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Practical guide for SME managers and REACH coordinators

How to fulfil your information requirements at tonnages 1-10 and 10-100 tonnes per year

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Practical guide for SME managers and REACH coordinators – How to fulfil your information requirements at tonnages 1-10 and 10-100 tonnes per year

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Table of Contents

LIST OF FIGURES

LIST OF TABLES

1. Introduction

This Practical Guide is intended for people responsible for gathering all information needed to compile a technical dossier for a substance to be registered under the REACH Regulation. It is not an exhaustive guidance for experts or consultants, but it is aimed at business managers or REACH coordinators, mainly in small and medium-sized enterprises (status of SMEs).

This Guide is on **information requirements**, *i.e.* on what information is needed in the registration dossier. It will focus on the following aspects for each required element:

- What is it/what does it mean?
- Why is it relevant/what is influenced by it?
- When is it needed?
    - Not all elements are needed in every dossier.
- Who can do it?
    - Many elements require an expert to gather and evaluate the information to draw conclusions, but some elements may be done by non-experts.
- How can the information be gathered?
    - A brief indication of relevant methods with links to further information.
- How much time does it take?
    - Some information needs to be created, e.g. through a test; this can take substantial time.

For many activities in the preparation of a registration dossier, you will need expert help. To show the level of expertise needed for specific activities, a colour coding scheme is used in this Guide.

If only administrative expertise is needed, *i.e.* if you do not have to be an expert in a specific scientific field, this will be indicated by the words **administrative expertise**.

The words **scientific expertise** indicate that a certain level of scientific expertise in the relevant field is needed. A junior scientist with relatively limited experience should be able to do this activity.

In cases where you need an experienced, more senior scientist to do an activity properly, this is indicated by the words **advanced scientific expertise**. Generally, if you are an SME, the (advanced) scientific expertise may need to be hired from outside, e.g. from a contract research organisation or a consultant.

Throughout the Guide, you will find important messages and tips in boxes, similar to this one.

2. Seven phases to registration in REACH

This Guide is produced as part of ECHA's REACH 2018 Roadmap, which was published in January 2015 and documents the Agency's commitment to critically review the REACH registration process from start to finish and to enhance the process, support and documentation.

The aim of actions is to more effectively support inexperienced and SME companies with their obligations for the last registration deadline of existing substances that have been pre-registered: the deadline is 31 May 2018. The content of the Guide is also relevant for registrations regardless of their deadline.

> To stay on the market after 2018, you need to register the substances you manufacture or import in quantities of more than one tonne per year and less than 100 tonnes per year by **31 May 2018**.
>
> If you manufacture or import a substance in quantities above 100 tonnes per year, you need to register immediately as you will be in breach of legislation.

In the REACH 2018 Roadmap, the process of registration has been split into seven phases to make them easier to follow. For each phase, the support material is organised in three layers: 'Getting started' for all interested, 'Essential reading' for the responsible managing person, and 'Going deeper' for the expert performing the work. The seven phases of registration are:

1. Know your portfolio.
2. Find your co-registrants.
3. Get organised with your co-registrants.
4. Assess hazard and risk.
5. Prepare your registration as a IUCLID dossier.
6. Submit your registration dossier.
7. Keep your registration up-to-date.

This Practical Guide focuses on phase 4 of the process. Phases 1 to 3 are briefly discussed, because they are critical to the success of phase 4.

> All the phases are explained at the ECHA 'REACH 2018' web pages. Then, click on <Where do I start?>

Phase 1: you have to know what substances are part of your product portfolio and make a decision on whether you need to register them. Each substance is registered separately. If you are reading this Practical Guide, you most likely know or anticipate that you will register at least one substance. You can find more help on whether you need to register.

Many existing substances on the market in the European Union are considered to be 'phase-in substances'. Manufacturers and importers of phase-in substances profit from specific transition periods for registration in the REACH Regulation. You can find the criteria for deciding whether your substance is a phase-in substance in Section 2.3.1 of the *Guidance on Registration*.

If you intend to register a phase-in substance, you have either already pre-registered it, or you still need to do a late pre-registration. A late pre-registration is only possible if you started

manufacturing or importing the phase-in substance after 1 December 2008 and you need to do this late pre-registration within six months after exceeding the one tonne per year threshold and no later than 31 May 2017.

If you need to register a substance that you did not pre-register or if you missed the deadlines for (late) pre-registration, you have to submit an inquiry (through REACH-IT) to ECHA before manufacturing your substance or placing it on the market.

You can find more information on how to submit a pre-registration through the central IT system, REACH-IT, including how to sign up for the system.

> REACH-IT is the central IT system you have to use to submit a registration dossier.

Phase 2: independent of whether you intend to register a phase-in substance or a non phase-in substance, you have to cooperate with other (potential) registrants of the same substance. A basic principle of REACH is 'one substance, one registration'.

The pre-registration and inquiry processes help you to find (potential) co-registrants through the 'pre-SIEF' and 'Co-registrants' pages of REACH-IT. A SIEF is a substance information exchange forum that helps you and your co-registrants to organise the work and to share information. It is formed when co-registrants have agreed that their substance is indeed the same, based on detailed considerations on the substance identity. If a SIEF already exists for your substance, you have to join that SIEF.

Once a SIEF is formed, the co-registrants have to start to cooperate and decide who will take the lead in the registration and how every company will contribute. Industry associations and consultants can help you with organising the cooperation within the SIEF. For example, some industry associations have created standard agreement documents. Some consultants specialise in administrative support to the cooperation of registrants.

> Ensure proper identification of your substance, and comparison with the substances of your (pre-)SIEF members as soon as possible. This way you will avoid difficulties if you find out late that substances are not the same and need their own separate registration.

Phase 3: data sharing is an important principle of the REACH Regulation. However, information that are sensitive in relation to competition law, such as information on market behaviour, production capacities, production, sales or import volumes, market shares, product prices and similar information must not be exchanged.

> You must share information involving tests on vertebrate animals. You are encouraged to also share other information on intrinsic properties of substances as well as general information on uses and use conditions with (pre-)SIEF members and co-registrants.

You have to reach an agreement with your SIEF members or co-registrants on how to share information and the costs of data as well as the costs of administrating the SIEF and other joint activities: this is a joint responsibility for all. The costs of registration need to be shared in a fair, transparent and non-discriminatory way, and you have to make every effort to reach an agreement.

> You only pay for the information and the management of the SIEF that directly relates to your own registration. You have the right to know the basis for the costs you pay.

More information about data-sharing and related disputes is provided by ECHA.

The main objective of the REACH Regulation is to ensure a high level of protection for humans and the environment. Therefore, the properties of substances and their risks to humans and the environment need to be assessed (phase 4 of the process). This includes gathering, evaluating and reporting information by the SIEF, on:

- Uses of the substance and conditions of use in the whole supply chain;
- Properties of the substance; according to requirements that are triggered by the volume manufactured/imported per year. If all the information are not yet available, you have a data gap, and you will either have to generate new data or propose a testing strategy;
- Classification and labelling, based on the properties of the substance;
- Carrying out a chemical safety assessment and recording it in a chemical safety report, if the volume manufactured/imported per year is higher than 10 tonnes per year.

When all necessary information have been gathered and assessed, the dossier creation is done with the IT tool IUCLID (International Uniform Chemical Information Database). Dossier submission is done through REACH-IT. Manuals on preparing REACH dossiers are available at: http://echa.europa.eu/manuals.

If you work on a joint registration, the lead registrant will have to submit the lead registration dossier first, and will if the submission was successful, provide the co-registrants with a token that is needed to submit the member registration dossier.

> The lead registrant is advised to submit their registration dossier well before 31 March 2018 to ensure that co-registrants are able to submit their registration dossier before the deadline of 31 May 2018.

After you have registered your substance, your obligations under the REACH Regulation continue. You have to keep your registration up-to-date.

2.1 Key messages

Take note of the key messages below when preparing your registration dossier.

> Good quality dossiers are required. This is a common obligation for all co-registrants.

All conclusions in your dossier need to be supported by sufficient, relevant, appropriate and adequate information. Check the 'Support' pages of the ECHA website, to find guidance on what good quality information is: http://echa.europa.eu/support.

> Animal testing is **the last** option.

One of the goals of the REACH Regulation is to promote the use of alternative methods to reduce the number of tests on animals. Therefore, you have to consider the possibilities of using alternative methods. If you are not able to gather sufficient reliable data through alternative methods, you may perform a test on animals. Check the Practical Guides on "How to use alternatives to animal testing"" and on "How to use and report (Q)SARs" available at: http://echa.europa.eu/practical-guides.

Data sharing is **compulsory** for information involving tests on vertebrate animals to avoid unnecessarily duplicating (animal) tests.

Co-registrants have to share relevant data involving tests on vertebrate animals to ensure that any duplication of testing is avoided, and to save time and costs. Of course, an appropriate cost-sharing mechanism should be agreed.

If you decide to use alternative methods instead of standard methods listed in the REACH annexes, you need to scientifically justify this choice in your registration dossier and keep a record of it.

To provide equivalent information than the test required, the use of already existing information on your substance or from (an)other, very similar, (group of) substance(s) (which is called 'read-across' or 'category approach') may be adequate.

Other methods exist such as computer calculations (sometimes called *in silico* or 'quantitative structure activity relationships' ((Q)SARs) and testing on cultured cells (called *in vitro* methods). Lately, annexes to REACH were amended, making non-animal test methods the default for more information, if the level of information provided by an *in vitro* method is equivalent to that of an *in vivo* method and if it is, at least, sufficient to draw a conclusion on the classification.

When using alternative methods to fulfil your requirements, you will need to adequately justify their use, interpret the results, and provide proper documentation supporting the validity and applicability of the methods used.

Check the Practical Guides on "How to use alternatives to animal testing" and "How to use and report (Q)SARs": http://echa.europa.eu/practical-guides, for more instructions and assess how certain information can be used in alternative approaches.

QSAR Toolbox can help you to fill data gaps for (eco)toxicity data needed to assess the hazards of chemicals.

Read-across and category/grouping approach is explained also at:
http://echa.europa.eu/support/grouping-of-substances-and-read-across

Start in time with gathering data to allow preparation of the dossier well before the deadline.

Gathering, analysing and reporting all the necessary information is very time consuming. The more information you need to gather, the earlier you need to start. You also need to reserve additional time for reaching agreement with your co-registrants, finding and contracting a research laboratory, and discussing and concluding on the results after the information is gathered. This Practical Guide will provide you with some rough estimates of time in the appropriate sections.

You have to consider that **the whole process** of deciding what information needs to be gathered, how, when, where, by whom, and the process of discussing and coming to conclusions can also take quite some time.

2.2 Information to be gathered

You need to gather five main types of information for your registration dossier:

1. Substance identification information.
2. Physical and chemical characteristics.
3. Environmental properties.
4. Human health properties.
5. Use and conditions of use of the substance.

In a joint registration, the lead registration dossier should describe the composition of the substance in such a way that all variations within the composition of single registrants are covered by the profile in the lead registration dossier. Such a profile is called a 'substance identification profile'. In each single registration dossier, the composition of the single substance should cover all day-to-day variation in the exact composition of the substance.

Note that a 'substance' is not the same as 'a single chemical component'. A substance as defined in REACH can consist of one or more chemical components, usually called 'constituents'. A substance can have one main constituent, a mono-constituent substance, and may still contain impurities or additives. A substance can also consist of several constituents, a multi-constituent substance. A substance can also have many constituents of (largely) unknown composition and ratio, 'substances of unknown or variable composition, complex reaction products or biological materials' (UVCBs).

Chapter 3 will describe the information requirements for substance identification. You need to gather sufficient information to unambiguously identify your substance, and to ensure that a joint registration is indeed for one and the same substance.

The conditions of manufacturing, the use of the substance and the conditions of use influence in how far a substance is emitted into the environment and in how far humans can get into contact with the substance. This, together with the characteristics and properties of the substance, determines whether there is a risk of negative effects to humans or the environment.

Physical and chemical characteristics influence both the fate and properties in the environment and the human health properties of the substances.

This Practical Guide for SMEs explains how the various characteristics and properties of substances influence each other and how the information is used to further assess the hazards and risks of a substance.

The amount of information you need to gather depends on the tonnage you manufacture and/or import (officially: per 'legal entity'). Annex VI to the REACH Regulation describes four steps you need to follow to fulfil the requirements, valid for each information described in Annexes VII to X:

1. Gather and share existing information.
2. Consider information needs.
3. Identify information gaps.
4. Generate new data/propose testing strategy.

Step 1: The use of information on some chemical and physical characteristics from handbooks is quite common and can be accepted if there are sufficient independent sources of information.

Consider the information published in literature: they have to be of appropriate quality to be used and sufficient detail is needed to assess their usefulness.

Registrants must be in legitimate possession or have permission to refer to data they use in their registration dossier. Publicly available data may be subject to copyright and/or other relevant data protection provisions. If it is not clear that publicly available data can be used freely, it is recommended to contact the owner or publisher to obtain a Letter of Access that will allow you to use the data.

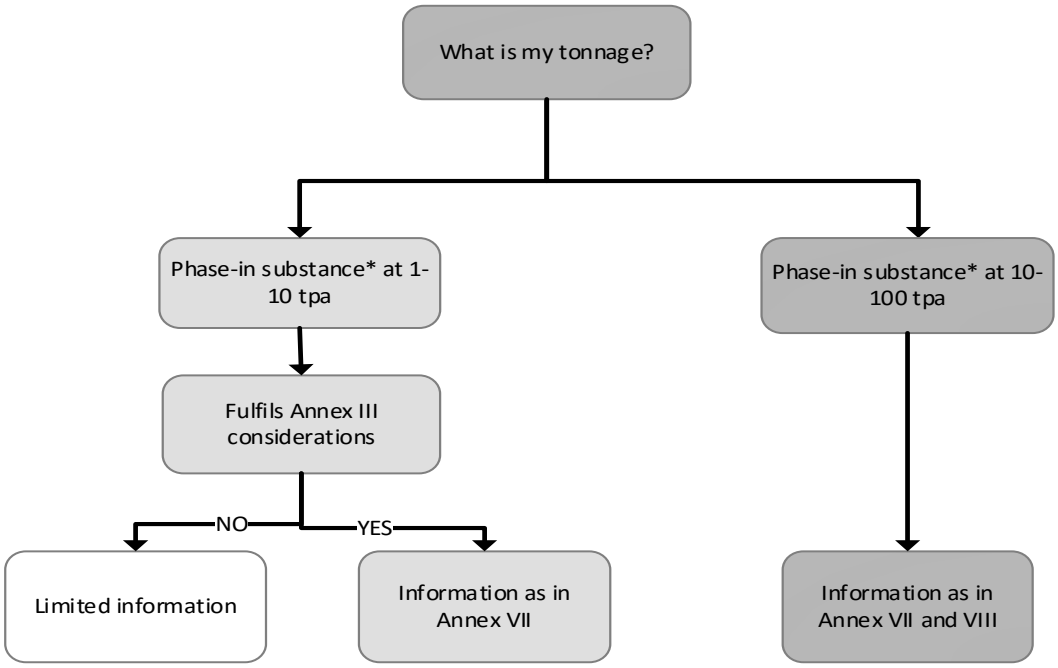
Step 2: you must review Annex VII to REACH for the information needed for your substances manufactured or imported from 1 to 10 tonnes per year, and in addition, Annex VIII for the information required for your substances from 10 to 100 tonnes per year.

Note that substances at a low tonnage (1-10 tonnes per year), known or predicted to be of low risk (according to the considerations in Annex III) can be registered with less information: only the dataset of information on physical and chemical characteristics is obligatory and needs to be gathered, if not yet available. In addition, you should submit any already available information on the (lack of) effects of the substance on humans and the environment, but no new information are required.

For more information, check: http://echa.europa.eu/support/registration/reduced-information-requirements, including the published inventory of substances (ECHA's Annex III inventory).

Figure 1 explains how to decide which information needs to be provided in the registration dossier depending on the tonnage manufactured or imported per year.

Figure 1: Decision scheme on the requirements for substances manufactured or imported in 1-100 tonnes per year (tpa)



* A phase-in substance is a substance that you already manufactured or imported in a specific timeframe before REACH came into force, and that you pre-registered. See the glossary. For non-phase-in substances, Annex III cannot be used.

Information on certain properties may in some cases be omitted: this is called 'data waiving', and is described in Column 2 of the REACH Annexes (VII to X) providing specific rules to follow. For example, a boiling point test is not needed for gases or for substances that decompose before boiling. Information also do not need to be provided if a test is technically not possible.

Step 3: The result of the gathering and assessment of available information may mean that your substance needs to be further studied. You need to identify all information gaps and decide by which means to fulfil the information requirement (alternative methods, data

waiving, or a standard test.

Step 4: Note that if you need to generate a test which is normally only required for substances produced or imported in high volumes (and listed in Annexes IX and X to REACH), you cannot perform the test straightaway. For example, if your substance is poorly water soluble, instead of the standard requirement for short-term toxicity testing on fish in Annex VIII, the long-term toxicity testing on fish, as required in Annex IX, should be considered.

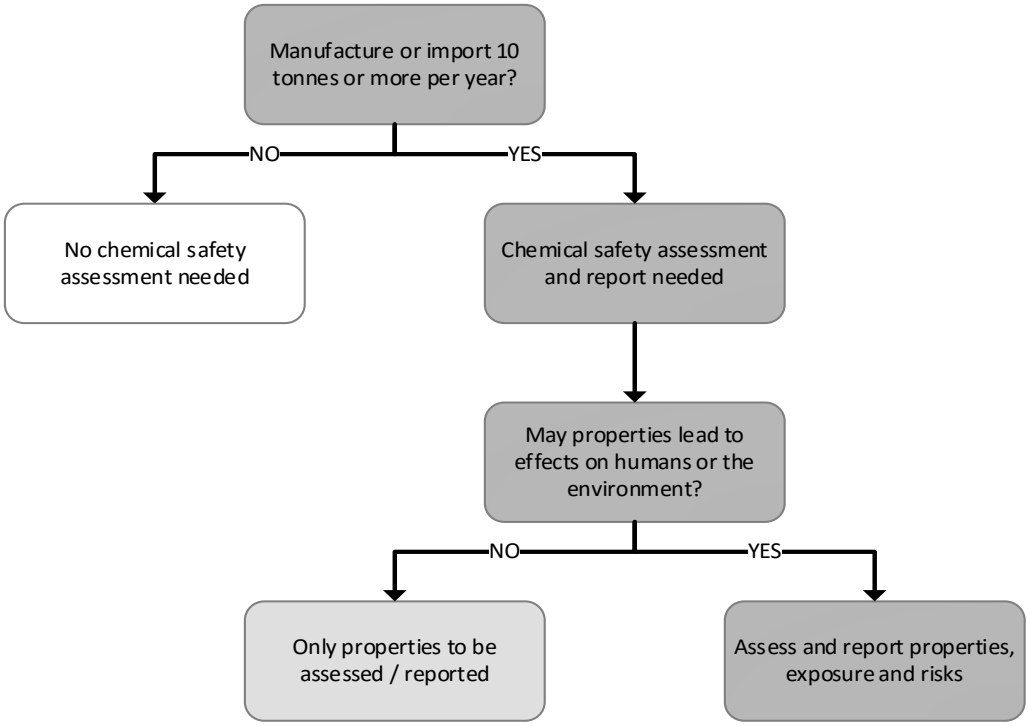
You first have to submit a testing proposal to ECHA. Only after approval of the testing proposal, can you and the co-registrants perform the test.

More guidance on how to submit a testing proposal to ECHA is available in the Manual on "How to prepare registration and PPORD dossiers" (9.7.4. Examples of completing endpoint study records).

Finally, if you manufacture or import 10 tonnes or more per year of a substance, you have to perform a chemical safety assessment and produce a chemical safety report in which you will assess and report the physical and chemical characteristics, the human health and the environmental properties of your substance.

An assessment of concentrations in the environment and the level and duration of contact of humans with the substance as well as a characterisation of the resulting risks can also be required, depending on the properties of the substance. In addition, exposure scenarios indicating conditions of safe use for an identified use or group of uses may need to be generated. The relevant exposure scenarios need to be attached to the safety data sheets delivered to your customers.

Figure 2: Decision scheme for the requirements for chemical safety assessment.



2.3 Use appropriate tests

Where results from tests, either already available or newly performed, are used to fulfil information requirements, it is very important that:

1. Appropriate test methods are used, and
2. Tests are relevant for your substance.

In this guide, we provide you with references to the appropriate test methods relevant for each piece of information.

Ensure that you identify your substance as precisely as possible and that test materials are representative of your substance, as the tested material should fit the same substance identification profile as the registered substance.

If the composition of the tested material is different from the composition of your substance, you have to carefully consider whether you should use the test results in your registration, as this will depend on qualitative and quantitative variations.

A relatively high concentration of an impurity can influence the properties of the substance, while the same impurity in very low concentrations will not influence the test results. It is therefore critical to confirm if an impurity of the test material is present in the substance you register.

The ultimate aim of gathering all the required information is to ensure appropriate protection of humans (workers and the general population) and of the environment. You will do that by classifying and labelling your substance correctly and by attaching the exposure scenarios (if needed) to the safety data sheets.

3. Requirements for substance identity

3.1 What is it?

A substance can be a chemical that is made by a manufacturing process, generated from waste, or that exists in nature. A substance does not necessarily contain just one constituent, but can also be made up of more constituents. There are three types of substances: mono-constituent, multi-constituent and UVCBs.

Table 1: Name of substance – examples for mono-constituent

Substance types	
Type	**Description**
Mono-constituent	Your substance contains at least 80 % of one main constituent. There can also be unintentional constituents present in your substance; these constituents are the results of side reactions, they are called impurities and their amount is below 20 %.
Multi-constituent	Your substance contains more than one main constituent, and each main constituent is present between 10 % and 80 %. There can also be unintentional constituents present in your substance; these constituents are the results of side reactions, they are called impurities and their amount is below 10 %.
UVCB	Your substance is a UVCB (*unknown or variable composition, complex reaction product or biological material*) substance if it contains a high number of constituents in varying, and often not well-known amounts. It is made from a manufacturing process that may consist of several steps, or it is obtained from a biological source, such as a plant material or an animal material.

A multi-constituent substance should not be confused with a mixture:

- a multi-constituent substance is formed as a result of a chemical reaction during the manufacturing process.

- a mixture is formed by blending two or more chemicals. Blending is not considered a chemical process, but a physical process.

3.2 Why should it be determined?

Knowing your substance in a REACH sense is very important because that will help you to find the correct SIEF. According to the REACH Regulation, a 'substance' can consist of one single constituent or several different constituents. The substance identity is therefore based on information about the constituents and their amount. The concentration of each constituent in a substance is important and must be determined. If the substance is not correctly identified, the data used in the registration dossier may not fit the substance and errors may be made in the conclusions on how to handle the substance. All information in the registration dossier should be relevant for the identified substance and therefore the correct identification is critical.

If your substance differs in composition from the substance of another company, it may still be registered as the same substance. For example, if the majority of constituents that define the substance are identical, but the difference is defined only by the presence or absence of a few constituents at low concentration, such as impurities, you and the other registrant still have the same substance. Also for a multi-constituent substance, a different ratio of the main

constituents in your substance and in the one of your co-registrants, does not mean that it is a different substance. However, the resulting properties of the two variants of the same substance may require a different classification for some hazard.

A UVCB from two co-registrants may still be registered as one substance if you can demonstrate that both co-registrants have the same 'structural depiction' (e.g. in relation to main types of constituents, such as aliphatic substances within a certain range of carbon atoms), the same source and the same manufacturing process. For example, a substance can be mainly formed by cracking and hydrotreatment (process) of a petroleum fraction (source) and consist mainly of Cx to Cy alkanes (structural depiction), where Cx and Cy represent different carbon chain lengths. Within such a substance, there can be substantial variation in composition, but for registration it is considered as one substance.

The substance that you will use for the tests described in the following chapters should be identical or very similar to the substance that is going to be registered. The type of information needed here is chemical analytical data, such as spectral data. Information on the source material and the production process may also be needed.

3.3 When should it be determined?

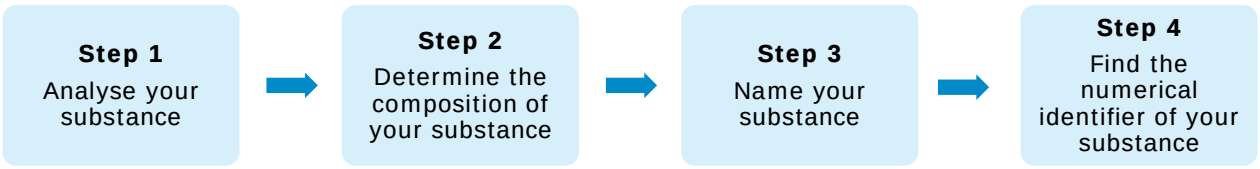
The identity of your substance needs to be determined before you register.

> The identity of your substance needs to be known before you can decide that your substance is the same as the substance of another (potential) registrant.

3.4 How should it be determined?

A stepwise approach for the determination of the identity of your substance is developed by ECHA. If you follow this approach, you will be able to successfully identify your substance.

Figure 3: Stepwise approach for determining substance identity



3.4.1 Analyse your substance

> The identity of a mono-constituent, multi-constituent or UVCB substance is confirmed with spectral data and other analytical information.

First, you will need to check if you already have the necessary spectral data and other analytical information available. It is possible you already have this information in your own records. If you import the substance, you can ask your supplier for the analytical information.

If you need to generate new spectral data and other analytical information, you need to select a representative sample of your substance. This analysis needs to be carried out by a competent person, but does not have to be carried out in compliance with the principles of Good Laboratory Practice (GLP). Therefore, some of them can be carried out by the registrant themselves (such as UV/Vis, IR, GC, HPLC – see Table 2). Other more complex tests or tests requiring expensive instrumentation (such as NMR, MS – see Table 2) might need to be subcontracted to a university lab or contract research organisation.

The spectral data and other analytical information should be of high quality and a full evaluation and interpretation of the analytical data will need to be included in the registration dossier.

For each substance you manufacture or import, you will need to confirm the chemical structure and the concentration of the constituents. Analytical methods to follow for organic and inorganic substances are provided in Table 2. If you have knowledge of other analytical methods that are suitable for identifying and quantifying your substance, you are allowed to use these other methods as well.

Table 2: Spectral data and analytical information

Recommended spectral data and analytical information	
Organic substance	**Inorganic substance**
Ultraviolet and visible absorption spectroscopy (UV/Vis) (OECD TG 101)	X-ray diffraction (XRD)
Infrared spectroscopy (IR)	X-ray fluorescence (XRF)
Nuclear magnetic resonance spectroscopy (NMR)	Atomic absorption spectroscopy (AAS)
Mass spectrometry (MS)	Inductively coupled plasma optical emission spectrometry (ICP-OES)
Gas chromatography (GC) or high-performance liquid chromatography (HPLC)	Ion chromatography (IC)
Any other method that is known to be suitable for identifying and quantifying your substance	

Spectral and analytical data need to be provided independently from the substance type (i.e. mono-, multi- and UVCB substances) unless it is technically not possible or does not appear scientifically necessary.

You need then to include a scientific justification for not providing the respective spectrum/ chromatogram method in the registration dossier. For example, for the identification of UVCB substances (obtained from petroleum), boiling range and carbon number in addition to the spectroscopic and analytical data are required.

You, as a manufacturer or importer, should be as complete as possible so ECHA can confirm the identity of your substance.

3.4.2 Determine the composition of your substance

The spectral data and other analytical information are used to make a representation of the composition of your substance, including the concentration of the constituents and its ranges.

The examples below show what the composition of a substance may look like (in reality each constituent/impurity A, B, C,…H would have its respective chemical name).

Mono-constituent		
Name	**Typical concentration (%)**	**Concentration range (%)**
Constituent A	85	80 – 90
Impurity B	12	9 – 15
Impurity C	2	1 – 3
Impurity D	1	0 – 2

Multi-constituent		
Name	**Typical concentration (%)**	**Concentration range (%)**
Constituent A	40	30 – 50
Constituent B	45	40 – 50
Impurity C	8	5 – 10
Impurity D	7	5 – 10

UVCB		
Name	**Typical concentration (%)**	**Concentration range (%)**
Constituent A	21	1 – 50
Constituent B	30	10 – 70
Constituent C	33	10 – 50
Constituent D	10	1 – 20
Constituent E	3.7	0 – 20
Constituent F	1	0 – 5
Constituent G	0.3	0 – 1
Constituent H	1	0 – 10

3.4.3 Name your substance

Based on the composition of your substance, you have to define the name for your substance. For each type of substance, there are different rules to follow when naming them.

Mono-constituent substances
A mono-constituent substance is named after its main constituent, and it is recommended to follow the IUPAC rules (**advanced scientific expertise** required).

Table 3: Name of substance – examples for mono-constituents

Name of substance – example for mono-constituent		
Name	**CAS number**	**EC number**
formaldehyde	50-00-0	200-001-8
o-xylene	95-47-6	202-422-2
sodium hydroxide	1310-73-2	215-185-5

Multi-constituent substances

A multi-constituent substance is named after its main constituents, by combining the IUPAC name of each main constituent. For example, for two main constituents, the name of the multi-constituent substance will then be 'Reaction mass of *[IUPAC name of constituent 1]* and *[IUPAC name of constituent 2]*'.

Table 4: Name of substance – examples for multi-constituents

Name of substance – example for multi-constituent		
Name	**CAS number**	**EC / List number**
Reaction mass of ethylbenzene and m-xylene and p-xylene	*Not available*	905-562-9
Reaction mass of cyclohexanol and cyclohexanone	*Not available*	906-627-4
Reaction mass of chromium hydroxide sulphate and sodium sulphate	*Not available*	914-129-3

UVCB substances

A UVCB substance is named after its starting materials (biological or non-biological) and the chemical process used to manufacture the UVCB substance.

Table 5: Name of substance – examples for UVCBs

Name of substance – example for UVCB		
Name	**CAS number**	**EC / List number**
Formaldehyde, oligomeric reaction products with phenol	9003-35-4	500-005-2
Reaction products of tall-oil fatty acids, diethanolamine and boric acid	*Not available*	400-160-5
Coriander, ext., acetylated	93571-77-8	297-403-9
Zeolite, cuboidal, crystalline, synthetic, non-fibrous	*Not available*	930-915-9

Defining the name of a UVCB substance can be (very) complicated and requires **advanced scientific expertise**.

For some UVCB substances, industry sector-specific substance identification guidance is available. You can check on ECHA's sector-specific support for substance identification web page. More general information can be found in ECHA's *Guidance for identification and naming of substances under REACH and CLP*.

3.4.4 Find the numerical identifier of your substance

To check if your substance already has an EC number or List number, you should consult the 'Search for Chemicals' tool on ECHA's website. It is possible that an inventory number, such as a CAS and/or EC/List number, is also available for your substance. If this number is available to you, for instance from a safety data sheet (SDS) you received from your supplier, you can also use this CAS and/or EC/List number for the description of your substance.

3.5 Expertise required

Administrative expertise	Based on the analytical information, the substance is completely identified and the information can be used directly as input in the registration dossier.
Scientific expertise	Analytical information are available for a mono- or multi-constituent substance, and there is a need to interpret the results and to conclude on the composition, name, numerical identifiers of the substance; There are no analytical information available to decide on the determination of the appropriate analysis, and further assessment of the substance identity is necessary.
Advanced scientific expertise	Analytical information are available for a UVCB (complex) substance, and there is a need to interpret the results and to conclude on the composition, name, and numerical identifiers of the substance.

3.6 Timelines

The different spectral data and analytical information of a substance can be obtained within one month. In addition, time should be reserved for finding a contract laboratory, making contractual arrangements and the preparation, packaging and delivery of test samples.

Although normally a test (or a test package) can start about four weeks after contractual agreement, this is largely dependent on the capacity of the available test laboratories.

Interpretation of the spectral data and analytical information, can be done in one day for a mono-constituent substance, or in up to a month for a complicated UVCB substance.

It should also be noted that contacting other registrants who (pre-)registered your substance can also take up to two months.

