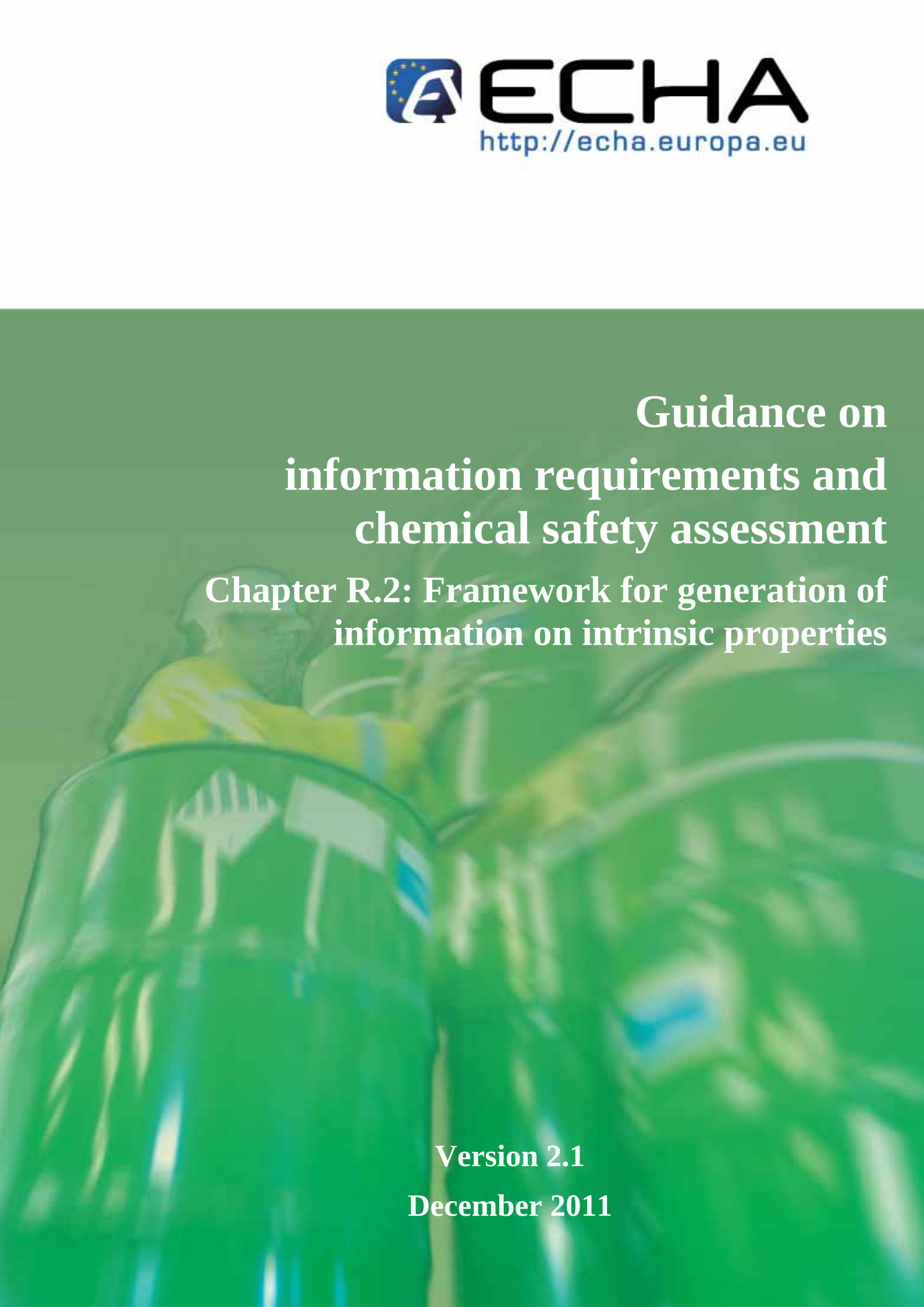

Guidance on information requirements and chemical safety assessment

Chapter R.2: Framework for generation of information on intrinsic properties

Version 2.1

December 2011

Guidance on information requirements and chemical safety assessment
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PREFACE

