

*Practical guide 10:*

# How to avoid unnecessary testing on animals



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### ***Practical guide 10: How to avoid unnecessary testing on animals***

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# 1. INTRODUCTION

The purpose of this practical guide is to highlight the opportunities & obligations that registrants have to avoid unnecessary new animal studies, yet still assessing the properties of their substances adequately for classification and hazard communication and also for a satisfactory risk assessment to enable appropriate risk management measures to be taken to manage any risks that arise from manufacture or use.

The guide explains alternative and non-test methods of assessing the properties of chemical substances in order to provide the information required by the REACH Regulation<sup>1</sup>. The resulting data can be used for REACH registration and CLP classification. More detailed explanations of the methods involved are provided in the European Chemicals Agency's (ECHA) guidance documents which are referenced at the end of this paper.

The overall purpose of both the REACH and the CLP<sup>2</sup> Regulations is to ensure a high level of protection of human health and the environment. One of the main reasons for developing and adopting the REACH Regulation was to fill the data gaps for the large number of substances already in use. For many of these substances there is inadequate information on the hazards they pose to human health and the environment. Filling the data gaps will enable industry to assess hazards and risks, and to identify and implement any risk management measures that are necessary to protect human health and the environment.

A primary means of avoiding unnecessary tests on animals is the requirement that REACH registrants share test data with one another. This means that any existing studies involving tests on vertebrate animals conducted by one registrant must be shared for use by all registrants of that substance. Also, information from any new animal studies will need to be provided to all registrants that need them for registration. While data sharing will influence the number of animals tests, that process is only briefly described here as much greater detail is already available in "*Guidance for the implementation of REACH – Guidance on data sharing*" (2007).

Many of the standard test methods use vertebrate animals as a model to predict the effects of chemicals on humans and the environment. However, there are other means to assess the properties of substances without using tests on animals. Hence another key means of avoiding unnecessary testing on animals is to use what are called alternative methods for assessing the hazards of substances – the rationale for this guide.

The CLP Regulation does not require new studies<sup>3</sup>. Instead, suppliers have to obtain and evaluate all the available relevant information to classify their substances and mixtures. In practice this means that many substances can be classified on the basis of the data obtained during the preparations for registration under REACH. Nevertheless, some suppliers may themselves choose to generate new information to improve their classifications.

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<sup>1</sup> Regulation (EC) No 1907/2006 concerning the registration, evaluation, authorisation and restriction of chemicals.

<sup>2</sup> Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures.

<sup>3</sup> Except for physicochemical properties which is outside the scope of this document.

This Guide sets out four steps: the gathering and sharing of information; considering information needs; identifying information gaps; and generating new data. It also highlights that, should testing be needed, registrants should first consider: the use of *in vitro* testing; the opportunities to avoid testing provided by the specific rules for adaptation in column 2 of Annexes VII to X of REACH; and the general rules for adaptation in Annex XI. Recommendations have also been made based on ECHA's experience so far with the registration and dossier evaluation process.

Finally, there is a brief description of what ECHA does when it receives registrations, outlining the processes of the technical completeness check and of dossier evaluation.

## 2. WHO SHOULD READ THIS PRACTICAL GUIDE?

This document is for manufacturers and importers of substances (and their only representatives). The document may also be useful for companies outside the European Community who need to check that companies importing their products into the Community are complying with the information requirements that the REACH and CLP Regulations place on them.

This guide is aimed especially at management and less experienced regulatory affairs professionals to help them to make decisions on their registrations and assess advice they might be given by other parties. It is also intended to introduce readers to the subject and to point them to more detailed information necessary in order to prepare registration dossiers. Hence this document should be especially useful to small and medium sized enterprises (SME) who have responsibilities under the REACH or CLP Regulation.

