recorded in the CSR and the SDS and communicated to downstream users (DUs) as information.

Table 5-1 Examples of determinants of exposure

Determinants of exposure	Examples (not exhaustive)	Remarks
Substance characteristics		
Molecular properties	Molecular weight Molecular size	Gives an indication of bioavilability
Physico-chemical properties of substance	Vapour pressure Octanol-water partition coefficient Water solubility	Exposure determinant at workplace and in the environment
Stability	Biological degradation, hydrolysis Photodegradation, atmospheric degradation (half-life in water, soil, air)	Exposure determinant related to degradation in environmental compartments incl. sewage treatment
Characteristics of processes and products		
Lifecycle stage of substance or product to which the ES refers	Manufacture of substance, formulation, final use of chemical products, service life of substances in articles, waste phase.	Identify relevant exposures for all target groups, supports selection of suitable broad ES; supports the selection of pre-set process or product categories in tier 1 tools for exposure assessment.
Type of activity or process	For example: synthesising substances; mixing substances; using substances as process aids; using chemicals by spraying or by dipping or by brushing; using substances in articles e.g. wearing textiles, spending time in house;	
Time pattern of use	Duration of activity/use Frequency of activity/use	Determinant related to pattern of exposure (short term vs. long term) and corresponding choice of PNEC or DNEL
Technical conditions of use	Level of contaminant of process Temperature, pH, etc	Determinant related to exposure of humans and environment
Characteristics of chemical product	Weight fraction of substance Fugacity, dustiness, volatility of product	Determinant related to exposure of humans and environment for preparations or products
Use quantity	Kg [t] per time or activity	Determinants for the exposure potential per time or per activity
Risk Management Measures (RMMs)	Local exhaust ventilation (workplace) Personal Protective Equipment (workplace) On-site waste (water) treatment e.g. oil-water separation Municipal sewage treatment, waste treatment Package design preventing dermal or inhalation exposure (product safety)	RMMs as integrated element of the technical product or process, or as additive measure; determinant of the extent to which exposure can be mitigated or prevented;
Characteristics of surrounding		
Surrounding absorbing or diluting release	Room size and ventilation rate; river water flow; capacity of sewage system	Exposure determinant based on the assumption that even distribution of substance takes place
Biological exposure factors	Inhalation volume, body weight	Determinant of the dose to which a human is exposed and corresponding choice of PNEC or DNEL

Some of the determinants listed in Table 5-1 are usually not iterated by the registrant but are set realistic (default) values, namely substance characteristics and surrounding characteristics. Other parameters can and have to be determined in the ES during the iterative process by the registrant. REACH distinguishes two types of these changeable determinants to be reflected in the exposure scenario: the operational conditions (OCs) and risk management measures (RMMs).

5.4 Development of Exposure Scenario

Exposure scenarios shall be developed for;

i) The manufacturing process and
ii) For identified use including own uses by the M/I, and uses further down the chemical supply chain and consumer uses,
iii) Life cycle stages resulting from manufacture and identified uses (article service lie and waste life stages).

M/I will start his assessment with all available relevant information on the operational conditions and the existing risk management measures in manufacture, identified uses and resulting life cycle stages (initial exposure scenario). Downstream users or their organisation may have already compiled such information in a generic ES format so that M/I can directly proceed with completing the initial ES and estimating exposure for the uses covered. He will then estimate exposure corresponding to the available information. Often in a first iteration, standard tools for exposure estimates that are sufficiently conservative will be applied (Initial step: Tier 1).

If measured data on exposure levels are available, reliable, and representative for the operational conditions and risk management measures described in the initial exposure scenario, these data can be used for the exposure estimate. The same applies for cases where there is enough information to use higher tier (Tier 2 assessment) exposure models for the first estimate.

M/I will collect further details on release and exposure determinants when it is not possible to demonstrate control of risk based on the initial ES. In some cases hazard data are also refined as well, but that is not further described here.

The process of developing the ES may vary case by case depending on the available information, but in particular when relatively little information is available upfront, the general process will follow the 14 steps presented in Figure 5-2 and Table 5-2. The standard workflow is based on categorising processes and products in which the substance is used. The choice for specific categories leads to a selection of preset generic exposure scenarios which can be connected to existing tier 1 exposure estimation tools. If M/I has sufficient information available to build exposure scenarios and document the corresponding exposure estimates based on measured data or higher tier models he can shortcut the process. In such situations he can directly go to step 6 described in Figure 5-2 and Table 5-2 (invite DUs for feedback) or step 10 (run CSA based on measured data or higher tier models), depending on the state of dialogue with the downstream users (See CSA Concise Guidance Document Part D.2, D.3).

The general workflow for the building an exposure scenario is shown in Table 5-2 and Figure 5-2.