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

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

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

1 1 Corrigendum to Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006); amended by amended by: Council Regulation (EC) No 1354/2007 of 15 November 2007 adapting Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), by reason of the accession of Bulgaria and Romania, Commission Regulation (EC) No 987/2008 of 8 October 2008 as regards Annexes IV and V; Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures; Commission regulation No 453/2010 of 20 May 2010 as regards Annex II; Commission Regulation No 252/2011 of 15 March 2011 as regards Annex I; Commission Regulation No 366/2011 of 14 April as regards Annex XVII (Acrylamide), Commission Regulation No 494/2011 of 20 May 2011, as regards Annex XVII (Cadmium).

Document History

Version	Comment	Date
Version 1	First edition	May 2008
Version 2	First revision	July 2008
Version 2.1	Corrigendum replacing references to DSD/DPD by CLP references Editorial changes	December 2011

Convention for citing the REACH regulation

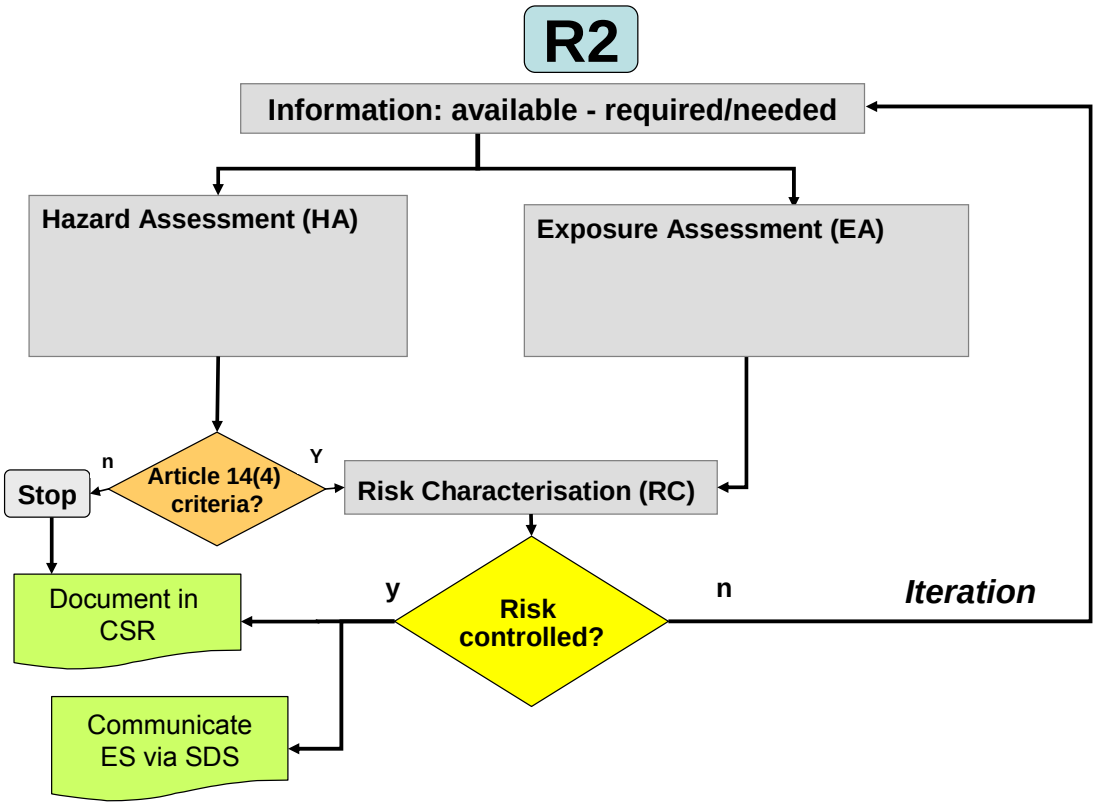
Where the REACH Regulation is cited literally, this is indicated by text in italics between quotes.