## 3. DUTIES OF POTENTIAL REGISTRANTS

### 3.1. Data sharing

**The important principle is that in order to avoid unnecessary tests on animals, the REACH Regulation requires registrants to share test data with one another. This means that any existing studies using vertebrate animals conducted by one registrant are shared for use by all registrants of that substance. It also means that any new animal studies that do have to be conducted are also used by all the registrants that need them for their registration. This principle lies behind the processes summarised below.**

REACH prescribes that, in general, all substances manufactured or imported in quantities of 1 tonne or more per year have to be registered before being manufactured or placed on the market. In order to avoid unnecessary testing it also contains an obligation for companies to share the results of tests involving vertebrate animals with other companies registering the same substance.

REACH discriminates between non-phase-in substances and phase-in substances, i.e. essentially speaking, new substances and substances that are already manufactured and marketed.

Before registering a non-phase-in (new) substance<sup>4</sup>, a potential registrant is obliged to submit an inquiry to ECHA as to whether that substance has already been registered and, if so, whether any information required by the potential registrant is already available<sup>5</sup>. If the substance has already been registered, ECHA informs both the previous registrant and the potential registrant of this fact and the potential registrant is then obliged to request the information involving tests on vertebrate animals from the previous registrant. In particular, studies involving tests on vertebrate animals must not be repeated. The previous registrant and the potential registrant shall make every effort to reach an agreement on the sharing of the data, and ECHA's role is to decide if the potential registrant should be granted permission to refer to the data in question if the two parties cannot reach agreement on the sharing of the study.

For phase-in substances, REACH introduced pre-registration. Registrants could pre-register their phase-in substances from 1 June to 1 December 2008 to benefit from a transitional regime for registration. One of the main purposes of pre-registration was to set up the Substance Information Exchange Forums (SIEFs) consisting of potential registrants of the same substance, in which the potential registrants must collaborate on obtaining and sharing data on the substance ensuring that unnecessary animal testing is avoided. REACH requires that available studies involving tests on vertebrate animals are shared among the potential registrants. Essentially, members of SIEFs must make every effort to reach agreements on data sharing and as long as the SIEF members are able to do so, ECHA has no role in the data sharing process within the SIEFs. ECHA is only obliged to step in if an owner of a study is not willing to share the study, if the SIEF members cannot agree on sharing the costs, or if the SIEF members cannot agree on who should carry out a new study for filling data gaps.

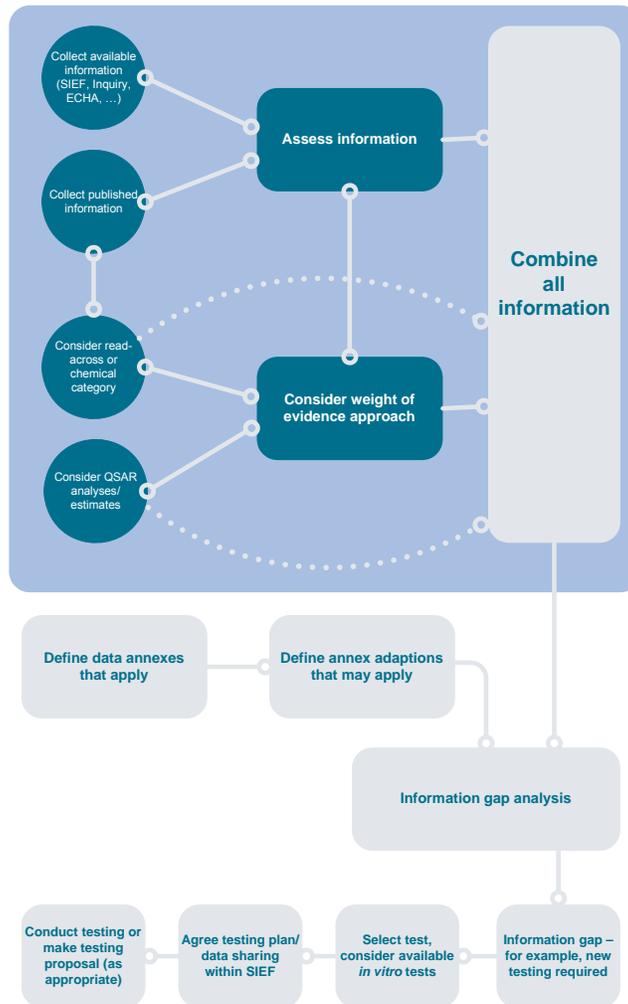
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<sup>4</sup> This applies also to phase-in substances that were not pre-registered.