Table 5-2: Workflow of building exposure scenarios

	Workflow
1	**Map use of substance** Analyse the market of the substance based on existing in-house information. Invite DUs to provide information on is needed
2	**Compile all available information on OCs and RMMs and related release/exposure levels during the life cycle of the substance** Start with existing in-house information. Invite DUs to provide information if needed.
3	**Select appropriate process or product categories related to the uses identified.** Define the information needs based on ES standard format and the selection of the tool (exposure estimation models). Take into account the domain of the tool with regard to the hazard profile and the physical state of the substance to be assessed.
4	**Build initial exposure scenarios based on the input data needed for Tier 1 exposure estimate** Check further available information on OCs and RMMs from • DUs and/or their organisations (including initial exposure scenarios) • Product or branch specific RMM packages in the RMM library. Make an initial exposure estimation and initial risk characterisation by obtaining relevant exposure data for the ES.
5	**Complete initial ES** Where control of risk can be demonstrated on the basis of initial risk characterisation, complete the initial ES by further describing the corresponding operational conditions and risk management measures.
6	**Invite and receive feedback from representative customers or DUs organisations** • Relevant uses are (not) covered • RMMs or OCs are appropriate or not • The descriptions in the ES are understandable to the addressees
7	**Identify and use additional information (if needed), based on feedback;** • Refine RMM and OC in the initial ES before and/or • Refine information on substance properties (e.g. DNEL for a certain route needed)
8	**Carry out further CSA runs (exposure estimates, risk characterisation and uncertainty analysis)** Decide on further iteration needed, and/or control of risk can be demonstrated, and/or further testing is needed.
9	If initial model (Tier 1) cannot demonstrate the control of risk, **decide whether measured data or higher tier model is needed.** If control of risk can be demonstrated based on tier 1, progress to step 11.
10	**Apply another model or use measured data to** Refine the ES and demonstrate control of risk.
11	**Conclude the exposure estimation and risk characterisation** (including uncertainty analysis)
12	**Derive the integrated exposure scenario** by linking all OCs and RMMs within the exposure scenarios. • Document the operational conditions and risk management measures required for human health and environment and corresponding exposure routes for each use covered by the ES. • Consider impacts of OC/RMM across exposure routes. Select the OC/RMM leading to control of risk related to all routes of exposure.
13	**Merge ES if appropriate** Carry out cross-comparison on the final exposure scenarios and conclude which scenarios to merge based on similarities in risk management and operational conditions.
14	**Document the deliverables of the exposure assessment** Document the results of exposure assessment in the CSR and SDS.

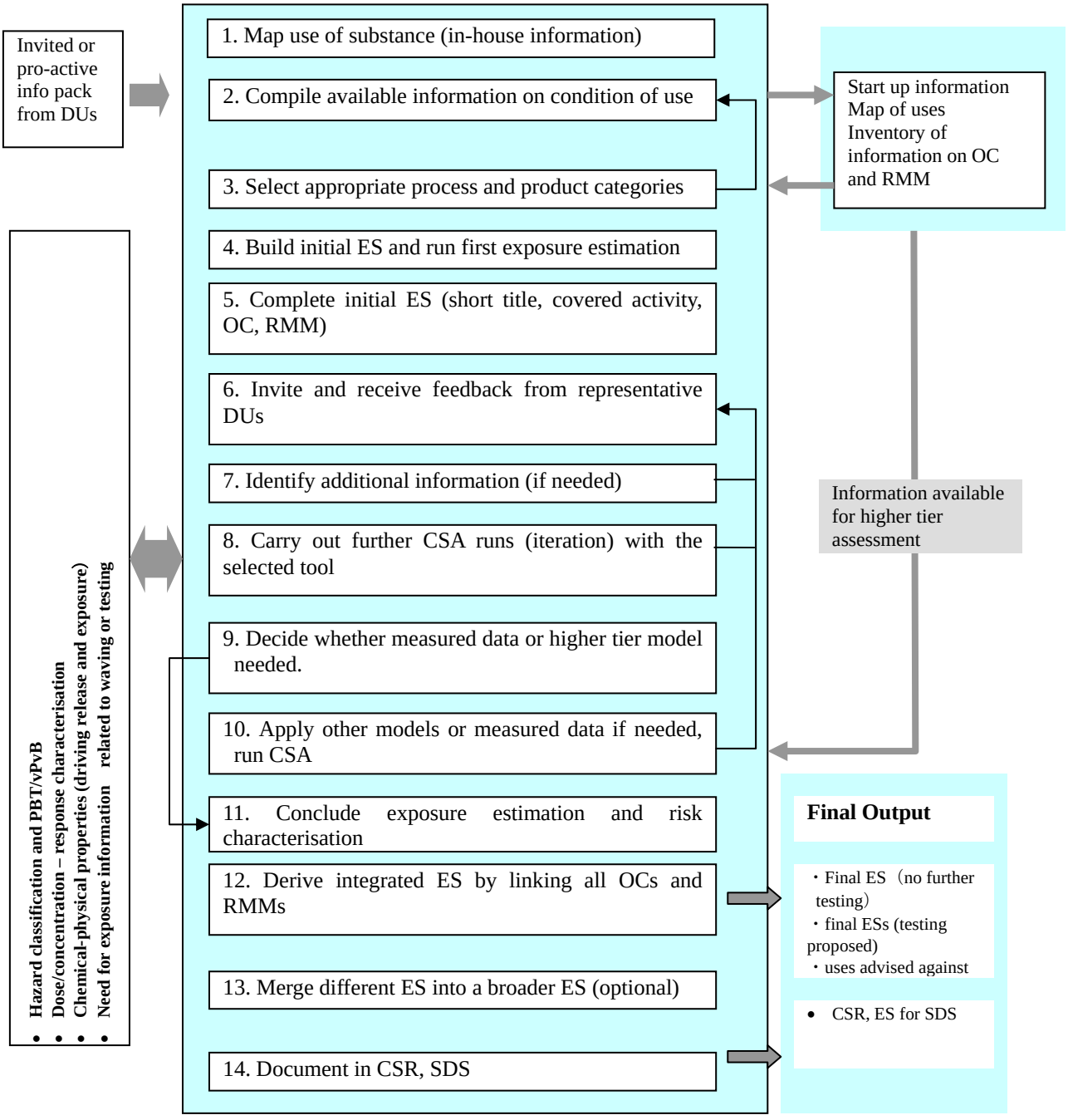

Figure 5-2 Steps for ES development
（each number corresponds to one in Table 5-2）

The process of developing the ES may vary case by case depending on the available information, usually implemented steps described in Figure 5-2 and Table 5-2. Standard workflow is based on the descriptors (categories) presented in chapter 5.5 and products in which the substance is used. Selection of a specific category is used for the selection of generic ES which is shown in section 5.13 of this document that the initial exposure estimation tool (tier 1). Where sufficient information for the development of the ES is available, these steps can be shortcut.