Table of Terms and Abbreviations

See Chapter R.20

Pathfinder

The figure below indicates the scope of part R.2 within the Guidance Document



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In the REACH Regulation, the standard information requirements are detailed in Annexes VI through X, while Annex XI includes general rules on how to adapt the standard information requirements set out in Annexes VII-X [2].

To achieve a high level of protection of human health and the environment while limiting the need for additional testing, all available data on the intrinsic properties of a substance must first be evaluated. Where available data are not adequate to meet the requirements of the REACH Regulation, additional testing may need to be generated. However, before embarking on animal testing, use of alternative methods and all other options must be considered.

In this context, Article 13(1) of REACH states that *information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set out in Annex XI are met. In particular for human toxicity, information shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example, in vitro methods or qualitative or quantitative structure-activity relationship models or from information from structurally related substances (grouping or read-across*[3]).

The information collected or generated will be used in a multiplicity of settings within REACH (e.g. for priority setting, classification and labelling, chemical safety assessment and PBT assessment). Chemical safety assessment within REACH is fundamentally dependent on an adequate conclusion on classification and PBT/vPvB assessment since exposure assessment and risk characterisation are triggered by classification and fulfilment of PBT/vPvB criteria. Therefore, data need to be adequate for both classification & labelling and for chemical safety assessment if the latter is required.

Regarding the classification and labelling:

- From 1 December 2010 until 1 June 2015, substances placed on the market on or after 1 December 2010 must be classified in accordance with both Directive 67/548/EEC and Regulation (EC) No 1272/2008 (the CLP Regulation).
- Substances shall be labelled and packaged in accordance with the CLP Regulation.[4] However, if a substance has been placed on the market before 1 December 2010 it is not required to be repackaged and relabelled according to the CLP Regulation until 1 December 2012.
- Mixtures must be classified according to the CLP Regulation from 1 June 2015 but may be classified according to Directive 1999/45/EC until this date (they may optionally also be classified according to the CLP Regulation in advance of this date[5].
- Mixtures classified, labelled and packaged in accordance with Directive 1999/45/EC and already placed on the market before 1 June 2015 are not required to be relabelled and repackaged in accordance with the CLP Regulation until 1 June 2017.

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[2] Throughout the document, all references to the REACH text refer to Regulation (EC) No.1907/2006 published in the OJ on 30.12.2006

[3] In this guidance these are described as category (grouping) and analogue (read-across) approaches respectively

[4] According to Article 61(3) of CLP

[5] According to Article 61(2) of CLP.

- Following the mentioned transitional period[6] Directives 67/548/EEC and 1999/45/EC will be completely repealed and replaced with the CLP Regulation that is based on the Globally Harmonized System[7] (GHS; see also Guidance on the Application of the CLP Criteria).

R.2.1 REACH Information requirements - Annexes VI – X

Under REACH, registrants are obliged to collect all relevant and available information on the intrinsic properties of a substance, regardless of the quantity manufactured or imported. However, the type and quantity of information on the intrinsic properties of a given substance that will be required as a minimum to meet the obligations of the regulation depends on the quantity of that substance that is manufactured or imported into the EU. Annexes VI-X of REACH specify these minimum data requirements for a given substance according to its tonnage for registration purposes (REACH Article 12), which however may be adapted as appropriate.

Column 1 of REACH Annexes VII-X lays down the standard information requirements for substances produced or imported in quantities of ≥1 t/y (tonne per year), ≥10 t/y, ≥100 t/y, and ≥1000 t/y, respectively. For physico-chemical properties and each of the health and environmental endpoints, more detailed specific guidance on meeting these information requirements is given in the appropriate subchapters of Chapter R.7

For the lowest tonnage band, the information required is that specified in Column 1 of REACH Annex VII, comprising certain physico-chemical data, toxicological information and ecotoxicological information. However, under the terms of Article 12 (1)(b) and Annex III of REACH, if the substance does not have a dispersive or diffuse use and it is predicted not to be likely to meet the criteria for classification for any human health or environmental hazard, the required minimum information is confined to the physico-chemical data.