3.7 Additional tips

If your substance is already registered, you may find the name of the registrants in the 'Search for Chemicals' tool. Otherwise, you will need to check within REACH-IT on the pre-SIEF page), because you have to cooperate with them and share data to prevent unnecessary animal testing.

> It is very important to ensure that your substance is indeed the same as that of another (potential) registrant.

Besides the name, the identification and description of your substances should cover CAS and EC numbers, if available, all variations in relation to concentrations ranges of constituents, impurities and additives to compare these with those of various co-registrants.

To be able to do this, many SIEFs have created a substance identity profile (SIP), which describes the identification parameters (such as substance name, constituents, concentration ranges, spectral data to be used, etc.) and can be used to facilitate the agreement of substance sameness.

The composition determined by the various spectral and analytical data need to cover the same constituents. Their concentration ranges will also need to fit within the boundaries given by the SIP.

> As a result of determining the boundaries of the SIP, you may have to register the substance on your own. That means that you will have to obtain or generate all information by yourself.

4. Classification and labelling

4.1 What is it?

Classification and labelling (C&L) is the approach to clearly present to users of substances and chemical products what properties substances may have. If substances can do harm, this is called a hazard. The C&L is the result of the analysis of all potentially harmful properties of substances, related to human health, to the environment and to physicochemical properties. The general requirements for C&L are described in the CLP Regulation (EC) No 1272/2008).

As requested under REACH, the information requirements and analysis of all properties may lead you to review the classification and labelling for your substance and to draw conclusions as a part of preparing your registration dossier.

In addition, for some substances, European experts have already agreed on 'harmonised classification and labelling' for a number of hazards.

> You always have to apply the 'harmonised classification and labelling' in the registration dossier and communicate it in the safety data sheets of substances. Harmonised classification and labelling is listed in Annex VI to the CLP Regulation.
>
> You also have to analyse whether there may be additional hazards, requiring separate additional classification (self-classification).

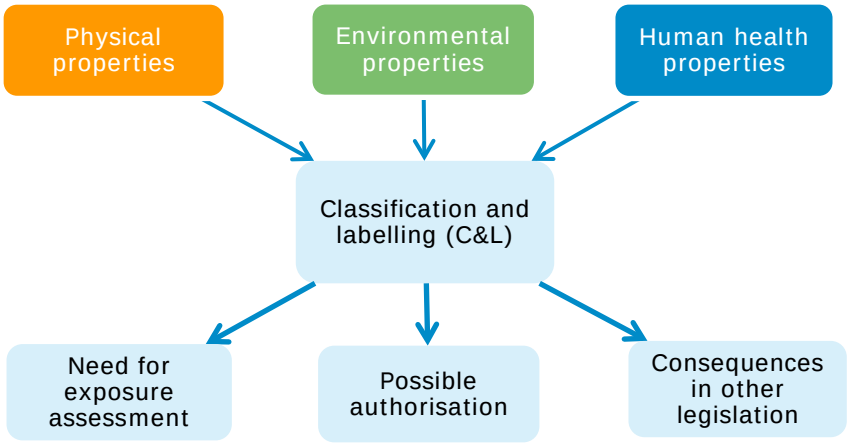
4.2 Why should it be determined?

You have to classify and label substances to ensure clear communication of the relevant properties of substances and products to those that come into contact with them.

This helps them to choose proper and safe methods of handling and controlling the substances and products.

The classification of a substance also influences the scope of the chemical safety assessment (see chapter 6) if your tonnage band registration is for 10 tonnes per year or more. The results of C&L also have an influence on the requirements in other pieces of legislation related to chemical substances. Figure 4 shows the relation between properties of substances and C&L and the consequences C&L may have within and outside the REACH Regulation.

Figure 4: Relationship between potentially harmful properties, C&L and consequences in REACH and other legislation

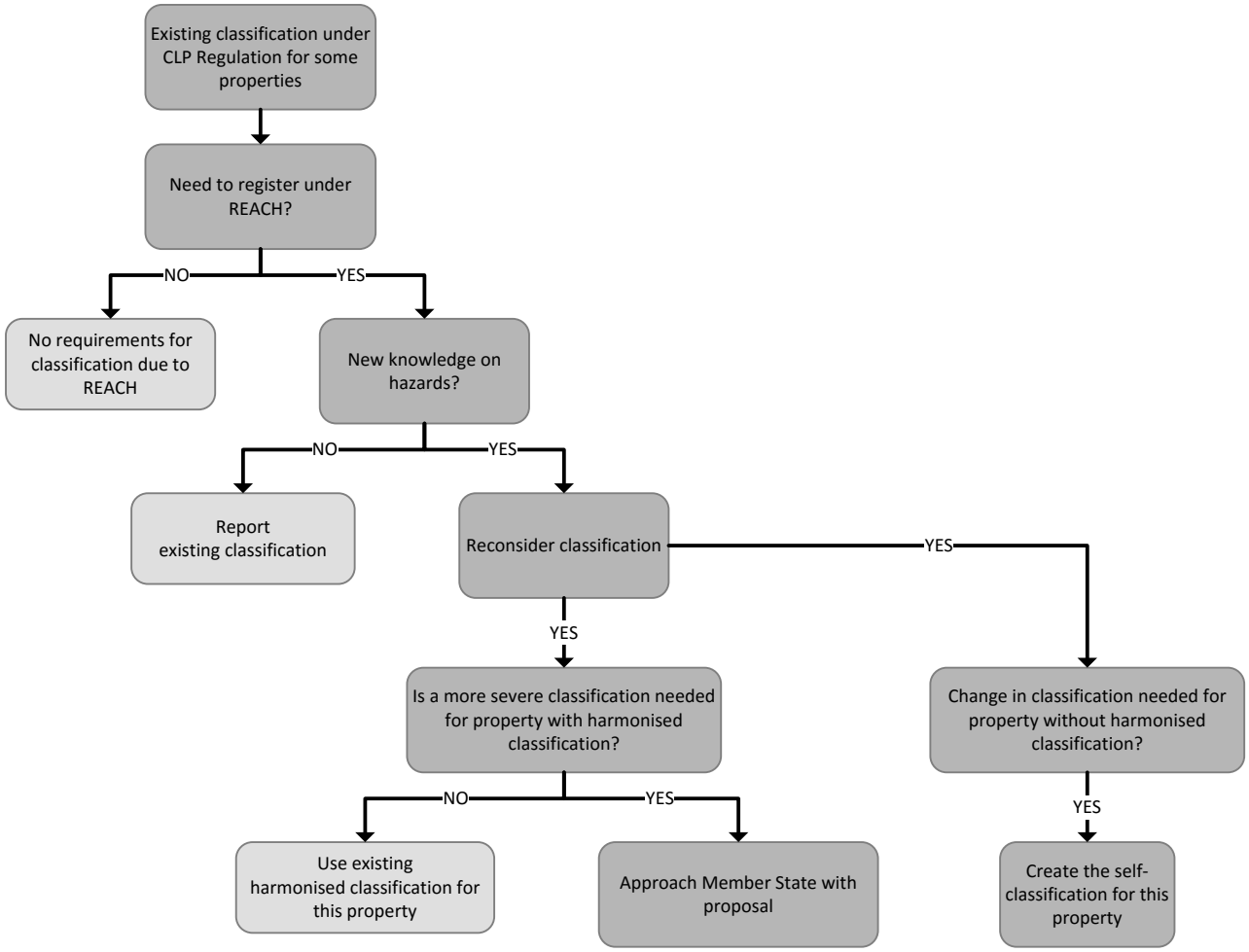


4.3 When should it be determined?

You should already have classified all substances that you put on the market (with some exemptions, as indicated in the CLP Regulation). Even if you do not need to register under REACH, you have to re-evaluate the properties of the substance, based on any new available data, and therefore you may need to reclassify the substance.

If there is a harmonised classification and labelling for a certain hazard, this is mandatory to follow and you should not self-classify for that hazard. If there is no harmonised classification and if you consider that your substance requires additional or more severe classification (Figure 5), you should update the self-classification in your registration dossier. If there is a harmonised classification and you think that this classification is not correct, you can approach a Member State competent authority with a proposal to reclassify the substance for that property. It is up to the Member State to decide whether or not to submit a formal proposal for reclassification to ECHA.

Figure 5: Decision scheme on revising an existing (self-)classification



4.4 How can it be determined?

You determine the classification of your substance based on the evaluation of the properties of the substance that you have established in accordance with the other chapters of this Guide. The criteria for classification are given in the CLP Regulation.

You can find more information on the CLP Regulation and the *Guidance on the application of the CLP criteria* on ECHA's website.

Expertise required

Administrative expertise	If clear results for one property are available.
Advanced scientific expertise	If classification needs to be based on several pieces of information or if the results of tests are not easily interpretable.

Timelines

LESS THAN 1 MONTH	• If there is no new information and the existing classification does not need to be reconsidered; • For properties with a clear test result.
UP TO 3 MONTH	• If you are the only registrant and if you need to obtain expert advice on unclear information for properties.
UP TO 6 MONTHS	• If you have to discuss unclear results with co-registrants and have difficulties in agreeing.

Additional tips

You can find the harmonised classification and labelling, if it exists, as well as the classification applied at this time by others in the data for the substance in the C&L Inventory.

You have to report any required classification, independently from whether a harmonised classification exists.

Co-registrants may report different classification according to the identity of their substances (for example, due to the presence of different impurities).

I- REQUIREMENTS FOR REGISTRATIONS AT 1-10 TONNES PER YEAR

I.1 Requirements for physicochemical characteristics

I.1.0 Test preparations and timelines

The physicochemical properties are described in detail in the following sections. The table below provides an overview of the standard tests that are available for each physicochemical property, including the expected turnaround time for performing the test and drafting a report as well as the amount of substance that is needed to perform the test.

Table 6: Physicochemical properties – overview

Physicochemical properties – overview			
Endpoint	**Standard test**	**Amount of substance per test**	**Turnaround time per test**
Melting point	OECD TG 102, EU TM A.1	50 grams	1-2 months
Boiling point	OECD TG 103, EU TM A.2	50 grams	1-2 months
Relative density	OECD TG 109, EU TM A.3	50 grams	1-2 months
Vapour pressure	OECD TG 104, EU TM A.4	50 grams	1-2 months
Surface tension	OECD TG 115, EU TM A.5	50 grams	1-2 months
Water solubility	OECD TG 105, EU TM A.6	50 grams	1-2 months
Partition coefficient n-octanol / water	OECD TG 107, EU TM A.8 OECD TG 117, EU TM A.8 OECD TG 123	50 grams	1-2 months
Flash-point	EU TM A.9	50 grams	1-2 months
Flammability	EU TM A.10, UN test N.1 EU TM A.11 EU TM A.13, UN test series N.2-4 UN test series A to H EU TM A.12; UN test N.5 UN test series A to H	50 grams	1-2 months
Explosive properties	EU TM A.14	50 grams	1-2 months
Self-ignition temperature	EU TM A.15 UN test N.4	50 grams	1-2 months
Oxidising properties	EU TM A.17 EU TM A.21 ISO 10156	50 grams	1-2 months
Granulometry	OECD TM 110	50 grams	1-2 months

The different physicochemical properties of a substance are usually tested at the same time in one test-package, which can take up to two months. Although for most endpoints the actual test duration is only one day, the rest of the time is needed for preparations and reporting.

Note that REACH determines a number of preferred standard methods for the testing of physicochemical properties, and that the CLP Regulation (see chapter 4) specifies certain

methods for the purpose of classifying physical hazard. Also, the CLP determines that certain internationally recognised quality standards must be met such as, for example, those of 'good laboratory practice' (GLP).

Tips

Defining the most appropriate test method for a specific physicochemical property sometimes depends on another endpoint. This is normally accounted for by following a 'phased approach'. However, when several tests for physicochemical properties are performed in a series, and not as a package, this may lead to a significant increase in the total turnaround time.

You should reserve time to find a contract laboratory, make contractual arrangements and prepare the test samples (packaging and delivery of ca. 50 grams per test). Although a test (or a test package) may start within four weeks after contractual agreement, this is largely dependent on how busy the test laboratories are.

The test lab assessing physicochemical characteristics does not need to be compliant with GLP.

We recommend that physicochemical testing is finalised before any of the studies on environmental fate and hazard or on human health are started, because the physicochemical properties of a substance will influence the study design of such studies and whether special precautions need to be taken.

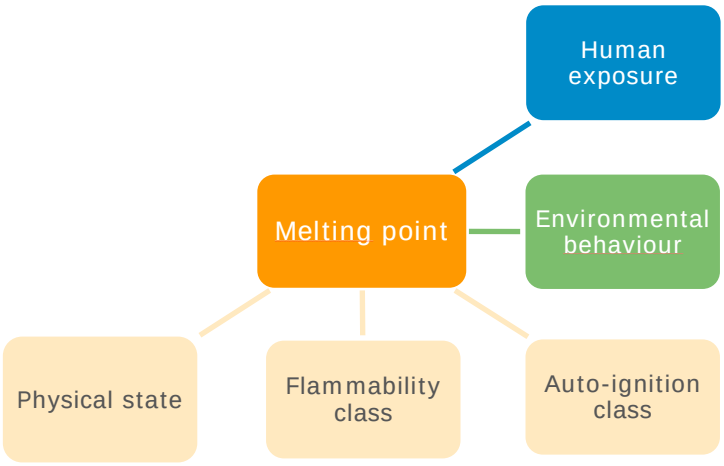
I.1.1 Melting point / freezing point

What is it?
The melting point is the temperature at which a substance changes from a solid to a liquid. The reverse change from a liquid to solid is generally referred to as the freezing point. As for most substances, the melting and freezing points are approximately the same, usually both are simply referred to as 'melting point'. Further, as transition from the solid to the liquid phase frequently takes place over a temperature range, also the term 'melting range' may be used. The melting point/range is expressed in °C.

Why should it be determined?
The melting point tells if the substance is a solid or a liquid at room temperature (20°C), industrial temperatures (generally higher than 20°C) or environmental temperature (12°C). Whether the substance is a solid or a liquid (or a gas) is referred to as the 'physical state' of a substance. This is important because a substance's physical state allows you to assess how humans are most likely to be exposed to a substance. Also, solids and liquids behave differently in the environment.

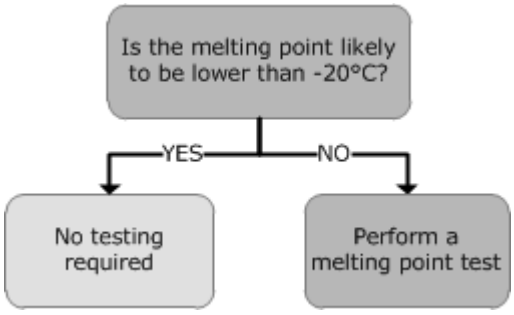
Furthermore, the physical state determines which 'physical hazard class' a substance belongs to, according to the CLP Regulation (see chapter 4).

Figure 6: Relationship of the melting point to other physicochemical (orange), environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.2, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 7.

Figure 7: Decision scheme for performing a melting point test



In addition to these arguments, other knowledge may exist based on which it is decided that

testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
The test guideline to determine the melting point describes several methods: thermal analysis is the preferred one. Some alternatives may however be considered, depending on the state of physical aggregation of a test sample and on whether the substance can be pulverised (easily, with difficulty, or not at all).

Table 7: Melting point / freezing point

Melting point / freezing point	
Standard test methods	**Alternatives to the standard test**
Melting point / melting range (OECD TG 102, EU TM A.1)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) Use of a QSAR predicted value is only possible for data 'waiving' (i.e. if the melting point is predicted to be lower than -20°C) and when accompanied by scientific justification and documentation according to REACH Annex XI, 1.3. Otherwise, QSARs are not sufficiently reliable to predict a final value for substance assessment.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA Guidance on Information Requirements and Chemical Safety Assessment	
Chapter R.7a: Section R.7.1.2 – melting point/freezing point	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If results of a test are available and can be used directly as input in the registration dossier.
Advanced scientific expertise	For use and interpretation of (Q)SAR data for preliminary assessment; for use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
For physicochemical endpoints, performing a test should always be considered: the use of stand-alone information from (Q)SAR, read-across and/or grouping as an alternative to

standard testing should only be considered if testing is technically not possible.

The test method for thermal analysis allows simultaneous determination of the boiling point and the melting point.

Determination of the melting point can be waived below a lower limit of -20°C. This lower limit should be confirmed through preliminary testing, except where a (Q)SAR indicates that the melting point is -50°C or lower.

If a substance decomposes or sublimes before the melting point is reached, that will be the outcome of the test. In that case, a boiling point study is not needed.

The test methods and physical hazard classifications for ‘flammability’ and ‘explosiveness’ differ for solids and liquids (and gases).

Finally, solids and liquids may require different measures for safe handling.

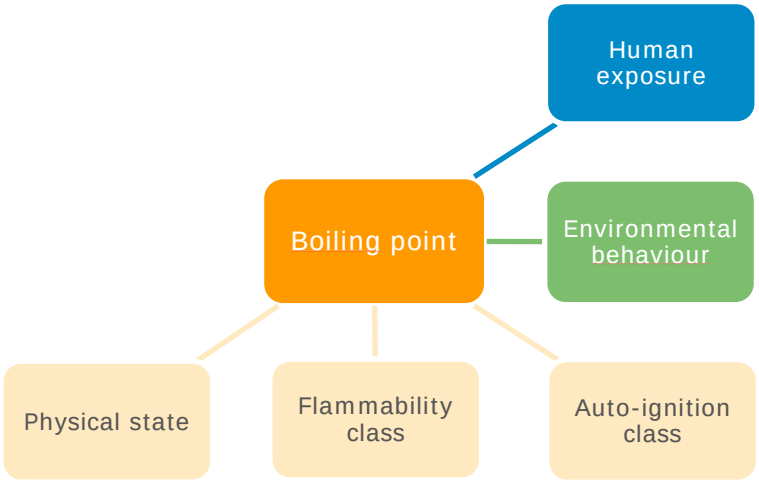
I.1.2 Boiling point

What is it?
The boiling point is the temperature at which a substance's physical state changes from a liquid to a gas. The boiling point is expressed in °C. If a substance has a boiling point of 20°C or lower, that substance is considered to be a gas.

Why should it be determined?
The boiling point tells if the substance is a liquid or a gas at room temperature (20°C), industrial temperatures (generally higher than 20°C) or environmental temperature (12°C). Whether the substance is a liquid or a gas (or a solid) is referred to as the 'physical state' of a substance. This is important information because a substance's physical state allows you to assess how humans are most likely to be exposed to a substance. Also, liquids and gases behave differently in the environment.

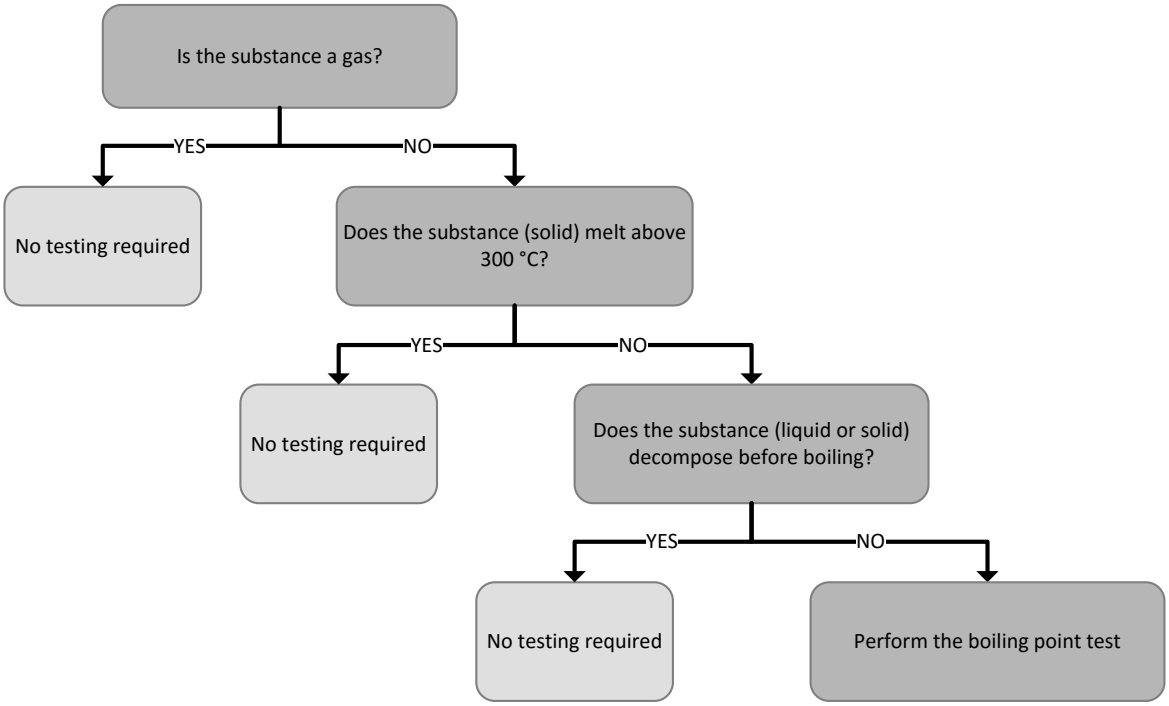
Furthermore, the physical state determines which 'physical hazard class' a substance belongs to, according to the CLP Regulation (see Chapter 4). For example, classifications for flammability (see Chapter I.1.9) and auto-ignition (see Chapter I.1.11) are different for liquids and gases (and solids). Finally, solids and liquids may require different measures for safe handling.

Figure 8: Relationship of the boiling point to other physicochemical (orange), environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.3, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 9.

Figure 9: Decision scheme for performing a boiling point test



In addition to these arguments, other knowledge may exist based on which it is decided that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?

The test guideline for determining the boiling point describes seven different methods which can be applied to liquid and low-melting substances, provided that they do not undergo chemical change below the boiling point. Normally, thermal analysis is the preferred method. Some alternatives to testing may however also be considered.

Table 8: Boiling point

Boiling point	
Standard test methods	**Alternatives to the standard test**
Boiling point (OECD TG 103, EU TM A.2)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A QSAR predicted value can be used only in combination with other information (i.e. "weight-of-evidence approach"). Reliable models are useful for substances with either very low or very high boiling points. In any case, each QSAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA Guidance on Information Requirements and Chemical Safety Assessment	
Chapter R.7a: Section R.7.1.3 – Boiling point	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment; For selection of the most appropriate test method (dependent on a number of factors).
Advanced scientific expertise	If computational models like (Q)SARs are used and for use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

For physicochemical endpoints performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

The test method for thermal analysis allows the boiling point and the melting point to be simultaneously determined.

Testing is technically not possible at least when the substance is an explosive, is self-reactive, or changes chemically during the melting point study. In addition, some substances will decompose before the boiling point is reached in which case that will be the outcome of the test.

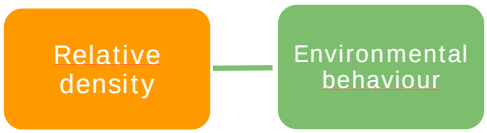
I.1.3 Relative density

What is it?
The density of a substance is the weight of a substance within a given volume. It is usually expressed as kg/m³. The *relative* density is the density of a substance compared to the density of a reference substance.

For gases, the reference substance is air which has a relative density of 1. For comparison, the relative density of helium is 0.138 (lighter), that of carbon dioxide is 1.52 (heavier). For liquids and solids, the reference substance is water which also has a relative density of 1. For comparison, the relative density of balsa wood is 0.2 (lighter), that of lead is 11.35 (heavier).

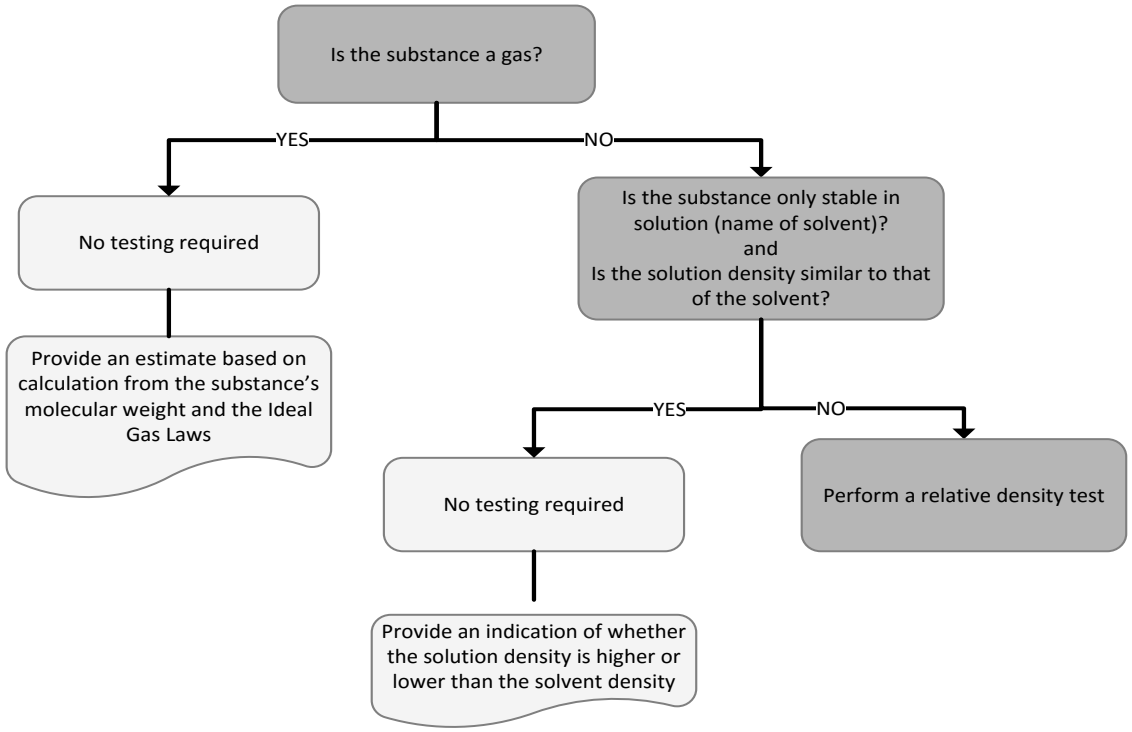
Why should it be determined?
The relative density tells us how a substance is likely to behave in the environment. For gaseous materials that are emitted into the atmosphere, the relative density is used to assess the tendency of that gas to settle (when a substance is heavier than air) or to disperse (in case a substance is equally heavy or lighter than air). For insoluble liquids and solids, the relative density is used to assess whether a substance will float or sink in water.

Figure 10: Relationship of the relative density to environmental endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.4) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 11.

Figure 11: Decision scheme for performing a relative density test



In addition to these arguments, other knowledge may exist based on which it is decided that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
The test guidelines for determining the density of substances describe seven methods, which can be applied to solids or liquids (or both). Some alternatives to testing may however also be considered.

Table 9: Relative density

Relative density	
Standard test methods	**Alternatives to the standard test**
Density of liquids and solids (OECD TG 109, EU TM A.3) **Relative density of gases** (No guideline: calculate from molecular weight using the Ideal Gas Law).	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) (Q)SAR is generally not applicable for determining relative density. Although some (Q)SARs are available, the documentation and validation of the methods is limited.
	Read-across / grouping of substances Use of experimental data from a single similar substance is not recommended. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA Guidance on Information Requirements and Chemical Safety Assessment	
Chapter R.7a: Section R.7.1.4 – Relative density	

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment; For selection of the most appropriate test method (dependent on whether the substance is a solid or a liquid and a number of other factors like, for example, how viscous the liquid is).

Additional tips
For physicochemical endpoints, performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

For gaseous substances, no test method exists and the relative density can be calculated (from the molecular weight using the Ideal Gas Law).

I.1.4 Vapour pressure

What is it?
When a liquid evaporates that means that particles escape from the liquid and form 'a vapour' above that liquid. If this were to happen in a closed box, the vapour above the liquid would apply pressure on the walls of that box. This is called the 'vapour pressure'. Solid substances can also vapourise and create vapour pressure although usually to a lesser extent than liquids. The vapour pressure is expressed in Pascals (Pa).

If a substance evaporates easily, the vapour pressure will be high. The vapour pressure is temperature–dependent: if the temperature increases, the vapour pressure also increases.

Why should it be determined?
Information on the vapour pressure tells if a substance is likely to be present as a vapour in air at room temperature (20°C), industrial temperatures (generally higher than 20°C) or environmental temperature (12°C).

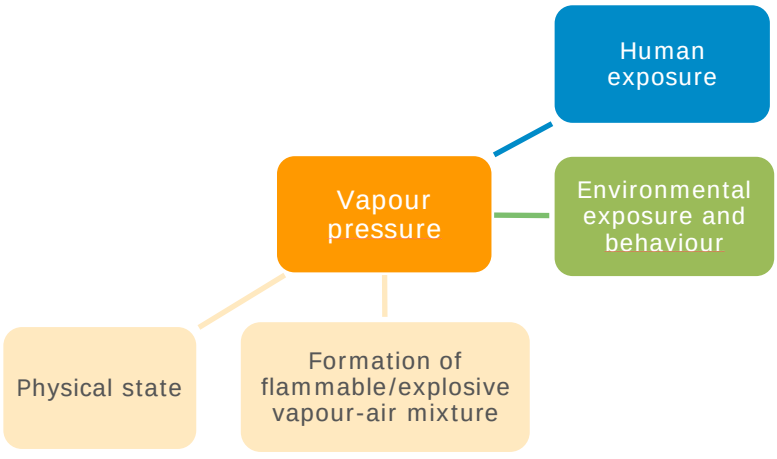
The vapour pressure, in addition to the melting point and boiling point, gives a more precise indication of whether a substance is a liquid or a gas and determines its physical state. Furthermore, the vapour pressure is used in physical hazard assessment and gives an indication of whether a substance may form flammable or explosive mixtures of vapour and air (for substances not classified as flammable themselves). It also determines which container/vessel is most suitable to ensure safety during storage, transport and use. Information on the vapour pressure may be used to assess, for example, how much of a substance will evaporate from a liquid spill into the atmosphere and will possibly be available for inhalation by humans.

The vapour pressure, combined with the water solubility, is used to estimate the degree of 'volatilisation from water', which is expressed in terms of 'Henry's law constant': one of the most important factors in describing how a substance will behave in the environment. As a general rule, the potential for volatility increases when the vapour pressure increases.

Finally, when a substance is likely to volatilise rapidly from water, it is considered to be a 'difficult substance' in relation to some other laboratory testing: special considerations need to be made on how the test is performed and/or the results interpreted.

The vapour pressure is a critical parameter in models used for assessing human exposure and environmental behaviour. Therefore, a particular effort is necessary to report the vapour pressure correctly and precisely.

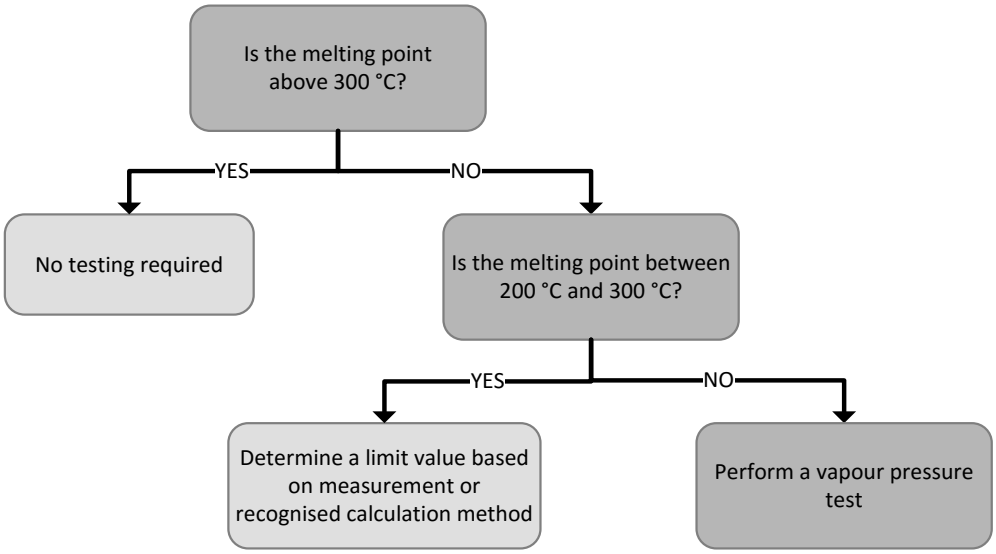
Figure 12: Relationship of the vapour pressure to other physicochemical (orange), environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.5, Column 2) provides some arguments based on which

you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 13.