5.5 Descriptors for Establishment of Exposure Scenario

Five types of descriptors are used in REACH with regard to the use of a chemical substance in order to develop the Exposure Scenario (ES) and to estimate the level of exposure. These are 1) Sector of Use (SU), 2) Chemical Product Category (PC), 3) Process Category (PROC), and 4) Article Category (AC). See CSA In-depth Guidance Document R.12 for details of each descriptor. In addition, Environmental Release Category (ERC) is used to assess the environmental exposure (see CSA In-depth Guidance Document R.16).

The first four descriptors are illustrated in Figure 5-3. These descriptors are the important decision criteria for the preparation of initial ES or in the use of the estimation model for the amount of exposure at the tier 1 stage.

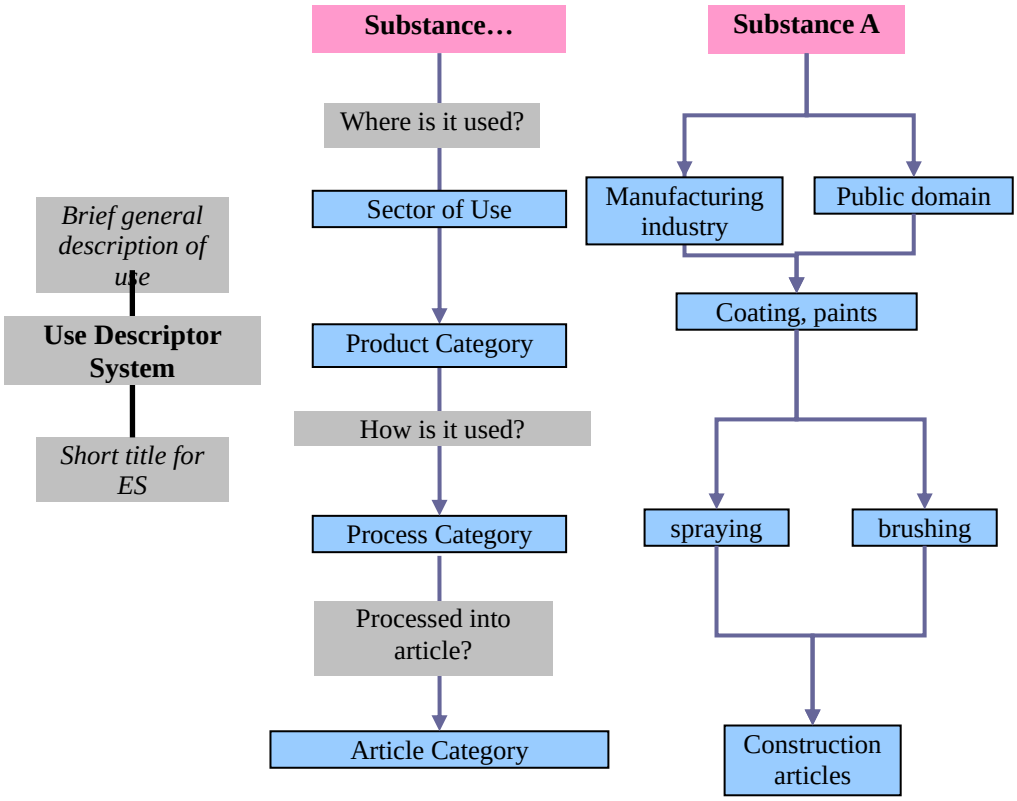

Figure 5-3 Descriptors for the development of ES

5.6 RMM: Risk Management Measures

In order to control the risk appropriately, RMM are used in REACH as measures to reduce exposure. The effect of RMM can be defined quantitatively as the reduction rate for the concentration of exposure and the amount of emission (release). However, the result of measurement of the actual exposure concentration may be a better index. In reality, the effect of RMM changes with various factors, and it is not possible to determine appropriately by a single value.

The effect of RMM can be obtained using a certain appropriate default value, which is used in the estimation model for the amount of exposure. The 31 RMM and the safety guideline listed in Table 5-3 are recommended in REACH and are included in the RMM library. The RMM library corresponds to measures such as a protective equipment to reduce exposure in various situations, product manufacturing / processing and to the workers within Europe. It is not recommended to refer to the contents of RMM library in the CSR since the efficacy evaluation has not been completed yet in the CSA Guidance Document. Although the RMM library can provide information regarding the effect of RMM, efficacy should be assessed individually by the actual downstream users (DUs), and RMM library should be utilized as the information source for this.

