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Introduction: Policy and Scientific Context of Chemicals Risk and Risk Management

This chapter acts as a foundation of understanding for the rest of the book. It introduces the regulatory systems that demand the evaluation of risk for chemical substances that are intended to be used and placed on the market. It sets out the development of risk assessment in the European, global and national contexts. This chapter also explains the key concepts of hazard and exposure. Hazard is defined as the inherent properties of a substance that may make it harmful – flammability, toxicity and so on. Exposure refers to the ways in which humans and the environment come into contact with substances. The reasons for bringing together hazard and exposure in order to understand risk are explained.

The focus of this book is the REACH Regulation (most often referred to just as 'REACH'), as this is the main regulatory driver for the risk assessment of chemical substances in the European Union. REACH (**R**egistration, **E**valuation, **A**uthorisation & restriction of **Ch**emicals), however, should be viewed in the context of other legislation that is either directly or indirectly connected to the REACH Regulation. With this in mind, the later sections of this chapter include consideration of United Kingdom legislation on chemicals, including worker and environmental protection. These sections are intended to serve as examples of how REACH is connected to prior legislation and how compliance with REACH works with such legislative regimes at national level.

The purpose of this book is to set out in a simple and concise way how to assess and manage the risks of chemicals to humans and the environment. This is done within the context of the main legislation that applies to the safety of the manufacture and use of chemicals in the European Union (EU) – the REACH Regulation. It is not the intention to give detailed guidance on each aspect of risk assessment or in depth assessment of specific aspects of REACH, but rather to explain the main aspects of chemical risk assessment and the processes that are applied, so that each aspect can be understood

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within the context of REACH. This book should act as a handbook, so the reader/user can find out about specific aspects of the process and technical elements in sufficient detail to understand where and how they fit in the risk assessment of chemicals, and where to look for more detailed information.

Legislation on chemicals has specific purposes and is aimed at control of particular processes or aspects of the manufacture, use, reuse and disposal of chemicals. In addition, some legislation is aimed at chemicals that are used in a particular way (for example pharmaceuticals or pesticides), or because they have specific dangerous qualities (carcinogens, explosives and highly flammable substances), and some legislation is aimed at protection of specific sections of the population (e.g. workers, consumers, pregnant workers). Other legislation is aimed at environmental protection by specific control of releases to the environment (e.g. integrated pollution potential and control – IPPC) or monitoring specific parts of the environment (e.g. the Water Framework Directive – WFD for water). Inevitably there is overlap between all this legislation on chemicals, and today companies manufacturing and using chemicals have to be aware of a wide range of legislation to ensure that they are complying with all the relevant laws to operate legally and safely.

REACH is concerned with the safety of chemical substances for placement on the European market. REACH is a 'Regulation' (as compared to a Directive[1]) meaning that REACH is a law that applies equally and with the same text in all EU Member States. REACH requires that industry supplies specific information on individual chemicals in order to demonstrate that its manufacture and specific uses in the EU market are safe[2] for humans and the environment.

Key features of REACH are:

- Those who make chemicals in the EU or import them into the EU (Manufacturers/Importers, i.e. 'industry') for placing on the EU and EEA (European Economic Area) market[3] are responsible for supplying information to demonstrate safe manufacture and use.
- The safety assessments done by industry are based on a risk assessment that examines the properties of the substance that may make it dangerous to humans and/or the environment, and the way the chemical is used that causes humans and/or the environment to come into contact with it.
- Information supplied is assessed by a central regulator: the European Chemicals Agency (ECHA).
- Each substance is assessed for safety on its own merit: that is, the potential risks or impact of each chemical and its uses are assessed on their own and not in combination with other substances.[4]
- The safety of chemicals is assessed only for the uses that the manufacturer puts forward; thus the assessment is valid for these uses only.
- The safety of all parts of the chemical's life cycle are relevant – from manufacture to final disposal (including recycling/reuse, if relevant).

[1] A Directive is applied (transcribed) by each Member State of the Union in its own law.

[2] What constitutes and is designated as 'safe' with the context of REACH is addressed in later chapters of this book.

[3] There are specific rules for substances that are used for the purposes of research – these are identified later (Section 4.1 and Appendix C).

[4] However, the breakdown products of the substance are relevant to the risk assessment.

- REACH is applied to the manufacture/import and use of chemicals substances, not chemicals that are used specifically as pharmaceuticals, biocides, plant protection products (pesticides), veterinary medicines and cosmetics. However, it does apply to the chemicals that are used to make these products.

The concepts that underpin the REACH Regulation are not new; what is new is the application of a single system for assessing the safety of chemicals being placed on the European market. To understand why REACH was created as a Regulation it is necessary to briefly look at what was in place prior to REACH coming into force in 2007.

The pre-REACH legislative framework comprised three main pieces of legislation, namely:

- Existing Substances Regulation (ESR).
- Dangerous Substances Directive (DSD) Seventh Amendment – concerning the placing on the market of 'new' substances (in the UK this was the Notification of New Substances Regulation or NONS). The legal basis was laid out in Directive 67/548/EEC.
- Marketing and Use (or 'Limitations') Directive.

In addition, the DSD set out the rules for the classification and labelling of substances. This is of key importance for hazard communication and also because the classification of substances leads to how the substance is dealt with in other legislation (Appendix A). This includes, importantly, how the substance should be handled and treated by users of the substance.[5]

Under this legislation prior to REACH, substances defined as 'new' (i.e. placed onto the European market after 1981) were required to be tested and notified before marketing in volumes above 10 kg. For higher volumes more in-depth testing – focused on long-term and chronic effects – had to be provided. On the basis of that information, the substances were assessed for their risks to human health and the environment. There were, however, no corresponding requirements for 'existing chemicals': chemicals that were on the European Community market between 1 January 1971 and 18 September 1981. These 'existing chemicals' were listed in the EINECS (European INventory of Existing Commercial chemical Substances), which consists of about 100 000 existing substances. This accounts for about 99% of the total volume of chemicals on the European market.

Risk assessment of new substances coming onto the market under pre-REACH legislation formed the basis of REACH and is the core of the registration of chemicals within REACH. For a new chemical to be placed on the EU market, the manufacturer had to chemically describe the substance and provide basic information on its properties in terms of hazard and use, and assess the potential risks to humans and the environment from the manufacture and use of the substance. The amount of information to be provided depended upon on the amount to be placed on the market. A manufacturer could present its information dossier to the 'Competent Authorities' of any of the Member States, who would assess the information and present a risk assessment of the substance and its uses for acceptance by all other Member States. The system was looked after

[5] Note that the regime for the classification and labelling of chemical substances is explained in Appendix A.

at EU level by the European Chemicals Bureau (part of the European Commission's Directorate General Joint Research Centre – DG JRC). The assessment could reach one of four possible conclusions:

1. **No immediate concern**: no need to consider again before next tonnage trigger.
2. **Concern**: define further information needs and requests at next tonnage trigger.
3. **Concern**: define further information needs and seek immediately.
4. **Concern**: immediately make recommendations for risk reduction.

For the existing EINECS substances, the risk assessment of these was the responsibility of the regulators at European and Member State level. Substances were placed on priority lists, four of which were established with about 50 substances on each. The prioritisation by the European Community (EC) and Member States was based on hazard, uses and high tonnage use. For this limited subset of substances, each substance was appointed a Member State 'Rapporteur' with the responsibility of conducting the risk assessment, retrieving and assessing all relevant information, and presenting the risk assessment to a Member State and EC expert group with representation from relevant industry sector groups for discussion and agreement. The assessments often required further information from industry (at the industry's expense) but the assessments were done by the Rapporteur and by their own government scientists. The assessments could conclude with one of three possible options for each of the different uses of the chemical and the risks they present to humans working with or using the substances as consumers, and each part ('compartment') of the environment (i.e. freshwater, marine, soil, air, and sewage treatment works). The three available conclusions were:

1. Need for further information and/or testing.
2. At present no need for further information and/or testing and no need for risk reduction measures.
3. Need for limiting the risk.