Figure 13: Decision scheme for performing a vapour pressure test



In addition to these arguments, other knowledge may exist based on which it is decided that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?

The vapour pressure can range from less than 10^{-10} to 10^{5} Pa. No single method is applicable to the entire range of values: in the available test guideline, eight methods are described which can be applied in different (expected) vapour pressure ranges. Some alternatives to testing may be considered.

Table 10: Vapour pressure

Vapour pressure	
Standard test methods	**Alternatives to the standard test**
Vapour pressure (OECD TG 104, EU TM A.4)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used if testing is technically not possible or combined with other information (i.e. "weight-of-evidence approach"). Reliable models are useful for substances with either very low or very high vapour pressure. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA Guidance on Information Requirements and Chemical Safety Assessment	
Chapter R.7a: Section R.7.1.5 – Vapour pressure	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment; For selection of the most appropriate test method as there is no single measurement procedure applicable to the entire range of possible vapour pressure values.
Advanced scientific expertise	If computational models like (Q)SARs are used and for use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules; If a substance is 'highly volatile' in relation to other tests and special considerations need to be made on how to perform such these tests and/or interpret the results.

Additional tips

For physicochemical endpoints performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

For a substance with a boiling point below 30°C, vapour pressure testing is not required because the vapour pressure of the substance will be too high to measure. Formation of a flammable/explosive vapour-air mixture might be the case for halogenated hydrocarbons.

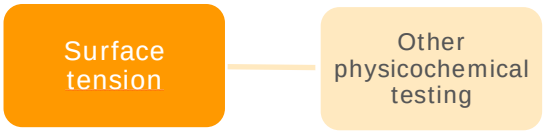
I.1.5 Surface tension

What is it?
Surface tension is a physical phenomenon: the surface of a liquid behaves as a resilient layer. It is also referred to as the 'elastic tendency of liquids'. It is normally expressed as newton per metre (N/m). A common example of the surface tension of water is that it allows certain insects, such as the pond skater for example, to 'walk' on water rather than to sink into it.

The surface tension 'of a substance' generally refers to the tendency of that substance to lower the surface tension of water instead of the surface tension of a liquid substance itself. If a substance alters the surface tension of water, it is referred to as a 'surface active' substance or 'surfactant'. Soap is a typical example.

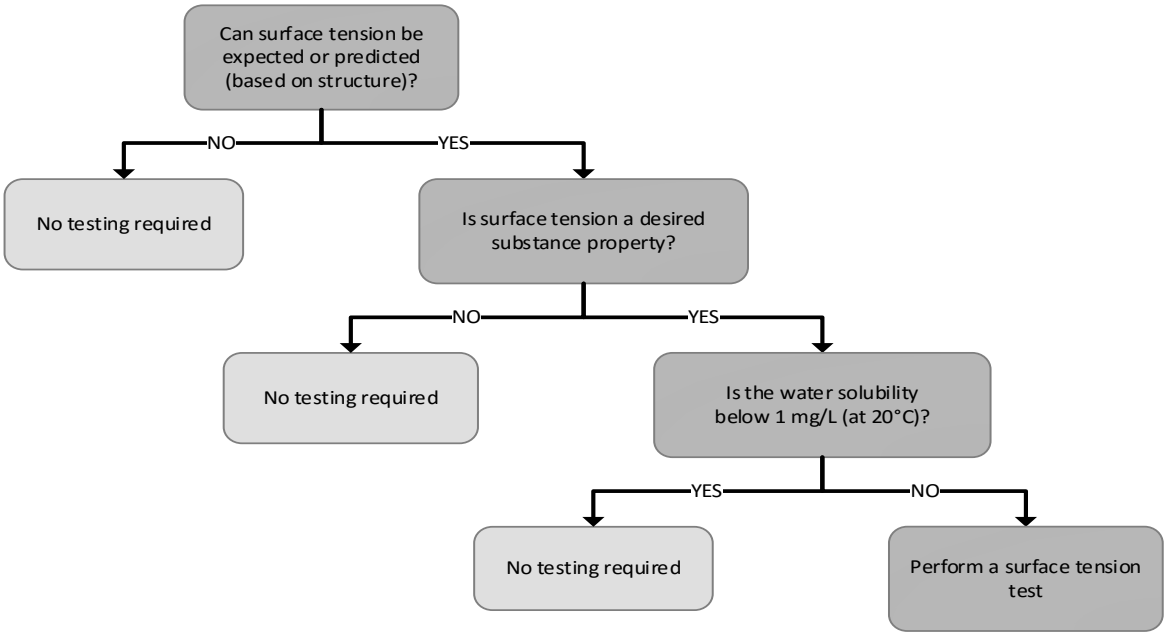
Why should it be determined?
Surface tension measurements of aqueous solutions are important because decreasing the surface tension of water may have an impact on the properties of the solution as a whole and thereby on other physicochemical measurements.

Figure 14: Relationship of the surface tension to other physicochemical endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.6, column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 15.

Figure 15: Decision scheme for performing a surface tension test



In addition to these arguments, other knowledge may exist based on which it is decided that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
Several methods can be used to determine surface tension. In the guideline for testing, four different methods are described, which are all based on measuring the force that is needed to 'detach' an object placed on the surface of a test solution. Some alternatives to testing may however also be considered.

Table 11: Surface tension

Surface tension	
Standard test methods	**Alternatives to the standard test**
Surface tension (OECD TG 115, EU TM A.5)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) No reliable (Q)SAR methods exist for sufficiently accurate predictions of surface tension.
	Read-across / grouping of substances Use of experimental data from a single similar substance is not recommended. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.6 – Surface tension	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test for selection of the most appropriate test method (dependent on some substance-specific information like water solubility and the chemical structure).
Advanced scientific expertise	For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules; If the surface active potential of a substance may have an impact on the testing for other physicochemical or (eco)-toxicological properties.

Additional tips
Testing may be technically not possible for substances that react with water or air (e.g. hydrolyse, are pyrophoric or evolve gases).

For physicochemical endpoints, performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

I.1.6 Water solubility

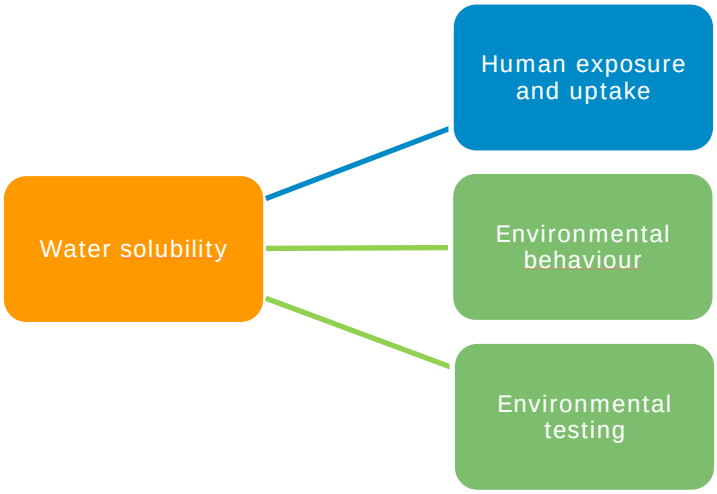
What is it?
The water solubility of a substance is the quantity that can be maximally dissolved in water (usually at room temperature, 20°C). It is expressed in grams per litre (g/L).

Why should it be determined?
The water solubility tells how much of a substance may be present in environmental water such as, for example, surface water, seawater or pore water in soil. Also, a substance with a high water solubility is considered to be mobile, meaning that it can move freely with environmental water flows and thus spread easily through the environment.

Furthermore, information on the water solubility allows the likeliness of exposure of humans, fish, plants etc. to be assessed. Substances with a high water solubility are more likely to be taken up by living organisms. The water solubility is a critical parameter in models used for assessing of environmental behaviour. Therefore, a particular effort is necessary to report the water solubility correctly and precisely.

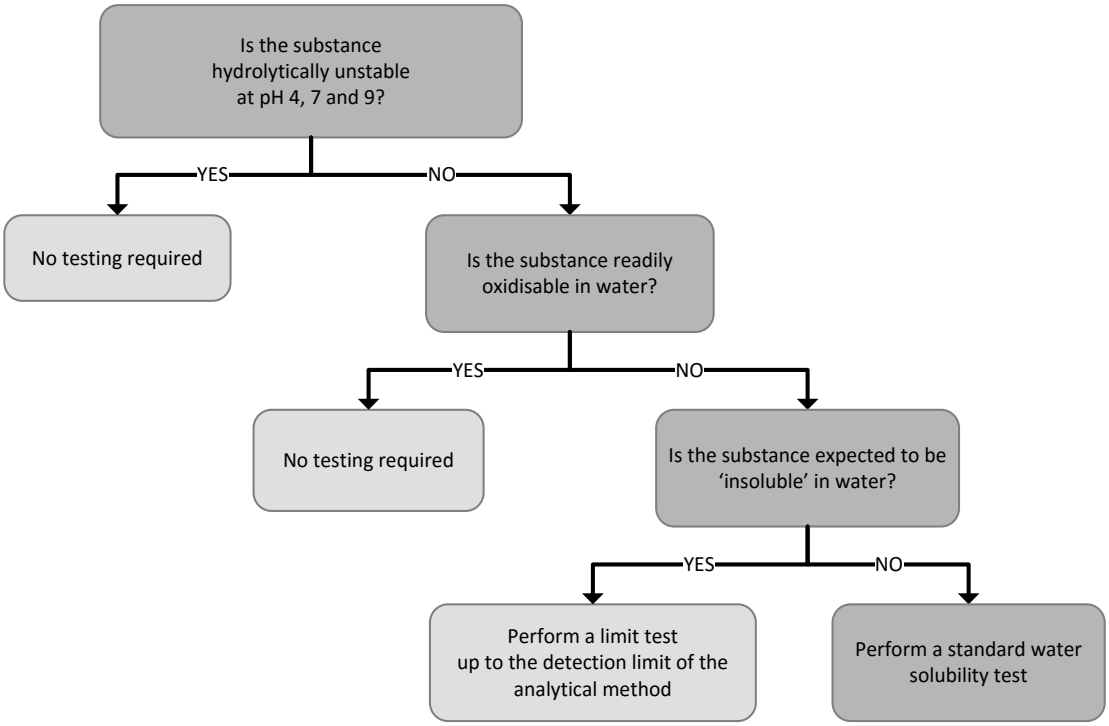
Finally, when a substance has a low water solubility, it is considered to be a 'difficult substance' in relation to some other laboratory testing (especially for environmental endpoints). Special considerations need to be made on how the test is performed and/or the results interpreted. Also, a low water solubility may be used as a regulatory argument that testing for other substance properties does not need to be performed in the first place.

Figure 16: Relationship of the water solubility to environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.7, column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 17.

Figure 17: Decision scheme for performing a water solubility test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?

No single method is available to cover the whole range of solubility values in water, from relatively to very low soluble substances. In the available test guideline, two methods are described covering the whole range of solubility values. The water solubility is normally determined at 20ºC. Some alternatives to testing may also be considered.

Table 12: Water solubility

Water solubility	
Standard test methods	**Alternatives to the standard test**
Water solubility (OECD TG 105, EU TM A.6)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can only be used in combination with other information (i.e. "weight-of-evidence approach"). Reliable models are useful for substances with either very low or very high water solubility, and which are not ionisable. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.7 – Water solubility	

Expertise required

Administrative expertise	If results of a test are available and can be input in the registration dossier
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	For use and interpretation of (Q)SAR data for preliminary assessment; For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules; If a substance is 'poorly soluble' in relation to other tests and special considerations are needed to perform these tests and/or interpret the results.

Additional tips

Testing of the water solubility is almost always possible and should normally be determined experimentally.

Substances are generally considered poorly soluble when their solubility lies below 100 mg/L. Technical difficulties with testing are more likely to occur at solubilities of about 1 mg/L.

For physicochemical endpoints performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

Complex substances (e.g. UVCBs) may be difficult to test as the constituents have different water solubilities. Hence, information on each constituent should be considered. For multiconstituent or UVCB substances, use of (Q)SAR methods can provide useful information on the water solubilities. If you can justify that that data will be irrelevant for subsequent assessments, you may decide not to perform the test.

I.1.7 Partition coefficient n-octanol / water

What is it?
The partition coefficient n-octanol/water reflects that a substance 'prefers' to be present in water or in fat/lipids in a system where both water and fat/lipids are present. N-octanol is used in test systems as a standard surrogate for fat/lipids. The partition coefficient n-octanol/water is most often referred to as the 'log K_{ow}'.

Log K_{ow} values usually range in between Log K_{ow} -2 and +12. The log K_{ow} is closely related to the water solubility. As a general rule, substances with a high log K_{ow} will have a low water solubility.

Why should it be determined?
The log K_{ow} tells if a substance is likely to be taken up by living organisms such as humans, fish, plants etc. After a substance is taken up, it determines how a substance will divide over different body tissues such as, for example, blood and fat. Substances that have a high log K_{ow} prefer to settle in fatty tissues and therefore have the potential to bioaccumulate in organisms (see Chapter 5). As an example, ethanol has a Log K_{ow} -0.3 (stays in water) whereas cholesterol has a Log K_{ow} > 6.5 (dissolves to fat). If Log K_{ow} is in the range 3-8, then the substance may be of special concern as it may accumulate in fat tissues.

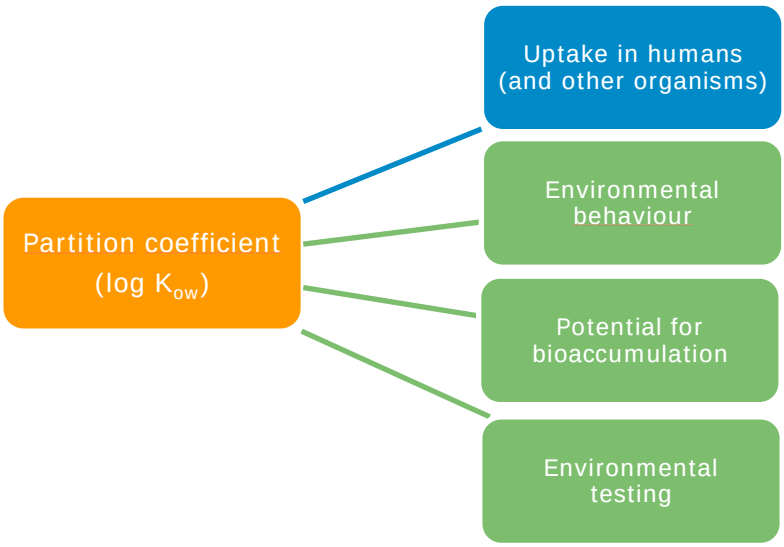
The log K_{ow} can be used to predict how a substance will behave after it enters the environment. The log K_{ow} is indicative of the potential of a substance to 'attach' to environmental particles present in for example soil and sediment. This process is called 'adsorption' and determines in which environments (e.g. water, soil or sediment) substances are likely to concentrate (see section II.1.2).

The higher the log K_{ow} value, the higher the probability to accumulate in soil/sediment. Finally, when a substance has a high log K_{ow} value, it may be necessary to make special considerations for the set-up of other tests (especially for environmental endpoints).

The log K_{ow} is a critical parameter in models used for assessing environmental behaviour. Therefore, a particular effort is necessary to report the log K_{ow} correctly and precisely.

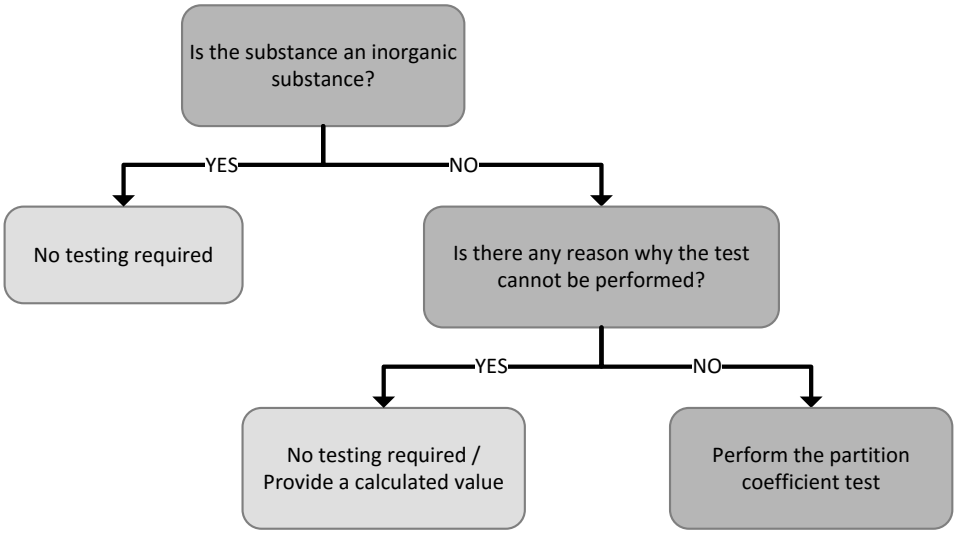
Also, for classification and labelling of substances according to the CLP Regulation (see Chapter 3) the log K_{ow} is used for environmental classification.

Figure 18: Relationship of the partition coefficient to other physicochemical (orange), environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.8) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 19.

Figure 19: Decision scheme for performing a partition coefficient test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
Three methods are commonly used for determination of the log K_{ow}. Two of these are direct methods which allow a substance to dissolve in a water/octanol system after which concentrations in each phase are determined. The third method determines the log K_{ow} indirectly through chromatography (High Pressure Liquid Chromatography or HPLC). All three methods cover a different log K_{ow} range. The applicability of the methods differs depending on substance specifics and the (expected) log K_{ow} of a substance. Some alternatives to testing may also be considered.

Table 13: Partition coefficient n-octanol / water

Partition coefficient n-octanol / water	
Standard test methods	**Alternatives to the standard test**
Shake flask method (OECD TG 107, EU TM A.8) **Slow-stirring method** (OECD TG 123) **HPLC method** (OECD TG 117, EU TM A.8)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used on its own or in combination with other information (i.e. "weight-of-evidence approach"). (Q)SARs for the calculation of the partition coefficient n-octanol/ water are available and may be used if determination by experiment is not possible. Additional caution is required for ionisable substances. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.8 – Partition coefficient n-octanol/water	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier
Scientific expertise	If a decision needs to be made on whether to perform a test for selection of the most appropriate test method (dependent on a number of factors); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment
Advanced scientific expertise	for use and interpretation of (Q)SAR data for preliminary assessment; For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules; If a substance has a 'high log K_{ow}' and special considerations need to be made on how to perform other tests and/or interpret their results.

NB: Substances are generally considered to have a high log K_{ow} at a value of about 5-6 although that may vary between different tests.

Additional tips

For physicochemical endpoints, performing a test should always be considered. As a general rule, the use of standalone information from QSAR, read-across and/or grouping as an alternative for standard testing should be considered only if testing is technically not possible.

I.1.8 Flash-point

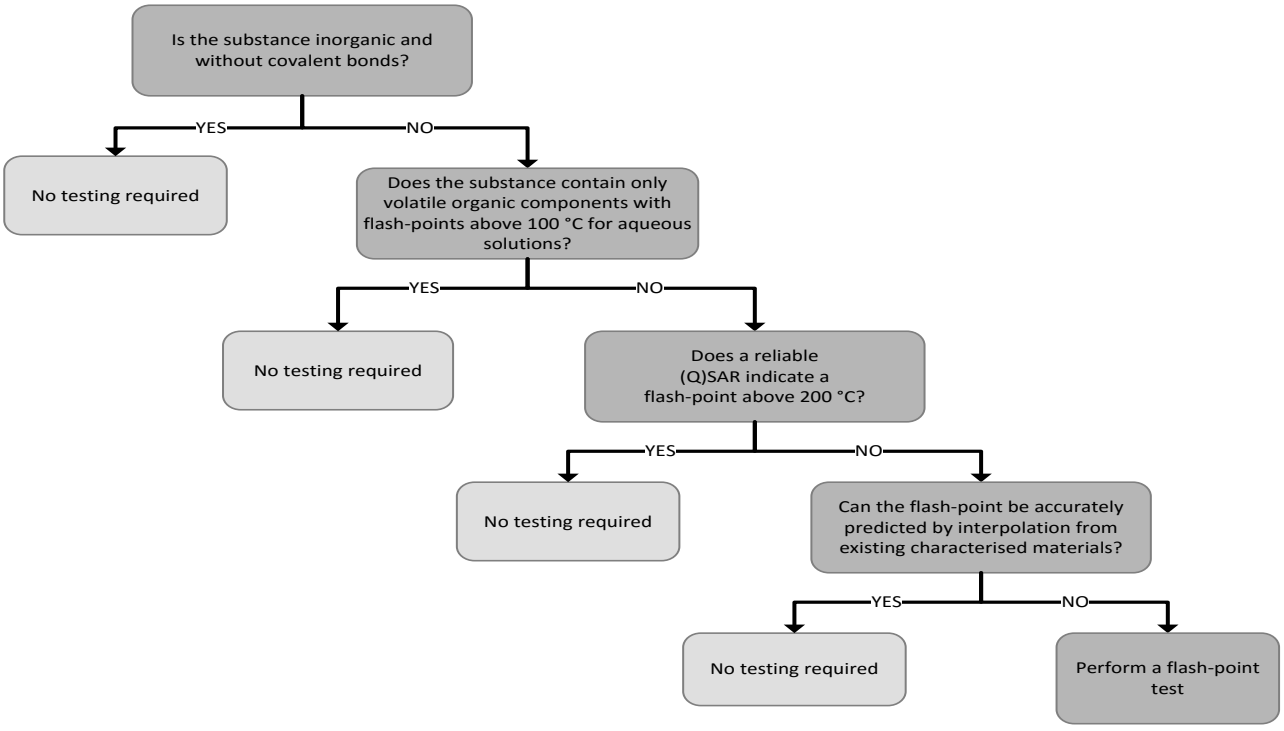
What is it?
The flash-point is the lowest temperature of a liquid at which applying an external energy source, for example a flame or a spark, causes the vapour of that liquid to catch fire (i.e. 'ignite') directly and the flame to spread across the surface of the liquid. The flashpoint is expressed in ºC.

Why should it be determined?
The flash-point is an important property for physical hazard assessment. The flash-point of a liquid is directly related to its 'flammability' as it is defined as 'a liquid with a flash-point of no more than 60°C'. It is used to characterise the fire hazard of liquid substances and to determine rules for safe handling.

Figure 20: Relationship of the flash-point to other physicochemical endpoints

When should it be determined?
The REACH legal text (Annex VII, 7.9, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 21.

Figure 21: Decision scheme for performing a flash-point test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
The flash-point is determined by increasing a liquid's temperature while being exposed to electrical sparks. The temperature at which the liquid catches fire is the flash-point. A range of methods can be used to determine the flash-point: the exact method is chosen taking into account other properties of the liquid. Some alternatives to testing may also be considered.

Table 14: Flash-point

Flash-point	
Standard test methods	**Alternatives to the standard test**
Flash-point (EU TM A.9)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) Use of a (Q)SAR-predicted value is possible for data 'waiving' (i.e. if the flash-point is predicted to be above 200°C). (Q)SARs are not sufficiently reliable to predict a final value for substance assessment but may be used in combination with other information (i.e. "weight-of-evidence approach"). In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.9 – Flash-point	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test for selection of the most appropriate test method (dependent on some substance-specific information and knowledge on classification and labelling according to CLP); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	For use and interpretation of (Q)SAR data for preliminary assessment; For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
For physicochemical endpoints performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

For non-halogenated liquids, calculation based on the vapour pressure curve and lower explosion limit of the substance can be used as a screening approach. When the calculated value is at least 5°C higher than the relevant classification criterion, no flash-point test needs to be performed.

I.1.9 Flammability

What is it?
A flammable substance may be defined as a substance that easily catches fire (i.e. 'ignites') and is capable of burning rapidly when it comes in contact with an external energy source such as a flame or an electrical spark. The criteria based on which a substance is considered to be flammable differ for gases, liquids and solids.

In addition to the definition above, there are some other forms of flammability that need to be considered:

(i) substances that ignite *without an external energy* source but solely by reaction with air (at room temperature) are referred to as 'self-heating' or 'pyrogenic';

(ii) substances that are so 'unstable' that they may even ignite in the *absence of air* and are referred to as 'self-reactive';

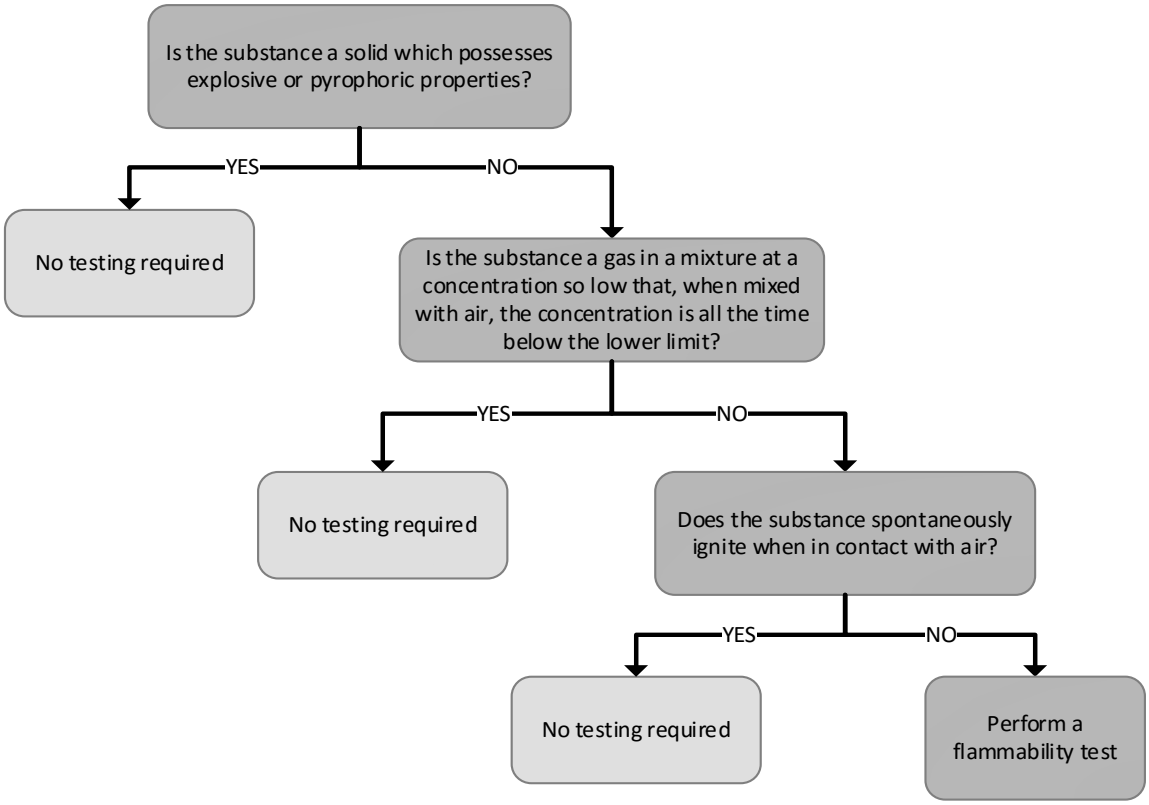
(iii) substances that become flammable when in contact with water; and

(iv) substances referred to as 'organic peroxides', which have some unique properties separate from the previous definitions.

Why should it be determined?
The flammability is not related to any other endpoint. It is a very important property for hazard assessment, as it is used to characterise the fire hazard of substances and to determine rules for safe handling of these substances.

When should it be determined?
The REACH legal text (Annex VII, 7.10, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 22.

Figure 22: Decision scheme for performing a flammability test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?

According to the physical state of your substance, a different test method should be used: testing of the flammability of liquids is covered by the flash-point test (see Section I.1.8). Testing the flammability of solids and of gases, as well the pyrophoric properties and reactivity to water, can be determined by one of the methods in the table below.

For self-reactive substances and organic peroxides a range of methods is available, focusing on explosive capacity more than on flammability as such. Indeed, these two hazard classes can have explosive and/or flammable properties which are assessed in a single test.

Table 15: Flammability

Flammability	
Standard test methods	**Alternatives to the standard test**
Flammability (liquids) Covered by flash-point test **Flammability (solids)** (EU TM A.10, UN test N.1) **Flammability (gases)** (EU TM A.11) **Self-heating/pyrophoric substances** (EU TM A.13, UN test series N.2-4) **Flammability in contact with water** (EU TM A.12, UN test N.5) **Self-reactive substances** (UN test series A to H) **Organic peroxides** (UN test series A to H)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI **Computer calculation (QSAR)** For most flammability sub-endpoints, use of (Q)SAR is not applicable. For the few sub-endpoints where (Q)SAR data are available, this can be used only in combination with other information (i.e. "weight-of-evidence approach") and when accompanied by scientific justification and documentation according to REACH Annex XI, 1.3. **Read-across/grouping of substances** For all flammability sub-endpoints, use of experimental data from a single similar substance or interpolation from data of a group of similar substances is not applicable/ possible.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.10 - Flammability	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on some substance-specific information and knowledge on classification and labelling according to CLP); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models like (Q)SAR are used as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

For physicochemical endpoints, performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

Testing of flammability of liquids is technically not possible if the liquid is explosive, pyrophoric or self-reactive.

Assessment of the chemical structure may be used to anticipate pyrophoric properties of a substance.

Testing of the flammability in contact with water is not necessary if the substance is known to be soluble in water (while remaining stable) or to not react with water (for example, because it is manufactured in/with water).

If a substance is pyrophoric, a number of other tests on physicochemical, toxicological and eco-toxicological endpoints cannot be conducted.

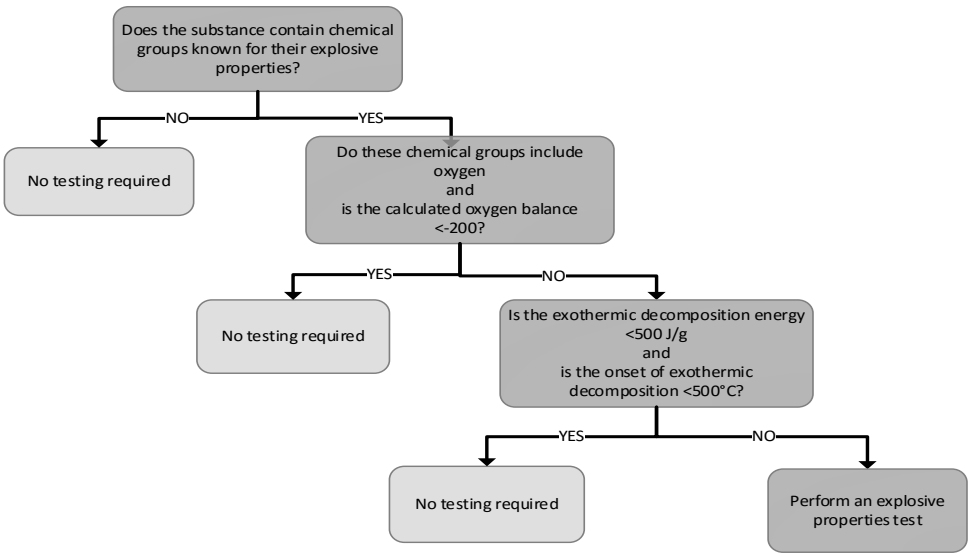
I.1.10 Explosive properties

What is it?
An explosive substance is a solid or a liquid that can explode due to a chemical reaction. 'Explosion' is further defined as producing 'gases at such pressure, speed and temperature that it causes damage to the surroundings'. Pyrotechnic substances (such as fireworks) are also considered to be explosives even when they do not produce gases.

Why should it be determined?
The potential for explosion is not related to any other endpoint. It is a very important property for hazard assessment, as it is used to characterise the explosion hazard of substances and to determine rules for safely handling these substances.