<sup>5</sup> See Article 26 of the REACH Regulation.

### 3.2. The process of gathering Information

Potential registrants are required to obtain data on their substances as specified in the Annexes VI to X of REACH. Annex VI of REACH provides a basic four-step procedure for fulfilling the information requirements. Note that these steps are not necessarily consecutive. In practice, this is an iterative process which is also illustrated in the diagram below. A comparable process can be used for the classification of substances under the CLP Regulation, although as noted above, there is no obligation to conduct new studies.



## **STEP 1 – Gather and share existing information**

The potential registrant should collect all the existing physicochemical, toxicological and ecotoxicological information that is available on their substance, regardless of whether information on a given endpoint is required or not at the specific tonnage level (the Annexes of REACH specify exactly what is required for which tonnage level). This includes information possessed by the potential registrant, other potential or previous registrants, information available from ECHA or from a literature search. This includes:

- Existing data on the substance whether from testing or other sources;
- Use, exposure and risk management information;
- Data on analogous substances if ‘read across’ or membership of a ‘chemical category’ is possible (consider contacting SIEFs with related substances);
- (Q)SAR estimated results for the substance if suitable models are available;
- Weight of evidence approach to fill data gaps for particular endpoints, if this is appropriate.

The potential registrant has to make an assessment of the reliability, relevance and adequacy of the data obtained.

## **STEP 2 – Consider information needs**

The potential registrant needs to identify from Annexes VII to X of REACH the standard information requirements according to the tonnage he manufactures or imports. These standard requirements may have to be varied according to the specific criteria for the endpoint in question (as provided in column 2 of the Annexes), or in accordance with the general criteria for adaptation of information requirements (Annex XI of REACH).

## **STEP 3 – Identify information gaps**

The potential registrant needs to compare the information needs for the substance identified in step 2 with the reliable and relevant information already available as identified in step 1. For endpoints where the REACH regulatory requirements cannot be fulfilled with relevant and available information, data should be obtained in accordance with step 4.

## **STEP 4 – Generate new data or propose a testing strategy**

When a data gap has been identified in step 3, the potential registrant needs to conduct a test in accordance with Article 13(3) of REACH. It should be noted that new ‘higher-tier’ studies from Annex IX and X (which include those tests requiring the largest number of vertebrate animals and which are the most expensive) for substances at 100 or 1,000 tonnes per annum respectively, should not be conducted by the registrant at the stage of registration. Instead, when a data gap has been identified in step 3, the potential registrant needs to develop a testing proposal and include it in the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) and (e). Pending the availability of results from any further testing, the registrant must also implement the appropriate risk management measures as well as document those they recommend to downstream users.

It is a precondition that before any new tests are carried out to fulfil the information requirements, all available *in vitro* data, *in vivo* data, historical human data, data from

valid (Q)SARs and data from structurally related substances (read-across or categories) shall be assessed first. In practice, this means the registrant should carefully consider the rules for adaptation of column 2 (see section 3.5 below) and the general rules for adaptation (see Annex XI of the REACH Regulation and also section 3.3 below) before conducting testing on animals. Furthermore, the available guidance on integrated testing strategies to fulfil the information requirements should also be consulted (see *Guidance on information requirements and chemical safety assessment. Chapter R.7a: Endpoint specific guidance*). Therefore, before considering testing on animals registrants should check that they have considered the possibilities offered by such alternative approaches before actually conducting testing on animals.

### 3.3. Strategies to avoid unnecessary testing on animals

#### 3.3.1. In vitro methods

A test performed *in vitro* (Latin: in the glass) is performed in a controlled environment, such as a test tube or Petri dish, and does not use a living organism. A test performed *in vivo* (Latin: in the living) is one using a living organism, e.g. a vertebrate animal.