While the system for assessing new substances was generally regarded to work well and efficiently, the system for existing substances was slow (albeit thorough) and came under increasing criticism. This was both from industry, who wanted to show that their substances were risk assessed as safe, and pressure groups, who wanted to see the existing substances assessed and risky uses banned.

The solution was REACH, in which all substances new and existing are treated the same way, and the burden of information provision is on those who are placing the products on the market. Existing substances are brought into REACH as 'phase-in' substances; the timing for registration of these substances is based on particular hazard and the volume placed on the market. Former 'new' substances are considered to be registered within REACH, but the registrations must be updated before the next tonnage band is reached.

1.1 Overview of the Risk Assessment of Chemical Substances

This section describes the main concepts that underpin risk assessment of chemicals (although these concepts also underpin many other assessments of risk). The assessment

of risk is based on the likelihood of something (usually undesirable) happening; this is based on assessing the quality of the 'thing' (in this case a chemical) that might have an effect and the likelihood that the effect will take place. Thus, how and how often the chemical comes into contact with the systems ('receptors') it can impact on (i.e. humans or the environment) forms part of the risk assessment.

The two sides of risk assessment of chemicals are:

1. The inherent properties of a substance that can cause harm (adverse effects).
2. The likelihood of contact with those hazards.

In terms of chemical risk assessment it is useful to think of 1 and 2 above as 'properties' and 'exposure', respectively.

It is the inherent properties of a substance that both define the hazard and influence how it comes into contact with humans and the environment. The likelihood of humans and the environment coming into contact with these hazards is determined by how the substances are used and how much of them are used. In this context, 'inherent properties' are those that cannot be altered since they are a consequence of the molecular structures of the constituents of the substance itself. In risk assessment of chemicals, the main hazards that relate to the ability of substances to poison humans or wildlife are referred to as toxicity. Toxicity can, of course, vary in severity or nature of effect and some substances are very toxic (i.e. small amounts can be very harmful). Other hazards, such as flammability, also vary in severity and the degree of process control needed to make the risk acceptable.

Risk is the likelihood that a hazard will actually cause its adverse effects, together with a measure of the effect. Likelihoods can be expressed as probabilities (e.g. '1 in a 1000'), frequencies (e.g. '1000 cases per year') or in a qualitative way (e.g. 'negligible', 'significant' etc.). The effect can be described in many different ways (HSE, nd) and this depends upon what effect is happening, that is what harm.

The 'risk' in chemical risk assessment, and in particular in REACH, is determined by establishing a national safe level, below which effects will not happen to a particular receptor (e.g. human or part specific part of a human such as skin or particular organ or system or the specific part of the environment), expressed as a concentration. This is then compared to the concentration that the receptor of concern in exposed to. If the exposure concentration is higher than the safe level, then there is a risk and that needs to be controlled to get back to a level (concentration) that is safe.

1.2 Chemical Hazard and Risk Programmes

1.2.1 REACH Overview

REACH brings all EU chemical regulation into a standardised approach, apart from the exemptions. It provides a system of hazard and risk assessment and sets out how these must be communicated. It does not deal with the overlap with other types of regulation but does in reality share many technical objectives with national and EU regulation. It is also at the centre of generic worldwide legislation, affecting decisions from research through to continuing commercial viability (Figure 1.1).

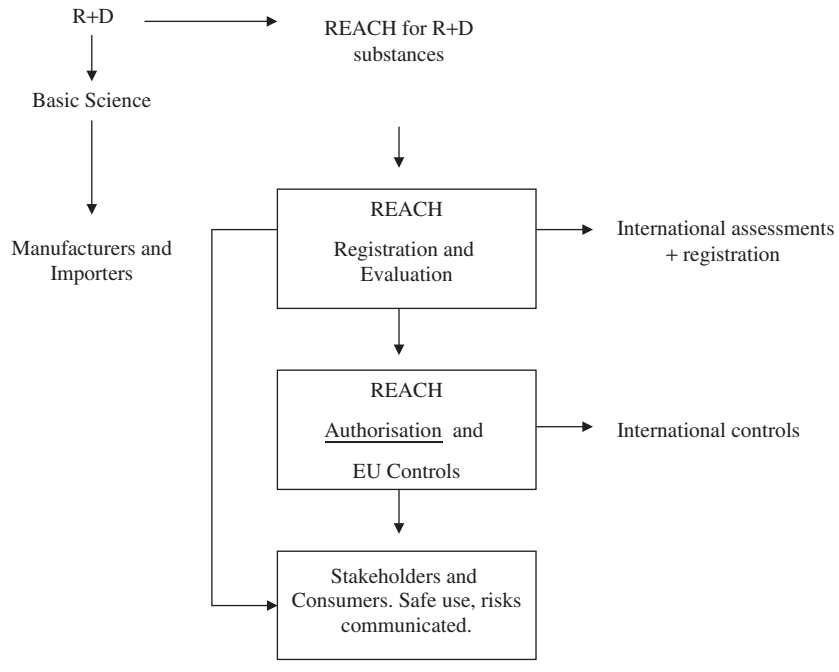

Figure 1.1 *REACH Overview*

1.2.2 Registration

The registration of chemicals under REACH applies to each importer or manufacturer of a substance (either on its own or present in a mixture) that is intentionally released in the EU in quantities ≥ 1 tonne/year.

1.2.2.1 Registration Strategy: 'Existing' and 'New' Substances

REACH applies different registration strategies depending on the tonnage level and whether a substance is considered as an 'existing substance' or a 'new substance'. Substances manufactured in or imported into the EU before December 2008, that is 'existing substances', were entitled to be pre-registered as phase-in during the pre-registration period (1 June to 1 December 2008). Substances eligible for 'phase-in' are:

- Those listed in the EINECS.
- Those that have been manufactured in the EU (including accession countries) but have not been placed on the EU market after 1 June 1992.
- Those that qualify as a so-called 'no-longer polymer' (ECHA, 2008).

These pre-registered substances are in the process of being phased-in according to their REACH requirements.

If a phase-in substance has not been pre-registered, it must be registered immediately (applicable from December 2008) in order for manufacturing and import in the EU to be legal, otherwise all activities must cease until registration is complete.

First-time manufacturers or importers[6] of a substance in quantities ≥ 1 tonne/year from December 2007, that is 'new substances', are required to register within six months of trading reaching the one tonne threshold and no later than twelve months before the relevant registration deadline.

New substances registered under the previous chemicals regulation process, that is the NONS, are considered to be registered under REACH. However, should the production volume increase or new information become available, REACH requires that the registration must be updated.

A process exists for substances to be used for R&D purposes, without full registration.

1.2.2.2 Product and Process Oriented Research and Development (PPORD)

REACH defines this as:

> *any scientific development related to product development or the further development of a substance, on its own, in preparations or in articles in the course of which pilot plant or production trials are used to develop the production process and/or to test the fields of application of the substance.*
>
> (Article 3 (22))

The PPORD exemption of five years from the obligation of registration is for substances intended to be used for product and process orientated research and development (PPORD) (ECHA, nd-a). ECHA imposes the following constriction on PPORD Substances:

- The substance must be handled in a reasonably controlled conditions for the protection of workers and the environment.
- It is only made available to selected customers.
- The substance will be handled only by staff of a number of listed customers.
- The substance will not be made available to the general public at any time, either in the form of the substance on its own, in a preparation or in an article.
- Remaining quantities of the substance will be re-collected for disposal after the exemption period.