Table 5-3: RMMs in tentative RMM library and summary of safety guidelines[11]

Product-substance Related: 1. Limiting concentration of hazardous or non-hazardous ingredient 2. Change of physical state (e.g. powder -> pellet) 3. User friendly packaging (reducing handling) 4. Info /Guidance /Manual other than label and Safety Data Sheet **Marketing and use related** 5. Marketing and Use – General 6. Product safety/ advice **Process/ Control Changes:** 7. Process Control/ Change 8. Automation 9. Containment of process equipment 10. Cleaning of process equipment 11. Spill Containment Measures 12. Reduction and cleaning of air emissions 13. Reduction and cleaning of waste water 14. Reduction of waste, disposal of waste **Ventilation Control:** 15. Local Exhaust Ventilation – (partial) enclosure 16. Laminar Flow Booths & Laminar Flow Benches 17. Local Exhaust Ventilation – captor hoods	18. Local Exhaust Ventilation – receptor hoods 19. applications **General Dilution Ventilation:** 20. Dilution Ventilation **Organisational:** 21. Management Systems 22. Operating Practice 23. Competence and training 24. Supervision 25. Monitoring 26. Health Surveillance **Good Hygiene Practice & Housekeeping:** 27. Good Hygiene Practice & House keeping **Personal Protective Equipment** 28. Body protection 29. Hand protection 30. Respiratory protection 31. Face/ Eye protection

5.7 Outline of the Exposure Estimation Method

When an initial exposure scenario has been developed it has to be assessed whether the information collected is sufficient to demonstrate that the risks occurring from the manufacture and all identified use(s) are controlled. Often the collection of information and the risk characterisation will be an iterative process until it can be confirmed that the risk is controlled. The risk characterisation requires the comparison of exposure estimates and derived no-effect or minimum effect levels (DN(M)EL, PNEC). This can be done by generating exposure estimates for all identified uses described in the exposure scenario.

The process for estimating exposures during the development of ES is usually conducted in two steps:
The first step (also termed Tier 1) aims at estimating the "reasonable worst-case" exposure for the conditions of use described in the initial ES. Such estimate can be obtained using actual measurements or standard exposure models and selecting from preset conditions of use as defined for Process Category (PROC) or Chemical Product Category (PC).

A subsequent step (Tier 2) is required if control of risk cannot be demonstrated for the initial ES in the first step (Tier 1).

Tier 2 focuses on typical well-defined exposures with appropriate knowledge on the confidence limits involved, based on uncertainty and variability of the relevant parameters. The estimation model for the amount of exposure used in Tier 2 generally requires more detailed input on conditions for processing or use, physiochemical properties, and RMM, etc. compared to that in Tier 1. Although a certain level of expert knowledge is required in the Tier 2 model, it can derive a result which seems closer to the actual exposure compared to the Tier 1 model.

[11] At present, the library is in an early stage of development. An outline of the library can be obtained at CEFIC's web site below.
http://www.cefic.org/Templates/shwStory.asp?NID=494&HID=645&PHID=643

5.8 Use of Measured Data

Ideally, the process for estimating exposure would be based on actual measurements for the use of the substance in each scenario. However, this will not always be possible. Therefore, it will often be necessary to either combine actual and modelled estimates of exposure, or to rely solely on modelled estimates. Sometimes it may also be possible to estimate exposure based on the measured data of another substance which however processes similar properties regarding its environmental fate.

However, the use of measured data needs special attention i.e.

- Are the data appropriate for the scenario being investigated, i.e. is there sufficient information on RMM and OC that were in place when measurements were performed?
- Are the data supported by sufficient contextual information such that their relevance to the scenario can be determined?
- Have the data been obtained using appropriate sampling and analytical techniques to yield the necessary sensitivity?
- Are sufficient data points available to be seen to be representative of the exposure scenario being evaluated?

For measured data related to environmental concentrations a number of additional considerations have to be made:

- Have the data been properly assigned to the appropriate spatial scale (local or regional scale) by taking into account sources of exposure and the environmental fate of the substance?
- Have background concentrations been taken into account for naturally occurring substances?

Provided such data are of a suitable quality and are supported with sufficient information that enables them to be seen as being representative of an Exposure Scenario, then such data will reflect the reality of the use rather than any modelled representation (see CSA in-depth Guidance Document R.14 – R.18).

5.9 Occupational Exposure Estimation Assessment

In the workplace, exposure to chemicals may occur via three exposure routes: inhalation, dermal contact and oral intake. However, when proper hygienic measures are taken the direct oral intake is generally considered to be negligible and is not assessed for workers. For the determination of exposure through the other routes, one can use either measured data and/or predictive estimation models. Where measured data are available, then these are preferred to exposure estimates derived from models. Furthermore, while measured data might often be available for inhalation exposure, data that characterises dermal exposure is much less frequent. It will therefore be necessary to develop any estimate of exposure for the Scenario based upon combinations of available data (real and modelled estimates) (see CSA in-depth Guidance Document R.14).

5.10 Consumer Exposure Estimation

Consumer exposure estimation will need to consider 3 exposure routes (i.e. dermal, oral, inhalation). Each exposure route needs to be calculated separately. An exposure scenario can be derived using a tiered approach to exposure estimation. Initially a 1st tier exposure estimate can be used to derive a “reasonable worst case” scenario. Subsequent higher tired (tier 2) estimates can be used to further characterise the exposure (see CSA in-depth Guidance Document R.15).

Inhalation: In a Tier 1 assessment, it is assumed that all substance is released as a gas, vapour or airborne particulate into a standard room. This may be due to direct release or by evaporation from a liquid or a solid matrix. At subsequent iterations or in higher tier assessments, other parameters are considered such as concentration of substance in the air, the number of rooms, ventilation rate of the room or rooms and the rate at which a substance is released into the room or rooms.

Dermal, two options:
A: The substance is contained in a preparation. This option is e.g., applicable when hands are put into a solution containing the substance under evaluation.
B: Substance migrating from an article; applicable for example when residual dyes in clothing are in contact with skin and migrate from the clothing.

Oral, two options:
A: Substance in a product unintentionally swallowed during normal use.
B: Substance migrating from an article; applicable for example when a substance migrates from a pen or textile that is mouthed.