As each new tonnage level is attained, the requirements of the next corresponding REACH Annex must be addressed. These standard requirements may, however, be adapted (waived or increased) when appropriately justified (REACH Annexes III and VI-XI). Thus, for each individual substance the precise information requirements will differ, depending on tonnage, use and exposure, and the properties of the substance. The Annexes should thus be considered as a whole, and in conjunction with the overall requirements of registration and the duty of care. Further guidance on the information requirements for each individual endpoint is given in the appropriate subchapters of Chapter R.7.

For each of the REACH Annexes VII to X, Column 2 lists the conditions under which the standard information requirements for individual endpoints may be modified (e.g. on the basis of characteristics of the substance itself or its exposure pattern). If the conditions for adaptation in Column 2 are met and applied, the fact that an adaptation has been made, together with its justification, must be indicated clearly in the registration. Further guidance on the possibilities for adaptation of the information requirements for the individual endpoints is given in the appropriate subsections of Chapter R.7.

In addition to these specific rules, the required standard information set may also be adapted according to the general rules contained in Annex XI of the REACH Regulation e.g. in cases where testing is not technically possible, or testing does not appear scientifically necessary, or based on exposure consideration. In such cases the reasons for each adaptation should be clearly indicated in the registration. Further guidance on these rules/conditions is detailed below in Chapter R.5. It should be noted that although this guidance will provide assistance in developing the reasoned justification for asking for derogations/waiving from the standard information requirements, in

[6] According to Article 61 of CLP.

[7] Globally Harmonized System of Classification and Labelling of Chemicals (GHS), first revised edition, United Nations, New York and Geneva, 2005 (ST/SG/AC. 10/30/Rev. 1)

certain cases available data showing hazardous effects could trigger the need for additional information including new testing.

In general terms, Column 1 of Annexes VII-X provides the standard information requirements and Column 2 of each Annex specifies the adaptation possibilities for the specific endpoints.

R.2.2 Information Gathering and Evaluation

Annex VI of the REACH Regulation describes a general scheme embodying four steps to be followed by the registrant to fulfil the information requirements detailed above for a given substance. These steps are relevant for all substances to be registered:

Step 1: Gather and share existing information

Step 2: Consider information needs

Step 3: Identify information gaps

Step 4: Generate new information or propose a testing strategy

Figure R.2-1 illustrates how these four steps are related to other processes and the deliverables under REACH.