When should it be determined?
The REACH legal text (Annex VII, 7.11, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 23.

Figure 23: Decision scheme for performing an explosive properties test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
The explosiveness of a substance is tested under different conditions: by using fire, using friction and dropping a weight on the substance, as they may be considered as common in a workplace. It is not necessary to investigate explosiveness under *any* (other) conditions. Some alternatives to testing may also be considered.

Table 16: Explosive properties

Explosive properties	
Standard test methods	**Alternatives to the standard test**
Explosive properties (EU TM A.14) **UN Test series 1 to 3** (further test series 4 to 6 are necessary for classification)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) No reliable (Q)SAR methods exist for sufficiently accurate predictions.
	Read-across / grouping of substances Experimental data from one or more similar substances should not be used. However, assessing the chemical structure may be used to anticipate explosive properties of a substance.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.11 – Explosive properties	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on some substance-specific information and knowledge on classification and labelling according to CLP); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.

Additional tips

For physicochemical endpoints, performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

Assessment of the chemical structure may be used (based on 'oxygen balance') to anticipate explosive properties of a substance.

Testing for explosives does not need to be performed if it can be justified that it is technically not possible based on substance properties.

Gases do not need to be tested for explosiveness. Liquids do not need to be tested for sensitivity with respect to friction.

Self-reactive substances and organic peroxides are discussed in the section on 'Flammability', as both hazard classes can have explosive and/or flammable properties.

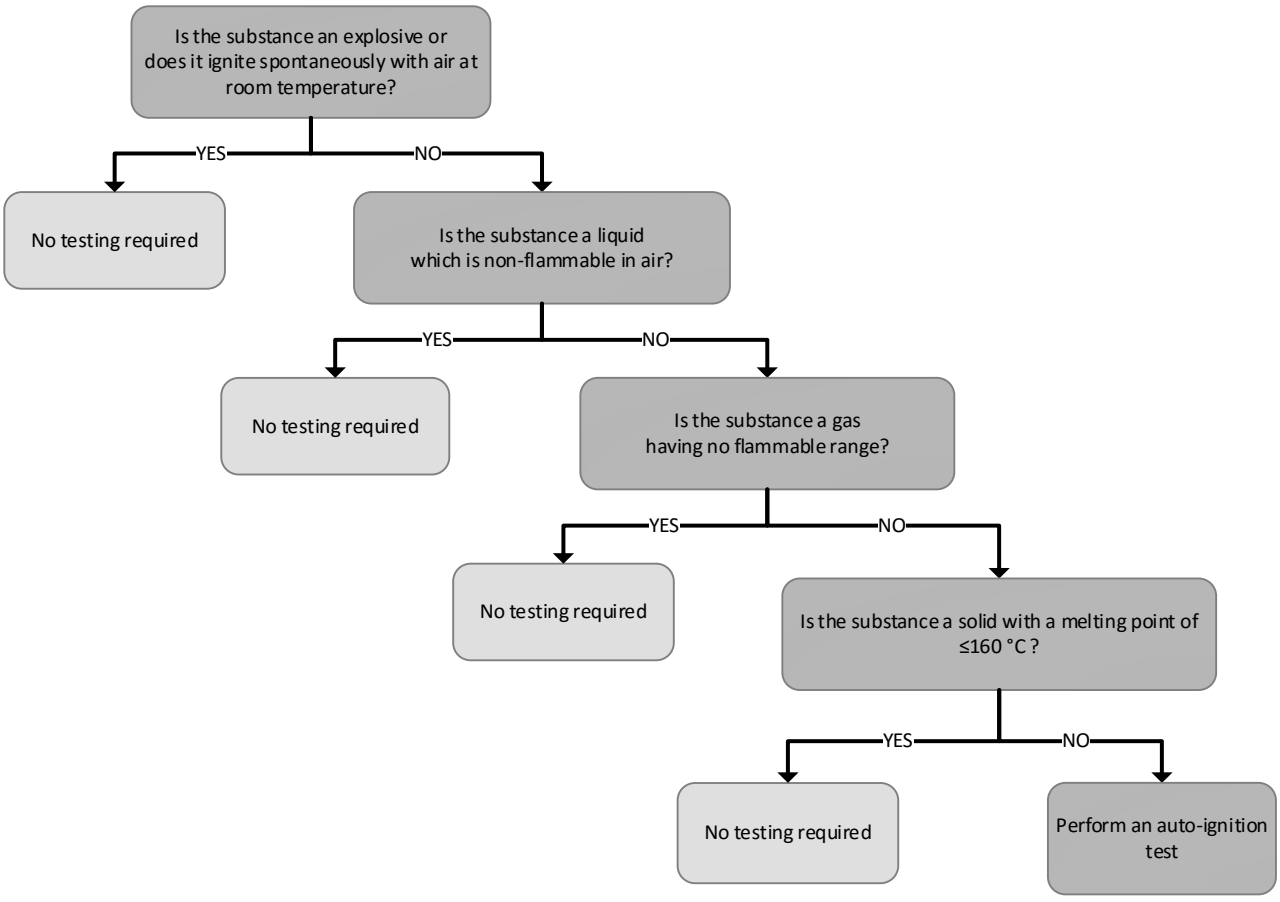
I.1.11 Self-ignition temperature

What is it?
The self-ignition temperature is the lowest temperature at which a substance will spontaneously heat up or catch fire (i.e. 'ignite') when it is mixed with air. Spontaneous means that no external energy source such as a flame or electrical spark is needed. For liquids and gases, self-ignition is more commonly referred to as 'auto-ignition'.

Why should it be determined?
The potential of a substance to auto-ignite is not related to any other endpoint. It is of high importance for hazard assessment, as it is used to determine rules for safely handling these substances, more specifically for the assignment of temperature classes to protect against fire accidents and explosion of plants and equipment.

When should it be determined?
The REACH legal text (Annex VII, 7.12) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 24.

Figure 24: Decision scheme for performing a self-ignition temperature test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
Depending on the physical state of your substance, different test methods should be used to determine the auto-ignition temperature of a substance. The principle of these tests is the same: a test sample is placed in an oven, and the temperature is increased until the substance spontaneously ignites or until the oven reaches a determined maximum temperature, whichever comes first. Some alternatives to testing may also be considered.

Table 17: Self-ignition temperature

Self-ignition temperature	
Standard test methods	**Alternatives to the standard test**
Auto-ignition temperature (liquids and gases) (EU TM A.15) **Relative self-ignition temperature for solids** (UN test N.4)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) No reliable (Q)SAR methods exist for sufficiently accurate predictions.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may, however, be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.12 - Self-ignition temperature	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on some substance-specific information and knowledge on classification and labelling according to CLP); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models, (Q)SARs, and experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing. Use of, justification for, and documentation of such data is subject to very specific rules.

Additional tips
For physicochemical endpoints, performing a test should always be considered: the use of standalone information from (Q)SAR, read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible. The determination of the self-ignition temperature or auto-ignition temperature is not relevant for self-reactive substances and organic peroxides.

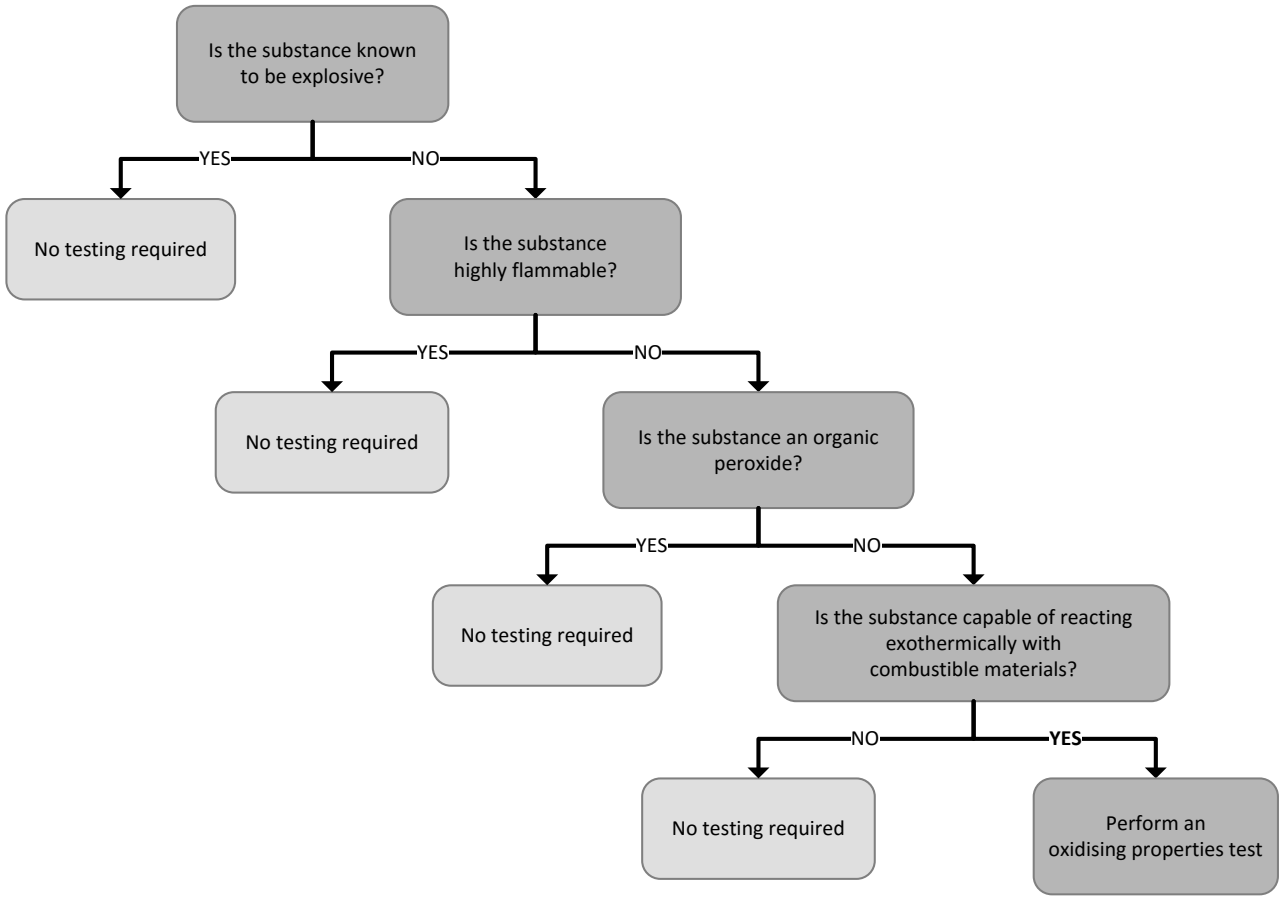
I.1.12 Oxidising properties

What is it?
A substance is oxidising when it causes, or contributes to, the burning (i.e. 'combustion') of another material. This does not necessarily mean that the substance is combustible. The potential to be oxidising applies to solids, liquids and gases although the number of gases that are known to be oxidising is limited.

Why should it be determined?
The oxidising potential is not related to any other endpoint. It is an important property for physical hazard assessment. It is used to characterise the fire hazard of substances and to determine rules for safely handling these substances.

When should it be determined?
The REACH legal text (Annex VII, 7.13, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 25.

Figure 25: Decision scheme for performing a test for oxidising properties



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
Depending on the physical state of your substance, different test methods should be used to determine the oxidising potential of a substance. The principle of these tests is the same: a substance is mixed with another material that is known to be able to combust (generally cellulose) and the maximum burning rate of that mixture is compared to the burning rate of a reference substance. Some alternatives to testing may also be considered.

Table 18: Oxidising properties

Oxidising properties	
Standard test methods	**Alternatives to the standard test**
Oxidising properties (solids)* (EU TM A.17) **Oxidising properties (solids)** (UN Test O.1) **Oxidising properties (liquids)*** (EU TM A.21) **Oxidising properties (liquids)** (UN Test O.2) **Oxidising properties (gases)** (ISO 10156)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI **Computer calculation (QSAR)** No reliable (Q)SAR methods exist for sufficiently accurate predictions. **Read-across / grouping of substances** Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may, however, be possible when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5. Assessment of the chemical structure may be used if no oxidising groups are present in the substance.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.13 – Oxidising properties	

* Not recommended to be used as they are not linked with classification.

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on substance-specific information and knowledge on classification and labelling according to CLP); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	For use and interpretation of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
For physicochemical endpoints, performing a test should always be considered: the use of standalone information from read-across and/or grouping as an alternative to standard testing should only be considered if testing is technically not possible.

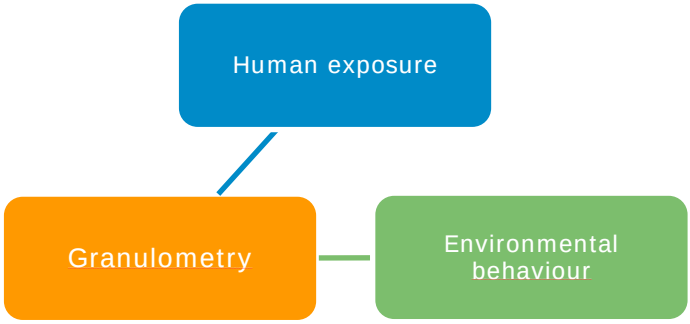
I.1.13 Granulometry

What is it?
Granulometry is only relevant for solids in powdered form and provides information on the size of particles in that powder. The range of particle sizes is referred to as 'particle size distribution'. Particles can be present in the form a single particle, as a collection of bound particles (agglomerates and aggregates) or as fibres.

Why should it be determined?
Although granulometry is not a true 'physicochemical property' of a substance, it is of considerable importance for the toxicological properties of a substance: it influences the route of entry and the distribution in the body of a substance after uptake. It is especially important when uptake occurs through inhalation as a substance's particle size influences how deep a particle will penetrate the lungs.

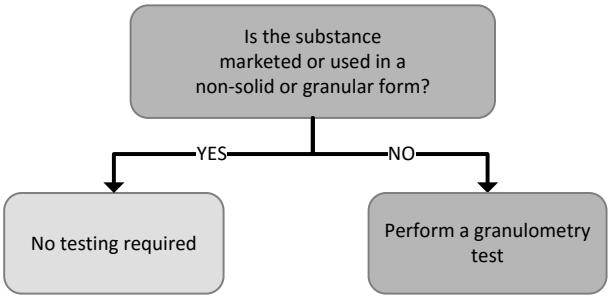
The particle size also influences how a substance behaves after it enters the environment, especially its transportation to and its sedimentation of insoluble particles in water and air.

Figure 26: Relationship of the granulometry to environmental (green) and human health (blue) endpoints



When should it be determined?
The REACH legal text (Annex VII, 7.14) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 27.

Figure 27: Decision scheme for performing a granulometry test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How can it be determined?
Many methods for determining particle size distribution exist, such as sieving, microscopic sedimentation and elutriation techniques, but none of these methods are applicable to the entire range of possible particle sizes. Some alternatives to testing may however also be considered.

Table 19: Granulometry

Granulometry	
Standard test methods	**Alternatives to the standard test**
Particle Size Distribution / Fibre Length and Diameter Distributions (OECD TM 110)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) There are no QSPR/(Q)SAR tools available for predicting particle size.
	Read-across / grouping of substances Experimental data from one or more similar substances cannot be used.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.14 - Granulometry	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on a number of factors); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.

Additional tips
When particles of the same size have different shapes, this may result in different physical hazards of the powder. Therefore, not only the physical appearance, but also other parameters should be considered when identifying the form, since it may trigger different classifications of the same substance or mixture.

Very small particles (nano particles, size <100nm) can differ with their properties from bulk substances and require tailored testing. These substances should be marked as 'nanomaterials' when registered. ECHA's *Guidance on Information Requirements and Chemical Safety Assessment* provides separate guidance to know if you have a nanomaterial and how to register it.

I.2 Requirements for environmental fate and ecotoxicological properties

I.2.0 Test preparations and timelines

The environmental fate and ecotoxicological properties, required at a tonnage band of 1-10 tonnes per year, are described in the following sections. In the table below, an overview is provided of the standard tests, available for each environmental fate and ecotoxicological property, including the expected turnaround time for performing the test and drafting a report as well as the amount of substance that is needed to perform the test.

Table 20: Environmental fate and ecotoxicological properties – overview

Environmental fate and ecotoxicological properties – overview			
Endpoint	**Standard test**	**Amount of substance per test**	**Turnaround time per test**
Development of method for substance analysis	-	50 grams	1 month
Ready biodegradability	OECD TG 301 A-F, EU TM C.4	50 grams	3 months
Short-term toxicity testing on aquatic invertebrates *	OECD TG 202, EU TM C.2	50 grams	3 months
Toxicity testing on aquatic plants (preferably algae) *	OECD TG 201, EU TM C.3	50 grams	3 months

* An analytical method needs to be determined before these tests are started.

For some studies, the amount of test substance present in the test system during the test needs to be analytically verified. Therefore, an analytical method needs to be developed before these studies are started. This can take up to one month. Any available analytical information from the process of substance identification (see Chapter 3) may speed up the process and reduce the costs.

Most of the environmental fate and ecotoxicological properties of a substance can be tested at the same time in one test-package, within approximately three months. Although the actual duration per test ranges from a couple of days (e.g. toxicity testing) to about a month (e.g. ready biodegradability), the additional time is needed for preparation and reporting.

Note that REACH determines a number of preferred standard methods for the testing of environmental fate and ecotoxicological properties, and in addition requires that ecotoxicological studies are performed in compliance with the criteria for good laboratory practice (GLP).

You should also reserve time to find a contract laboratory, make contractual arrangements and prepare the test samples (packaging and delivery). Although a test (or a test package) may start within six weeks after contractual agreement, this is largely dependent on how busy the test laboratories are.

I.2.1 Ready biodegradability

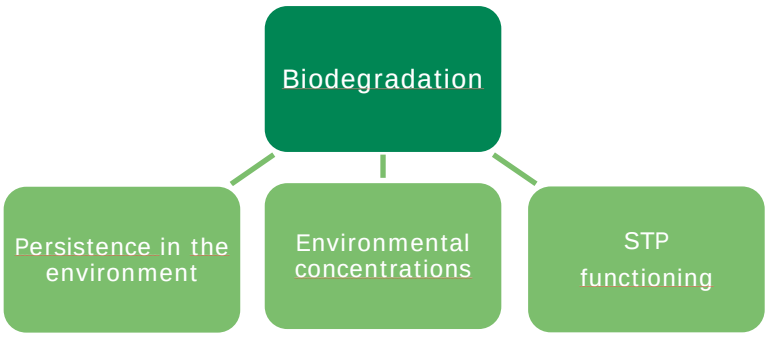
What is it?
Biodegradation is a naturally occurring process where microorganisms, such as bacteria, feed themselves by breaking-down (organic) substances into smaller fragments which may themselves be further degraded to even smaller fragments. When 'complete' biodegradation takes place, all that will be left of the substance is water, carbon dioxide and salts.

The term 'ready' or 'readily' is used when a substance is degraded rapidly and completely in a laboratory test that has very unfavourable conditions for biodegradation compared to those in the environment.

Why should it be determined?
The amount and speed of biodegradation will allow you to predict how much of the substance will eventually be present in different environmental areas (e.g in surface water, sediment or soil). When a substance is biodegraded very slowly or not at all, it is possible that it is 'persistent' in the environment (see Chapter 5). This means that with continued emission of the substance, the concentrations in the environment will keep increasing and organisms are continuously exposed to the substance.

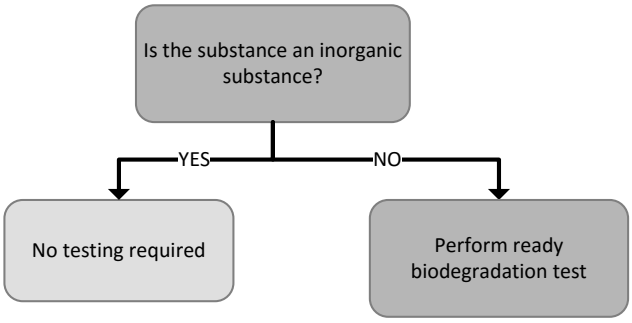
Biodegradation is also essential for the treatment of wastewater in biological sewage treatment plants (STP). When a substance is readily biodegraded, concentrations in the water that leaves the STP will be very low. When, however, no biodegradation takes place, all of the substance that enters the STP may leave the STP unchanged and may enter the surface water or remain in the sewage sludge.

Figure 28: Relationship of biodegradation to other environmental endpoints



When should it be determined?
The REACH legal text (Annex VII, 9.2.1.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 29.

Figure 29: Decision scheme for performing a ready biodegradation test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

The ready biodegradability is assessed by mixing a substance with microorganisms after which it is left standing, usually for a period of 28 days. The test guideline for ready biodegradability testing describes six different methods. The choice for one method depends on a substance's physicochemical properties such as the solubility in water. Some alternatives to testing may also be considered.

Table 21: Ready biodegradability

Ready biodegradability	
Standard test methods	**Alternatives to the standard test**
Ready biodegradation test (OECD TG 301 A-F, EU TM C.4)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used normally in combination with other information (i.e. "weight-of-evidence approach") and when accompanied by scientific justification and documentation according to REACH Annex XI, 1.3
	Read-across / grouping of substances Experimental data from one (or more) similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.9 - Degradation / biodegradation	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; For selection of the most appropriate test method (dependent on a number of factors); If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) and experimental data from one or more similar substances from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

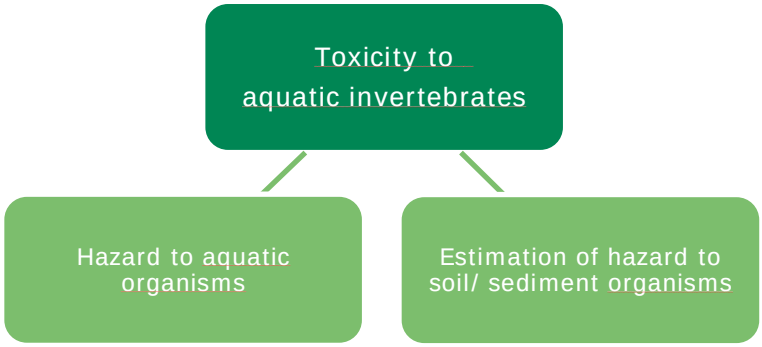
I.2.2 Short term toxicity testing on aquatic invertebrates

What is it?
Aquatic invertebrates are found in all water environments. A typical example of an aquatic invertebrate is the water flea. Short-term aquatic toxicity (also referred to as 'acute' toxicity) is assessed by exposing aquatic organisms to relatively high concentrations of a chemical for a relatively short period of time (several days).

Why should it be determined?
Aquatic invertebrates are an important part of the aquatic food chain. A negative effect of a chemical on a water flea may be predictive of a negative effect on other organisms of the food chain. Information on the effects of a substance to aquatic invertebrates is used to assess the possible hazard of a substance to aquatic ecosystems at a larger scale.

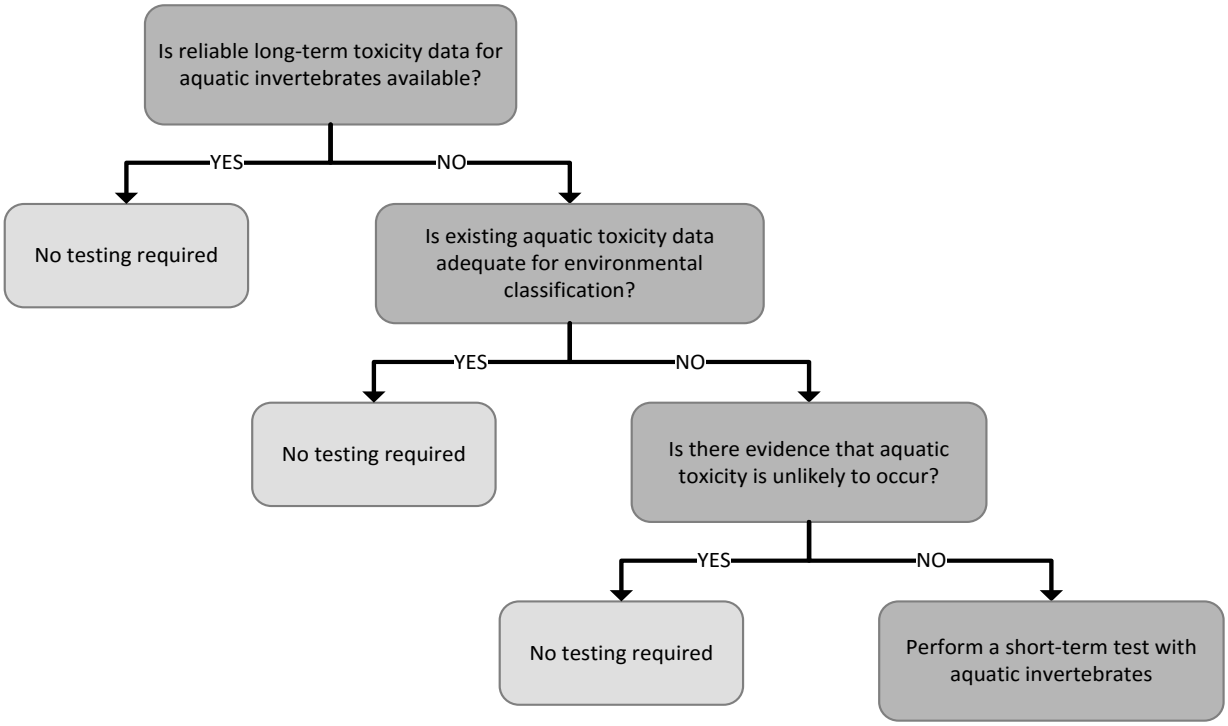
Aquatic toxicity data is also used to predict the hazard to soil or sediment organisms when no experimental results with these specific organisms are available.

Figure 30: Relationships of aquatic toxicity data to other environmental endpoints



When should it be determined?
The REACH legal text (Annex VII, 9.1.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 31.

Figure 31: Decision scheme for performing an aquatic invertebrates short-term toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

Aquatic invertebrate testing is preferably done with the water flea, more specifically with *Daphnia magna*, which is a common species worldwide. The mobility of water fleas is monitored during a 48-hour period after treatment. Some alternatives to testing may also be considered.

Table 22: Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates	
Standard test methods	**Alternatives to the standard test**
***Daphnia* sp., Acute Immobilisation Test** (OECD TG 202, EU TM C.2)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR-predicted value can be used normally combined with other information (i.e. "weight-of-evidence approach"). (Q)SARs can be used on their own for some simple organic and sufficiently water soluble substances and if several reliable models are predicting similar toxicity levels. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3. (see Chapter 8)
	Read-across / grouping of substances Experimental data from one (or more) similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.8 - Aquatic toxicity; long-term toxicity to sediment organisms	

Expertise required

Administrative expertise	if results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; if results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If the substance is poorly soluble in water, you need to consider performing a long-term (testing proposal needed) instead of a short-term toxicity test; If a substance is a 'difficult substance', for example, very unstable or highly volatile, special considerations need to be made on how to perform such a test and/or interpret the results; For use and interpretation of (Q)SAR data for use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

Short-term toxicity tests with freshwater species are preferred but if a substance is released mainly directly into seawater, tests with marine species are more relevant.

Aquatic toxicity is 'unlikely to occur' when the substance is highly insoluble in water or when the substance is likely not to cross biological membranes.

If the substance is poorly soluble in water, you need to consider performing a long-term instead of a short-term toxicity test, normally required only for substances produced or imported in high volumes (and described in Annexes IX and X to REACH). Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) go ahead with performing the test.

If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

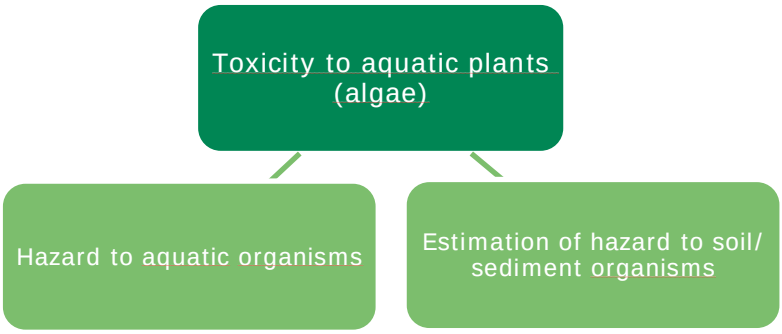
I.2.3 Toxicity testing on aquatic plants (preferably algae)

What is it?
Aquatic plants are found in all water environments. The use of algae is preferred because they are easy to maintain in culture. The short-term toxicity (also referred to as 'acute' toxicity) in algae is assessed by exposing aquatic plants to relatively high concentrations of a chemical for a relatively short period of time (several days). The test also provides data that can be used for the assessment of long-term toxicity (also generally referred to as 'chronic' toxicity).

Why should it be determined?
Aquatic plants, and aquatic algae in particular, are an important part of the aquatic food chain. A negative effect of a chemical on a certain alga species may predict a negative effect on other organisms of the food chain. Information on the effects of a substance to aquatic algae is thus used to assess the possible hazard of a substance to aquatic ecosystems at a larger scale.

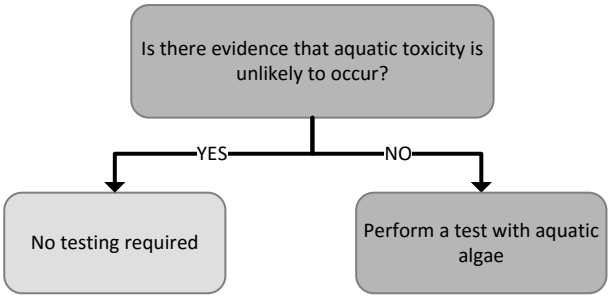
Aquatic toxicity data is also used to predict the hazard to soil or sediment organisms when no experimental results with these specific organisms are available.

Figure 32: Relationship of aquatic toxicity data to other environmental endpoints



When should it be determined?
The REACH legal text (Annex VII, 9.1.2 Column 2) provides some arguments based on which you may decide that testing is not necessary and maybe 'waived'. These arguments are presented in Figure 33.

Figure 33: Decision scheme for performing a aquatic plants short-term toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that

testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
Normally, the effect of a chemical substance on the growth rate of algae is measured during a 72-hour test period. Some alternatives to testing may also be considered.

Table 23: Short-term toxicity testing on aquatic algae

Short-term toxicity testing on aquatic algae	
Standard test methods	**Alternatives to the standard test**
Freshwater Alga and Cyanobacteria, Growth Inhibition Test (OECD TG 201, EU TM C.3)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used only in combination with other information (i.e. "weight-of-evidence approach"). (Q)SARs can be used on their own for some simple organic and sufficiently water soluble substances and if several reliable models are predicting similar toxicity levels. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.8 - Aquatic toxicity; long-term toxicity to sediment organisms	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If a substance is a 'difficult substance', for example, poorly soluble in water, instable or highly volatile, special considerations need to be made on how to perform such a test and/or interpret the results; For use and interpretation of (Q)SAR data for use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

Short-term toxicity tests with freshwater species are preferred but if a substance is released mainly directly into seawater, tests with marine species are more relevant.

Aquatic toxicity is 'unlikely to occur' when the substance is highly insoluble in water or when the substance is likely not to cross biological membranes.

I.3 Requirements for human health properties

I.3.0 Test preparations and timelines

The human health properties required at a tonnage band of 1-10 tonnes per year are described in detail in the following sections. In the table below, an overview is provided of the standard tests, available for each human health property, including the expected turnaround time for performing the test and drafting a report as well as the amount of substance that is needed to perform the test.