PPORD exemptions for less than 1 tonne/year can be for an indefinite length.

PPORD exemption for more than 1 tonne/year can be exempted for a maximum of five years. This exemption applies to the manufacturer, importer or producer of the articles and listed customers. The Regulation does not limit the quantities of the substance manufactured, imported, incorporated in articles or imported in articles, provided the quantities are limited to the purpose of PPORD.

A further five years needs to be justified (or 10 years for substances for human or veterinary use and substance not placed on the market). The justification must include the improvements and achievements obtained during the first five years of exemption, the reason for the previous research programme not being completed over the five-year exemption period and the expected achievement during the duration of the extension requested.

[6] First-time importers refers to companies which import or export a substance in the EU for the first time after REACH came into force, that is 1 June 2007.

1.2.2.3 Registration Process

The registration process consists of the submission to the ECHA (ECHA, nd-b) of a dossier containing hazard information and, where relevant, a risk assessment of the uses of the substance. The technical dossier should include a summary of the substance's properties and provide guidance on its safe handling. If a substance is produced or imported at >10 tonnes/year, then a chemical safety report (CSR), which illustrates the safe use of the substance through the hazard and risk assessments, should also be provided.

REACH registration has been divided into three phases in order to process a high number of submissions:

Phase 1: Substances with a production or import volume in the EU of ≥ 1000 tonnes/year OR classified as Carcinogenic, Reprotoxic or Mutagenic 1 and 2 (CMR 1 and 2) OR substances which are classified for the environment as Aquatic Acute 1 or Aquatic Chronic 1, corresponding to the old DSD classification criteria R51–53, and manufactured or imported at ≥ 100 tonnes/year were required to be registered first, that is 1 December 2010.

Phase 2: Substances with a production or import volume 100–1000 tonnes/year required registration by 1 June 2013.

Phase 3: Substances with an import or production volume 1–100 tonnes/year require a registration by 1 June 2018.

The information requirements that need to be presented in the technical dossier depend on the tonnage and phase requirements. The information requirements can be found in Annexes VI to IX of the REACH regulation (ECHA, nd-c).

1.2.2.4 Substances Exempt from REACH

Not all substances imported or manufactured in the EU at ≥ 1 tonne/year require registration. REACH regulation Annex IV lists specific substances exempt from REACH. These include well-understood substances such as water, hydrogen, oxygen and the noble gases, as well as some naturally occurring substances such as ores and minerals. Other classes of substances that currently do not require registration under REACH include: polymers, monomers bound into polymers at $<2\%$, cosmetics, food additives, by-products, and products from reaction with additives or waste.

1.2.3 Evaluation

After the registration is submitted, one or more forms of evaluation are carried out by the authorities.

1.2.3.1 Technical Completeness Check (TCC)

The evaluation process initially takes the form of an automated electronic check that all the required technical contents of the dossier are included at a basic level. This is referred to as the technical completeness check (TCC). If the TCC is failed, it will lead to immediate rejection of the dossier, and it will then be necessary for the registrant to make the necessary corrections and re-submit. A tool is available for the registrant to ascertain in advance if the TCC will be passed. This tool works as a plug-in or

application within the IUCLID (International Uniform ChemicaL Information Database) software (which most registrants use to compile their technical dossier). The tool has been regularly updated and registrants should ensure that they use the latest version.

The TCC does not evaluate the science or approach, only that entries are present and/or specific fields completed, including:

- substance composition
- business information
- volume and use pattern
- chemical property data (or waiver) for all of the endpoints associated with the appropriate Annex level (VII–X)
- guidance on safe use
- attachments.

A TCC pass does not necessarily indicate a successful registration.

1.2.3.2 Compliance Checks

ECHA may make a more in-depth review on a selective basis. These compliance checks are made by ECHA technical staff. The review is likely to cover such elements as:

- Adequacy and completeness of the data in technical terms
- Grounds for any data waiving
- Full compliance with the regulatory requirements
- Exposure
- Suitability of scientific approaches used in the chemical safety assessment (CSA).

During the phase-in period, the compliance check is the most commonly used in-depth review of scientific approach. Due to the volume of dossiers received, ECHA expects to conduct compliance checks for only approximately 5% of submissions received in that period. Dossiers are prioritised for compliance checking based on specific criteria: for example, if the substance is hazardous or used in widely-dispersed applications, or contains numerous data waivers. However, a proportion of dossiers are compliance checked on the basis of randomised selection.

The ECHA communicates its findings to the registrant through Decision Letters, which alert the registrant to non-compliance with the regulatory requirements, and/or Quality Observation Letters, which recommend adjustments to the methods used in the submission. The changes called for are required rather than optional. The ECHA gives feedback in a practical way, making clear reference to specific guidelines, and has been willing to participate in discussion meetings. The ECHA may request additional further testing as a result of the Compliance Check.

The ECHA is obliged to undertake consultation with the registrant, the member states and any other interested parties.

1.2.3.3 Testing Proposal Examination (TPE)

In accordance with the REACH Regulation, certain types of new experimental studies should be proposed by the registrant rather than being conducted before registration. ECHA reviewers make specific checks on dossiers which contain such test proposals,

to assess whether the proposed tests are appropriate. Whilst scientific factors from the chemical safety assessment and chemical data from elsewhere in the dossier are taken into account, the testing proposal examination checks are not comparable with the compliance check.

Test proposals for vertebrate animal studies are published for consultation and calling in of any existing data held within Europe for sharing. The ECHA communicates its findings to the registrant through Decision Letters. All test proposals must be checked by the ECHA. Fixed deadlines have been set out for completion of these checks associated with each tranche of phase-in registrations.

1.2.3.4 Substance Evaluation – Community Rolling Action Plan (CoRAP) Programme

Substances which are identified as posing a particularly serious concern are prioritised for full substance evaluation, undertaken by member state competent authorities. Through this form of evaluation, under the community rolling action plan (CoRAP) programme, information from all individual registrations of the same substance is brought together by the member state reviewers.

The priority lists for this form of evaluation are developed on the basis of hazards, tonnage, and exposure. This being a rolling action plan, the priority list will be regularly updated to reflect current issues and concerns.

The purpose of the CoRAP evaluation is to ascertain, using risk-based methods, whether the substance is adequately controlled and to identify whether any courses of action, such as EU-wide risk management, are necessary. In the course of this evaluation, additional information may be required from registrants (e.g. monitoring data; property data outside the normal regulatory requirements outlined in the relevant REACH Annex).

Experience from the member state-led assessments under the previous legislation (Existing Substances Regulation) and the early work suggest that CoRAP will involve a process of detailed assessment made on a substance-by-substance basis, led by a nominated member state; with regular in-depth technical discussion meetings Some Member States appear to view the CoRAP process as a risk management option (RMO) process within which an evaluation of the risk is made followed by an assessment of the most appropriate measures for control of the risk/s. The risk management option process is somewhat similar in essence to the risk reduction strategy process under the Existing Substances Regulation and should involve the consideration of the practicability, effectiveness, ease of monitoring and proportionality of the proposed measures. This involves some consideration and comparison of the costs and benefits of the possible measures. The measures considered may be processes within REACH (such as Authorisation or Restriction) as well outside REACH, for example specific legislation at EU level (e.g. the Carcinogens and Mutagens Directive, Water Framework Directive or Industrial Emissions Directive) or specific legislation at national level.