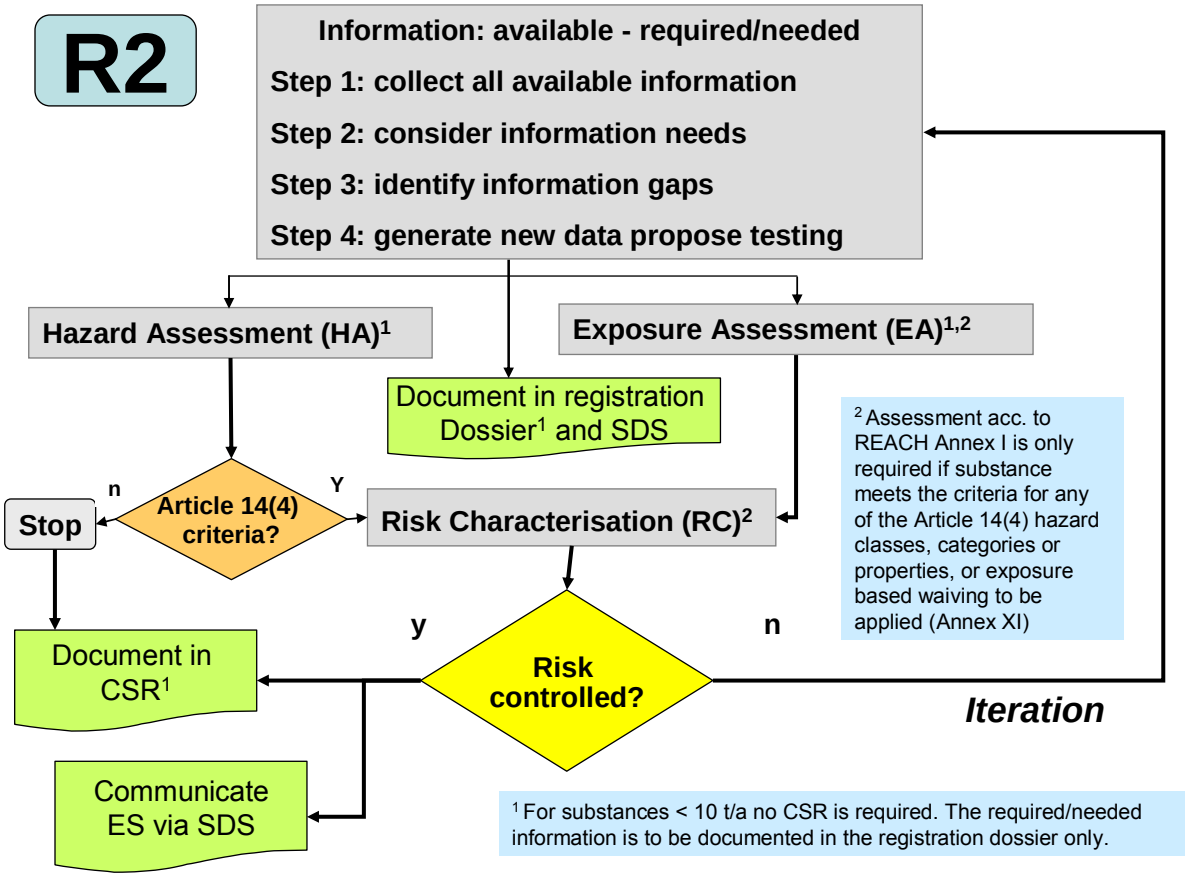

Figure R.2-1: Overall framework of information generation under REACH

General guidance on how all available existing information should be gathered, evaluated and what new data may be needed for the assessment of the properties of substances under the REACH Regulation is given below. More specific guidance for each endpoint is given in Chapter R.7 including an Integrated Testing Strategy (ITS) developed specifically for each endpoint.

R.2.2.1 Step 1: Gather and share existing information

R.2.2.1.1 Information on substance properties

In step 1, the registrant must collect all physicochemical, toxicological and ecotoxicological information that is relevant and available to him regardless of whether information on a given endpoint is required or not at the specific tonnage level. This includes available existing test data as required in accordance with REACH Annexes VII-X, including:

- Physicochemical data
- Human data, incl. epidemiological data
- Testing data: incl. all *in vitro* and *in vivo* testing data
- Non-testing data: i.e. data obtained with (Q)SAR models, grouping of substances, read-across, weight of evidence etc.
- Any other data that may assist in identifying the presence or absence of hazardous properties of the substance

Such information may be obtained from a variety of sources such as in-house data of companies, from other manufacturers and importers of the substance by cooperation in a SIEF (REACH Article 29), from the Agency upon request (REACH Article 26) or from databases or other sources in the open literature or accessible on the internet. This information gathering step should (if possible) also include the establishment of membership of the substance in a proper chemical category (cf. Annex XI, 1.5) and the information this provides (incl. read-across from other substances), as well as the information that is retrievable from computational tools, i.e. (Q)SAR models. For details see Sections R.4.3.2 and Chapter R.6. Acquiring of results from non-testing methods would be especially important for substances for which the testing data set is limited or non-existent.

It may well be that the available information on these intrinsic properties of the substance go beyond the tonnage triggered requirements of test data (referred to in Step 2): it is a requirement of REACH Article 12(1), that *"The technical dossier referred to in Article 10(a) shall include […] all physico-chemical, toxicological and ecotoxicological information that is relevant and available to the registrant […]"*.

R.2.2.1.2 Assessment of reliability, relevance and adequacy of information

The registrant should assess all relevant and available information on physicochemical and environmental fate properties, toxicity and ecotoxicity of the substance for its reliability, relevance, adequacy and completeness. Although the reliability criteria are of a general nature, the decision on whether a single piece of information is reliable (i.e. how to assign it a specific level of reliability, e.g. using the Klimisch score) is endpoint specific (Section R.4.2). Therefore, the section on *Evaluation of available information* for the relevant endpoint(s) in Chapter R.7 should be consulted.