5.11 Environmental Exposure Assessment

For the environmental exposure assessment, consideration should be made for;

- Fresh surface water (including sediment)
- Marine surface water (including sediment)
- Terrestrial ecosystem
- Top predators via the food chain (secondary poisoning)
- Micro-organisms in sewage treatment systems
- Atmosphere – mainly considered for chemical with a potential for ozone depletion, global warming, ozone formation in the troposphere, acidification
- Man indirect, i.e. man exposed via the environment

Based on the identified use by the ES, estimation of the level of exposure should be done for all possible target routes separately (see CSA in-depth Guidance Document R.16).

5.12 Use of the Final ES in the Supply Chain

The final exposure scenario(s) for a substance must be communicated down the supply chain. The format and the phrasing of the exposure scenario should meet three requirements:

1. The RMM advice should be practically useful for the recipient of the exposure scenario:
    - The recipient may be a formulating downstream user for whom the ES is a source of three types of information:
        - Practical advice relating to the formulator's own technical activity (mixing substances and/or preparations)
        - Information relevant to the formulator's choices on product composition and design.
        - Information and advice relevant to the formulator's customers and further downstream users
    - The recipient may be an end-user for whom the ES is a source of i) practical advice relating to its own technical activity and ii) information relevant with regard to control of risk further down the supply chain (articles and waste).
2. The assumptions under which the supplier regards the uses of his customer and the uses further down the chain as safe must be transparent to the downstream user
3. The ES should include brief advice on how the recipient of the ES can check whether the conditions in the ES are met in practice at the user's level.

5.13 Features of Exposure Estimation Models

Following exposure estimation models are recommended to use under REACH. Outlines of each model are shown below.

ECETOC TRA occupational	
URL	https://www.ecetoc-tra.org/index.asp
Target	Occupational exposure
Strengths	• Clear structure • A parameter related to process category is used as basis for assessment • Duration of process/activity is taken into account • Scenarios (process categories) based on EASE and expert input from industry stakeholders • The calculated effectiveness of local exhaust ventilation depends on process and is thus not set at a constant value. This is in accordance with observations. However, the tool is currently not able to distinguish between different types and efficiencies of LEVs.
Limitations	• Some process categories appear to overlap; the choice is not always clear • The number of process categories appears to be insufficient to cover every first Tier assessment • Processes categories are described in expert language; non experts in the field of worker exposure (assessment) therefore find the tool difficult to use • Except through differentiation of processes/activities/operation units and in duration of activity, influence of amount of product used on exposure level cannot be taken into account • Only “local exhaust ventilation” and (indirectly) changes in processes/activities/operation units and duration can be chosen as “risk management measures” • Web-based version and paper version (ECETOC Technical Report No. 93) do currently not fully agree; the paper tool is at the moment the preferred choice. The foreseen update of the tool will include streamlining in this respect. • Compared to measured data (RISKOFDERM project) the dermal exposure for situations with local exhaust ventilation is underestimated.
Compensation for limitations	• Using the most conservative estimate of both process categories if the choice is not clear • Assume that small amounts are related to short durations of use • Consistently use the paper version as basis for the estimations (the report can be downloaded from the internet) • Assume no local exhaust ventilation for dermal exposure estimates (to reach a conservative estimate)

COSHH-BAuA-Tool	
URL	http://www.REACH-helpdesk.de/en/Exposure/Exposure.html
Target	Occupational exposure
Strengths	• Very clear and user friendly structure • The output has been shown basically sound for a number of ES • Provides control strategies for a range of common tasks, e.g. mixing, filling, etc. • Control guidance sheets are available on the Internet
Limitations	• The estimates are generic in nature and therefore uncertain to some extent. • It is not possible to use the assessed exposure ranges as a basis for further iterations, e.g. considering the duration of exposure (only the influence of short term exposure, i.e. < 15 min/day, is considered) • Validation of the concept is, as always for exposure estimation models, limited • Not suited for gases (handled or released) • Should not be used for tasks where fumes are generated or where dusts are formed through abrasive techniques • Not suited for CMR substances.
Compensation for limitations	• The substance concentration (in products) is assumed to be 100%. • The duration of exposure is assumed to be the shift length. If the activity is carried out for less than 15 minutes a day the next lower range of predicted exposure can be assumed and compared with the DNEL.

ConsExpo	
URL	http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp
Target	Consumer exposure
Strengths	• Builds on the EU-TGD for *existing and new* substances (2004), which is accepted within the EU. • Contains a database with default values for a range of products and uses (although input data mostly relate to higher tier models, not Tier 1) • Documentation for default values is available in so called 'fact sheets'. • Free of charge.
Limitations	• ConsExpo currently has no explicit facility to work with a diversity of consumer product categories at Tier 1. If default pre-set values for product categories are being developed in near future, a link between these categories or incorporation of these categories in the database of ConsExpo is needed. • Risk management measures are not mentioned explicitly.
Compensation for limitations	• Product-related RMMs can be accommodated in ConsExpo by changing the input parameters to the Tier 1 equations (see Section D.4.5).

EUSES Consumer	
URL	http://ecb.jrc.ec.europa.eu/euses/
Target	Consumer exposure
Strengths	• Builds on the current EU-TGD, which is accepted within the whole EU • Requires few data • Free of charge
Limitations	• EUSES currently has no explicit facility to work with consumer product categories subdivided in preparation categories and article categories. Initial product category settings need to be transferred to the input of EUSES. • As in any other available consumer exposure tool, risk management measures are not mentioned explicitly.
Compensation for limitations	The inclusion of RMM for the consumer can be handled manually in the tools.