1.2.3.5 Annual Reporting

Every February, the ECHA issues an annual Evaluation Report via its web site. This presents some statistical details of progress, useful reference information on common issues and findings from the evaluation processes conducted in the year to date.

1.2.4 Authorisation and Restriction

This section explains these processes within REACH; both authorisation and restriction are revisited and discussed in more depth in relation to additional supporting analysis including socio-economic analysis (SEA) in Chapters 13 and 14 of this book.

The main objective of REACH is the systematic collection of data on the properties and uses of substances that are intended to be placed on the EU market and the assessment of those data to show safe use. The main process driving that in REACH is the registration of individual substances, providing information in dossiers as described in Chapters 2–10 of this book. The concept of safe use in REACH is expressed as adequate control, in which the levels of exposure of humans and the environment due to use are compared to notional safe levels that are deemed protective specific receptors, that is for humans in the workplace, for the general public and for specific parts of the environment. The data presented in registration dossiers must demonstrate adequate control for each use pattern and for each relevant receptor in order for the use to fulfil the requirements of REACH, and thus to be placed on the market for those uses.

For some substances, due to their intrinsic hazardous properties and associated uncertainties on the type of harmful effects they may have, it is not possible to indicate a safe level and, therefore, in theory adequate control cannot be demonstrated (i.e. substance of very high concern (SVHC) – Chapters 6 and 13 of this book). Alternatively, there may be substances that are not SVHCs and for which is possible to demonstrate adequate control, but there is still the possibility of a risk from cumulative uses (not accounted for by individual and separate chemical safety assessments from a number of different registrants). The process within REACH for additional controls on SVHCs is *Authorisation* and the process by which additional controls on substances that may pose risks not accounted for individual registrations is *Restriction*.

Authorisation and Restriction, therefore, represent an additional layer of precaution and assessment that is applied to hazardous and risky substances. The aim of Authorisation is to progressively replace SVHCs with safer substances and the aim of Restriction is to provide a ‘safety net’ for the imposition of risk reduction measures that would not be otherwise put in place though the registration process. The processes of Authorisation and Restriction in REACH are concerned with placing limits on the use of dangerous substances. They are similar processes with complimentary objectives, but have key differences.

The process of Authorisation effectively places ‘ban’ of all uses of a SVHC unless an authorisation is granted to allow a specific use or uses to continue. It is for industry (manufacturers and users) to make the case for continued use in the form of an application for authorisation and for ECHA committees and, ultimately, the European Commission and the European Parliament to decide on the validity of the case.

The authorisation process is driven by hazard (i.e. the intrinsic properties of the substances that cause it to be dangerous) and starts with identification of a substance as an SVHC (Chapters 6 and 13 of this book). Substances identified as a SVHC (by way of a dossier submitted by a Member State to the ECHA or ECHA on behalf of

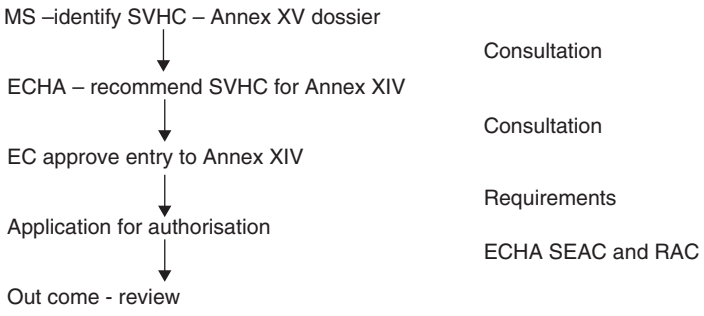

Figure 1.2 *Flow Diagram of SVHC, Placing on ANNEX XIV, Authorisation and Review Process*

the Commission) are placed on a 'Candidate List'.[7,8] From this list substances may be selected for assessment against criteria for recommendation to require authorisation (placing on Annex XIV). There are specific exemptions to authorisation; it applies only to the marketing and use of substances; it does not apply to manufacture alone, that is substances manufactured solely for export out of the EU, or use as an intermediate only.

The assessment for placing a substance on Annex XIV is done by the ECHA and takes account of the volume placed on the market, the uses (in particular if there is a large number of different uses, distributed widely across the EU, so-called wide and dispersive use) and alternatives (particularly if there appear to be viable alternatives, since authorisation seeks to replace the most hazardous substances, this depends upon alternatives being available). On the basis of this assessment a recommendation (with a supporting report) is made to the Commission for inclusion on Annex XIV. The recommendation also includes proposals for when the substance should be no longer used from unless an authorisation is granted for specific uses – this is called the sun-set date as well as possibly a review date (i.e. a maximum time that the authorisation can be granted for before it is re-assessed by the ECHA and the Commission). Note that all authorisations are time limited; the length of time that the authorisation is granted for is dependent on the production cycle of the substance and the information submitted in the authorisation application.

Figure 1.2 illustrates the 'route' for a substance from identification as a SVHC though possible selection for the need for authorisation – placing on Annex XIV of REACH.

There are two possibilities for an authorisation to be granted:

1. The substance does not have a safe level (i.e. non-threshold CMR (carcinogen, mutagen, reproductive toxin) or PBT/vPvB (persistent, bioaccumulative and toxic/very persistent and very bioaccumulative)); therefore, 'adequate control' cannot be demonstrated. For these substances an authorisation can only be granted if it is demonstrated in the authorisation application that there are no technically or economically feasible

[7] Designation as a SVHC and listing on the Candidate List have consequences within REACH, even if the substance is not then selected for Annex XIV. Obligations under Article 33 of REACH mean that producers of articles (products that are objects) that contain 0.1% of a SVHC or more by weight must inform their customers about that and supply information on how to use the article safely with respect to the SVHC content.

[8] Once a substance is placed on the Candidate List, it will not be removed, unless there is new information to demonstrate that is no longer fulfils the criteria for SVHC – this is, of course, unlikely.

or available alternatives for the substance and also that the socio-economic benefits outweigh the risks. This is called the socio-economic analysis route.

2. Substances for which a safe level can be derived, that is adequate control can be demonstrated. For these substances, an application can be granted so long as adequate control is demonstrated. If suitable alternatives are available, then a substitution plan must be presented.

The application for authorisation must include a chemical safety report (unless one has already been submitted to ECHA in a registration dossier) and an analysis of alternatives, in addition it *may* include a socio-economic analysis (although in practice this *must* be included because it will be very difficult to present the socio-economic arguments to support the benefits outweighing the risk without such an analysis). The theory and practice of socio-economic analysis in support of authorisation applications and restriction proposals are explained in Chapters 13 and 14 of this book.

Restriction is a ban on a specific use or uses, with all other uses being permitted (so long as they have been registered appropriately). The cases for restrictions are made by Member State Competent Authorities or by the ECHA (at the request of the Commission). As with authorisation, the case for restriction is assessed by the ECHA committees, with the ultimate decision made by the Commission and the Parliament.

There may also be potential risks from substances for which it is possible to demonstrate safe use. Because registration in REACH is done per substance and per legal entity, it means that it is possible that a number of chemical safety assessments for the same substance (submitted by different registrants) can demonstrate safe use, but there may be a cumulative risk when all the safety assessments are considered together. For example, it is only possible for a registrant that is a manufacturer to consider releases from its plants and processes and those of its customers (whose uses are being supporting in the registration). The registrant can assess these uses as safe when it considers the releases and control of releases of the substance. There are also other manufacturers with customers with similar or different uses, which are also assessed as safe. However, when the cumulative releases are considered, there may be the need for additional measures to control the risks – that is risks that are only apparent when the releases from all uses are considered together. Since it can only be the ECHA that can be in possession of all the dossiers (and therefore chemical safety reports) for a substance, it can only be the ECHA that can identify such risks. There is particular concern when there is additional risk at a European-wide scale.