Results obtained from suitable *in vitro* methods may indicate the presence of a certain dangerous property or may be important in relation to understanding the mode of action of the substance. In this context “suitable” means sufficiently well developed according to internationally agreed test development criteria (e.g. the European Centre for the Validation of Alternative Methods (ECVAM) pre-validation criteria).

#### Recommendations:

1. Data generated from *in vitro* test methods (validated and pre-validated) can be used under REACH provided that the information for the hazard endpoint is sufficient for the purpose of classification and labelling and/or risk assessment.
2. Where a pre-validated method is used, the registrant should assess the method according to the ECVAM pre-validation criteria and justify its suitability for use in the registration dossier.
3. Advanced *in vitro* technologies may provide valuable information on the mode of action of the substances and can be part of a read-across and category justification.
4. *In vitro* data produced using other methods (i.e. non-prevalidated methods) can be used only as supportive information (e.g. as part of a weight of evidence justification).
5. A detailed, clear description of the results, the test conditions and the interpretation of the usefulness of the results should always be provided in the registration dossier. This is necessary if the study is used as a key study or as part of a weight of evidence approach.
6. Limitations of the method should be clearly communicated; for example *in vitro* test methods may not replicate all of the metabolic processes relevant to chemical toxicity that occur *in vivo*.

7. In all cases the conditions set out in the REACH Regulation Annex XI, Section 1.4 must be met.

Further information can be found in *Practical Guide 1: How to report in vitro data* and at: <http://ecvam.jrc.it/>

### 3.3.2. Grouping of substances and read-across

Animal tests on a substance can be avoided if there is enough evidence on similar substances which the registrant can show should be “read across” to their own substance. Substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity, may be considered as a “group”, or ‘category’ of substances. Applying the group concept means that the physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for one substance within the group by interpolation to other substances in the group (read-across approach). This avoids the need to test every substance in the group for every hazard endpoint. Preferably, a category should include all similar substances. REACH Annex XI, Section 1.5. sets out the requirements for the application of this strategy.

#### Recommendations:

1. Results from the read-across approach should be adequate for the purposes of classification and labelling and/or risk assessment (see section R6.2.3 of *Guidance on Information Requirements and Chemical Safety Assessment*).
2. Substance identity must be specified and documented for all relevant members of the category, including purity / impurity profiles. The *Guidance for identification and naming of substances under REACH* should be used.
3. Where substances have been accepted as members of categories under other regulatory programs (for example OECD HPV categories), the registrant should refer to them in the dossier. The registrant must nevertheless include all available information (including information which became available after assessment in the other regulatory programme) and reassess the validity of the category.
4. The read-across hypothesis used and its justification must be detailed in the dossier. An acceptable read-across justification is normally based on multiple lines of evidence. Different routes of exposure should also be taken into account. A consideration of information from studies on toxicokinetics may improve the robustness of the read-across hypothesis.
5. The documentation must detail which hazard end-points are covered by the read-across, and the source chemical which is used for the read-across must be identified. It is also important that the reliability indicator (Klimisch score<sup>6</sup>) reflects the *assumptions* of similarity. Thus, a score of 1 (reliable without restrictions) should normally not be used for results derived from read-across.

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<sup>6</sup> Klimisch H., Andreae M. and Tillmann U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regulatory Toxicology and Pharmacology* Volume 25, Issue 1, pages 1-5.

6. A comparison of experimental data for hazard endpoints for all category members (also presented in a tabular data matrix) is recommended, ideally highlighting trends within the category.

Further information can be found in the *Guidance on information requirements and chemical safety assessment in Chapter R.6: (Q)SARs and grouping of chemicals* and in the *Practical Guide 6: How to report read-across and categories*.

### 3.3.3. Quantitative Structure-Activity Relationship (QSAR) models

Animal tests can be avoided if the hazardous properties of a substance can be predicted using computer models. The [(Q)SAR] [(quantitative) structure-activity relationship] approach seeks to predict the intrinsic properties of chemicals by using various databases and theoretical models, instead of conducting tests. Based on knowledge of chemical structure, QSAR quantitatively relates characteristics of the chemical to a measure of a particular activity. QSAR should be distinguished from SAR, which makes qualitative conclusions about the presence or absence of a property of a substance, based on a structural feature of the substance.