For all available data, an assessment must be made of the adequacy of the available information for arriving at conclusions on hazard assessment, i.e. C&L, PBT/vPvB assessment, and identification of (a) dose descriptor(s) enabling the derivation of (a) DNEL(s) and (a) PNEC(s). DNEL(s) and PNEC(s) are subsequently to be used in the risk characterisation when a substance fulfils the criteria for any of the hazard classes or categories, or is assessed as having properties listed in Article 14(4) of the REACH Regulation, as amended from 1 December 2010 by Article 58(1) of Regulation (EC) No 1272/2008 (CLP Regulation), namely:

- hazard classes 2.1 to 2.4, 2.6 and 2.7, 2.8 types A and B, 2.9, 2.10, 2.12, 2.13 categories 1 and 2, 2.14 categories 1 and 2, 2.15 types A to F.
- hazard classes 3.1 to 3.6, 3.7 adverse effects on sexual function and fertility or on development, 3.8 effects other than narcotic effects, 3.9 and 3.10.
- hazard class 4.1:
- hazard class 5.1,
- or PBT, vPvB properties,:

These classes, categories and properties will henceforth be described as "Article 14(4) hazard classes, categories or properties".

The term *adequate* refers to the ability to meet the defined information requirements (Annexes VII-XI), and to allow a conclusion on the above mentioned aspects in hazard assessment. Different conclusions may be obtained:

- the information available is considered *adequate* for the objectives mentioned (C&L, PBT and vPvB assessment, and DNEL and PNEC derivation)
- the information available is considered *inadequate* for at least one of the objectives and further information is needed

It is possible that the data may be adequate for C&L and PBT (or vPvB), but not for DNEL and/or PNEC derivation, or *vice versa*, as data requirements for these conclusions may differ.

It is also emphasised that it may not always be possible to establish a DNEL for risk assessment purposes via the identification of a concrete quantitative dose descriptor value, e.g. a NOAEL etc. In these situations it may be possible nevertheless to define some quantitative or semi-quantitative dose descriptor or a qualitative approach that may also allow a conclusion that the use and handling of the substance may be regarded as adequately controlled.

A decision on *adequacy* relies often on *Weight of Evidence* (WoE) approaches for the various endpoints (also mentioned in REACH Annex XI, Section 1.2), see Chapter R.4 Section R.4.4. Further details on the *adequacy of data* can be found in Chapter R.4 on *Evaluation of available information*, Chapter R.5 *Guidance on Adaptation of Information Requirements*, and in Chapter R.7 on endpoint specific guidance.

R.2.2.1.3 Information on use and exposure

In addition, the registrant should collect information on use, exposure and risk management measures. This may require more details on, e.g., manufacture (if within EU), use, handling and disposal of the substance or of articles containing the substance (i.e. covering its whole life cycle) as well as the nature of the exposures, i.e. routes, frequency and duration (see REACH Annex VI, Sections 3, 5, and 6). This information will guide further information requirements, e.g. if limited and well controlled human exposure is only taking place at the workplace during a few days a month, chronic toxicity studies may not be needed. Considering all this information together, the registrant will be able to determine the need to generate further information.

The further elaboration of these data on exposure characteristics in terms of deriving associated exposure estimates is required under REACH only when available and/or required information indicates that the substance fulfils any of the criteria of the Article 14(4) hazard classes, categories or properties[8], as only under these conditions a full risk assessment is requested (see Guidance information requirements and chemical safety assessment: Part E).

[8] In this context "properties" refers to PBT and vPvB (see Section R.2.2.1.2)

All data gathering activities should be well documented, to allow a proper assessment of the completeness of the registration dossier and to avoid repetition at a later stage. Each manufacturer or importer (and downstream user and distributor) is required to assemble and keep available all information he requires to carry out his duties under REACH for 10 years after the last manufacture or import of the substance.

R.2.2.2 Consider information needs

At step 2, the registrant needs to identify from REACH Annexes VII to X the standard information requirements according to the tonnage he manufactures or imports. These standard requirements may be adapted in accordance with Annex III, in accordance with specific criteria for the endpoint in question as provided in column 2 of the mentioned annexes, or in accordance with the general criteria for adaptation of information requirements given in Annex XI (Section R.5.1).