The objective of Authorisation is the progressive removal and replacement of a SVHC from the EU market, whilst the objective of Restriction is to act as a 'safety net' to impose limitations (restrictions) on the uses of a substance that present a European-wide risk. Restriction applies to all substances, whereas authorisation applies only to a SVHC (and substances which have properties of equivalent concern to a SVHC).

Authorisation and restriction are possibly the most contentious, controversial and misunderstood parts of the REACH process. This is largely because, at the time of writing, these processes within REACH are untested. Certainly for authorisation, no substances have yet been fully through the process, as no application has yet been assessed by the ECHA. However, a few restriction proposals have been made and decisions on restriction for specific uses of specific substances made.

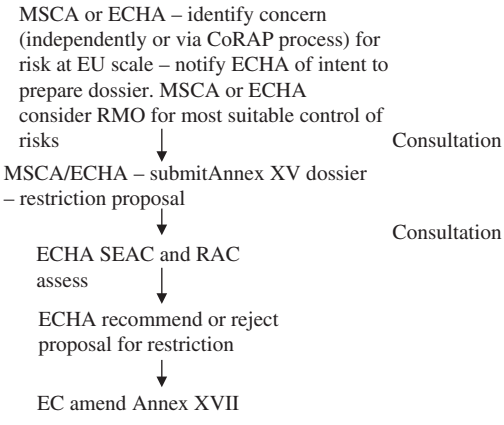

Figure 1.3 *Flow Diagram of CoRAP, ANNEX XV Dossier and Placing on ANNEX XVII, Restriction Process*

Figure 1.3 illustrates the 'route' for restriction from registration, the CoRAP process to a restriction being placed on Annex XVII of REACH.

1.2.5 Hazard and Risk Communication

In this section, the chemical supply chain as defined in REACH is discussed. This is an area which caused many stakeholders concerns before any substance was registered. With the experiences gained since then, it is possible to refine and, in part, eliminate those fears, but many areas remain difficult for all.

The composition of what constitutes the supply chain is well-defined in the REACH guidance. Although taken from the environmental guidance 'Guidance on information requirements and chemical safety assessment, Chapter R.16: Environmental Exposure Estimation', page 12 (ECHA, 2012), Figure 1.4 is a useful starting point, since it deals with life cycle rather than legal matters:

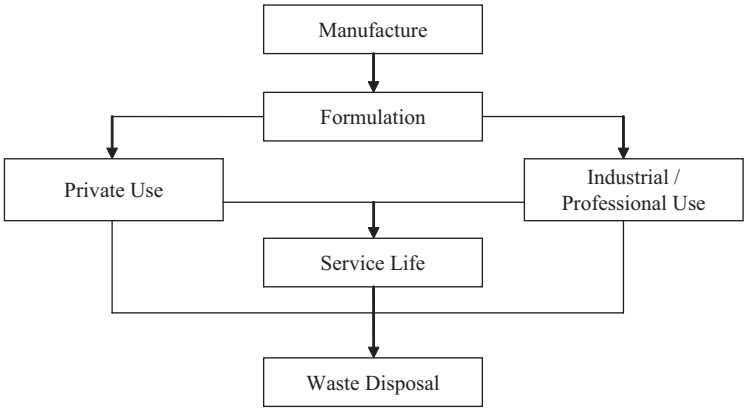

Figure 1.4 *Overview of Substance Use Patterns*

Within that structure, the supply chain can be seen as consisting of the following actors:

- **Manufacturers or importers**, the import of substances, preparations or articles are all included here.
- **Downstream users**, someone who uses a substance, either on its own or in a preparation, in the course of their industrial or professional activities. Many different types of companies can be downstream users (DUs), including formulators of preparations, producers of articles, craftsmen, workshops and service providers or re-fillers.
- **Retailers**, may be involved and do have responsibilities in respect of provision of information.
- **Private consumers**, where relevant in the life cycle.
- **Waste processors and recyclers**.

Some key elements of supply chain actions can be identified:

- Formulators have a key place in this chain, because the process of mixing substances to make a preparation adds a whole new dimension to the assessment of hazard and risk. Formulators need to prepare safety data sheets to cover the preparation.
- REACH requires a considerable amount of information to be communicated to downstream users by suppliers, to enable them to use chemicals safely. In addition, REACH requires downstream users to communicate new information on hazards and also use information when the supplier's advice seems to be incomplete.
- Downstream users need to communicate upstream and downstream, for example when identifying uses to a supplier or collecting information on customers' uses.

In such a context, there may be occasions when a DU simply does not want to take the commercial risk of giving information to a supplier about what exactly it is doing. Also, on occasion it has been found that suppliers are asking DUs questions that are far more detailed than is actually needed to fulfil their responsibilities. Such scenarios do not need to give rise to a tense relationship – that is not in anyone's interests. However, a well-prepared supplier could perhaps gain advantage over another supplier by handling DUs well. The DU needs sufficient knowledge of REACH (and good advice) to be able to judge these and other matters. Indeed, it could be seen as one of the consequences of REACH that DUs and their support associations have had to learn many more 'new things' than suppliers have!

The general fears around REACH caused many DUs to make pre-registrations of substances just in case their suppliers did not! It is to be hoped that such examples will not recur. Since 2010 the focus of concern has shifted to DUs looking at eSDS (extended Safety Data Sheet) supplied to them, and finding them to be inconsistent and very hard to understand. Section 11.8 of this book helps with that, but some general statements can be made. How has it arisen that DUs have concerns about an eSDS from a manufacturer/importer? Whilst REACH has presented severe difficulties due to a highly compressed time line, typical problems include:

- Suppliers failing to communicate about hazards and exposure within the SIEF (Substance Information Exchange Forum).
- Suppliers failing to communicate with their customers.

- Suppliers and DUs have assumed that establishment of what the use pattern is (and assignment of descriptor codes) is enough information to characterise risk; in reality it often is not, because the default exposure values driven by the codes are very high. Agreement of codes must be accompanied by real understanding of what is actually happening!
- DUs not checking with suppliers that their use will be covered.
- Poorly-written eSDS.
- Insufficient technical expertise at both levels, including basic knowledge of admittedly very complex Guidance.
- Inadequate awareness of the implementation of the globally-harmonised system of Classification, Labelling and Packaging (CLP) alongside the implantation of REACH (Appendix A). This has had a positive benefit in gaining more consistency with transport regulations.

Another area of challenge for formulators is the communication of hazard and risk of preparations. They will need to collate information about all the ingredients and make an assessment, then report it in the SDS.

Whilst the above problems have been identified, the efforts of industry sector groups to establish clear and agreed descriptions of use pattern and exposure models must also be acknowledged. As with all things in REACH, findings must be supported by evidence, and this takes time to assemble.

The responsibilities in the supply chain are covered in more detail in Section 11.5 of this book.

1.2.6 Hazards

1.2.6.1 Physico-Chemical Hazards

Physico-chemical hazards such as flammability, explosivity, and auto-flammability may be manifested in standard laboratory tests when a sufficient quantity of the substance is present. There are established worldwide classification criteria for these properties.