#### Recommendations:

1. In order to use (Q)SAR predictions instead of testing, they must meet the conditions set out in the REACH Regulation Annex XI, Section 1.3.
2. The use of (Q)SAR analysis can also be used as part of a **weight of evidence approach** or an **integrated testing strategy**.

Further information can be found in the *Guidance on Information Requirements and Chemical Safety Assessment in Chapter R.6: (Q)SARs and grouping of chemicals* and in the *Practical Guide 5: How to report (Q)SARs*.

### 3.3.4. Weight of evidence approach

Animal tests can be avoided if there is a weight of evidence which points to the likely properties of a substance. This approach may be applied if there is sufficient information from **several independent sources** leading to the conclusion that a substance has (or has not) a particular dangerous property, while the information from each single source alone is regarded insufficient to support this assertion (see Annex XI, 1.2 for more detail).

#### Recommendations:

1. A weight of evidence approach **must be flagged** in the dossier; the flag can be used only if more than one study is provided for a hazard endpoint.
2. Weight of evidence **must not be flagged** if the registrant intends to waive a study.
3. **Robust study summaries** are recommended for each study used as part of a weight of evidence approach.
4. All relevant information for the hazard endpoint should be addressed and a scientifically justified weighting should be assigned to it in the overall assessment.

5. The quality of the available data, the consistency of the results, the severity and the type of effect of concern and the relevance of the available data for the hazard endpoint should all be considered.

Further information can be found in the *Practical Guide 2: How to report weight of evidence*.

### 3.4 The need for registrants to provide adequate and transparent justifications

In ECHA's *Evaluation under REACH - Progress Report* (last published 2009), experience showed that whilst there has been some use of alternative methods by registrants, testing has frequently been omitted based on inappropriate or poorly justified scientific arguments.

It is a clear principle of REACH that potential registrants are obliged to use *in vitro* test methods and or non-testing property estimation methods, as well as data sharing to the fullest extent in order to avoid unnecessary testing on animals to obtain the information necessary to assess the hazards and risks of the registered substance. However, omitting testing on animals must not compromise the safe use of substances. Therefore, registrants should note that every adaptation they apply to the standard information requirements needs a valid justification. Analysis of the registration dossiers already received by ECHA shows that some adaptations have been poorly justified. Registrants should be aware that any adaptation to the standard testing regime must meet the conditions set out in REACH (Annex XI or in column 2 of Annexes VII to X). Every justification that supports waiving for testing of a specific endpoint must be scientifically justified by the registrant. Clear and robust justifications are needed for the regulator to independently assess their validity. Poor quality or minimalistic justifications will lead to follow-up action from ECHA or Member States in cases where the safe use of a substance may be compromised. More detailed feedback based on the ECHA's experience with such justifications can be found in the *Evaluation under REACH - Progress Report*.

### 3.5. Additional scientific or technical approaches to avoiding unnecessary new testing on animals

The standard REACH information requirements can be found in column 1 of the tables in Annexes VII to X.

In column 2 of Annexes VII to X there are rules for 'adapting' the standard tests specified in column 1; these rules outline the circumstances in which a particular animal test does not have to be conducted or can be deferred to a higher tonnage level. Therefore, it is of the utmost importance for registrants to check these rules and the associated detailed *Guidance on Information Requirements and Chemical Safety Assessment*. Examples of the adaptation rules for animal studies are presented in the table below to illustrate the possibilities for avoiding or deferring animal testing.