Table 24: Human health properties - overview

Human health properties – overview				
Endpoint	**Standard test**	***In vivo* test**	**Amount of substance per test**	**Turnaround time per test**
Skin corrosion/ irritation	OECD TG 430, EU TM B.40 OECD TG 431, EU TM B.40bis OECD TG 435 OECD TG 439, EU TM B.46 OECD TG 404, EU TM B.4	 Y	10 grams	2 – 3 months
Severe eye damage/ Eye irritation	OECD TG 437, EU TM B.47 OECD TG 438, EU TM B.48 OECD TG 460 CM Test Method (draft OECD) OECD TG 491 OECD TG 492 OECD TG 405, EU TM B.5	 Y	10 grams	2 – 3 months
Skin sensitisation	OECD TG 442C OECD TG 442D h-CLAT (draft OECD) OECD TG 429, EU TM B.42 OECD TG 442A/ OECD TG 442B OECD TG 406, EU TM B.6	 Y Y Y	10 grams	2 – 3 months
In vitro mutagenicity[1]	OECD TG 471, EU TM B.13/14		10 grams	2 – 3 months
Acute toxicity: oral	OECD TG 420, EU TM B.1bis OECD TG 423, EU TM B.1tris OECD TG 425 3T3 NRU (no OECD, no EU)	Y Y Y	100 grams	2 – 3 months

[1] For mutagenicity, a 'phased approach' is required under REACH (see Chapters I.3.4, II.2.1 II.2.2, II.2.3). This may influence the total turnaround time.

REACH determines a number of preferred standard methods for the testing of human health properties, and in addition requires that toxicological studies are performed in compliance with the criteria for good laboratory practice (GLP).

You should also reserve time to find a contract laboratory, make contractual arrangements and prepare the test samples (packaging and delivery). Although a test (or a test package) may start within 2-3 months after contractual agreement, this largely depends on how busy the test laboratories are.

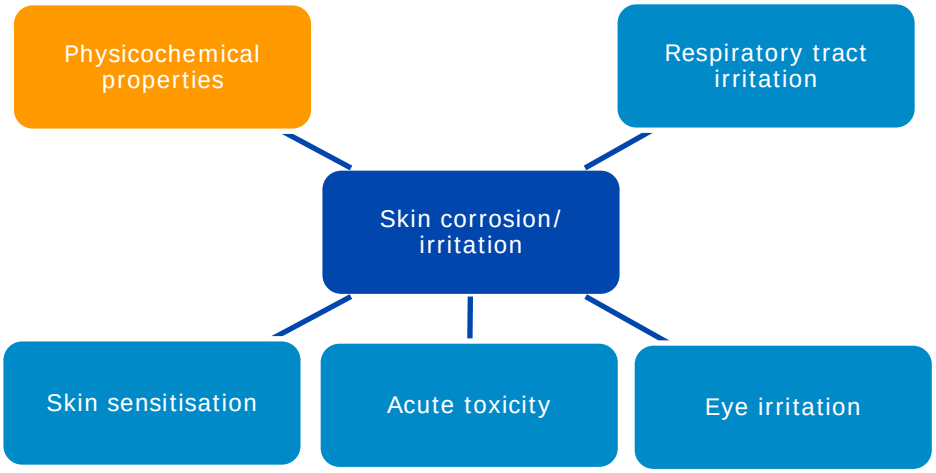
I.3.1 Skin corrosion / irritation

What is it?
A skin irritating or corrosive substance causes irritating or corrosive effects after contact with the skin. If the substance is present in a mixture, its concentration in the mixture determines whether contact with the mixture can lead to effects.

Why should it be determined?
A substance irritating or corrosive to the skin may provoke effects such as pain, a burning feeling or even permanent skin damage when brought into contact with the skin.

Information about the skin irritation or corrosion potential also has an impact on the determination of other properties (Figure 34).

Figure 34: Relationship of skin corrosion / irritation to human health and physicochemical properties

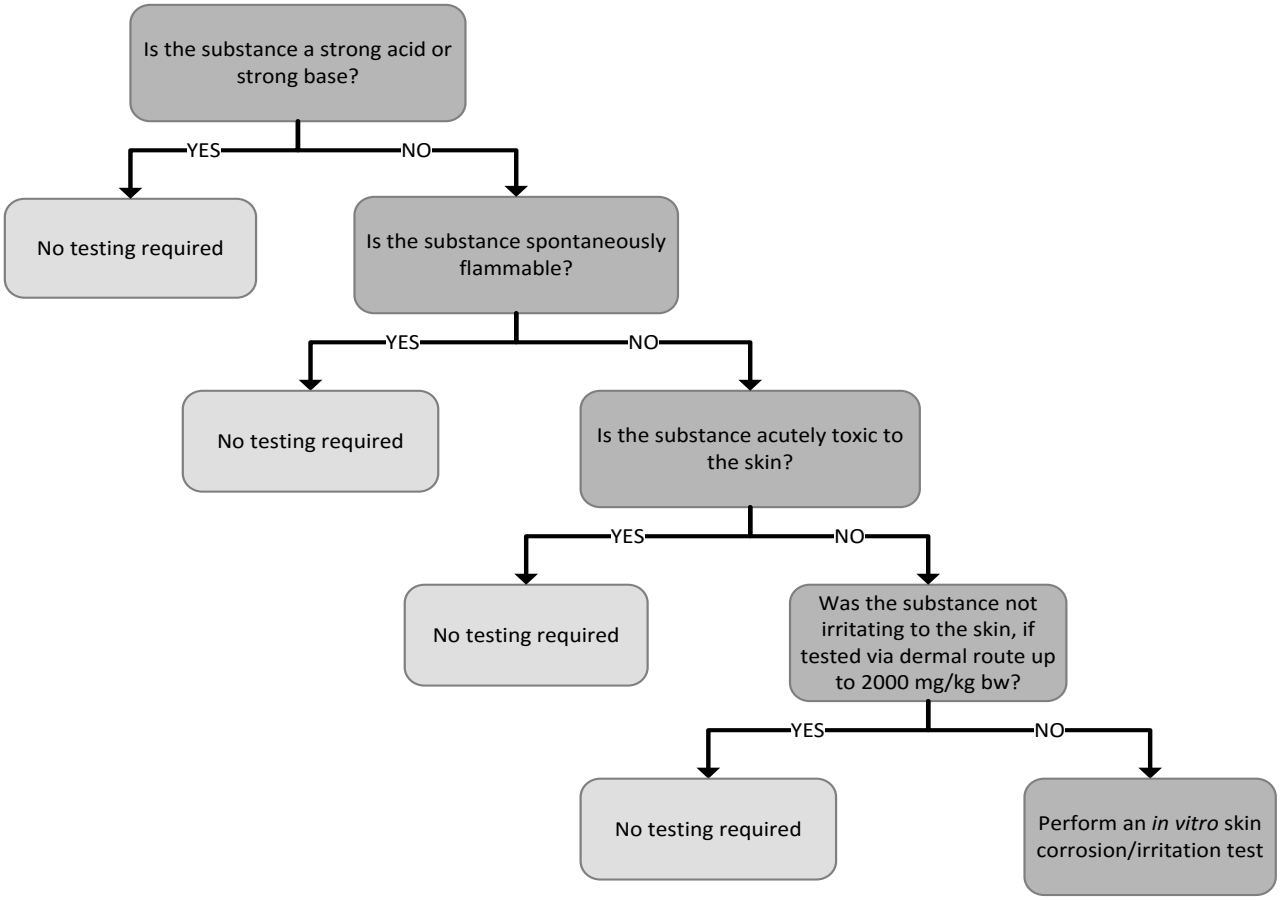


When should it be determined?
When you register a substance at a tonnage band of 1-10 tonnes per year, you must perform and submit an *in vitro* test.

The REACH legal text (Annexes VII and VIII, 8.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 35.

When you register a substance at a tonnage band higher than 1-10 tonnes per year, you may only submit an *in vivo* test if you were not able to draw conclusions on classification and/or risk assessment from the *in vitro* results.

Figure 35: Decision scheme for performing a skin corrosion / irritation test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument is used for not performing a test should be accompanied by a clear explanation on a scientific basis in the registration dossier.

How should it be determined?

The skin corrosion or irritation potential can be determined using a variety of methods, depending on whether the substance is expected to be corrosive or irritant, always starting first with an *in vitro* method. *In vivo* methods can only be used for substances registered at 10-100 tonnes per year (and higher) if *in vitro* results were inconclusive.

Table 25: *In vitro* and *in vivo* skin corrosion / irritation

***In vitro* and *in vivo* skin corrosion / irritation / corrosion**	
Standard test methods	**Alternatives to the standard test**
In Vitro Skin Corrosion; Transcutaneous Electrical Resistant Test Method (OECD TG 430, EU TM B.40)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex VIII • According to REACH Annex XI
In Vitro Skin Corrosion; Reconstructed Human Epidermis Test Method (OECD TG 431, EU TM B.40bis)	
In Vitro Membrane Barrier Test Method for Skin corrosion (OECD TG 435)	**Computer calculation (QSAR)** Computational models are available but discouraged to be used (except as supporting information).
In Vitro Skin Irritation Reconstructed Human Epidermis Test Method (OECD TG 439, EU TM B.46)	
Acute Dermal Irritation/Corrosion (OECD TG 404, EU TM B.4)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.2 - Skin corrosion/irritation, serious eye damage/eye irritation and respiratory irritation	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is not a strong base or acid, not spontaneously flammable, not acutely toxic to the skin, and further assessment of the skin irritation or corrosion potential is needed; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

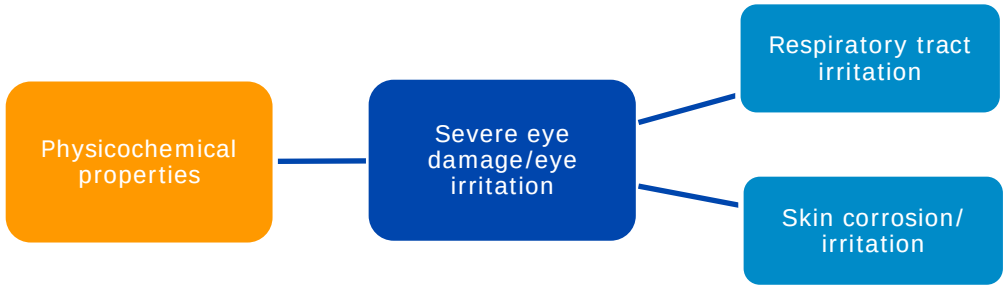
If a substance is irritating or corrosive to the skin, it might also be irritating or corrosive to the eyes and respiratory tract.

I.3.2 Serious eye damage / eye irritation

What is it?
An eye irritating substance causes irritating effects or damages after contact with the eyes. If the substance is present in a mixture, its concentration in the mixture determines whether contact with the mixture can lead to effects.

Why should it be determined?
If a substance is irritating to the eyes it may provoke effects such as redness, itching, swelling, a burning sensation, pain, or blurry vision. If eye damage is severe, it may be permanent i.e. no repair may occur.

Figure 36: Relationship of eye irritation to human health and physicochemical properties

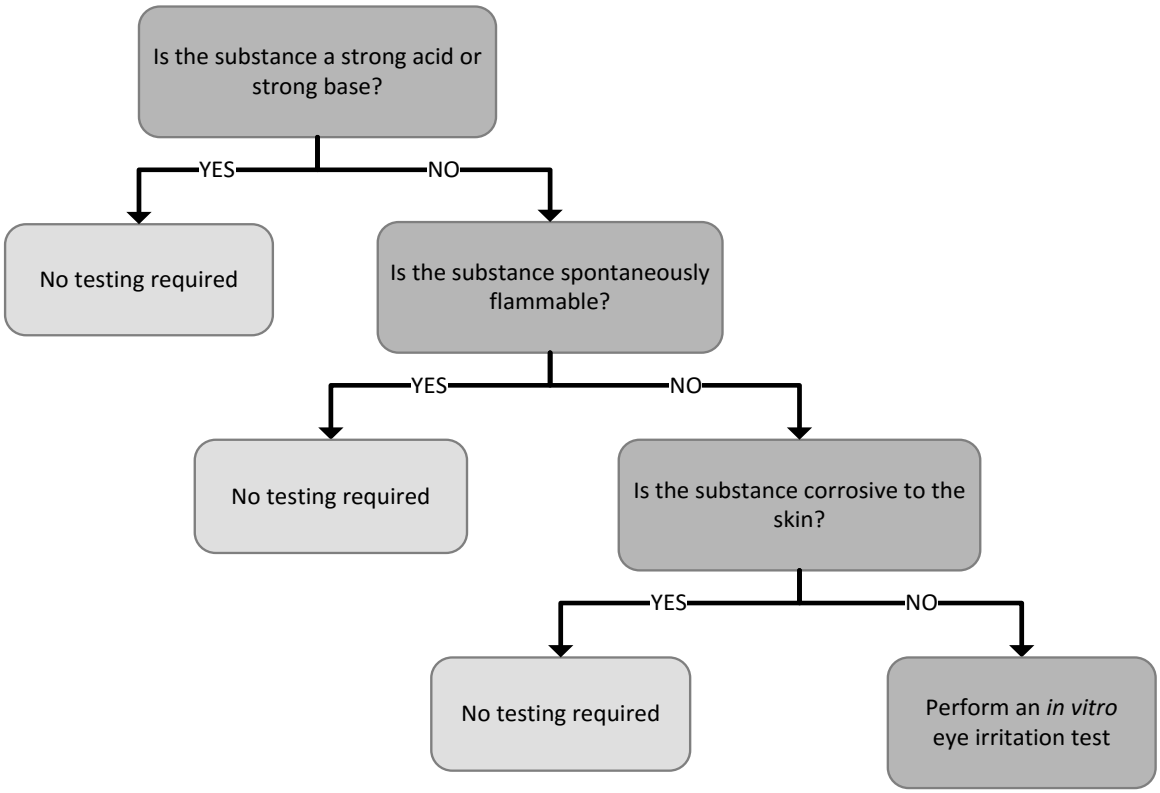


When should it be determined?
When you register a substance at a tonnage band of 1-10 tonnes per year, you must perform and submit an *in vitro* test.

The REACH legal text (Annexes VII and VIII, 8.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 37.

When you register a substance at a tonnage band higher than 1-10 tonnes per year, you may only submit an *in vivo* test if you were not able to draw conclusions on classification and/or risk assessment from the *in vitro* results.

Figure 37: Decision scheme for performing a severe eye damage / eye irritation test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument is used for not performing a test should be accompanied by a clear explanation on a scientific basis in the registration dossier.

How should it be determined?

The eye irritation potential can be determined using a variety of methods, depending on whether the substance is expected to be corrosive or irritant, always starting first with an *in vitro* method. *In vivo* methods can only be used for substances registered at 10-100 tonnes per year (and higher) if *in vitro* results were inconclusive.

Table 26: *In vitro* and *in vivo* severe eye damage / eye irritation

***In vitro* and *in vivo* severe eye damage / eye irritation**	
Standard test methods	**Alternatives to the standard test**
Bovine Corneal Opacity and Permeability Test Method (OECD TG 437, EU TM B.47)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex VIII • According to REACH Annex XI
Isolated Chicken Eye Test Method (OECD TG 438, EU TM B.48)	
Fluorescein Leakage Test Method for Identifying Ocular Corrosives and Severe Irritants (OECD TG 460)	**Computer calculation (QSAR)** Computational models are available but discouraged to be used (except as supporting information).
The Cytosensor Microphysiometer Test Method (Draft OECD TG)	
Short Time Exposure *In Vitro* Test Method (OECD TG 491)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
Reconstructed human Cornea-like Epithelium (RhCE) Test Method (OECD TG 492)	
Acute Eye Irritation/Corrosion (OECD TG 405, EU TM B.5)	
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R7.2 - Skin corrosion/irritation, serious eye damage/eye irritation and respiratory irritation	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is not a strong base or acid, not spontaneously flammable, not corrosive to the skin, and further assessment of the eye irritation potential is needed; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

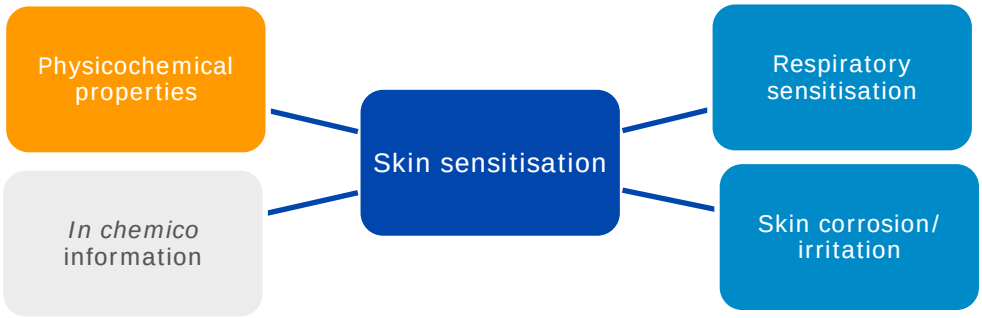
I.3.3 Skin sensitisation

What is it?
A skin sensitising substance has the potential to cause an allergic reaction after contact with the skin.

Why should it be determined?

A substance that is sensitising to the skin may provoke an allergic reaction, including redness, and itching of the skin, which may be combined with small blisters. Repeated contacts can lead to susceptible persons, already reacting at very low levels of a substance, to increasingly severe allergic reactions (up to death). It is therefore important to know whether a substance or mixture is sensitising to the skin, to choose correct protective measures and handling methods to avoid skin contact.

Figure 38: Relationship of skin sensitisation to human health and physicochemical properties

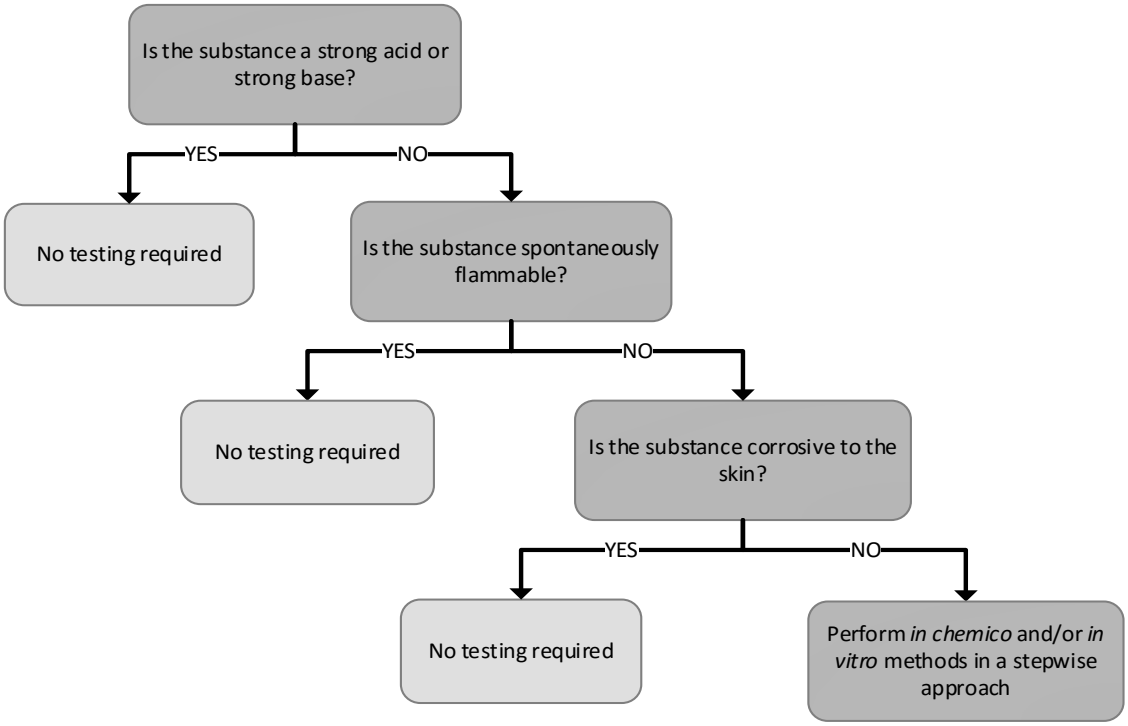


When should it be determined?
As of the end of 2016, you must perform and submit *in chemico or in vitro* methods in a stepwise approach (combinations of several studies may be needed) to correctly classify and define whether the substance can produce significant effects in humans.

The REACH legal text (Annex VII, 8.3 Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 39.

You are only allowed to perform the *in vivo* test if you were not able to draw conclusions on classification and/or risk assessment from the *in chemico* or *in vitro* tests.

Figure 39: Decision scheme for performing a skin sensitisation test



How should it be determined?

The skin sensitisation potential can be determined by various methods, always starting first with *in chemico* or *in vitro* methods, in a stepwise approach, combining one to three studies, to correctly classify according to the potency of sensitisation. *In vivo* methods can only be used for substances registered at 10-100 tonnes per year (and higher) if *in chemico/in vitro* results were inconclusive.

Table 27: Skin sensitisation

Skin sensitisation	
Standard test methods	**Alternatives to the standard test**
In Chemico Skin Sensitisation: Direct Peptide Reactivity Assay (DPRA) (OECD TG 442C)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method (OECD TG 442D)	
In Vitro Skin Sensitisation: human Cell Line Activation Test (h-CLAT) (Draft OECD TG)	**Computer calculation (QSAR)** Computational models are available and can be used usually together with other information (i.e. "weight-of-evidence approach") but must be scientifically substantiated and documented according to REACH Annex XI, 1.3.
Skin Sensitisation: Local Lymph Node Assay (OECD TG 429, EU TM B.42)	
Skin Sensitisation: Local Lymph Node Assay: DA or BrdU-ELISA (OECD TG 442A or OECD TG 442B)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
Skin Sensitisation (OECD TG 406, EU TM B.6)	
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.3 - Skin and respiratory sensitisation	

Expertise required

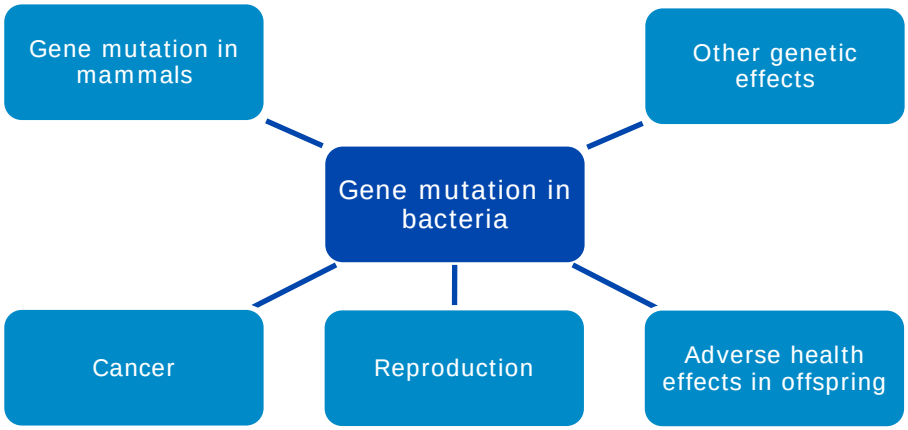
Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is not a strong base or acid, not spontaneously flammable, not corrosive to the skin, and further assessment of the skin sensitisation potential is needed; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

I.3.4 *In vitro* gene mutation in bacteria

What is it?
In vitro gene mutation in bacteria refers to the ability of a substance to change the genetic material (DNA) of bacteria.

Why should it be determined?
If a substance causes gene mutations in bacteria, it may also impact the genetic material in humans which in turn could lead to the development of cancer, affect reproduction or lead to an adverse health effect in offspring. It is therefore important to know whether a substance or mixture causes these types of effects, to choose correct protective measures and handling methods to avoid skin and inhalation contact.

Figure 40: Relationship of gene mutation in bacteria to human health properties



When should it be determined?
The REACH legal text (Annex VII, 8.4.1) does not provide an argument based on which you may decide that testing is not necessary (thus testing cannot be 'waived').

However, you may have other knowledge from which you may decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
In vitro gene mutation in bacteria is determined by performing an Ames test, with five different types of bacteria.

Table 28: *In vitro* gene mutation in bacteria

***In vitro* gene mutation in bacteria**	
Standard test methods	**Alternatives to the standard test**
Bacterial reverse mutation test (OECD TG 471, EU TM B.13/14)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex XI
	Computer calculation (QSAR) Computational models are available. They can be used to provide predictions on its own or together with other information (i.e. "weight-of-evidence approach") and must be scientifically substantiated and documented according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.7 - Mutagenicity and carcinogenicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment, or to decide whether further testing is needed.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

Further mutagenicity studies must be considered if there is a positive result (see Chapter II-2.3): first *in vitro* testing, as foreseen in testing required for substances at tonnages 10-100 tonnes per year. Then, you need to consider performing *in vivo* mutagenicity testing, normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH).

Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test.

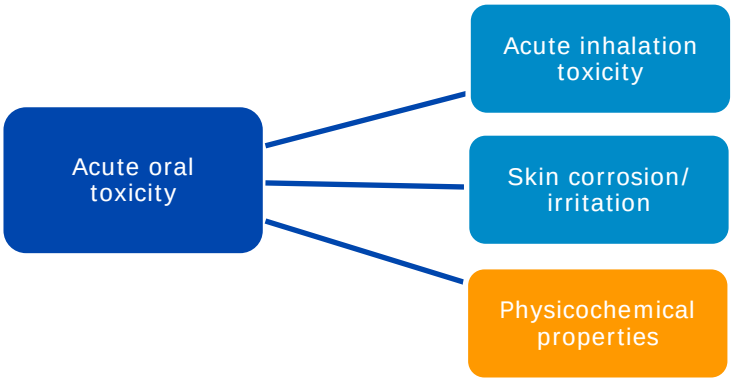
If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

I.3.5 Acute toxicity: oral

What is it?
The acute oral toxicity of a substance is a measure for health effects that may occur after a single (accidental) ingestion of the substance.

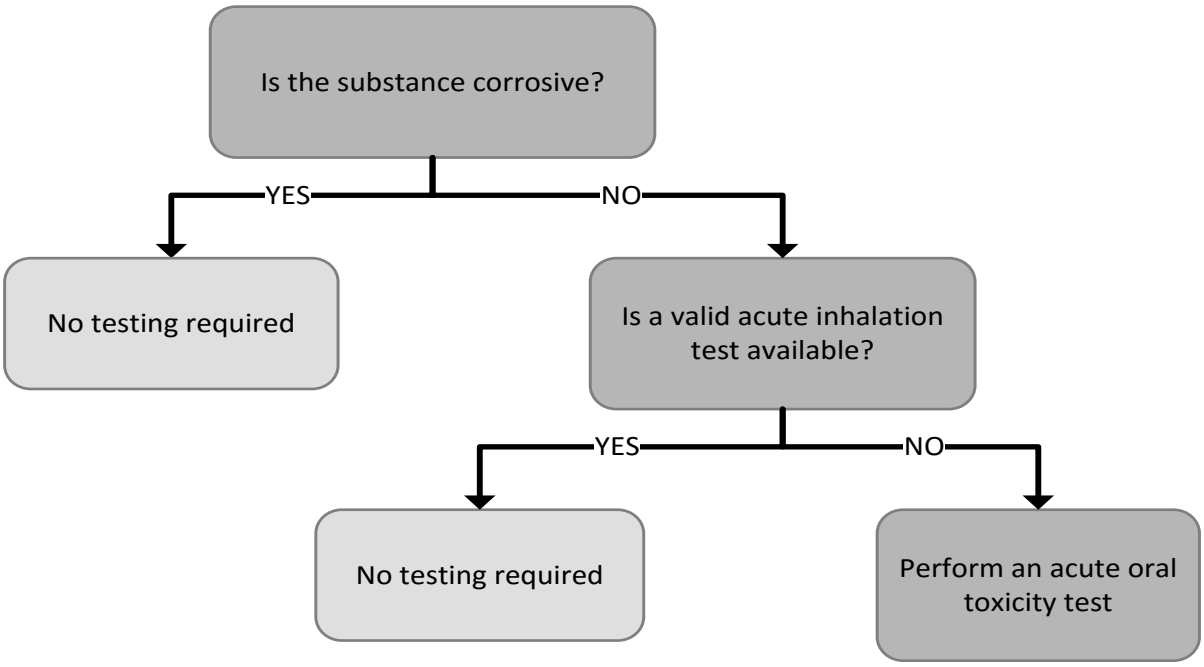
Why should it be determined?
If a substance is acutely toxic after (oral) ingestion, it may induce serious health effects, including death (that may occur after (accidental) ingestion).

Figure 41: Relationship of acute oral toxicity to human health properties



When should it be determined?
The REACH legal text (Annex VII, 8.5.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 42

Figure 42: Decision scheme for performing an acute oral toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

The acute oral toxicity can be determined by various methods.

Table 29: Acute toxicity: oral

Acute toxicity: oral	
Standard test methods	**Alternatives to the standard test**
Acute oral toxicity – Fixed dose procedure (OECD TG 420, EU TM B.1bis)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VII • According to REACH Annex XI
Acute oral toxicity – Acute toxic class method (OECD TG 423, EU TM B.1tris)	**Computer calculation (QSAR)** Computational models are available and can be used to provide predictions together with other information (i.e. "weight-of-evidence approach") but must be scientifically substantiated and documented according to REACH Annex XI, 1.3.
Acute oral toxicity – Up-and-down procedure (OECD TG 425)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
3T3 Neutral Red Uptake (3T3 NRU) Cytotoxicity Assay (no OECD TG or EU TM)	
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.4 - Acute toxicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is not corrosive to the skin, and further assessment of the acute oral toxicity is necessary; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

If a substance is acutely toxic after ingestion, it may also be acutely toxic after skin contact or after inhalation.

Remember that to reduce the number of tests on animals, animal testing is the last option and you have to consider the possibilities to use alternative methods.

If your registration tonnage band is at 10-100 tonnes per year, or higher, it is recommended to define a testing strategy to avoid unnecessary animal tests and therefore address this test in combination with other requirements (see Chapter II.2.6).

ECHA presents a workable approach in its guidance: see the annex, which gives more detailed and practical advice.

II - REQUIREMENTS FOR REGISTRATIONS AT 10-100 TONNES PER YEAR

II.1 Requirements for environmental fate and ecotoxicological properties

II.1.0 Test preparations and timelines

The environmental fate and ecotoxicological properties required at a tonnage band of 10-100 tonnes per year, are described in detail in the following sections. In the table below, an overview is provided of the standard tests that are available for each environmental fate and ecotoxicological property, including the expected turnaround time for performing the test and drafting a report as well as the amount of substance that is needed to perform the test.

Table 30: Environmental fate and ecotoxicological properties – overview

Environmental fate and ecotoxicological properties – overview			
Endpoint	**Standard test**	**Amount of substance per test**	**Turnaround time per test**
Hydrolysis as a function of pH *	OECD TG 111, EU TM C.7	50 grams	3 months
Adsorption/desorption screening	OECD TM 106, EU TM C.18 OECD TG 121, EU TM C.19	50 grams	3 months
Short-term toxicity testing on fish *	OECD TG 203, EU TM C.1	50 grams	3 months
Toxicity to microorganisms in activated sludge (STP toxicity)	OECD TG 209, EU TM C.11	50 grams	3 months

* An analytical method needs to be determined before these tests are started.

For some studies, the amount of test substance present in the test system during the test needs to be analytically verified. Therefore an analytical method needs to be developed before these studies are started. This can take up to one month. Any available analytical information from the process of substance identification (see Chapter 3) may speed up the process and reduce the costs.

Most of the environmental fate and ecotoxicological properties of a substance can be tested at the same time in one test package, within approximately three months. Although the actual duration per test ranges from a couple of days (e.g. toxicity testing) to about a month (e.g. ready biodegradability), the additional time is needed for preparations and reporting.

If you conclude that the substance is 'readily biodegradable' based on the ready biodegradability study (see Chapter I.2.1), no new hydrolysis and STP toxicity tests are needed. Any other conclusion however, means that a test will still have to be carried out. As the ready biodegradability study needs to be finalised before the hydrolysis and STP studies are started, the total duration of data gathering would be three months for the biodegradation study plus three months for hydrolysis/STP toxicity studies and thus adds up to six months total.

Note that REACH determines a number of preferred standard methods for the testing of environmental fate and ecotoxicological properties, and in addition requires that ecotoxicological studies are performed in compliance with the criteria for good laboratory practice (GLP).

You should also reserve time to find a contract laboratory, make contractual arrangements and prepare the test samples (packaging and delivery). Although a test (or a test package) may start within six weeks after contractual agreement, this is largely dependent on how busy the test laboratories are.