EUSES/ERCs	
URL	http://ecb.jrc.ec.europa.eu/euses/
Target	Environmental exposure
Strengths	・ Builds on the current EU-TGD, which is accepted within the whole EU ・ Requires few data for a first assessment ・ Refined data on operational conditions and RMM can be directly inserted into the calculation of emissions at Tier 1 level during the CSA process. The same applies for refined substance characteristics that can be entered into the tool ・ Available free of charge from http://ecb.jrc.it/euses/
Limitations	・ For the default emission factors in the current EUSES is it not clear which operational conditions and which risk management measures are assumed to be already in place. Thus iteration may lead for example to a duplication of RMMs already included in the default emission factor. ・ The correlations used for the derivation of substance parameters, i.e. mainly partition data, are not valid for inorganics and surfactants. Whenever measured partition and degradation data are available, these should be used in the calculations. This is of very high importance for metals, inorganic compounds and surfactants.
Compensation for limitations	・ These limitations are the reasons for introducing the ERCs. The ERCs can be loaded in EUSES from input files. ・ To introduce the effect of RMMs and changes in the conditions of use, the presets for the ERCs can be replaced with own estimates, information from downstream users or measured data. ・ When dealing with metals, inorganic compounds and surfactants, use - if available - measured partition data. For cationic (positively charged) compounds, you may use very high partition coefficients (soil-water, sediment-water, sludge-water). For anionic (negatively charged) compounds you may use very low partition coefficients (soil-water, sediment-water, sludge-water). If no measured partition data are available, you may run a set of simulations: one where you use very high partition coefficients (soil-water, sediment-water, sludge-water) and one with very low partition coefficients. You can then use the results giving the highest predicted risk quotients.

EUSES Spreadsheet	
URL	RIVM（www.rivm.nl） and CEFIC（www.cefic.org）
Target	Environmental exposure
Strengths	・ Similar advantages as EUSES for environment and indirect exposure of man ・ For the experienced user having specific release data at his disposal, the emission estimation module in the spread sheet version provides more transparency of the calculations. ・ Allows integration in dedicated exposure calculation tools. ・ Available free of charge
Limitations	・ Not linked to any process or product categories, thus, release data are to be entered manually by user and the effect of RMMs needs to be introduced by reduced emission factors.
Remark	Spreadsheet software needs to be protected for algorithm stability since it is vulnerable to introducing mistakes. As a default, the sheets in the TGD Excel are write-protected, except the cells for specifying the variable input parameters. Great care should be taken if disabling this write-protection.

6 Risk Characterisation

6.1 An Overview of Risk Characterisation

In REACH, it is required to demonstrate in CSA that the risk of the registered substance to humans or environmental organisms under the condition of identified use (IU) is at the acceptable level.

This is called Risk Characterisation, which is to compare the amount (concentration) of exposure and quantitative or qualitative hazard information. When suitable Predicted No-Effect Concentrations (PNECs) or Derived No-Effect Levels (DNELs) are available, the results are shown by Risk Characterisation Ratios (RCRs) to decide if risks are adequately controlled. When these no-effect levels cannot be established for certain effects, a qualitative assessment of the likelihood that these effects are avoided when exposure scenarios are implemented shall be carried out

It is verified that risks are adequately controlled if the results of both hazard assessment and exposure assessment are reliable, and RCR for all exposure (in all environmental compartments, route, group, and duration) associated with all exposure scenarios (ES) and all endpoints is less than 1, or if it is possible to verify by qualitative risk characterisation that the effects can be avoided when performing ES (See Topic-7). RCR can be obtained with the following formula.

$$RCR = \frac{PEC}{PNEC} \ or \ \frac{amount\ of\ exposure}{DNEL}$$

6.2 Procedures for the Risk Characterisation

Risk characterisation is normally conducted as following steps:

Step 0	If the substance is classified for physiochemical danger, carry out a risk characterisation for physicochemical properties.
Step 1	Collect the predicted or derived no-effect levels or minimal effect levels (PNECs, DNELs or DMELs if appropriate) for the relevant time scales, environmental ecosystems, human populations, health effects, and routes of exposure. For endpoints where no DNEL can be derived, collect other information on potency of the substance.
Step 2	For each exposure scenario collect the exposure values, measured or estimated, for the relevant time scales and spatial scales, environmental compartments, human populations and human routes of exposure.
Step 3	Compare matching exposure and predicted or derived no-effect levels or minimal effect levels for all relevant matching combinations.
Step 4	If no predicted or derived no-effect level or minimal effect level could be derived for a substance for a certain environmental compartment or human effect, carry out a qualitative risk characterisation for that compartment/effect. This is done if also a PNEC or DNEL/DMEL is available for other compartments/effects.
Step 5	Calculate the sum of risk characterisation ratios of combined exposure, e.g. for each human population and for the general population (combined worker and consumer exposure).
Step 6	Decide on possible iterations of the CSA, taking uncertainties in the assessment into account. The risk characterisation should demonstrate control of risks, based on a sufficiently robust hazard and exposure assessment.
Step 7	Finalise the risk characterisation.

Procedures related to step 0 to 6 are described below.

6.3 Risk Characterisation for Physicochemical Properties

Substances which are dangerous because of their physicochemical hazard trigger the additional requirements for the CSR and SDS under REACH in the same way as substances which are dangerous because of their (eco)toxicological properties.

Risk characterisation with regard to human health must be carried out as a minimum for explosivity, flammability or oxidising potential. For those previously mentioned physicochemical properties, the assessment shall entail an evaluation of the likelihood (risk) that an adverse effect will be caused under the reasonably foreseeable conditions of use in the workplace or by consumers.

The assessment of the potential effects arising from the capacity of hazardous chemical agents to cause accidents, in particular fires, explosions or other hazardous chemical reactions covers:

- hazards resulting from the physicochemical nature of the chemical agents,
- risk factors identified in their storage, transport and use, and
- the estimated severity in the event of occurrence.