R.2.2.2.1 Adaptation under Annex III (Substances in the 1-10 t/y range)

Information requirements on toxicological and ecotoxicological properties should be provided for all non-phase-in substances and for phase-in substances meeting the criteria specified in REACH Annex III. The criteria given in REACH Annex III are:

(a) *Substances for which it is predicted (i.e. by the application of (Q)SARs or other evidence) that they are likely to meet the criteria for category 1A or 1B classification in the hazard classes carcinogenicity, germ cell mutagenicity or reproductive toxicity or the criteria in Annex XIII* (i.e. the PBT or vPvB criteria)

or

(b) Substances

i. with dispersive or diffuse use(s) particularly where such substances are used in consumer mixtures or incorporated into consumer articles; and

ii. for which it is predicted (i.e. by application of (Q)SARs or other evidence) that they are likely to meet the classification criteria for any health or environmental hazard classes or differentiations under Regulation (EC) No 1272/2008.

Specific rules apply to phase-in substances manufactured or imported in a tonnage of more than or equal to 1 t/y, but below 10 t/y, if they do not fulfil the criteria in Annex III. In this case, the standard information requirements are restricted to all physicochemical, toxicological and ecotoxicological information that is relevant and available to the registrant and as a minimum the physicochemical endpoints in Annex VII. The registrant needs to document thoroughly that the criteria of Annex III are not fulfilled, i.e. by submitting available and reliable information on properties relevant for the classification criteria and/or on the uses as appropriate.

All available information should be used in the evaluation of the toxicity and ecotoxicity of the substance including information from non-testing methods. In case no testing (eco)toxicity data are available predictions from non-testing methods would exclusively provide the basis for the assessment. The registrant needs to obtain reliable information that allows the comparison with the criteria for all the Article 14(4) hazard classes, categories or properties[9] If based on the comparison it is concluded that the substance is likely to meet classification criteria for any effect endpoint or the criteria for CMR category 1A or 1B or the criteria for PBT or vPvB, then the

[9] In this context “properties” refers to PBT and vPvB (see Section R.2.2.1.2)

substance should be considered as meeting the requirement (a) or (b) (ii) according to REACH Annex III. In general any results (both testing and non-testing) assessed as reliable (i.e. meeting the validity criteria) would be sufficient to predict that the substance would be likely to meet these criteria (see Chapter R.11 and criteria for Classification and Labelling, as specified in Annex I of the CLP Regulation).

According to REACH Annex III if *dispersive use* or *diffuse use* (particularly where such substances are used in consumer mixtures or incorporated into consumer articles) cannot be excluded, the criterion (b) (ii) should be considered as fulfilled (see *Chapter R12* for further explanation of *dispersive* and *diffuse use*). In the case, based on available information, the substance is likely to meet any of the criteria specified in REACH Annex III, the full information requirements specified in REACH Annex VII are required. The classification of the substance based on the available data should be recorded.

However, if it can be demonstrated with sufficient certainty from reliable information that the substance is not likely to meet either of the criteria for CMR category 1 or 1B or PBT/vPvB, or for any other classification endpoint (i.e. health and the environmental) and it has no dispersive or diffuse use, no further information generation on this substance is required at the ≥1-10 t/y level. In any case all the gathered reliable information should be provided in the registration dossier.

R.2.2.2.2 Adaptations of information requirements according to column 2

For specific endpoints, column 2 specifies rules according to which the standard information is required or can be omitted . Based on intrinsic properties a test may be waived or replaced by another, better suited for the substance. In many cases, these rules refer to information on other properties or endpoints of the substance in question and such information should also be reliable, i.e. have undergone the assessment under step 1 (Chapter R.7).