1.2.6.2 Toxicological Hazards

Potential effects on humans are assessed firstly on the basis of studies with non-animal laboratory tests (termed '*in vitro* assays') or with animals (if required by legislation or there is no alternative to provide the data needed). Studies with animals are only models for possible effects on humans and, as such, are not perfect predictors.

Study schemes are set out to assess hazard step-by-step, with the following targets:

- Genetic toxicology
- Short-term toxicity
- Long-term toxicity
- Effects on reproduction and development
- Carcinogenicity.

Animal testing can be minimised through the use of read-across strategies and other alternatives, such as (Q)SAR modelling. However, it is widely thought that there is

much research to be done before use of *in vivo* animal models of human hazard can be eliminated.

For certain carcinogenic, mutagenic or reprotoxic substances, authorisation of each use must be obtained. This is independent of any risk characterisation.

1.2.6.3 Environmental Hazards

A substance's potential environmental hazard is investigated through testing for toxicity to environmentally-relevant organisms (ecotoxicity). There are standardised tests for ecotoxicity to aquatic organisms (including sediment) and terrestrial organisms. Effects on microorganisms present in biological waste-water treatment plant are also examined.

REACH sets out precautionary criteria as regards environmental fate. If a substance has a high potential for bioaccumulation in the absence of degradability, it is regarded as a hazard, even if there is no evidence of toxicity.

As part of this precautionary approach, substances decided to be PBT or vPvB require authorisation for specific uses (Section 1.2.4 in this chapter).

1.2.7 Overview of Types of Exposure

The inherent hazard of a substance may trigger various risk and safety concerns for humans and the environment during its use. The potential for and consequences of such risk are determined, to a large extent, by the nature and level of exposure during the use of the substance. The term 'exposure' in risk assessment of chemical substances means the form and/or route of contact, and potential interaction of different substances with humans and the environment. The exposure may be short term or long term, once or repeatedly, by different pathways, in low or possibly in high concentrations (CEFIC/VCI, 2009).

The exposure of a chemical substance can be direct and intentional, as in the case of consumer use of personal care products or washing-up liquid. Exposure can also be indirect and unintentional, as in the case of the loss of dyestuff from a dyeing process. The dyestuff which was intended to be taken up by the fibre or fabric is then lost to waste water, leading to exposure of the environment (rivers: fresh water and/or sea: marine water) and possible subsequent exposure of humans through intake of fish and/or drinking water.

1.2.7.1 Human Health Exposure

The underlining principle/concept for human health exposure is very well captured and explained by the definition of exposure by the International Programme on Chemical Safety (IPCS, 2001): the 'contact of an organism with a chemical or physical agent, quantified as the amount of chemical available at the exchange boundaries of the organism and available for absorption'.

In the case of human health exposure, the contact with a physical or chemical agent occurs with the visible exterior of a person (i.e. target), such as the skin, and openings, such as the mouth, nostrils and lesions (EPA, 2011). Depending on the use and life cycle stages of the physical or chemical agent, the target individual may cut across different population categories: workers, professionals and consumer users of the substance or products containing the substance.

The way a substance is used and the population that would be affected (e.g. workers, adult consumers or children) can also define the significance of the point of contact and route of exposure. For example, the oral route of exposure is typically generally not considered relevant for workers. Mouth contact and oral exposure are, however, significant for children, as they are exposed during the normal oral exploration of their environment (i.e. hand-to-mouth behaviour) and by touching floors, surfaces and objects such as toys (EPA, 2011).

The individual's population category and activity patterns, as well as the nature and concentration of the chemical, will determine the frequency, duration, route and magnitude of the exposure.

1.2.7.2 Environmental Exposure

The process of environmental exposure begins with a chemical substance released into the environment from a point source (e.g. emissions from an industrial stack), or wide dispersive sources such as multiple emissions from cars. Point source releases are to the 'local environment', while releases into a larger area from multiple point sources or wide dispersive uses are to the 'regional environment' (ECHA, 2012; EPA, 2011). A chemical substance's contact with the environment will be through one or more of the various 'environmental compartments': air, water and soil.

Once in the environment, the chemical substance follows an exposure pathway, along which it can be transformed and transported through the environment via air, water, soil, dust and diet. The physico-chemical properties of the substance determine the overriding fate and transport mechanisms of the substance in the environment.

1.2.7.3 Exposure of Humans via the Environment

As well as the direct exposure from use of a chemical substance or its products, indirect exposure of humans can also occur through releases to the environment, exposure to humans via the environment may result from releases to the air and water, and solid and hazardous waste disposal.

Chemical releases to rivers, lakes and streams may result in a substance's accumulation in fish and other marine life. These may be subsequently used as a source of food, or ingested by persons using the downstream reaches of rivers as a water supply. Those living downwind of a chemical manufacturing facility may be exposed to fugitive and point source releases of chemical toxins to the atmosphere. Disposal of solid and hazardous wastes on the land, either in repositories such as landfills, or into subterranean strata by injection into wells, may result in contamination of potable groundwater if the waste is not isolated from the surrounding environment.

The significance of the exposure of humans via the environment is dependent on the tonnage of the substance produced, the tonnage used and the inherent chemical hazard of the substance.

Risk assessment of a chemical substance involves producing an 'exposure scenario'. This means the set of conditions, including operational conditions and risk management measures, which describe how the substance is manufactured or used during its life cycle. An exposure scenario also includes how the manufacturer or importer controls, or recommends downstream users to control, exposures of humans and the environment.

These exposure scenarios may cover one specific process or use, or several processes or uses, as appropriate (ECHA, 2012).

1.2.8 Overview of Risk Characterisation

The purpose of risk characterisation is to identify uses of a substance that present an unacceptable risk to the environment or to human health, and to reduce these risks to an acceptable level. Under REACH, risk characterisation must be carried out and documented for all substances that are either:

1. Classified according to the CLP Regulation (European Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures) as having health, environmental or physical hazards or
2. Meet the criteria set out under REACH for PBT substances, and are manufactured or imported in the EU at a volume of > 10 tonnes/year.

As discussed in the introduction to this section, risk characterisation brings together two different types of information:

1. The properties of the substance and an assessment of any hazards, where possible quantified to give a maximum safe level of exposure (discussed further in Chapters 7 and 9 of this book);
2. The use patterns of the substance and quantification of predicted exposure levels for the environment and humans (this is discussed further in Chapters 8 and 10 of this book).

Whenever possible, risk is quantified by calculation of a risk characterisation ratio (RCR). This is the ratio of the predicted exposure level to the safe level of exposure. A RCR greater than one (where the predicted exposure is greater than the safe level) indicates an unacceptable risk, whereas RCRs less than one indicate that the use of the substance may be considered safe.

A separate risk characterisation is performed for each identified use of the substance (e.g. manufacturing, use as a chemical intermediate or use in household cleaning products). For human health, RCRs are calculated for the different routes of exposure (oral, dermal or inhalation), short- and long-term exposure and the different types of people who may be exposed (workers at industrial sites, professionals, adult consumers and children and humans exposed via the environment). If exposure via more than one route or from more than one source is possible, a combined RCR is calculated. For the environment, RCRs are calculated for the different types of environment that may be exposed to the substance (marine and fresh water, marine and fresh water sediment, soil, microorganisms in the sewage treatment plant and predators) at both regional and local scales.