**Table 1:** Specific rules for adapting the standard REACH information requirements in column 1 Annexes VII to X are in column 2 – examples

<b>Opportunities to adapt tests - Annex VII (1 to 10 tonnes/annum)</b>	
Column 1 STANDARD INFORMATION REQUIRED	Column 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
<p>Skin sensitisation (Section 8.3.)</p> <p>The assessment of this endpoint shall comprise the following consecutive steps: (1) an assessment of the available human, animal and alternative data, (2) <i>In vivo</i> testing.</p>	<p>Step 2 does not need to be conducted if:</p> <ul style="list-style-type: none"> <li>– the available information indicates that the substance should be classified for skin sensitisation or corrosivity, or</li> <li>– the substance is a strong acid (<math>\text{pH} \leq 2,0</math>) or base (<math>\text{pH} \geq 11.5</math>), or</li> <li>– the substance is flammable in air at room temperature.</li> </ul>
<b>Opportunities to adapt tests - Annex VIII (10 to 100 tonnes/annum)</b>	
<p>Skin irritation (Section 8.1.1.)</p>	<p>The study does not need to be conducted if:</p> <ul style="list-style-type: none"> <li>– the available information indicates that the criteria are met for classification as corrosive to the skin or irritating to eyes, or</li> <li>– the substance is a strong acid or base, or</li> <li>– the substance is flammable in air at room temperature, or</li> <li>– the substance is classified as very toxic in contact with skin, or</li> <li>– an acute toxicity study by the dermal route does not indicate skin irritation up to the limit dose level (2 000 mg/kg body weight).</li> </ul> <p>[To note that now it is now possible to conduct skin irritation testing <i>in vitro</i>, EU Test Method B.46 (see Regulation (EC) No 440/2008, as amended). Both positive and negative findings are acceptable. ]</p>
<b>Opportunities to adapt tests - Annex IX (100 to 1000 tonnes/annum)</b>	
<p>Reproductive study (Section 8.7.)</p> <p>Screening for reproductive/developmental toxicity, one species (OECD 421 or 422), if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from <i>in vitro</i> methods that the substance may be a developmental toxicant.</p>	<p>The studies do not need to be conducted if:</p> <ul style="list-style-type: none"> <li>– the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or</li> <li>– the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or</li> <li>– the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.</li> <li>– If a substance is known to have an adverse effect on</li> </ul>

	<p>fertility, meeting the criteria for classification as Repr Cat 1 or 2: R60, and the available data are adequate to support a robust risk assessment, then no further testing for fertility will be necessary. However, testing for development toxicity must be considered.</p> <ul style="list-style-type: none"> <li>- If a substance is known to cause developmental toxicity, meeting the criteria for classification as Repr Cat 1 or 2: R61, and the available data are adequate to support a robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered.</li> </ul> <p>[Please note that the requirement for a two-generation reproductive toxicity study (Section 8.7.3.; OECD TG 416) is a standard information requirement at 100 tonnes/annum (Annex IX) if adverse effects on the reproductive tissues are observed in the available repeated dose studies. Where no such adverse effects are observed, the 2-generation study would only need to be conducted if the tonnage reached 1000+ tonnes/annum (Annex X).]</p>
<b>Opportunities to adapt tests - Annexes IX and X (100 to1000 and 1000+ tonnes/annum)</b>	
<p>Bioaccumulation in aquatic species, preferably fish (Section 9.3.2.)</p>	<p>Need not be proposed if the substance has a low potential for bioaccumulation (for instance a log Kow &lt; 3) and/or a low potential to cross biological membranes; or</p> <ul style="list-style-type: none"> <li>- direct and indirect exposure of the aquatic compartment is unlikely</li> </ul>

## 4. ANIMAL WELFARE

Where animal tests prove essential, the legislation requires that the minimum of distress and suffering be caused to the animals. Article 13(4) of REACH stipulates that toxicological and ecotoxicological tests shall be carried out in compliance with EU Directive 86/609/EEC on animal protection. This Directive sets out the basic requirements for the care and accommodation of laboratory animals, and stipulates that experiments shall be designed to avoid distress and unnecessary pain and suffering to the animal. Furthermore, when new animal testing is necessary, where possible, scientifically sound approaches to the implementation of the 3Rs (reduction, refinement or replacement of animal use) which are already stipulated under the REACH Regulation, should be used.