Also considerations on exposure may be used for adapting the information requirements. Different descriptors for exposure considerations are used in these Annexes varying from *limited* to *no relevant* exposure. These descriptors may not always be easily interpretable and may be difficult to define in operational terms, indeed their application requires practical experience and expert judgement applied on a case-by-case basis taking account of all the relevant supporting information. Also results of Chemical Safety Assessment may guide further information gathering. Further guidance on their interpretation may be found in the Integrated Testing Strategies (ITS) for specific endpoints in the relevant subsections of Chapter R.7.

R.2.2.2.3 Adaptations of information requirements according to Annex XI

When the registrant makes use of the Annex XI criteria (i.e. regarding the scientific necessity of the information, the technical possibility for testing, and exposure-based waiving) to adapt the standard information requirements, he should base this on reliable and adequate information as it is specified in Annex XI and should document this in accordance with the guidance provided (Chapter R.5).

If control of risks can be demonstrated based on exposure scenarios, the need for testing in accordance with section 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be waived, cf. REACH Annex XI Section 3. Evidently, this requires a documented knowledge of all exposure scenarios and accurate estimation of all associated exposures (see for further details Section R.5.1, and the corresponding endpoints chapters in Chapter R.7). It is noted that in specific cases, e.g. wide dispersive use of the chemical, information (from test or non-test sources) beyond that indicated by the respective tonnage level may be considered necessary.

R.2.2.3 Identify information gaps

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. The adaptation rules described in step 2 should be carefully considered before deciding on performance of a new test.

For endpoints 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.

R.2.2.4 Generate new information or propose a testing strategy

When a data gap has been identified in step 3 for information requirements included in Annexes VII or VIII, the registrant needs to conduct a test in accordance with Article 13 of REACH. However, a number of issues may need to be considered before deciding on conducting a new test.

R.2.2.4.1 Conclude on what exactly is unclear or insufficient to fulfil the requirements

If it is conceivable that the information gathering has not been as extensive as possible, i.e. that further information gathering could potentially yield further existing data, this should be addressed following the guidance described. This includes also *in vitro* and non-testing information. However, where all possible information sources have been consulted, it is important to develop a clear idea about exactly what additional information is needed to be able to conclude on hazard and/or risk assessment (i.e. Classification & Labelling, PBT/vPvB assessment, and/or DNEL and PNEC derivation including identification of dose descriptors).

R.2.2.4.2 Is testing technically possible?

In accordance with REACH Annex XI Section 2, testing for specific endpoints may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance, e.g. very volatile, highly reactive or unstable substances (specific cases can be found in Column 2 of REACH Annexes VII-X). Any omission of testing should be thoroughly justified and the technical limitations explained. Case-by-case expert judgement is required.

R.2.2.4.3 Consider if in vitro testing may be adequate

At present, with the exception of the endpoints skin corrosion and skin irritation, it is possible in specific cases to conclude on a classification according to the existing EU or GHS criteria on the basis of *in vitro* studies alone, e.g. for identification of severe eye irritants using organotypic methods. See Chapter R.7 on specific endpoints.

However, the combination of various pieces of evidence, including *in vitro* test data, may provide adequate information for a decision on classification and/or risk assessment, when applied in an integrated manner.

R.2.2.4.4 Conduct or propose an appropriate test

When a data gap has been identified in step 3 for information requirements included in REACH Annexes VII or VIII, the registrant should obtain this information before submitting his registration dossier. New testing should be conducted in accordance with REACH, Article 13, i.e. using one of the methods included in the Commission's Test Method Regulation[10] or an international test method recognised by the Commission or the Agency as being appropriate. Moreover, toxicological and ecotoxicological tests shall be carried out in compliance with the principles of Good Laboratory Practice and with the provisions of Directive 86/609/EEC, if applicable.

When a data gap has been identified in step 3 for information requirements included in REACH Annexes IX or X, the registrant needs to develop a testing proposal and include it in the registration dossier in accordance with Article 10(a)(ix) of REACH. In developing the testing proposal, the same requirements as specified above for conducting a new test should be taken into account. Whilst waiting for the results of this testing, the registrant should implement and/or recommend interim risk management measures and include them in his exposure scenarios and chemical safety report as documentation for control of risks (cf. REACH, Annex I, 0.5).

[10] Council Regulation (EC) No 440/2008

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