A substance may possess hazardous properties for which it is not possible to define a safe level, either because there is no threshold below which exposure can be considered safe (e.g. genotoxicity or carcinogenicity) or because the standard tests for that property do not provide this information (e.g. flammability or irritation). For the former group, semi-quantitative risk characterisation may be appropriate. This involves calculating a level corresponding to a low, possibly theoretical, risk. RCRs are then calculated in the same way as for a quantitative risk characterisation. For the latter group of substances,

qualitative risk assessment must be carried out. This involves consideration of the severity of the hazard and how risks associated with it are controlled. A qualitative assessment is then made of the likelihood that these controls are adequate to prevent harm to relevant groups. For health hazards, the general principle is to limit or avoid contact with the substance. For physical hazards, the aim is to eliminate or reduce the likelihood of accidental events occurring. The degree of control required is proportional to the severity of the hazard. If a substance possesses both hazards that can be quantified and those that cannot, both quantitative and semi-quantitative or qualitative risk characterisation is required.

All uses to be covered in a submission under REACH must be shown to be safe by the risk characterisation. If an initial risk characterisation gives one or more RCRs higher than one (or the qualitative risk characterisation indicates that a hazard is inadequately controlled), there are several options:

- Refine the estimates of exposure levels. Initial estimates of exposure levels often make use of various default values (e.g. the percentage of a substance unintentionally lost to the environment during mixing of substances, or the concentration available for inhalation when spraying a substance). These defaults are intended to cover the worst case of a very general situation and, therefore, are often unrealistically high. If use of the defaults still results in RCRs less than one, there is no need for refinement. However, consideration of the specific use often means that it is possible to justify reducing these estimates if necessary. This can involve making measurements of exposure levels.
- Refine the estimates of the safe level of exposure. In some cases, gaining greater knowledge of the properties of the substance (for example by carrying out longer-term animal studies) can result is a more accurate estimate of a safe level of exposure (although this may be higher or lower than the original estimate).
- Put in place additional measures to manage the identified risks. For example: wearing gloves whenever a substance is handled can reduce worker exposure; reducing the concentration of the substance in a cleaning product can reduce consumer exposure; and fitting technology at a manufacturing site to limit emissions can reduce environmental exposure.
- Do not support the affected use(s). If a risk is still present after all possible refinement of the estimates, and it is not possible (or not commercially viable) to introduce further controls, it may be necessary to advise against the use.

The choice of approach can depend on many factors, both technical and commercial. An iterative approach of refinement followed by review of the risk characterisation is usually appropriate. During this process, uncertainty in the calculated RCRs should be considered. Uncertainty in the RCRs results from uncertainties in the estimates of both hazards and exposures, and is relevant to deciding whether risks are adequately controlled. If there is too much uncertainty in the outcome of the risk characterisation, further iterations may be required.

The iteration ends when the qualitative and quantitative risk characterisation indicates that risks are controlled to a level of very low concern, or it is concluded that it is not possible to demonstrate control of the risks. The conditions which allow safe use, or the information that the use is advised against, must then be communicated down the supply chain.

1.2.9 Successful Interaction with REACH: Registration, Evaluation and Authorisation

1.2.9.1 Introduction: How EU Chemical Legislation Evolved

REACH is, of course, the culmination of a series of directives and regulations enacted by the European Parliament since the end of the 1960s (Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the CLP of dangerous substances). It is difficult to understand how REACH relates to other chemical legislations without taking into consideration how they came by in the first place. Historically, the primary consideration of the European Commission and of the Member States was initially worker and consumer protection. Later on, especially after the accession of Sweden to the European Union (in 1995), more emphasis has been placed on environmental protection. In particular, many of the non-enforceable environmental goals of OSPAR (Oslo–Paris Commission, historically piloted by Sweden and composed by several EU and non-EU states), which predates the European Union, were gradually included in European legislation, such as the Water Framework Directive (2000/60/EC). While, retrospectively, the gradual development of chemical legislation may have been seen as haphazard, the underlying reason was that both regulators and industry (through various associations) were struggling to find middle ground between command and control and hazard-based legislation, potentially affecting the competitiveness of the European chemical industry, and a more constructive approach based on industry's experience in the safe handling of hazardous substances and self-regulation.

While REACH was intended to provide a EU-wide, directly applicable (as opposed to nationally enacted) legislation ensuring a harmonised market within its borders, the conflicting positions of non-governmental organisations (relayed by media and by public opinion) and industry, with the EU authorities caught in the middle, continue. The former advocate rapid bans of potentially problematic substances, based solely on their hazard profiles, while the latter accepts the need to adapt the EU's chemical policy but at the same time enhance or at least maintain its competitiveness, protecting and strengthening the internal market and reaching decisions based on risk.

Until the early 1970s the first task of the chemical industry and of the regulators (EU Commission and the Member States represented by their various health and environment protection agencies) was to inventory the thousands of chemicals in commerce and their known properties. Simultaneously, internationally agreed test protocols to generate (eco)toxicological data under Good Laboratory Practices were developed under the auspices of organisations such as the OECD (Organisation for Economic Co-operation and Development).

It should be noted that the Classification and Labelling Directive 65/548/EEC did not impose an obligation for manufacturers to develop new (eco)toxicological data. Manufacturers had a tendency to focus on measuring physical property data (critical for transportation and storage safety) and short-term toxicity data. With the exception of Germany, which had developed its own system of water endangering classification (WGK – Wassergefährdungsklassen), and with its manufacturers agreeing to voluntarily sponsor basic environmental testing of its products, generally little of the more expensive long-term toxicity data were developed. The only exceptions were for certain chemicals

that belonged to families suspected of repeated-exposure hazard properties, such as sensitisation, carcinogenicity, reprotoxicity and mutagenicity, or for other substances in wide dispersive use or with a high potential for human exposure, as in cosmetics. More recently the potential effects of endocrine-mimicking substances on the unborn child are being investigated but there is still some controversy whether existing methods to determine reproductive effects are sufficient. Similarly, the concepts of synergistic health effects between exposure to low doses of chemicals and the long-term environmental effects or secondary poisoning due to a combination of persistency, bioaccumulation and toxic properties have gained increased traction, with the latter now fully part of REACH.

The chemical industry had accumulated a huge amount of practical experience in handling safely several hazardous substances without necessarily undergoing extensive testing. This experience was based on the effects observed during the time where the methodology to assess them in a systematic way was not yet fully developed. Some notorious examples are the use of some metals, inorganic or organic compounds in cooking (lead utensils and lead acetate as a condiment by the Romans), medicine (arsenic for the treatment of leukaemia, psoriasis, mercury for syphilis etc.), cosmetics (lead in eyeliners), jewellery (nickel plating), marine coatings (organotin antifouling additives), pesticides (DDT), herbicides (2,4-D or dichlorophenoxy acetic acid), refrigerants (chlorofluorocarbons), felt hats (mercury) and even transformer cooling oils (polychlorinated biphenyls). The remaining uses of all of these substances are now strictly controlled or banned. New technologies have made possible complete substitution of some of these substances in essential applications, such as mercury in thermometers or in the production of chlorine by separation cells.

Margot Wallström, the EU Environment Commissioner when REACH was enacted, had called for decisive action by claiming that had REACH been in place, asbestos would not have caused and still be causing 100 000 industrial deaths, although one can hardly call asbestos a man-made chemical, the control of which is the primary purpose of REACH. While that remark was widely criticised or applauded, depending on which side the comments were coming from, it was effective in instituting the principle of substitution of CMR Cat. 1a or 1b substances. However, for the reasons explained above, such as greater awareness of the effects of certain chemicals, exposure to them has dropped significantly between the 1930s and the 1970s, showing that the early chemicals legislation has achieved its goals.

Nevertheless, the growing awareness that exposure to certain substances can have some long-term effects that were originally unsuspected has resulted in adopting a more precautionary attitude towards innovation. In the USA, for example, there is a requirement for industry to report to the EPA (Environmental Protection Agency) significant new uses rule (SNUR), which would be authorised once they are demonstrated to be safe. In the EU, the Commission published in 2000 its interpretation of the Precautionary Principle (EC, 2000),[9] which is referred to in all chemical legislations enacted since then.