## 5. WHAT HAPPENS AFTER SUBMISSION OF A REGISTRATION DOSSIER?

### 5.1. Technical completeness check

All registration dossiers submitted to ECHA will undergo an automatic technical completeness check (TCC), followed by a manual verification of any further information to be requested in the case of TCC failure. This corresponds to the check that the potential registrant himself can conduct in advance of finalising and submitting the registration dossier by use of the TCC IUCLID plug-in. The purpose of the TCC is to check that all the elements required have been provided (i.e. that the relevant fields in the IUCLID dossier have been filled in) and that the fee has been paid. The quality or adequacy of any data or justifications for adapting the information requirements will not be checked at this stage.

If the registration dossier is deemed to be technically complete, ECHA will assign a registration number to the substance and inform the registrant, once the corresponding fee has been paid. Having received the registration number, the registrant can start or continue the manufacture or import of the registered substance.

If the registration dossier does not pass the first technical completeness check, the registrant will be informed about what additional information is needed and requested to complete the dossier within a reasonable deadline. If submitted within the deadline set, ECHA will conduct a further technical completeness check, but if the dossier still fails the registration will be rejected and the fee forfeited.

### 5.2. Examination of testing proposals

Registrants have to submit a testing proposal prior to undertaking testing for obtaining information as defined in REACH Annexes IX and X. The testing proposal is submitted with the registration dossier, in which the need for the test is justified. When a testing proposal concerns a study involving vertebrate animals, ECHA publishes the name of the substance (which in some cases can be a partial name to preserve trade secrets for the full chemical structure) and the hazard endpoints for which testing is proposed

inviting third parties to submit scientifically valid information and studies that address the relevant substance and hazard endpoint. This public consultation is a call for data, i.e. the specific studies on the substance that might already have been conducted or relevant information on close chemical analogues that can be read-across and used instead of new studies being carried out. Data submitters are invited to include a scientific justification to support their data. Following the end of the consultation period, ECHA will draft one of the following decisions: a decision accepting the testing proposal, a decision accepting the testing proposal with modified conditions (e.g. test species, route of exposure), a decision rejecting the testing proposal, or a decision accepting (with or without modified conditions) or rejecting the testing proposal but requiring one or more additional tests to be carried out. These draft decisions can also be made if several registrants or downstream users have submitted proposals for the same test. In preparing the draft decision ECHA will take into account all information contained in the registration dossier as well any scientifically-valid information obtained from the public call for data. It may be that ECHA has to add extra vertebrate animal studies to the testing proposal if the registrant has omitted Annex IX or X endpoints without fulfilling the specific rules for adaptation including an adequate scientific justification. Hence, it is advisable to provide adequate explanations in the registration dossier as to how all the higher-tier endpoints are to be addressed. The decision of ECHA involves the consultation of the registrant who submitted the testing proposal, the Member State competent authorities and, if necessary, ECHA's Member State Committee (MSC). If the MSC does not reach a unanimous agreement, ECHA refers the draft decision to the European Commission which takes the final decision after further consultation with the Member States. This procedure was established to ensure that the best possible use is made of existing information, and that animal testing is required only when there is broad consensus that such testing is indeed necessary.

### 5.3. Compliance check of a registration dossier

ECHA checks at least 5% of all registration dossiers received within each tonnage band for compliance with the information requirements of REACH. In contrast to the technical completeness check, this means that the quality and adequacy of data is assessed. If ECHA considers that the dossier is not in compliance with the information requirements, ECHA will draft a decision requiring the registrant to submit the missing information, which may be studies, including those to be conducted on vertebrate animals.

Part of the compliance check is making sure that the hazard information provided complies with the requirements of REACH. If the information requirements specified in REACH Annexes VII to X have been adapted, ECHA checks the scientific validity of the adaptation justifications. If, for example, the information required has been provided by use of alternative methods, the documentation for their use will be evaluated in accordance with the basic preconditions and specifications provided in REACH Annex XI and explained in the *Guidance on information requirements and chemical safety assessment*. In any case, it is up to the registrant to justify that alternative data are adequate for the purpose of classification & labelling and/or for risk assessment.