The accident scenarios to be especially considered linked to REACH are minor accidents which might occur in the workplace and those related to consumer use. As major accidents caused by chemicals and the requirements to manage these risks are regulated under the Seveso II Directive (Council Directive 98/82/EC2)[12] it can be assumed that major accident risks are adequately covered at the workplace level.

Independently of the assessment method applied the M/I shall prepare an analysis of the processes and procedures a hazardous substance is used in and describe the measures taken to prevent accidental release or negative effects on human health in case of an event. This should include a hazard ranking of the substance (e.g. using the R-phrases as criteria) and a possible frequency and assumed severity of an accident. A rational judgement should be provided which describes the underlying assumptions and the conclusions made. Based on the assessment one can either conclude that the use of the substance can be considered of no immediate concern or that recommendations for risk reduction are necessary (see CSA Concise Guidance Document Part E.2).

6.4 Risk Characterisation For Human Health

Having conducted the hazard assessment for all relevant human health endpoints and populations and the exposure estimation; a quantitative, and in some cases also a qualitative, risk characterisation is carried out.

It should be acknowledged that the whole risk characterisation process, whether quantitative or qualitative, depends heavily upon expert judgment. Therefore, the approach taken in reaching a conclusion needs to be as transparent as possible and needs careful explanation/justification as to assumptions, decisions, uncertainties and adequacy of the available data set.

The risk characterisation for human health is conducted as follows;

1. Collect and evaluate of all hazard information
2. Development of exposure scenario and estimation of amount of exposure for all the possible exposure route
3. Quantitative and semi- quantitative risk characterisation

The target population exposed are 1) workers, 2) general population (consumers and humans exposed via the environment).

The exposure routes of 1) inhalation, 2) dermal, 3) oral are needs to be considered and the risk characterisation should be carried out for all possible combinations.

The quantitative risk characterisation for human health is conducted as follows:

[12] Further guidance see
http://mahbsrv.jrc.it/GuidanceDocs-SafetyManagementSystems.html#Section3-2

$$RCR = \frac{Exposure}{DNEL}$$

When RCR < 1, i.e. Exposure < DNEL, → Risk is adequately controlled;
When RCR < 1, i.e. Exposure > DNEL, → Risk is ONT controlled.

If hazards of which threshold (Non-Effect Concentration (Dose)) cannot be established (carcinogenic or mutagenic endpoint, etc.), risk characterisation is performed by using DMEL instead of DNEL. It is concluded that the risk is controlled if the amount of exposure is smaller than DMEL as similar to the DNEL (See CSA Concise Guidance Document Part E.3).

6.5 Risk Characterisation for the Environment

Risk Characterisation for the environment is performed by the same method as for human health. Generally, Predicted Environmental Concentration (PEC) and Predicted Non-Effect Concentration (PNEC) are compared, and it is considered that the risk is adequately controlled if PEC ＜ PNEC (See CSA Concise Guidance Document Part E.2).

Topic-7

Uncertainty Analysis

（See CSA In-depth Guidance Document R.19 for details）

In REACH, the risk characterisation is accompanied by uncertainty with the results of RCR calculation, hazard assessment such as DNEL or PNEC, etc., calculation of PEC or estimated amount of exposure, etc. For instance, if there is no information available when calculating the amount of exposure using an estimation model, the result obtained by using default values would be more safety side. As a result, the estimated risk may become excessively high. If it is can be demonstrated that risks are adequately controlled by the RCR obtained in the initial CSA, uncertainty analysis may not be required. However, if RCR is close to the acceptable border level, or if it is not possible to demonstrate that risks are controlled, the collect RCR may be obtained with the uncertainty analysis.

It may be possible to review values which are excessively safety side by re-evaluating the validity of all parameters. At least, it may be possible to avoid conducting unnecessary studies by performing uncertainty analysis before suggesting or performing collection of additional hazard data.

7 Chemical Safety Report (CSR)

7.1 The Standard Format of Contents Included in the Chemical Safety Report (CSR)

According to the CSA Guidance Document, CSR requires to include following items;

1. Conclusions from the CSA. If results were derived by means of quantitative methods, details should be presented to allow an evaluator to reproduce the results. If results were derived by means of a qualitative (weight of evidence) reasoning, this should be reported.

2. For any endpoints in the hazard or PBT/vPvB sections for which no relevant information is available, the relevant section shall contain the sentence: 'This information is not available'. In addition, a statement could be added if the information is not required for a tonnage band or that the results of the CSA do not indicate that it should be taken into account (e.g., when the CSA does not indicate an exposure-triggered risk to soil organisms as in REACH Annex X-9.4).

3. For an optional endpoint in the hazard section a statement that the hazard information is required or could be waived based on the exposure situation. This needs to be argued and documented in a weight of evidence or quantitative reasoning.

4. For any endpoints in Annex IX and X or REACH a testing proposal when needed.

5. The reason why information on specific exposure pathways is not reported. This should be clearly stated and argued. The absence of exposure information need to be argued in order to evaluate if exposure based triggers have been correctly considered.

7.2 The Format (Template) of Chemical Safety Report (CSR)

The CSR template and explanation of each heading are described in CSA Concise Guidance Document Part F Appendix.

The REACH registrant must prepare a document following a specific format upon preparation of CSR (See Topic-8). The below are the standard headings of CSR.