II.1.1 Hydrolysis as a function of pH

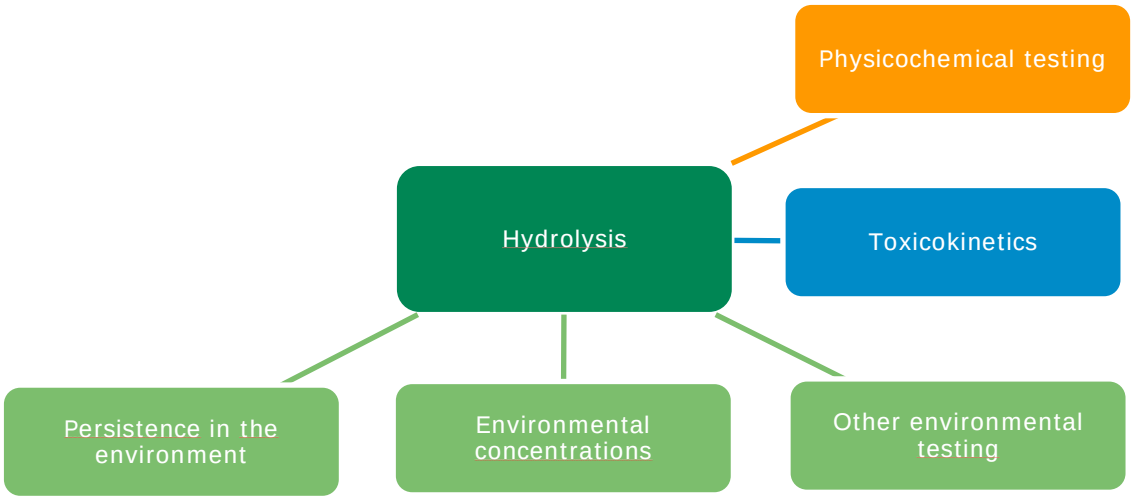
What is it?
Hydrolysis is a naturally occurring process where a chemical substance is broken down into smaller fragments as a result of reaction with water. Hydrolysis takes place in all environmental areas where water is present such as in surface water but also in sediment and soil.

The addition 'as a function of pH' means that hydrolysis needs to be assessed at different pH values. The pH of different environmental areas may vary, which can have a significant effect on the speed and amount of hydrolysis.

Why should it be determined?
The amount and speed of hydrolysis will allow you to predict how much of a substance will eventually be present in the environment (e.g. in surface water, sediment or soil). When a substance is hydrolysed very slowly or not at all, and also if no biodegradation takes place, the substance is likely to be 'persistent' in the environment (see Chapter 5). This means that with continued emission of the substance, the concentrations in the environment will keep increasing and organisms are exposed to the substance for the long-term.

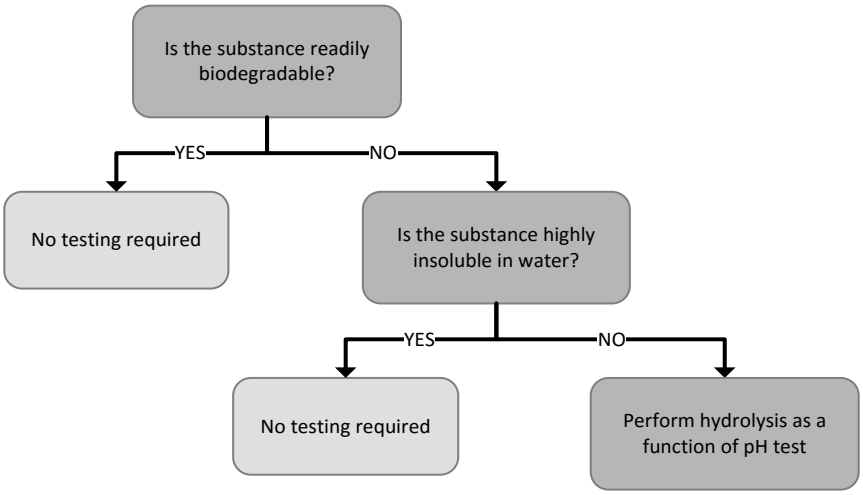
Hydrolysis may also be an important process in the transformation of a substance in an organism's body (i.e. 'toxicokinetics'). When a substance hydrolyses very rapidly (i.e. is 'hydrolytically unstable'), it is considered to be a 'difficult substance' and special considerations need to be made on how other tests are performed and/or the results interpreted.

Figure 43: Relationship of hydrolysis to other environmental (green), human health (blue) and physicochemical (orange) endpoints



When should it be determined?
The REACH legal text (Annex VIII, 9.2.2.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 44.

Figure 44: Decision scheme for performing a hydrolysis test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

The hydrolysis of a chemical substance is determined experimentally by dissolving the substance in water with varying pH and at varying temperatures. Some alternatives to testing may also be considered.

Table 31: Hydrolysis as a function of pH

Hydrolysis as a function of pH	
Standard test methods	**Alternatives to the standard test**
Hydrolysis as a Function of pH (OECD TG 111, EU TM C.7)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used only in combination with other information (i.e. "weight-of-evidence approach"). Some (Q)SARs are applicable only to limited types of substances. In addition, hydrolysis rates need to be calculated at several pHs for the (Q)SAR to be acceptable. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5. Assessment of the chemical structure may be used if no hydrolysable groups are present in the substance.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.9 - Degradation / biodegradation	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If you need to determine whether a substance is 'highly insoluble' in relation to hydrolysis testing; If a substance is 'hydrolytically unstable', special considerations need to be made on how to perform such a test and/or interpret the results; If computational models (QSARs) and experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing. Use of, justification for, and documentation of such data is subject to very specific rules.

Additional tips

The presence of specific groups within a substance's chemical structure triggers hydrolysis.

You may justify not performing a hydrolysis test, if such 'hydrolysable groups' are absent.

The substance is 'highly insoluble' when the solubility is so low that the test is difficult or impossible to perform; this should be assessed on a case-by-case basis.

When a substance is 'hydrolytically unstable', and therefore the breakdown products will likely exist in the environment instead of the substance itself, the behaviour of the breakdown products needs to be assessed.

II.1.2 Adsorption/desorption screening

What is it?
Adsorption describes the tendency of a substance to 'attach' to a solid such as a particle present in sediment or soil. Desorption is the opposite phenomenon, namely the tendency of a substance to release from the particle to the surrounding water. Adsorption and desorption combined refer to the 'sorption potential' of a substance.

The most used sorption parameter is the 'partition coefficient organic carbon-water' or 'log K_{oc}'. As a general rule, substances with a low log K_{oc} value will be mainly present in water, those with a high log K_{oc} value (typically >3) will be mainly present in sediment and soil.

The 'screening' refers to the possibility for a stepwise approach where an estimated log K_{oc} value is used in the chemical safety assessment (see Chapter 6) before a laboratory test is performed.

There is a strong relationship between the log K_{ow} (the 'octanol/water partition coefficient') of a substance (or its 'lipophilicity', see Section I.1.7) and its potential for adsorption (log K_{oc}).

Why should it be determined?
The sorption potential indicates where a substance is likely to be found in the environment: a substance with a high log K_{oc} will tend to concentrate in soil, and will be less mobile when it is attached to soil compared to substances that can move freely with environmental water flows. If a substance concentrates in soil, organisms living in soil will be exposed to the substance at relatively high concentrations and may therefore be at risk.

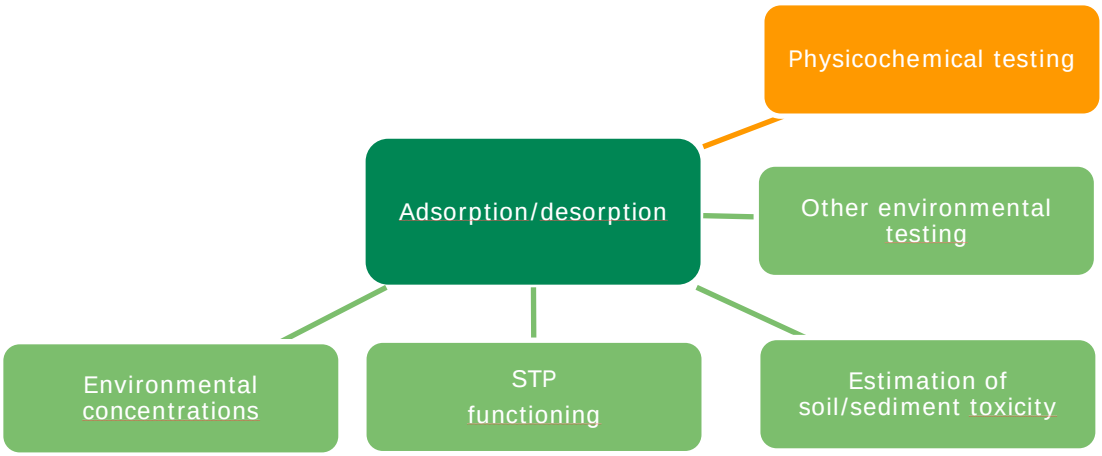
The sorption potential also informs about what may happen after a substance enters a biological sewage treatment plant (STP). Substances that bind firmly to particles (in this case in 'activated sludge') may no longer be available for biodegradation (see Section I.2.1).

On the other hand, the adsorption to sludge itself can lead to removal of the substance from the wastewater. And if the STP sludge containing the substance is used as fertiliser for agricultural soil, the concentration in that soil will increase.

The (log) K_{oc} is also used in combination with data from aquatic toxicity tests (see Chapters II.1.3 and II.1.4) to predict the hazard to soil or sediment organisms when no experimental results with these specific organisms are available.

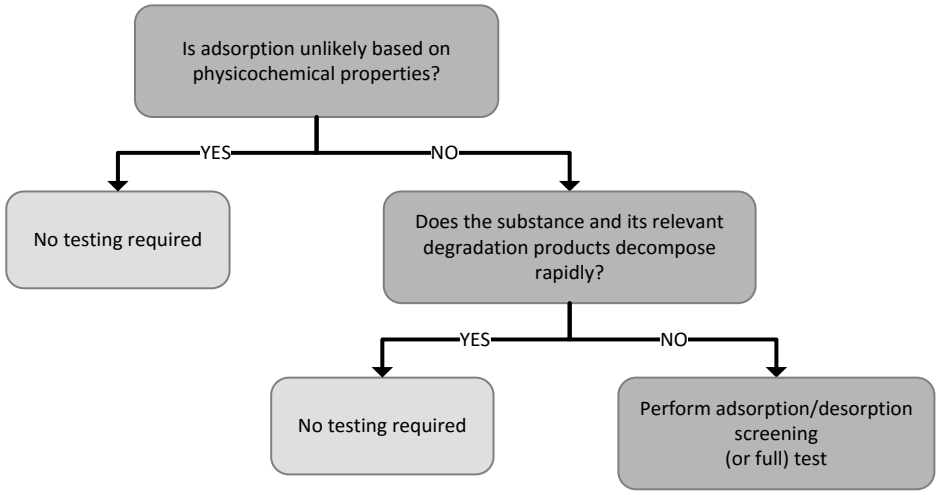
When a substance has a high log K_{oc}, it is considered to be a 'difficult substance' and special considerations need to be made on how other tests are performed and/or the results interpreted.

Figure 45: Relationship of adsorption / desorptions to other environmental (green) and physicochemical (orange) endpoints



When should it be determined?
The REACH legal text (Annex VIII, 9.3.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 46.

Figure 46: Decision scheme for performing an adsorption / desorption test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

However, as data on adsorption is critical for environmental exposure assessment, we recommend that adsorption/desorption screening or testing is always performed when you need to perform a chemical safety assessment (CSA).

How should it be determined?
The sorption potential may be estimated from the substance's log K_{ow} before a laboratory test is performed (as a screening approach), since there is a correlation between K_{ow} and log K_{oc}.

Then you should use computer calculations (QSARs) and/or read-across from substances with a similar structure and characteristics to predict the adsorption potential. However, you must demonstrate that these screening methods give reliable results. Finally you need to perform a test, if the chemical safety assessment shows that, based on the predicted value, not all substance uses are without risk.

Table 32: Adsorption / desorption

Adsorption / desorption	
Standard test methods	**Alternatives to the standard test**
First perform adsorption screening If no reliable results can be obtained from screening methods or the CSA indicates a risk based on a predicted value, than the following tests are first choice: **HPLC method** (OECD TG 121, EU TM C.19) **Adsorption-Desorption using a Batch Equilibrium Method** (OECD TM 106, EU TM C.18)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI **Computer calculation (QSAR)** A (Q)SAR predicted value can be used on its own or in combination with other information (i.e. "weight-of-evidence approach") when accompanied by scientific justification and documentation according to REACH Annex XI, 1.3.However, (Q)SARs should not be used in some cases, such as if the substance is ionisable or has surface active properties. **Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.1.15 - Adsorption / Desorption	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) and experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing. Use of, justification for, and documentation of such data is subject to very specific rules; If a step-wise approach is used for calculating a log K_{OC} value, assessing the reliability of the screening results, assessing the outcome of the chemical safety assessment, and deciding whether to perform a test and which test; For use and interpretation of (Q)SAR data for preliminary assessment; For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
If the substance is ionisable or has surface active properties, we do not recommend to use (Q)SAR as a screening approach. Read across or a HPLC test should be considered as alternatives.

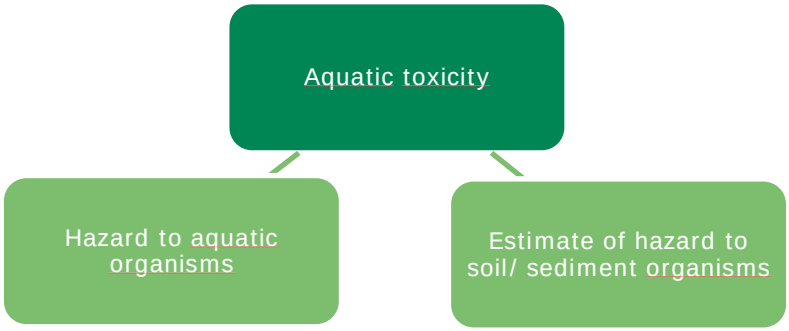
II.1.3 Short-term toxicity testing on fish

What is it?
Short-term aquatic toxicity to fish (also generally referred to as 'acute' toxicity) is assessed by exposing fish to relatively high concentrations of a chemical for a relatively short period of time (several days).

Why should it be determined?
Fish are an important part of the aquatic food chain. A negative effect of a chemical on fish may predict a negative effect on other organisms of the food chain. Information on the effects of a substance to fish is therefore used to assess the possible hazard of a substance to aquatic ecosystems at a larger scale.

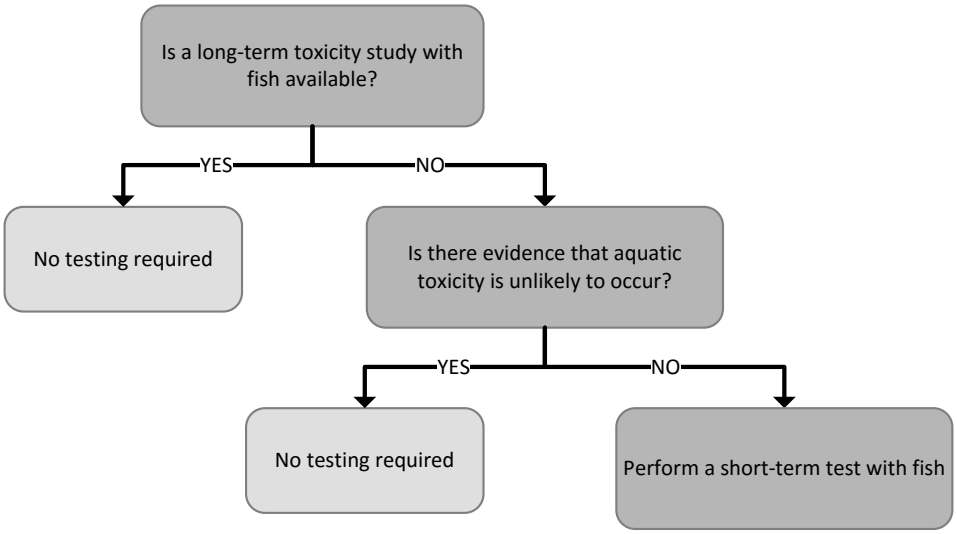
Aquatic toxicity data is also used to predict the hazard to soil or sediment organisms when no experimental results with these specific organisms are available.

Figure 47: Relationship of aquatic toxicity data to other environmental endpoints



When should it be determined?
The REACH legal text (Annex VIII, 9.1.3 Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 48.

Figure 48: Decision scheme for performing a fish short-term toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
The effect of a chemical substance on the mortality of fish is measured during a 96-hour test period. Some alternatives to testing may be considered.

Table 33: Short-term toxicity testing on fish

Short-term toxicity testing on fish	
Standard test methods	**Alternatives to the standard test**
Fish, Acute Toxicity Test (OECD TG 203, EU TM C.1)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
	Computer calculation (QSAR) A (Q)SAR predicted value can be used only in combination with other information (i.e. "weight-of-evidence approach"). (Q)SARs can be used on their own for some simple organic and sufficiently water soluble substances and if several reliable models are predicting similar toxicity levels. In any case, each (Q)SAR prediction should be accompanied by scientific justification and documentation according to REACH Annex XI, 1.3. (see Chapter 8)
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.8 - Aquatic toxicity; long-term toxicity to sediment organisms	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If the substance is poorly soluble in water, you need to consider to perform a long-term (testing proposal needed) instead of a short-term toxicity test; If a substance is a 'difficult substance', for example, very unstable or highly volatile, special considerations need to be made on how to perform such a test and/or interpret the results; If computational models (QSARs) and experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing. Use of, justification for, and documentation of such data is subject to very specific rules.

Additional tips

Short-term toxicity tests with freshwater species are preferred but if a substance is released mainly directly into seawater, tests with marine species are more relevant.

Aquatic toxicity is 'unlikely to occur' when the substance is highly insoluble in water or when the substance is likely not to cross biological membranes.

Remember that to reduce the number of tests on animals, animal testing is the last option and you have to consider the possibilities to use alternative methods. The OECD TG 236 Fish Embryo Acute Toxicity (FET) Test is an alternative to the standard test and could be used within a weight-of-evidence approach together with other supporting information justifying the reliability and adequacy of the test.

OECD developed a fish testing strategy to avoid (reduce) testing (OECD Short Guidance on the Threshold Approach for Acute Fish Toxicity (No. 126, 2010) and OECD Guidance on Fish Toxicity Testing Framework (No. 171, 2012)).

If the substance is poorly soluble in water, you need to consider performing a long-term instead of a short-term toxicity test. In that case, you need to submit a 'testing proposal' to ECHA before such a test is performed, and you need to await ECHA's decision before you can start testing. This is to ensure that generation of information is tailored to real information needs and thus avoiding unnecessary animal testing.

If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records) available at: http://echa.europa.eu/manuals

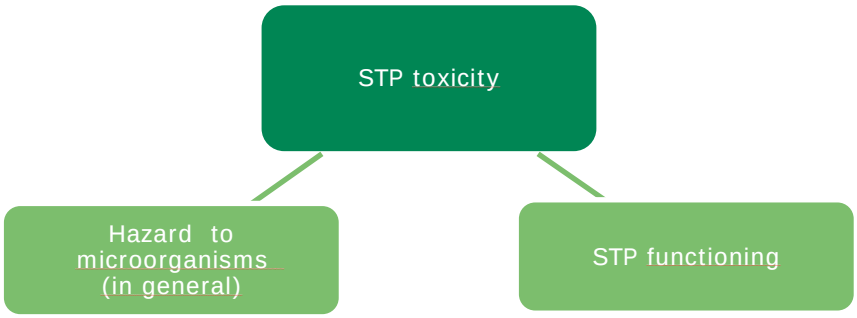
II.1.4 Toxicity to microorganisms in activated sludge

What is it?
Activated sludge that is present in biological sewage treatment plants (STPs), consists mainly of microorganisms that are responsible for breaking down chemicals present in both municipal and industrial wastewater (biodegradation). Toxicity to microorganisms in activated sludge is also generally referred to as 'toxicity to STP microorganisms' or simply 'STP toxicity'.

Why should it be determined?
Negative effects of chemicals on microorganisms in activated sludge may lead to reduced biodegradation in STPs. This affects not only the substance in question but also the other substances which need to be broken down in the STP. Consequently, the releases of treated water to surface water from STPs may contain much higher concentrations of chemicals than they do normally.

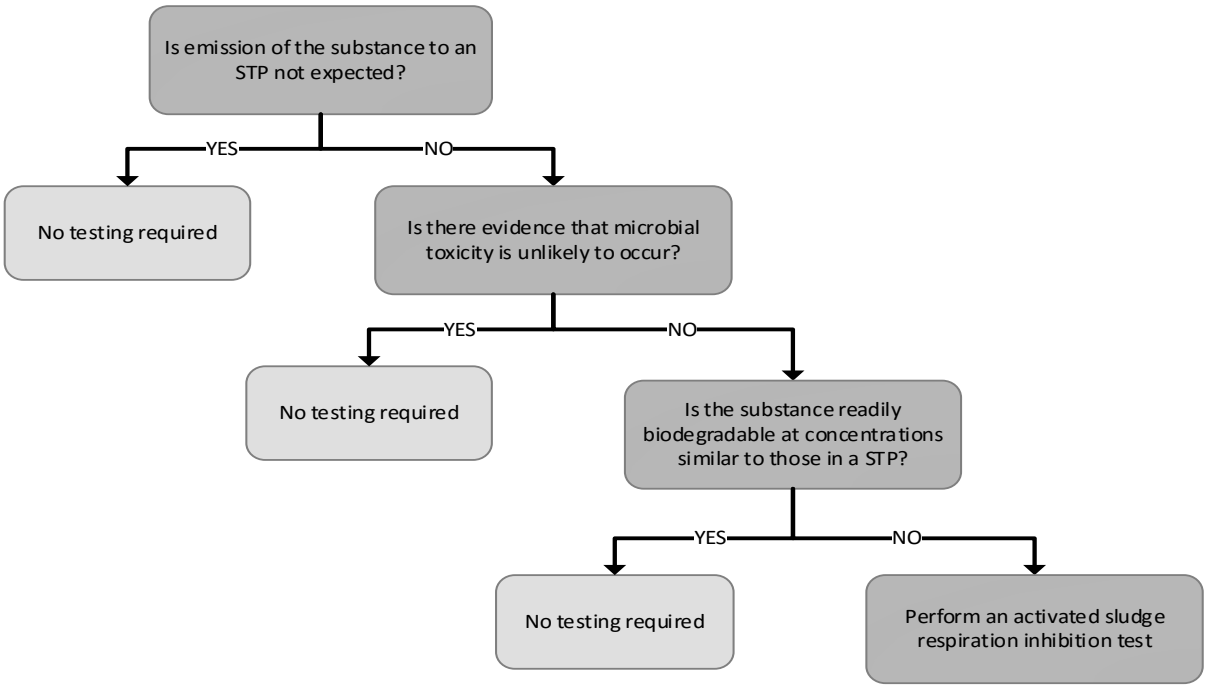
Toxicity to microorganisms in activated sludge is also indicative of toxicity to other microorganisms present in the environment such as those in surface water or in soil.

Figure 49: Relationship of STP toxicity data to other environmental endpoints



When should it be determined?
The REACH legal text (Annex VIII, 9.1.4 Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 50.

Figure 50: Decision scheme for performing an activated sludge microorganisms test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

The effect of a chemical on STP microorganisms is assessed by measuring the oxygen use of microorganisms in activated sludge (i.e. 'respiration') during a three-hour test period. Some alternatives to testing may also be considered.

Table 34: Toxicity to microorganisms in activated sludge

Toxicity to microorganisms in activated sludge	
Standard test methods	**Alternatives to the standard test**
Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation) (OECD TG 209, EU TM C.11)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
	Computer calculation (QSAR) The use of QSAR for STP toxicity is advised against.
	Read-across / grouping of substances Use of experimental data from a single similar substance is usually not possible. Interpolation from data of a group of similar substances may however be possible when accompanied by scientific justification and documentation as indicated in REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7b: Section R.7.8 - Aquatic toxicity; long-term toxicity to sediment organisms	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If a decision needs to be made on whether to perform a test; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.

Additional tips

Information on the toxicity to microorganisms in activated sludge may under certain conditions be derived from the already performed ready biodegradability test.

The standard test may be replaced by a nitrification inhibition test if there are indications that the substance may be toxic to nitrifying bacteria.

Toxicity to microorganisms is unlikely to occur when, for example, the substance is highly insoluble in water and is thus not likely to be present in an STP at high concentrations.

II.2 Requirements for human health properties

II.2.0 Test preparations and timelines

The human health properties, required at a tonnage band of 10-100 tonnes per year, are described in detail in the following sections. In the table below, an overview is provided of the standard tests, available for each human health property, including the expected turnaround time for performing the test and drafting a report as well as the amount of substance that is needed to perform the test.

Table 35: Human health properties - overview

Human health properties – overview				
Endpoint	**Standard test**	***In vivo* test**	**Amount of substance per test**	**Turnaround time per test**
In vitro mutagenicity[1]	OECD TG 487, EU TM B.49 OECD TG 473, EU TM B.10 OECD TG 476, EU TM B.17 OECD TG 490		10 grams	2 – 3 months
In vivo mutagenicity[1]	OECD TG 475, EU TM B.11 OECD TG 474, EU TM B.12 OECD TG 486, (EU TM B.39 OECD TG 488, EU TM B.58 OECD TG 489 OECD TG 483, EU TM B.23 OECD TG 478, EU TM B.22	Y Y Y Y Y Y Y	100 grams	2 – 3 months
Acute toxicity: inhalation	OECD TG 403, EU TM B.2 OECD TG 433 (draft) OECD TG 436	Y Y Y	3 – 5 kilograms	3 – 4 months
Acute toxicity: dermal*	OECD TG 402, EU TM B.3 OECD TG 434 (draft)	Y Y	100 grams	2 – 3 months
Short-term repeated dose toxicity	OECD TG 407, EU TM B.7 OECD TG 410, EU TM B.9 OECD TG 412, EU TM B.8 OECD TG 422	Y Y Y Y	3 kilograms (oral/ dermal) 100 kilograms (inhalation)	8 – 9 months (oral/ dermal) 10 – 11 months (inhalation)
Screening for reproductive/developmental toxicity	OECD TG 421 OECD TG 422	Y Y	3 kilograms (oral/ dermal) 100 kilograms (inhalation)	8 – 9 months (oral/ dermal) 10 – 11 months (inhalation)

[1] For mutagenicity, a 'phased approach' is required under REACH (see Sections II.2.1, II.2.2, II.2.3). This may influence the total turnaround time.
* Changes to annex requirements make the *in vivo* test a secondary requirement.

REACH determines a number of preferred standard methods for the testing of human health properties, and in addition requires that toxicological studies are performed in compliance with the criteria for good laboratory practice (GLP).

You should also reserve time to find a contract laboratory, make contractual arrangements and prepare the test samples (packaging and delivery). Although a test (or a test package) may start within two to three months after contractual agreement, this largely depends on how busy the test laboratories are.

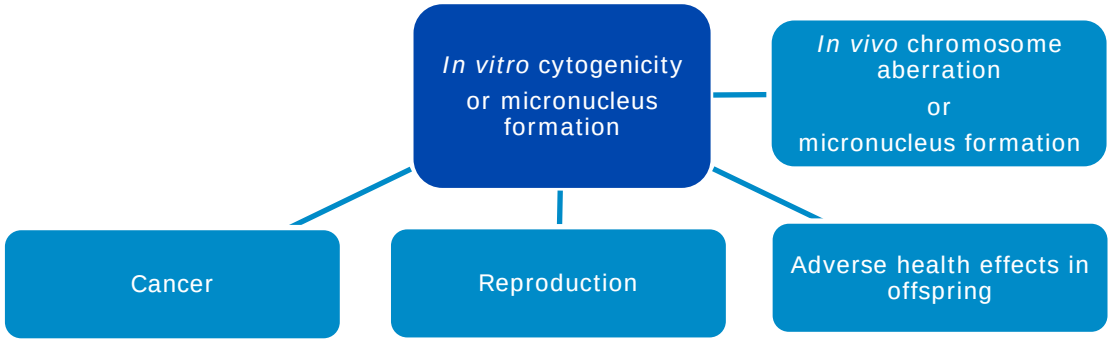
II.2.1 *In vitro* cytogenicity or micronucleus formation

What is it?
In vitro cytogenicity or micronucleus formation refers to the ability of a substance to disrupt the genetic material (DNA) of mammalian cells.

Why should it be determined?
If a substance causes cytogenicity or formation in mammalian cells of a micronucleus, it may also impact on the genetic material in humans which in turn could lead to the development of cancer. It is therefore important to know whether a substance or mixture causes these types of effects, to choose correct protective measures and handling methods to avoid skin and inhalation contact.

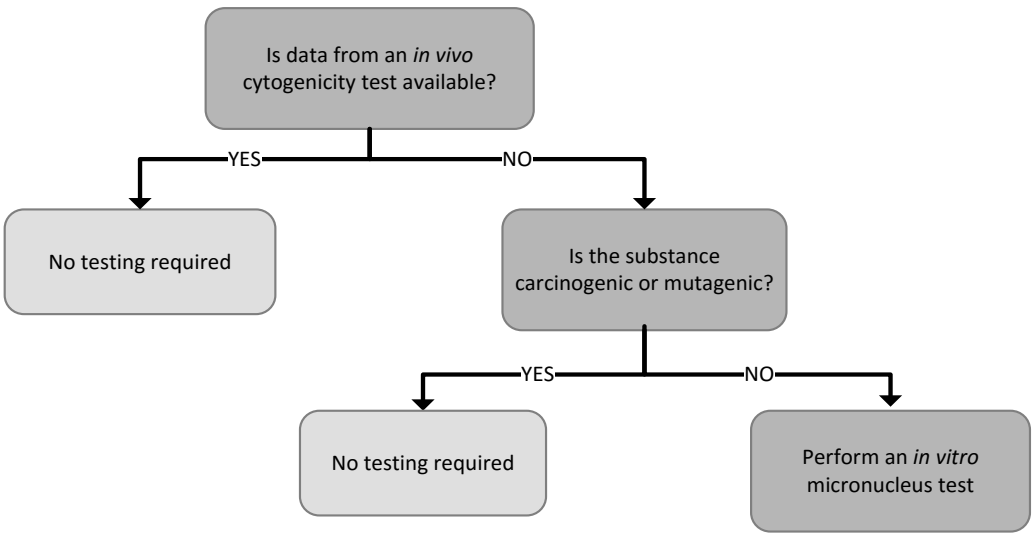
Information about the *in vitro* cytogenicity or micronucleus formation also has an impact on the determination of other properties.

Figure 51: Relationship *in vitro* cytogenicity or micronucleus formation to human health hazards



When should it be determined?
The REACH legal text (Annex VIII, 8.4.2, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 52.

Figure 52: Decision scheme for performing an *in vitro* cytogenicity or micronucleus test



In addition to these arguments, other knowledge may exist based on which you decide that

testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
In vitro cytogenicity or micronucleus formation can be determined using a variety of methods.

Table 36: *In vitro* cytogenicity or micronucleus formation

***In vitro* cytogenicity or micronucleus formation**	
Standard test methods	**Alternatives to the standard test**
In vitro micronucleus test (OECD TG 487, EU TM B.49)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
In vitro mammalian chromosome aberration test (OECD TG 473, EU TM B.10)	**Computer calculation (QSAR)** Some computational models are available but discouraged to be used (except as supporting information).
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.7 - Mutagenicity and carcinogenicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment; If a decision needs to be made on whether to perform a test.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
Further mutagenicity studies must be considered if there is a positive result (see Chapter II-2.3): according to the results of the *in vitro* testing, you need to consider performing *in vivo* mutagenicity testing, normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH).

Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test. If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

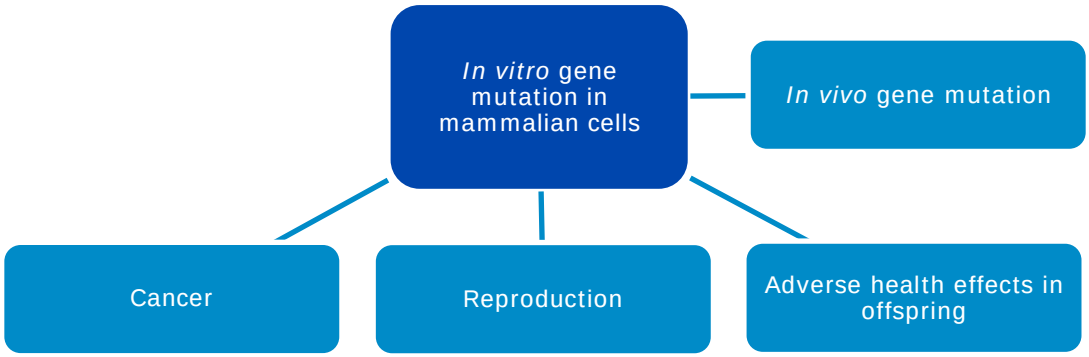
II.2.2 *In vitro* gene mutation in mammalian cells

What is it?
In vitro gene mutation in mammalian refers to the ability of a substance to change the genetic material (DNA) of mammalian cells.

Why should it be determined?
If a substance causes gene mutations in mammalian cells, it may also impact on the genetic material in humans, which in turn could lead to the development of cancer. It is therefore important to know whether a substance or mixture causes these types of effects, to choose correct protective measures and handling methods to avoid skin and inhalation contact.

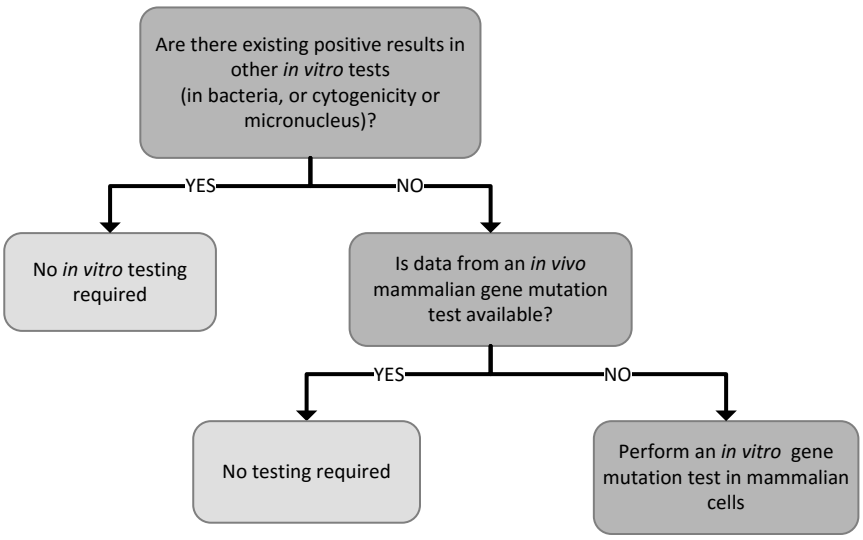
Information about the *in vitro* gene mutation in mammalian cells also has an impact on the determination of other properties.

Figure 53: Relationship of *in vitro* gene mutation in mammalian cells to human health hazards



When should it be determined?
The REACH legal text (Annex VIII, 8.4.3, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 54.

Figure 54: Decision scheme for performing an *in vitro* gene mutation in mammalian cells test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
In vitro gene mutation can be determined according to two methods.

Table 37: *In vitro* gene mutation in mammalian cells

***In vitro* gene mutation in mammalian cells**	
Standard test methods	**Alternatives to the standard test**
In vitro mammalian cell gene mutation test using the *Hprt* and *xprt* genes (OECD TG 476, EU TM B.17)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
In vitro mammalian cell gene mutation test using the Thymidine Kinase gene (OECD TG 490)	**Computer calculation (QSAR)** Some computational models are available but discouraged to be used (except as supporting information).
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.7 - Mutagenicity and carcinogenicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment. If a decision needs to be made on whether to perform a test.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
Further mutagenicity studies must be considered if there is a positive result (see Chapter II-2.3): according to the results of the *in vitro* testing, you need to consider performing *in vivo* mutagenicity testing, normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH).

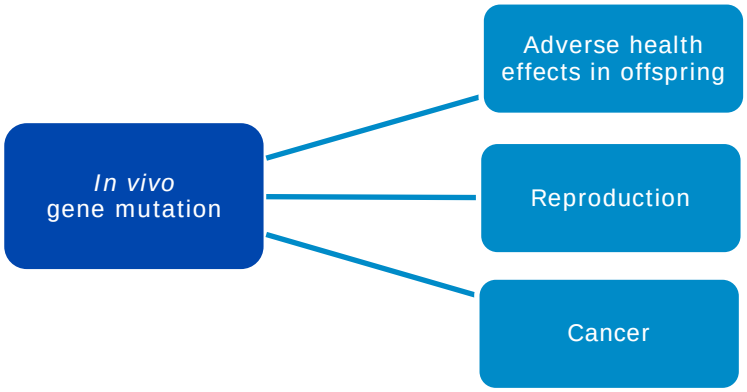
Before such a test is performed you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test. If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

II.2.3 *In vivo* mutagenicity (testing proposal)

What is it?
In vivo mutagenicity refers to the ability of a substance to damage the genetic material (DNA) of living mammals.

Why should it be determined?
If there is a positive result in one or more *in vitro* tests to assess these types of effects, the possible concern for effects in humans needs to be further assessed in a living animal test system.

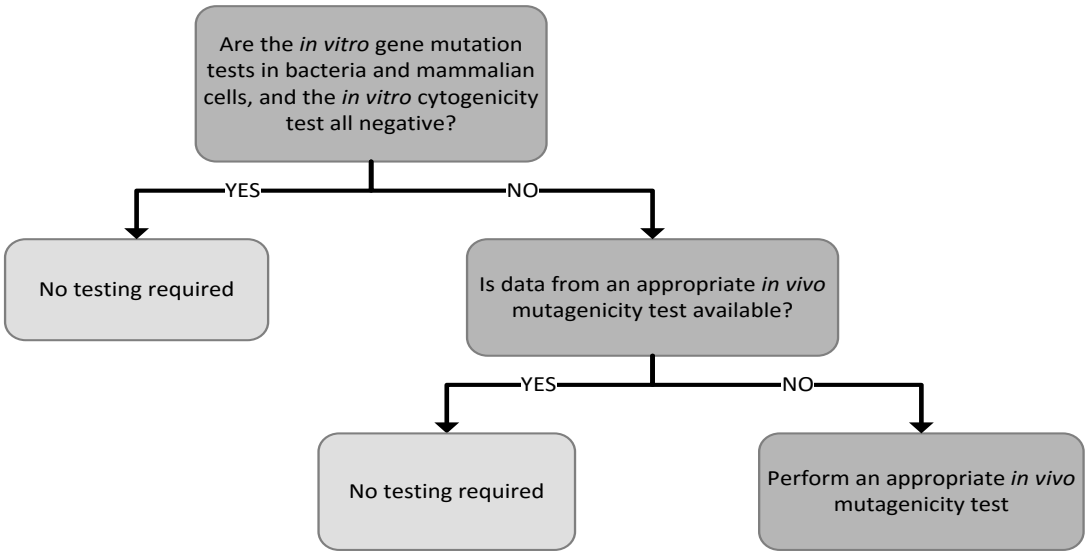
Figure 55: Relationship of *in vivo* mutagenicity to human health hazards



When should it be determined?
In vivo mutagenicity needs to be determined when at least one of the *in vitro* mutagenicity studies, described previously (see Chapters I.3.4, II.2.1, II.2.2) has produced a positive result.

The REACH legal text (Annex VIII, 8.4) does not provide an argument based on which you may decide that testing is not necessary (testing cannot be 'waived'). As the test is part of higher requirements, it cannot be performed before having the approval from ECHA on your testing proposal. Furthermore, to reduce the number of tests on animals, animal testing is the last option and you have to consider the possibilities of using alternative methods.

Figure 56: Decision scheme for performing an *in vivo* mutagenicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear

scientific justification and should be documented in the registration dossier.

How should it be determined?
Defining the suitable *in vivo* mutagenicity test depends on the existing *in vitro* results.

Table 38: *In vivo* mutagenicity

***In vivo* mutagenicity**	
Standard test methods	**Alternatives to the standard test**
In vivo mammalian bone marrow chromosome aberration test (OECD TG 475, EU TM B.11)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
In vivo mammalian erythrocyte micronucleus test (OECD TG 474, EU TM B.12)	
Unscheduled DNA synthesis (UDS) test with mammalian liver cells *in vivo* (OECD TG 486, (EU TM B.39)	**Computer calculation (QSAR)** Computational models are rare and discouraged to be used (except as supporting information)
Transgenic rodent (TGR) somatic and germ cell gene mutation assay (OECD TG 488, EU TM B.58)	
In vivo alkaline single-cell gel electrophoresis assay for DNA strand breaks (comet assay) (OECD TG 489)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
Mammalian spermatogonial chromosome aberration test (OECD TG 483, EU TM B.23)	
Rodent dominant lethal test (OECD TG 478, EU TM B.22)	
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.7 - Mutagenicity and carcinogenicity	

Expertise required

Scientific expertise	If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
Further mutagenicity studies must be considered if there is a positive result in at least one of the *in vitro* tests (see Chapters I.3.4, II.2.1.2.2), you need to consider performing *in vivo* mutagenicity testing, normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH).

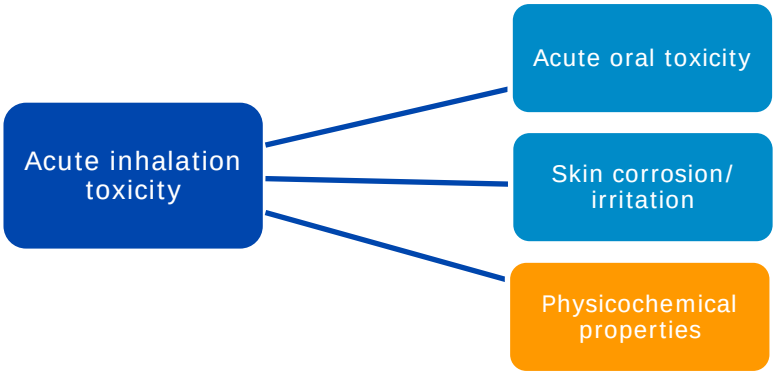
Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test. If you need to submit a testing proposal, follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

II.2.4 Acute toxicity: inhalation

What is it?
The acute inhalation toxicity of a substance is a measure for health effects that may occur after a single (accidental) contact through inhalation of the substance.

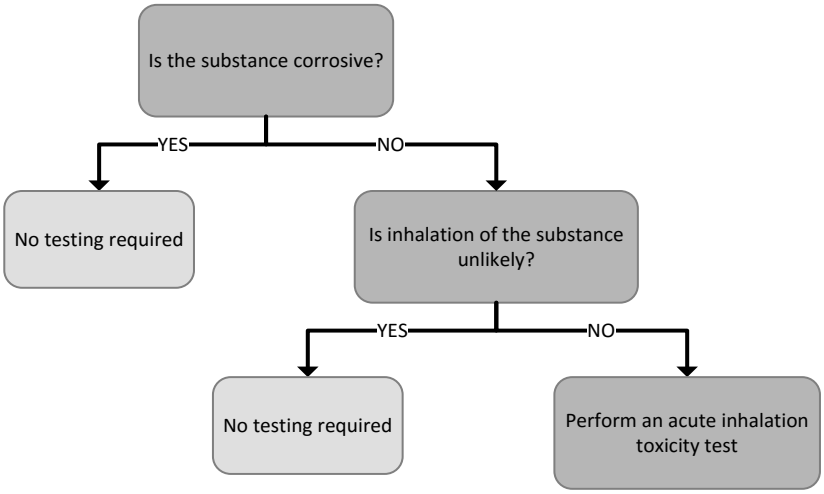
Why should it be determined?
If a substance is acutely toxic after inhalation/breathing, it may induce serious health effects, including death. To further protect humans/workers from accidents, REACH requires a second route for exposure to be assessed, after testing by ingestion.

Figure 57: Relationship of acute inhalation toxicity to human health properties



When should it be determined?
The REACH legal text (Annex VIII, 8.5.2, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 58.

Figure 58: Decision scheme for performing an acute inhalation toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
The acute inhalation toxicity can be determined using a variety of methods.

Table 39: Acute toxicity: inhalation

Acute toxicity: inhalation	
Standard test methods	**Alternatives to the standard test**
Acute inhalation toxicity (OECD TG 403, EU TM B.2)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
Acute Inhalation Toxicity, Fixed Dose Procedure (Draft OECD TG 433)	**Computer calculation (QSAR)** Some computational models are available but discouraged to be used (except as supporting information).
Acute Inhalation Toxicity, Acute Toxic Class Method (OECD TG 436)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.4 - Acute toxicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is not corrosive to the skin, inhalation of the substance is likely, and further assessment of the acute inhalation toxicity is necessary; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

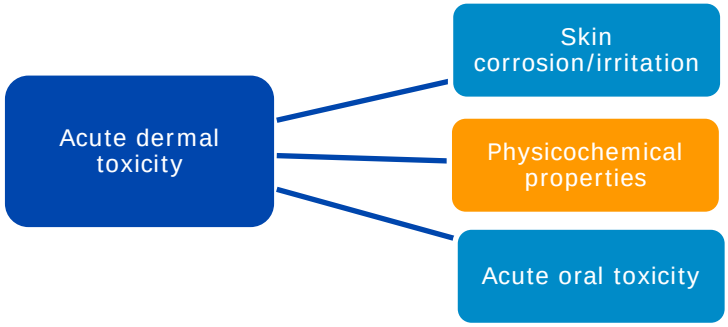
Additional tips
In addition to the oral route, only one second route is required: you have to decide whether, during the manufacturing, formulating, use, etc. of your substance, contact to humans is more likely by inhalation or onto the skin (see Chapter II.2.5).

II.2.5 Acute toxicity: dermal

What is it?
The acute dermal toxicity of a substance is a measure for health effects that may occur after single (accidental) contact of the skin to the substance.

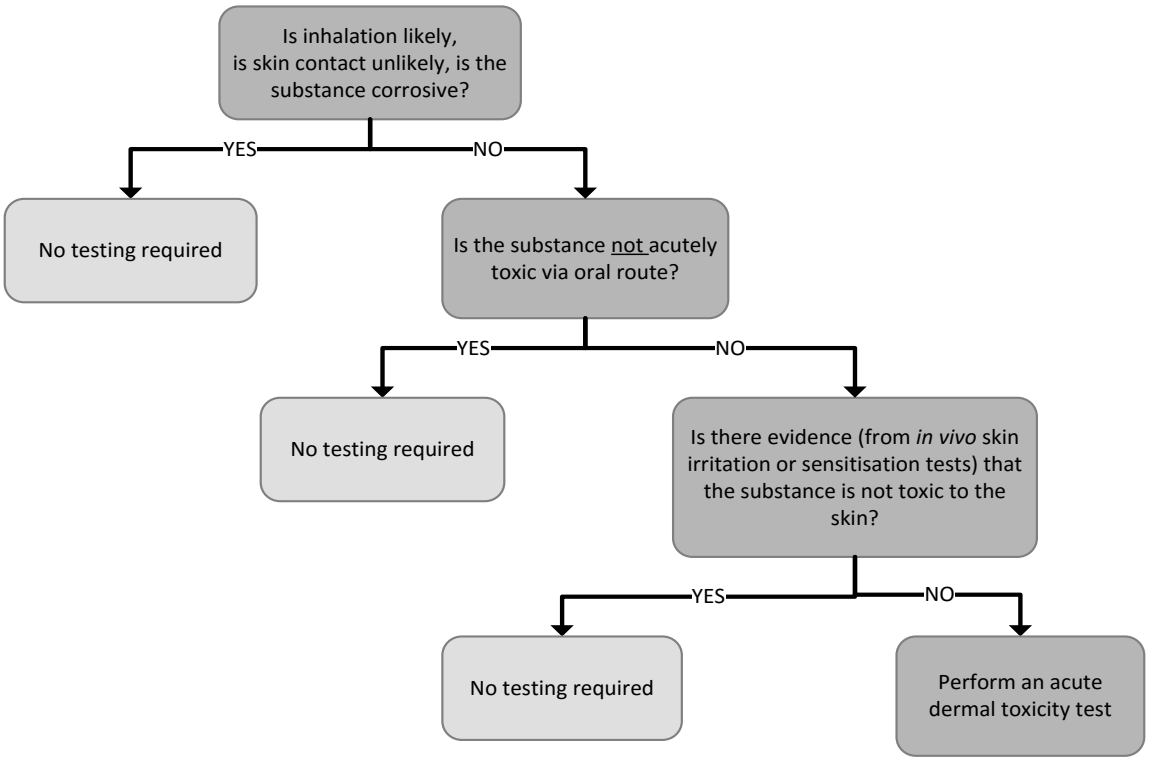
Why should it be determined?
If a substance is acutely toxic after contact with the skin, it may induce serious health effects, including death. To further protect humans/workers from accidents, REACH requires a second route for exposure to be assessed, after testing by ingestion. Results from an acute dermal toxicity test may also provide information about skin irritating effects.

Figure 59: Relationship of acute oral toxicity to human health properties



When should it be determined?
The REACH legal text (Annex VIII, 8.5.3, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 60.

Figure 60: Decision scheme for performing an acute dermal toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
The acute dermal toxicity can be determined using a variety of methods, if required.

Table 40: Acute toxicity: dermal

Acute toxicity: dermal	
Standard test methods	**Alternatives to the standard test**
Acute dermal toxicity (OECD TG 402, EU TM B.3)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
Acute Dermal Toxicity, Fixed Dose Procedure (Draft OECD TG 434)	**Computer calculation (QSAR)** Computational models are rare and discouraged to be used (except as supporting information).
	Read-across / grouping of substances Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.4 - Acute toxicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is highly absorbed through the skin, and the contact through the skin is most likely, and if the substance is acute oral toxic, there is no evidence from *in vivo* skin irritation or sensitisation tests that the substance is not toxic to skin, then further assessment of the acute dermal toxicity is necessary; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
In addition to the oral route, only one second route is required: you have to decide whether, during the manufacturing, formulating, use, etc. of your substance, contact to humans is more likely by inhalation (see Chapter II-2.4) or onto the skin.

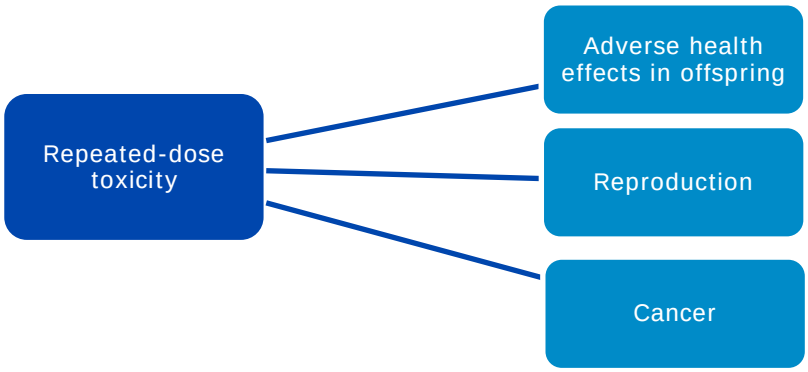
Changes to annex requirements make this *in vivo* test a secondary requirement.

II.2.6 Short-term repeated dose toxicity (28-days)

What is it?
The repeated dose toxicity of a substance describes the health effects that may occur after multiple contacts with a substance. A person can come into contact with a substance by inhalation, skin contact, or ingestion. 'Short-term' indicates that the time period of the recurring contacts of the animal with the substance is 28 days.

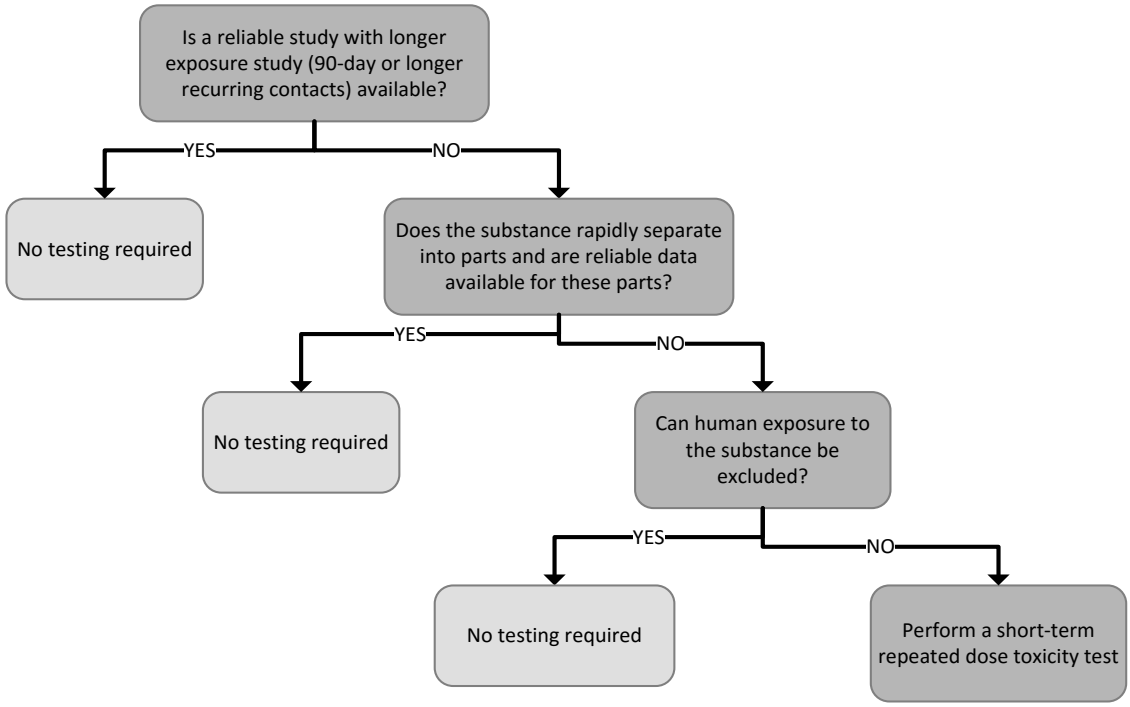
Why should it be determined?
If a substance is a toxicant after repeated-dose exposure, irrespective of the contact entry point, it may induce serious health effects, including damage to organs and death.

Figure 61: Relationship of repeated-dose toxicity to human health properties



When should it be determined?
The REACH legal text (Annex VIII, 8.6.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 62.

Figure 62: Decision scheme for performing a short-term repeated dose toxicity test



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?
The short-term repeated dose toxicity can be determined in a study performed with rodents (for instance, rats or mice).

Table 41: Short-term repeated dose toxicity

Short-term repeated dose toxicity	
Standard test methods	**Alternatives to the standard test**
Repeated dose 28-day oral toxicity study in rodents (OECD TG 407, EU TM B.7)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
Repeated dose dermal toxicity: 21/28-day study (OECD TG 410, EU TM B.9) Repeated dose inhalation toxicity: 28-day or 14-day study (OECD TG 412, EU TM B.8)	**Computer calculation (QSAR)** Computational models are available but discouraged to be used as they will never fulfil the information requirement (except as supporting information).
Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422)	**Read-across / grouping of substances** Experimental data from one or more similar substances may be used, when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.5: Repeated dose toxicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If there are no reliable long-term data available, the substance does not separate into parts, human exposure is likely, and further assessment of the short-term repeated dose toxicity is necessary; If there is an opportunity to address multiple information required while performing the minimum number of animal tests; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips
Remember that to reduce the number of tests on animals, animal testing is the last option and you have to consider the possibilities to use alternative methods.

There are opportunities to address multiple information requirements and avoid unnecessary animal testing. Below are a few situations, where you may define that testing is scientifically not necessary (Annex XI). Remember to always provide a clear argumentation which is scientifically justified and properly documented in the registration dossier.

If a screening for reproductive/developmental toxicity study also has to be performed (see Chapter II.2.8), these two tests can be combined by using the appropriate protocol, and only the screening study would need to be performed.

If the treatment of animals will occur by ingestion, we recommend to perform the screening test first, before the acute oral toxicity test. Indeed, depending on the results, you may have a justification to not conduct the 'acute' test (see Chapter I.3.5).

If some adverse effects are revealed in this study, they need to be investigated further and you will have to test the substance for a longer period, which is normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH). Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test.

If you need to submit a testing proposal follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

If your tonnage is likely to increase shortly, you may also have a justification to propose a test for a longer period rather than perform the short exposure treatment.

Remember to consult the relevant chapter of the ECHA guidance for more detailed advice.

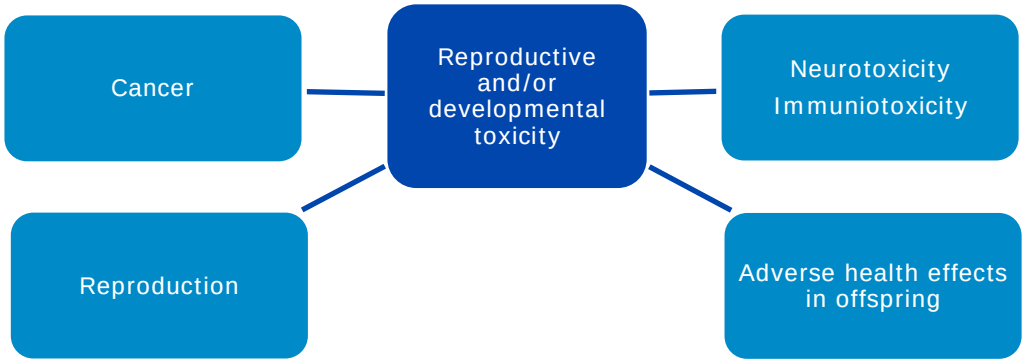
II.2.7 Screening for reproductive / developmental toxicity

What is it?
A reproductive and/or developmental toxic substance may affect fertility and can cause health effects in offspring after recurring contact. The exposure can occur by ingestion, inhalation, or skin contact.

Why should it be determined?

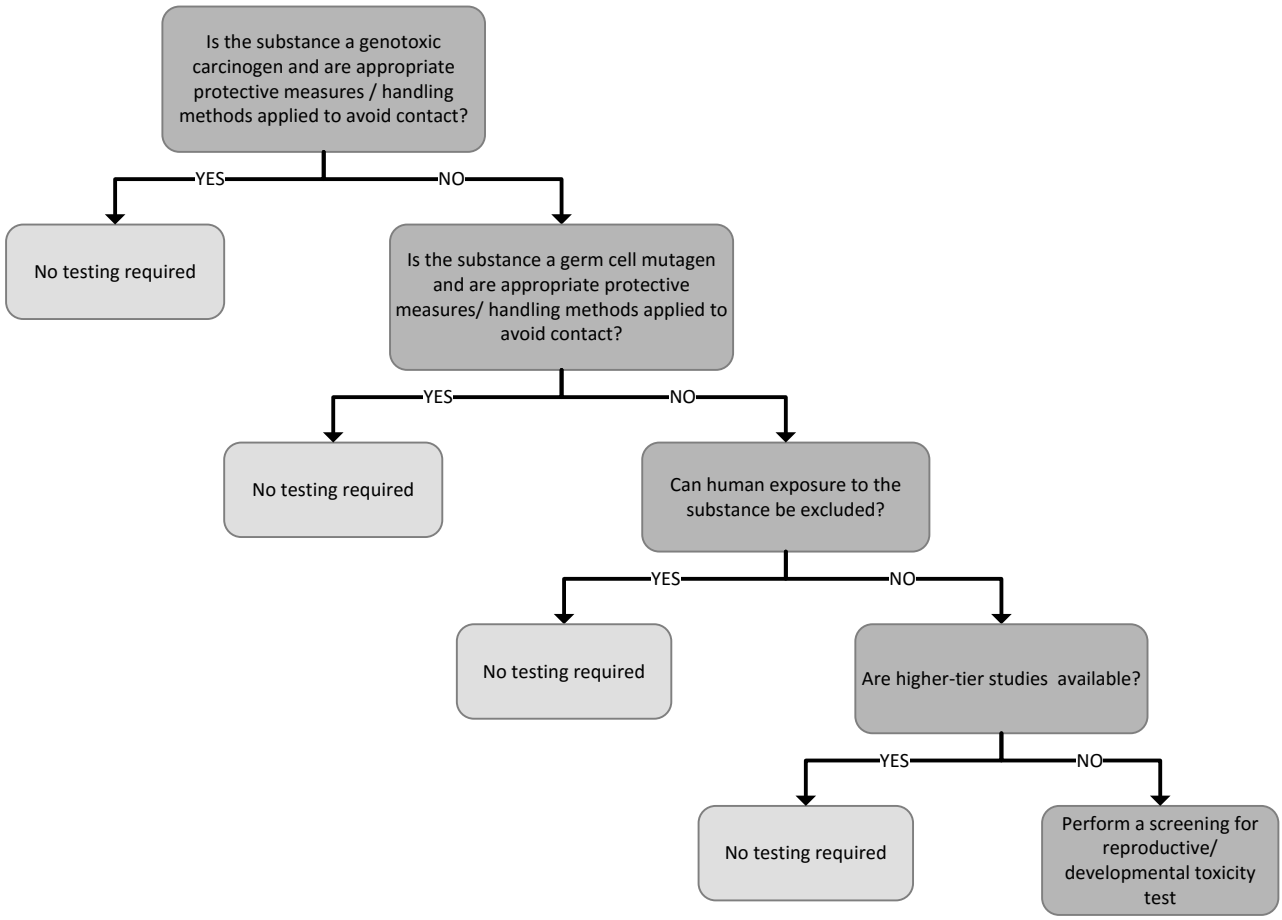
If a substance is a reproductive and/or developmental toxicant, it may induce fertility problems, problems with the ability to reproduce and serious health effects in the offspring. A screening test for reproduction/developmental toxicity gives a first impression of possible problems with the ability to reproduce.

Figure 63: Relationship of reproductive / developmental toxicity to human health properties



When should it be determined?
The REACH legal text (Annex VIII, 8.7.1, Column 2) provides some arguments based on which you may decide that testing is not necessary and may be 'waived'. These arguments are presented in Figure 64.

Figure 64: Decision scheme for performing a screening for reproductive/ developmental toxicity



In addition to these arguments, other knowledge may exist based on which you decide that testing is technically not possible or scientifically not necessary (REACH legal text, Annex XI).

Whichever argument you use for not performing a test should be accompanied by a clear scientific justification and should be documented in the registration dossier.

How should it be determined?

The screening for reproductive and/or developmental toxicity can be determined in a study performed with rodents.

Table 42: Screening for reproductive / developmental toxicity

Screening for reproductive / developmental toxicity	
Standard test methods	**Alternatives to the standard test**
Reproduction/Developmental Toxicity Screening Test (OECD TG 421)	**Waiving,** i.e. no test is performed based on justification: • According to REACH Annex VIII • According to REACH Annex XI
Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422)	**Computer calculation (QSAR)** Computational models are available but discouraged to be used as they will never fulfil the information requirement (except as supporting information).
	Read-across / grouping of substances Experimental data from one or more similar substances) may be used when accompanied by scientific justification and documentation according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7a: Section R.7.6 - Reproductive toxicity	

Expertise required

Administrative expertise	If results of a test are available and can be used directly as input in the registration dossier.
Scientific expertise	If the substance is a genotoxic carcinogen or germ cell mutagen and appropriate protective measures and handling methods to avoid contact are not applied, human exposure is likely, a pre-natal development study is not available, an extended one-generation reproductive toxicity study or a two-generation study are not available, and further assessment of the screening for reproduction/developmental toxicity is necessary; If results of a test are available but there is a need to interpret the results and to conclude on a relevant value for assessment.
Advanced scientific expertise	For use and interpretation of (Q)SAR data for preliminary assessment; For use of data from interpolation of a group of similar substances as an alternative for standard testing as the use of, justification for and documentation of such data is subject to very specific rules; If computational models (QSARs) or experimental data from one or more similar substances (read-across/grouping) are used as alternatives for standard testing as the use of, justification for and documentation of such data is subject to very specific rules.

Additional tips

Remember that to reduce the number of tests on animals, animal testing is the last option and you have to consider the possibilities to use alternative methods.