## 6. SUMMARY

The present practical guide can be summarised with a few key messages to potential registrants:

- A. Follow the “4 steps” for fulfilling information requirements:
  - 1. Gather and share existing information
  - 2. Consider the information needs
  - 3. Identify information gaps
  - 4. Generate new data or propose a testing strategy
- B. Share data with other potential registrants (in SIEFs for phase-in substances) or previous registrants.
- C. Document that the formal preconditions for the use of alternative data are fulfilled, including that they have been obtained with validated methods and that the results are adequate for classification and labelling and/or risk assessment.
- D. Note that the quality and adequacy of information are not evaluated before a registration number is assigned; however if ECHA identifies inadequate data the missing information will be requested from the registrant.

This practical guide should enable you to avoid unnecessary animal testing and to consider the use of alternatives to animal testing in order to comply with REACH. You may also want to consult the *Guidance on information requirements and chemical safety assessment Volume 3: Collection, evaluation, adaptation and generation of information (contains chapters R2, R3, R4, R5, and R6)*. The full guidance document provides more detailed examples and explanations of the concepts introduced here.

## 7. FURTHER INFORMATION

### Legal texts:

#### REACH Legislation

[http://echa.europa.eu/legislation/reach\\_legislation\\_en.asp](http://echa.europa.eu/legislation/reach_legislation_en.asp)

#### CLP Regulation

[http://echa.europa.eu/legislation/classification\\_legislation\\_en.asp](http://echa.europa.eu/legislation/classification_legislation_en.asp)

### Guidance:

#### Guidance on Information Requirements and Chemical Safety Assessment PATHFINDER

[http://guidance.echa.europa.eu/docs/guidance\\_document/information\\_requirements\\_en.htm?time=1270642981](http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm?time=1270642981)

#### Guidance on registration

[http://guidance.echa.europa.eu/docs/guidance\\_document/registration\\_en.pdf?vers=09\\_11\\_09](http://guidance.echa.europa.eu/docs/guidance_document/registration_en.pdf?vers=09_11_09)

#### Guidance for identification and naming of substances under REACH

[http://guidance.echa.europa.eu/docs/guidance\\_document/substance\\_id\\_en.pdf](http://guidance.echa.europa.eu/docs/guidance_document/substance_id_en.pdf)

#### Guidance on data sharing

[http://guidance.echa.europa.eu/docs/guidance\\_document/data\\_sharing\\_en.pdf](http://guidance.echa.europa.eu/docs/guidance_document/data_sharing_en.pdf)

#### Guidance on the Application of the CLP Criteria

[http://guidance.echa.europa.eu/docs/guidance\\_document/clp\\_en.pdf](http://guidance.echa.europa.eu/docs/guidance_document/clp_en.pdf)

### Practical Guides:

#### Practical guide 1. How to report *in vitro* data

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_in\\_vitro\\_data.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_in_vitro_data.pdf)

#### Practical guide 2. How to report weight of evidence

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_weight\\_of\\_evidence.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_weight_of_evidence.pdf)

#### Practical guide 3. How to report robust study summaries

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_robust\\_study\\_summaries.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_robust_study_summaries.pdf)

#### Practical guide 4. How to report data waiving

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_data\\_waiving.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_data_waiving.pdf)

#### Practical guide 5. How to report (Q)SARs

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_qsars.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_qsars.pdf)

#### Practical guide 6. How to report read-across and categories

[http://echa.europa.eu/doc/publications/practical\\_guides/pg\\_report\\_readacross\\_categ.pdf](http://echa.europa.eu/doc/publications/practical_guides/pg_report_readacross_categ.pdf)

### Technical manuals:

#### REACH-IT Supporting Documents

[http://echa.europa.eu/reachit/supp\\_docs\\_en.asp](http://echa.europa.eu/reachit/supp_docs_en.asp)

#### IUCLID 5

<http://iuclid.echa.europa.eu/index.php?fuseaction=home.documentation&type=public>

### Other:

#### Evaluation progress report 2009

[http://echa.europa.eu/doc/progress\\_report\\_2009.pdf](http://echa.europa.eu/doc/progress_report_2009.pdf)

#### European Centre for the Validation of Alternative Methods (ECVAM)

<http://ecvam.jrc.it/>

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