Title (CHEMICAL SAFETY REPORT) Substance Name EC Number CSA Number Registrant's identity
PART A
1. SUMMARY OF RISK MANEGEMENT MEASURES 2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED 3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED
PART B
1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES 2. MANUFACTURE AND USE 3. CLASSIFICATION AND LABELLING 4. ENVIRONMENTAL FATE PROPERTIES 5. HUMAN HEALTH HAZARD ASSESSMENT 6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES 7. ENVIRONMENTAL HAZARD ASSESSMENT 8. PBT AND vPvB ASSESSMENT 9. EXPOSURE ASSESSMENT 10. RISK CHARACTERISATION

Topic-8

Preparation of CSR Format Using Plug-in Software to IUCLID5

It is being considered in ECHA to add a function with which CSR or OECD SIDS report can be created automatically by adding Plug-in Software to IUCLID5. It is expected that the data entered in IUCLID5 are exported in the CSR specific format by using this software. ECHA has announced that they will first develop the software for CSR, which is required for REACH registration, and start the test operation from around the end of 2008.

The software will be released at the following ECHA website:
http://echa.europa.eu/reach/software_en.asp

8 Safety Data Sheet (SDS)

8.1 Objective of Safety Data Sheet in REACH

The objectives of SDS are to provide easily understandable information on the substance itself or substance incorporated into preparations to the actors in the supply chain. Since operational conditions (OC) and risk management measures (RMM) are different based on the condition of use, REACH requires that exposure scenarios for each of the use or a group of uses needs to be attached as an annex to the SDS.

An immediate downstream user of the registrant should confirm that ES for his own use or his customers use are relevant to the extended SDS which is provided by M/I. When the substance or the preparation are distributed further down the supply chain, he should include information on ES included in the extended SDS obtained from registrant and other information into his own SDS and provide such information to the customers. In case ES provided by the registrant do not cover his use or his customers, he should either contact his supplier and ask to have his use or his customers' use included in an ES or conduct a CSA himself and add the result into his own SDS for his DUs.

If the immediate DU is the formulator (or re-packer) of an end-use product for down-stream users: The DU is supposed to extract the relevant information on risk management and OC from the ESs, summarise and include it in Sections 1.2, 7, 8 and 13 of the SDS for the preparation. The SDS for an end-use product (substance or preparation) will often address a well defined group of downstream users, and hence the RMM advice does not need use-specific differentiation. If, however, the same substance/preparation (e.g. a solvent based cleaner) is used under different operational conditions and/or by means of different RMM, inclusion of the received ES may be best done by consolidating the received ES into two or more new exposure scenarios annexed to the SDS for the preparation. This may for example be relevant in situations where a manufacturer or large formulator supplies his products via distributors and re-packers to end-users (industrial or non-industrial).

If the immediate DU is the formulator of an end-use preparation to be offered or sold to the general public: The DU is supposed to extract the relevant information on risk management and OC from the received ESs, summarise and include it in the information for the users (e.g. by means of appropriate use instructions). Such information shall enable the users of the general public to take the necessary measures as regards the protection of human health, safety and the environment.

Distributors are no downstream users under REACH. Thus, the customer of the distributor is immediate downstream user next to M/I. It is recommended that M/I actively approach the distributors to seek agreement, how M/I can increase his knowledge on the conditions of use in the distributor's market, without requiring the distributor to disclose confidential business information (CBI). The feedback mechanism may be a suitable way of doing this, provided the distributor works as a sort of facilitator.

8.2 Requirements for Extended SDS in REACH

Descriptions of the following items are newly required in the SDS based on REACH in addition to the usual (M)SDS. Therefore, this is called Extended SDS (eSDS) in REACH.

- Assessment results of PBT/vPvB (Persistent, Bioaccumulative / very Persistent, very Bioaccumulative)
- Predicted No-Effect Concentration (PNEC) for environmental organisms and Derived Non-Effect level (DNEL) for human health
- ES, where risks can be adequately controlled as SDS appendix, and conditions of manufacturing / processing / use included in the ES.

List of Abbreviations

AC	Article Category
AF	Assessment Factor
CMR	Carcinogenic, Mutagenic and Reproductive (toxicant)
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
DMEL	Derived Minimal Effect Level
DNEL	Derived Non-Effect Level
DUs	Down Stream Users
ECHA	European Chemicals Agency
ERC	Environmental Release Category
ES	Exposure Scenario
GLP	Good Laboratory Practice
IU	Identified Use
IUCLID	International Uniform Chemical Information Database
M/I	Manufacturer or Importer
NOAEL	No Observed Adverse Effect Level
OC	Operational Condition
PBT	Persistent, Bioaccumulative and Toxic
PC	Chemical Product Category
PEC	Predicted Environmental Concentration
PNEC	Predicted No-Effect Concentration
PROC	Process Category
RCR	Risk Characterisation Ratio
RMM	Risk Management Measure
SDS	Safety Data Sheet
SIEF	Substance Information Exchange Forum
SU	Sector of Use
SVHC	Substance of Very High Concern
vPvB	Very Persistent and Very Bioaccumulative

Useful Links

Contains both English and Japanese materials

ECHA: European Chemicals Agency
http://echa.europa.eu/home_en.asp

ECB: European Chemical Bureau
http://ecb.jrc.ec.europa.eu/reach/

CEFIC: European Chemical Industry Council
http://www.reachcentrum.eu/

Japan Chemical Industry Association
http://www.nikkakyo.org/reach/

Japan Chemical Industry Ecology-Toxicology & Information Center
http://www.jetoc.or.jp/index.html

REACH Center, Japan Environmental Management Association for Industry
http://www.reachcenter.jp/

Network for Strategic Response on International Chemical Management
http://www.chemical-net.info/index.html

Ministry of Economy, Trade and Industry,
http://www.meti.go.jp/policy/chemical_management/int/reach.html

Ministry of the Environment
http://www.env.go.jp/chemi/reach/reach.html