There are opportunities to address multiple information requirements and avoid unnecessary

animal testing. Below are a few situations, where you may define that testing is scientifically not necessary (Annex XI). Remember to always provide a clear argumentation which is scientifically justified and properly documented in the registration dossier.

If a short exposure toxicity study also has to be performed (see Chapter II.2.7), these two tests can be combined by using the appropriate protocol, and only the screening study would be needed.

If the treatment of animals will occur by ingestion, we recommend to perform the screening test first, before the acute oral toxicity test. Indeed, depending on the results, you may have a justification to not conduct the 'acute' test (see Chapter I.3.5).

If some adverse effects are revealed in this study, you may further investigate and test the substance according to a test, which is normally required for substances produced or imported in high volumes (and described in Annexes IX and X to REACH). Before such a test is performed, you first need to submit a 'testing proposal' to ECHA. Only after ECHA has accepted the proposal, can you (and the co-registrants) perform the test.

If you need to submit a testing proposal follow the advice in the manual How to prepare registration and PPORD dossier (9.7.4. Examples of completing endpoint study records).

Remember to consult the relevant chapter of the ECHA guidance for more detailed advice.

II.2.8 Assessment for toxicokinetic behaviour from relevant information

What is it?
The toxicokinetic behaviour of the substance describes how it behaves after entering a living body (i.e. absorbed, distributed, changed and excreted from the body).

Why should it be determined?
The toxicokinetic behaviour of a substance indicates the relevance of different exposure routes and how the substance travels through the body.

The distribution provides indications of what sort of effects may occur where. It also indicates whether a substance is quickly removed from the body, or whether repeated exposure will induce an increase in internal concentrations. Information on metabolism can suggest what type of effects may occur.

The toxicokinetic information is also helpful for developing methods to monitor concentrations in urine or blood (biomonitoring). In general, it helps in understanding the interaction between a substance and the human body, and can also be used to create a comprehensive justification for read-across/grouping of substances.

How should it be determined?
It is not compulsory to generate toxicokinetic behaviour test information. An expert can do an assessment by using the available information: physicochemical characteristics, environmental information, and human health information that you already have available.

Table 43: Assessment for toxicokinetic behaviour from relevant information

Assessment for toxicokinetic behaviour from relevant information	
Standard test methods	**Alternatives to the standard test**
Toxicokinetics Test (OECD TG 417, EU TM B.36)	Information from physicochemical characteristics, environmental hazard information, and human health hazard information can be used to determine the toxicokinetic behaviour.
	Computer calculation (QSAR) Computational models are available but discouraged to be used as they will never fulfil the information requirement (except as supporting information).
	Read-across / grouping of substances Information on toxicokinetic behaviour from one or more similar substances can be used to create a comprehensive justification for the use of read-across according to REACH Annex XI, 1.5.
ECHA *Guidance on Information Requirements and Chemical Safety Assessment*	
Chapter R.7c: Section R.7.12 - Guidance on Toxicokinetics	

Expertise required

Advanced scientific expertise	To make an assessment on toxicokinetic behaviour based on all the available physicochemical characteristics, environmental information, and human health information.

Additional tips
Remember that animal testing is the last option and you need to consider any alternative.

5. Evaluation of whether substances are persistent, bioaccumulative and toxic

What is it?
Substances that breakdown slowly in the environment are called 'persistent'. Substances that have a tendency to stay in biological material, and whose levels in the biological material therefore increase with repeated exposure, are called 'bioaccumulative'. Substances that can harm organisms, coming into contact with them, are called 'toxic'.

In the evaluation of whether substances are persistent, bioaccumulative and toxic there are three possible relevant end-results:

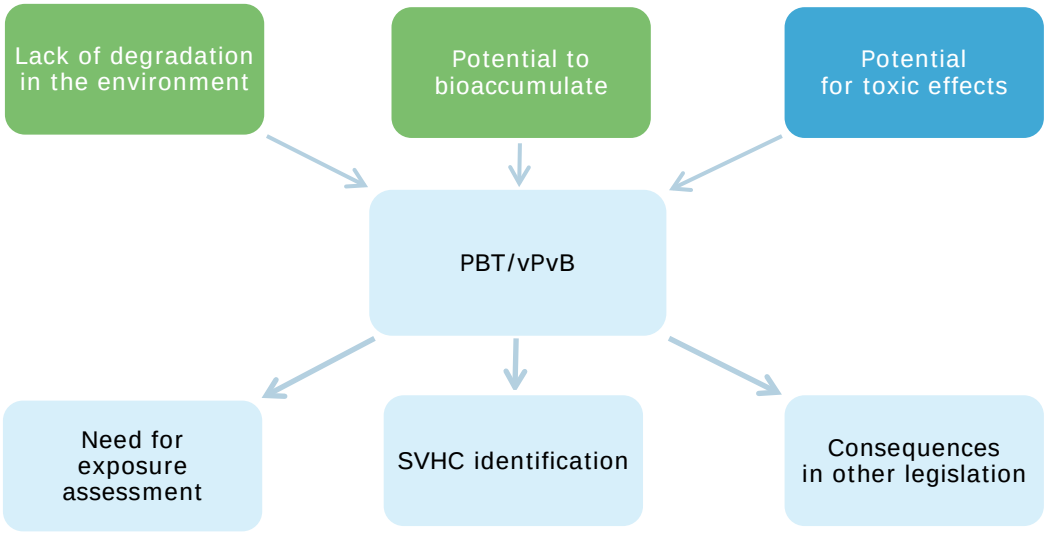
1. A substance is persistent and bioaccumulative and toxic (PBT);
2. A substance is very persistent and very bioaccumulative (vPvB)
3. A substance is neither PBT, nor vPvB.

Why should it be determined?
You have to evaluate whether a substance is a PBT or vPvB substance, because they may reach remote areas in the environment, even after a long time. They also tend to accumulate in organisms, and reach humans through the food chain. This can lead to unpredictable effects in the long-term and accumulation is difficult to reverse once it has occurred.

If your substance is a PBT or vPvB, you will have to perform an exposure assessment and risk characterisation in the chemical safety assessment (see Chapter 6). A PBT or vPvB substance may also be considered to be a Substance of Very High Concern (SVHC). This leads to a number of consequences, such as the need to request an authorisation under REACH. There are also restrictions for PBT or vPvB substances in other legislation.

Figure 65 shows the factors that help determine whether a substance is a PBT or vPvB substance and the consequences under the REACH Regulation and other legislation.

Figure 65: Relationship between factors, classification, PBT/vPvB characteristics and consequences in REACH and other legislation



When should it be determined?
You have to perform an assessment of whether a substance is PBT/vPvB when you need to conduct a chemical safety assessment, which has to be reported in a chemical safety report.

How should it be determined?

The criteria for PBT and vPvB substances are specified in Annex XIII to REACH and further explained in the Guidance document on PBT/vPvB assessment, Chapter R.11.

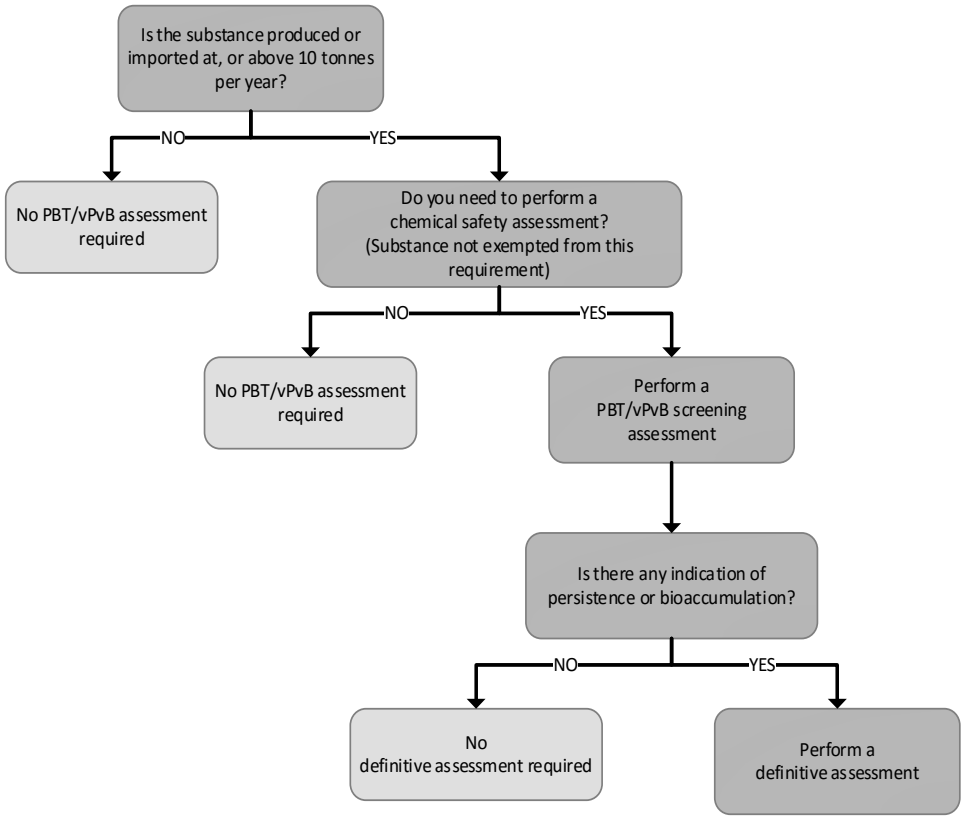
You have to use and combine all relevant available information, in an approach called 'weight

of evidence', to assess whether your substance is a PBT or vPvB substance.

Usually, for substances registered up to 100 tonnes per year, you will only have limited information on biodegradation, bioaccumulation and potential harmful properties related to human health and the environment. Information such as ready biodegradability, octanol water partition coefficient and short-term aquatic toxicity can be used in a **screening assessment**.

If this screening assessment provides indications that your substance is a PBT or vPvB substance, you will have to do a **definitive assessment.** This often requires additional tests which are part of the requirements for higher tonnage bands. You will have to make a testing proposal to ECHA if you need such additional tests, including testing on vertebrate animals.

Figure 66: Decision scheme on PBT assessment



Expertise required

Advanced scientific expertise	To assess the quality and relevance of existing data, to derive a conclusion on PBT/vPvB properties, either at a screening level or a definitive level (normally a multi-step process).

Timelines

UP TO 3 MONTH	• To perform and submit a PBT/vPvB screening if you are the only registrant and you need to hire expertise to assess the information and all relevant information is already available. All relevant information should be available because of requirements mentioned in other chapters of this Guide. The assessment itself, based on available information, does not require more than a day.
UP TO 6 MONTHS	• To perform further testing, once permission was obtained from ECHA for testing according to Annex IX to the REACH Regulation • To perform a definitive assessment if needed, as indicated by the screening assessment.

Factors that you need to consider in deciding the necessary timelines include:

- Finding and hiring expertise to perform the actual assessment.
- Agreeing with co-registrants on the results of the screening assessment.
- Agreeing with co-registrants and creating a testing proposal (if you need to) to be submitted as part of the registration dossier by the lead registrant.
- Finding a proper test laboratory to do the further testing and agreeing with the laboratory on the testing, contract, etc.
- Creating and sending samples for testing to the test laboratory.
- Evaluating the results and updating the registration document with the new PBT/vPvB assessment.

6. Chemical safety assessment and report

6.1 What is it?

The assessment of chemical safety is a stepwise approach to assess the hazard of a substance and exposure to it, to show whether and how a substance can be used safely. The chemical safety assessment (CSA) has to be done for each use in the life cycle of the substance: from manufacture to end use (with some exceptions). The CSA has to be reported in the chemical safety report (CSR) attached to the registration dossier.

6.2 Why is it needed?

You have to perform a CSA to assess whether the existing conditions of use of your substance are safe for all uses you identified. If you cannot demonstrate control of risks, you must define additional risk management measures or advise against such use.

Your CSR must describe the operational conditions and risk management measures that will sufficiently limit the exposure so that adverse effects do not occur. These use/use-group specific descriptions are given in the form of exposure scenarios (ESs). You must use the results of the CSA for checking and, where necessary, improving the conditions under which you manufacture and yourself use the substance.

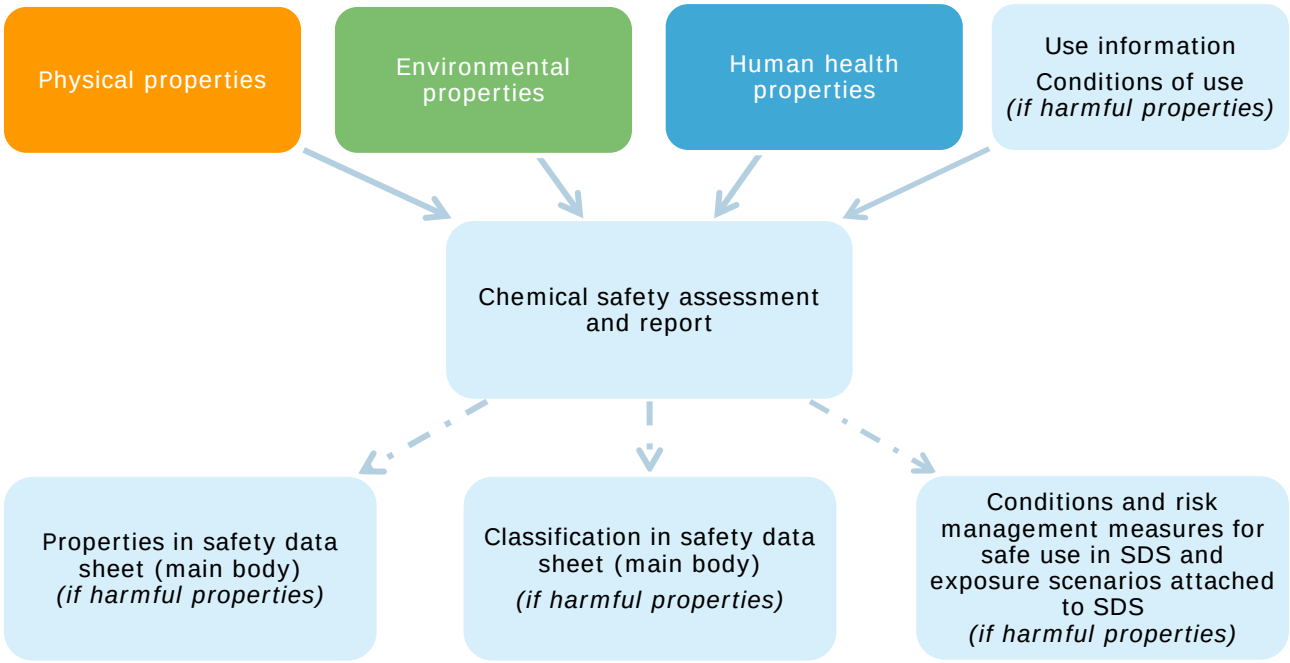
Furthermore, you must communicate the properties of the substance and the conditions and risk management measures needed for safe use in the safety data sheet (SDS) to your customers who are downstream users under REACH.

If ESs are needed in your CSR, you must also provide them to your downstream users, in a format and language facilitating communication on safe use. Formulators who mix your substance with other substances must use the information to create appropriate safety advice in the SDS of their products, and producers of articles must use this information to design their articles.

Finally, the non-confidential information on uses and exposures you submit in your IUCLID dossier are published on ECHA's website and your company name will be mentioned as a registrant unless you request it to remain confidential and this request is accepted as valid by ECHA. Therefore, we recommend your information on uses is valid and representative of the actual situation.

Figure 67 shows the relationship between the substance properties, CSA/CSR and resulting outputs.

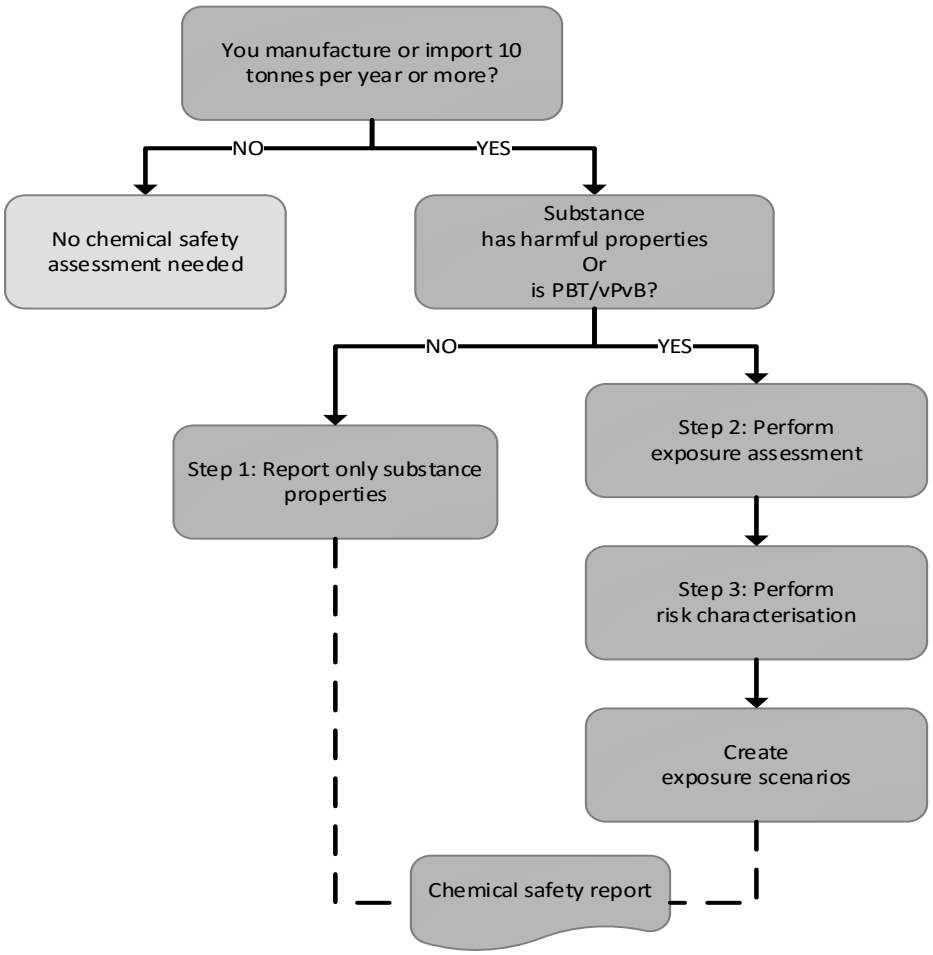
Figure 67: Relationship between properties of a substance, chemical safety assessment and report and resulting outputs of the process



6.3 When is it needed?

If you register a substance with a tonnage band of 1-10 tonnes per year, you need to provide the information on the properties of the substance and the uses in the registration dossier.

Figure 68: Decision scheme of CSA/CSR processing



If you register a substance with a tonnage band of 10-100 tonnes per year, you also need to perform a CSA and report it in CSR.

If you conclude that your substance is not hazardous or PBT/vPvB, the CSA can be limited to use description, hazard assessment and PBT assessment, and the CSR limited to Chapters 1-8.

If you conclude that your substance has harmful properties or is assessed to be a PBT or vPvB, you also have to perform, for each relevant use, an exposure assessment and risk characterisation.

Some uses are exempted from REACH or from the requirement to carry out a chemical safety assessment:

- If your substance is imported in a mixture in a concentration below certain concentration limits (usually 1% by weight, but dependent on e.g. the physical state of the mixture and the classification of the substance);
- If your substance is registered as an isolated intermediate used under strictly controlled conditions.

Furthermore, risks to human health do not need to be considered for the end-use of substances in food contact materials and cosmetic products, if the substances or the products are under the scope of relevant legislation, as indicated in the REACH text.

The full set of exemptions is rather complicated and you are advised to consult an expert or study the Guidance on registration.

In your IUCLID dossier, you need to clearly report uses exempted from the CSA.

6.4 How can it be determined?

6.4.1 Assessing the type and extent of hazards of the substance

You have to determine the (potentially harmful) properties of the substance. As described in other chapters of this Guide they are divided in three areas:

- Chemical/physical properties that may be harmful
- Environmental properties
- Human health properties

For **physicochemical** hazards you will have, as a minimum, to assess explosivity, flammability and oxidising potential. The assessment is a qualitative one, and the result will be either classification or not for these properties (see Chapter I.1).

For the **environment**, you will have to make assessments for the multiple parts of the environment, called environmental 'compartments', and for the short-term as well as long-term effects. Furthermore, you will have to assess whether your substance has so-called 'PBT/vPvB' properties (see Chapter I.2).

For **human health**, you will need to make different assessments depending on the routes of exposure, location of the effects, duration of exposure, type of effect and whether the study allows to draw conclusions on the quantitative relation between exposure and effects.

For many properties related to human health and the environment, you have to derive quantitative thresholds, i.e. levels below which no negative effects will occur. These thresholds are called derived no effect levels (DNELs) for human health and predicted no effect concentrations (PNECs) for the environment.

Based on the information on the properties, you will assess the type and extent of hazard related to your substance, and have to decide on the classification of the substance (see Chapter I.3).

If in the risk characterisation step (see below) you conclude that the risk is not sufficiently controlled, you may need to return to this step to obtain refined information on the threshold levels for safe use.

For more information, see the *Guidance in a Nutshell on Chemical Safety Assessment*.

6.4.2 Exposure assessment

Your exposure assessment for a use starts from the substance properties, identified uses and known existing conditions of use. This leads to an exposure estimate from that use. The full process is illustrated in Figure 69.

For use description, in addition to the textual descriptions, you must use the 'use descriptor system' to describe the uses of your substance, in terms of:

(i) types of activities/ processes (PROC),
(ii) type of environmental release (ERC),
(iii) sector of end-use (SU), and
(iv) type of product or article (PC/AC).

The use descriptor system is explained in the *Guidance on information requirements and chemical safety assessment, ChapterR.12*.

For **physicochemical** hazards, such as flammability, exposure assessments is nothing more than determining the conditions of use that prevent accidents at the workplace. For example, in the case of flammable substances, it has to be assessed whether the existing conditions of use, including risk management measures, are sufficient to ensure that the chances of a fire occurring are very low. Such an assessment is always a qualitative assessment.

For **the environment,** you also have to do several exposure assessments for several environmental compartments:

(i) assess the emission of the substance from the processes, and
(ii) (ii) assess the fate and distribution of the substance in the environment.

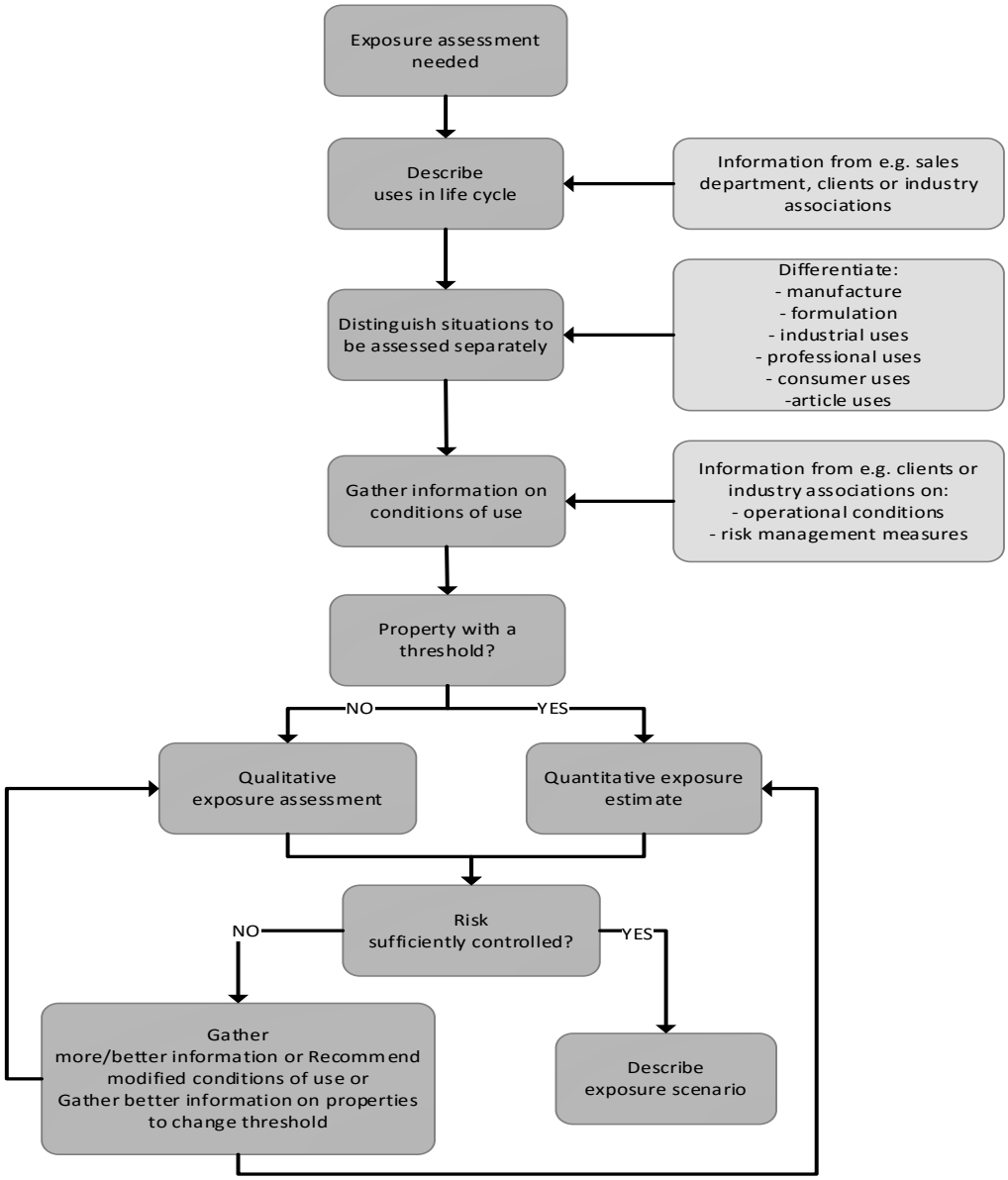
The emission and the fate and distribution, together with environmental conditions, result in concentrations in the environment.

You need to assess exposure separately around the local point sources and for regional exposure from several sources in a given region. You can do an emission assessment either by measuring emissions or by modelling. Environmental concentrations can also be measured. However, you will probably mostly use exposure modelling for estimating environmental concentrations.

For **human health,** you usually have to do several exposure assessments per identified use, e.g. for different routes and timeframes. The types of exposure assessment you need to do are related to the properties and uses of the substance.

Make sure that the exposure assessment methods and tools that you use fit to the property profile of your substance and the use conditions. The tools have their limitations. For example, exposure to fumes from hot work processes is difficult to model.

Figure 69: Illustration of the exposure assessment process.



If, in the risk characterisation step (see below), you conclude that the risk is not sufficiently controlled, you need to return to this step, to refine the operational conditions/risk management measures that you recommend to ensure safe use.

6.4.3 Risk characterisation

Risk characterisation, is the process whereby you balance the information on the hazards of substances with the information on the exposure to the substances (for humans and the environment and, where relevant, for physical and chemical properties).

For effects with a toxicological threshold (derived no effect levels (DNELs) or predicted no effect concentration (PNECs)), you need to compare the quantitative exposure estimates with the thresholds. In practice, this is done by dividing the exposure level (or concentration) by the effect level (or concentration). This leads to the 'risk characterisation ratio' (RCR).

You need to ensure that, for each relevant use and separate assessment, each RCR is below 1, i.e. the level of exposure is lower than the threshold level.

If an RCR is close to, or above 1, you need to iterate your assessment: either by refining the information on the substance's properties or by amending the recommended operational conditions and/or risk management measures.

6.4.4 Exposure scenarios

An exposure scenario (ES) is the description, given in a structured format, of operational conditions and risk management measures leading to safe use. You have to create ESs covering the full life cycle of the substance if the substance has harmful properties for humans, or for the environment, or has harmful physical and chemical properties.

Each separate activity - exposure situation - within the use that is assessed should be described separately in 'contributing scenarios'.

For example, manual spraying at industrial sites, which would be described in REACH terms as "application of paints at industrial sites", would have the following contributing scenarios:

- Preparing the paint to be sprayed (paint kitchen) (PROC 5)
- Filling equipment (PROC 8)
- Spraying (PROC 7)
- Cleaning of equipment (PROC 28).

For more details, please consult the templates of ES and examples.

6.4.5 Chemical safety report and Chesar

Finally, the results of the chemical safety assessment are documented in the chemical safety report (CSR).

The CSR structure is outlined in Annex I to REACH and contains 10 chapters: substance and uses are described in Chapters 1 and 2, and hazard assessment in Chapters 3-8. If no hazards are identified for your substance, Chapters 9 (exposure assessment) and 10 (risk characterisation) are not required.

For assisting in the exposure assessment and risk characterisation, ECHA has developed the chemical safety assessment and reporting tool (Chesar). You can use this tool to create the exposure assessment and the relevant part of the chemical safety report, as well as the corresponding ES for communication.

ECHA provides practical examples of chemical safety reports. This page includes a document with hints and tips to consider when planning and preparing a chemical safety report, a complete example of an imaginary substance and two data sets created from software tools (IUCLID and Chesar) that together can create a full CSR. See http://echa.europa.eu/support/practical-examples-of-chemical-safety-reports.

6.5 Expertise required

For several substances, you may be able to create a full chemical safety report relatively easily, including exposure assessment and risk characterisation from the report options in IUCLID combined with the report options in Chesar. However, you will have to engage sufficient expertise to do this.

Advanced scientific expertise	For assessing the hazards (including deriving appropriate thresholds), as well as assessing exposure (including the use of measured exposure data or exposure models); To use the tools which allow knowledge to be translated on the uses and conditions of use (expertise lies with the company) into correct input for the modelling.

These are activities that are very complex and need substantial expertise and experience.

6.6 Timelines

UP TO 1 MONTH	• To describe the uses in substance's life cycle and the conditions of use, if your substance has a very simple life cycle and you have proper relations with the relevant users; • To identify relevant uses of your substance from the use maps developed by downstream user sectors; • For each separate use, to create an exposure assessment for human health and the environment and to make qualitative assessments where needed; this does not include the element of finding and hiring experts to do this work.
UP TO 3 MONTHS	• To assess the properties of the substance, if all relevant information has already been gathered as described in the previous chapters, and • To derive thresholds and other conclusions on the properties of the substance.
UP TO 6 MONTHS	• To describe the life cycle and the starting point for conditions of use of your substance, if your substance has a complicated life cycle (e.g. a broad range of applications, long supply chain or distributors involved for a significant part of your market).
UP TO 12 MONTHS	• For a full chemical safety assessment, including exposure assessment and risk characterisation for a substance with multiple uses that has to be registered by multiple registrants; part of this time is needed to come to an agreement with your co-registrants.

6.7 Additional tips

To facilitate the information flow from downstream users and registrants, many downstream-user organisations develop use maps which cover typical uses and conditions of use in their sector. Check if such use maps exist for sectors relevant for your substance.

Your product development and technical department can provide input on the chemistry and composition of the substance. The marketing or sales department will have knowledge on the uses and may be able to obtain information from downstream users on conditions of use.

It is your decision (from a business or an assessment perspective) to widely/narrowly define the different uses of your substance for the CSA. There are benefits and risks in each approach. Importantly, you should not compromise your obligation to provide downstream users with useful safety data sheets (SDS), including ESs they can really use to ensure safe working conditions.

Ensure that your CSR is understandable for an outside reader and does not contain elements that are not relevant or even wrong (e.g. uses that are not relevant in practice). Note: this over-reporting of uses may trigger the selection of your substance for further actions by authorities, such as substance evaluation.

You need to agree with your co-registrants whether you want to create one joint CSR that fits all members in a SIEF. There may be reasons not to do this, e.g. if you have a specific use that you consider valuable business information.

If you opt for a joint CSR, you may also develop the content of the SDS with your co-registrants: all users will obtain the same information from their suppliers. Check if there are relevant differences in composition, such as e.g. impurities leading to differences in properties, as this has to be reflected in the respective SDS.

Consider developing a structured system for your downstream users to provide feedback on the ESs you send them, as you may need to update your dossier and the CSR accordingly.

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