At the same time it was realised that the undesirable effects of these substances were also a function of exposure. By restricting the use of these substances to those

[9] EC, 2000: 'The precautionary principle enables rapid response in the face of a possible danger to human, animal or plant health, or to protect the environment. In particular, where scientific data do not permit a complete evaluation of the risk, recourse to this principle may, for example, be used to stop distribution or order withdrawal from the market of products likely to be hazardous'.

applications where the benefits can be demonstrated versus the absence of risk, these negative effects can be avoided. For example, DDT is still used to treat mosquito nets, nickel is in every euro coin, a mercury compound is an essential preservative in certain vaccines and without lead metal and chemicals in batteries consumers would certainly have problems running automobiles.

The result of this approach was the so-called Marketing and Use Directive (Limitations Directive, i.e. Directive 76/769/EEC) restricting or banning the use of certain hazardous chemicals and the DSD 67/548/EEC setting up an in-depth review of existing priority chemicals selected for their hazard properties (CMR, PBT or vPvB, in other words: Carcinogenic, Mutagenic, Reprotoxic, Persistent, Bioaccumulative, Toxic or very Persistent and very Bioaccumulative) and all new chemicals. The experience with the implementation of both Directives was retrospectively viewed as too slow by the European Parliament and some member states (200 new and existing substances were assessed over a period of 30 years). The solution, ironically, was to turn over to industry the responsibility of preparing dossiers on all 30 000 commercial substances with strict deadlines.

The World Health Organization (WHO) had initiated a programme called IPCS (International Programme for Chemical Safety) which published 241 EHC (environmental health criteria) critical reviews on the effects of chemicals and physical and biological agents on human health and the environment. The first environmental health criterion concerned mercury and was published in 1976. One of the last for chemicals (2005) was on clay minerals but more recently the focus has been on methodology and on physical agents, such as extremely low frequency fields (2007).

The next step was to define a 'base set' of data that would cover the complete hazard profile of a chemical substance and from there to classify the substance, therefore ensuring that appropriate measures would be taken when managing the risk related to exposure. About the same time the OECD and industry through its trade associations (CEFIC in Europe, the ACC (American Chemistry Council) in the United States and the JCIA (Japan Chemical Industry Association) for Japan) reached an agreement to submit a defined data set (and to fill gaps if any) to an international review panel. The programme, called HPV (high production volume, prioritising substances manufactured at a rate greater than 1000 tonnes/year) is still underway but in a sense has been superseded in the EU by REACH. In the USA, the EPA has gone further, firstly by making this programme obligatory for US manufacturers and importers and, secondly, by lowering the reporting threshold to 1 million pounds/year or 450 tonnes/year. Also, more recently, the EPA has set up an Extended HPV programme by including substances that have reached the volume threshold since HPV was started.

As a result of all of this, knowledge about the hazards posed by chemical substances has increased considerably since the 1970s. The process of self-classification based on the new data has already resulted considerable changes in the production and the use of certain chemicals, which is the reason why industry is confident that the majority of existing chemical uses will be shown to be safe.

The following chapters look in more detail at the impacts and the links with REACH on three other important pieces of chemical legislation and their interactions with some of existing national implementations.

How in practice the potential risks associated with chemicals are identified and managed, and their impact on costs and liabilities, are reviewed in more detail. The specific risks are identified by scope and their relationship with REACH is noted.

As seen in Table 1.1, the regulations concerning chemicals fall into several categories:

- Regulations that overlap REACH in some respects:
  - Air
  - Water Framework Directive
  - Carcinogens at Work Directive
  - The cosmetics regulations
  - Biocidal products
  - Plant protection products.
- Regulations that may apply resulting from compliance with REACH, if new data or an evaluation generated under REACH trigger a change in the hazard classification of a substance:
  - Biocides
  - Construction products
  - Cosmetics
  - Ozone depleting substances (ODS)
  - 'Seveso' directives
  - Toys
  - Prior informed consent (PIC)
  - Transport
  - Waste.

The six regulations that have potential for overlapping REACH are now be reviewed in more detail.

1.2.10 Regulation and Assessment of Hazardous Chemicals Outside of the European Union

The REACH programme exists within a global context of regulatory regimes, many of which have similar objectives and methods, although the scope and focus varies considerably from one sphere of regulation to another.

Multinational companies are present or dominant in almost all areas of the modern chemicals industry. Therefore, it is not uncommon for the same company to face similar or equivalent legislative requirements for the same substance in different parts of the world. It is notable that the ECHA has entered into mutual memoranda of understanding with several other regulators around the world. Whilst not being legally binding, this implies recognition that acceptance of registration under other regulatory schemes suggests that certain technical standards have been met, hence this is taken into account when a registration is necessary under REACH (or vice versa). The ECHA website has further information and should be consulted for the latest information of MoU (Memorandum of Understanding) in place; those existing at the time of writing are shown in Table 1.2.

There are in place some voluntary programmes involving assessment of chemical hazard and risk. For example, HPV programmes, in progress internationally and in various global sectors, share some similar approaches with the assessments made under regulatory systems. In most cases, these programmes focus on hazard assessment and

Table 1.1 *Relation to REACH of chemical risk management.*

Chemical risk scope	EU legislation	Relation to REACH
Air Urban Indoor	Particulates, industrial emissions, solvent emissions 1999/19/EC and 2004/42/EC, IPPC 2008/1/EC	Each solvent use must be risk assessed and demonstrated to be safe
Biocidal products	Directive 98/8/EC and Regulation (EU) No 528/2012	Annex I listed substances are considered registered under REACH and are therefore exempted
Classification and labelling	CLP-Regulation (EC) No 1272/2008	Basis for identification as a substance of very high concern (SVHC)
Construction products	Construction Products Regulation (305/2011/EU – CPR)	Declaration of content of hazardous substances and identification of risks posed by construction materials
Cosmetics	Cosmetics Directive 76/768/EEC and recast as Regulation (EC) No 1223/2009	The environmental impact of cosmetics ingredients must be assessed. CMR ingredients are regulated
Food	Additives (Directive 89/107/EEC)	Excluded from REACH
Fresh and coastal waters	Water Framework Directive 2000/60/EC, IPPC 2008/1/EC	The Water Framework Directive (WFD) provides a framework to set Environmental Quality Standards for chemical substances found in surface waters. The methodologies may differ from REACH
Ozone depleting substances (ODS)	ODS (Office of Dietary Supplements) legislation, USA; Regulation (EC) No 2037/2000, Regulation (EC) 1005/2009, 2010/372/EU and (EU) 744/2010	By 2012 the consumption of ozone-depleting substances has dropped by 98%. REACH provides for an assessment of the ozone depleting potential of volatile substances
Greenhouse gases	EU implementation of the Kyoto Protocol	Monitoring of greenhouse gases emissions (especially certain fluorinated gases)
Health Consumers Workers	Carcinogens at Work Directive 2004/37/EC	REACH provides a mechanism for authorisation of Cat. 1a and 1b carcinogens

(*continued overleaf*)

Table 1.1 *(continued)*

Chemical risk scope	EU legislation	Relation to REACH
Laboratory animals	The Cosmetics Regulation (EC) No 1223/2009 contains provisions restricting animal testing of cosmetic ingredients	REACH contains provisions for adapting testing requirements and for reading across to minimise animal suffering and use
Major accident prevention	'Seveso' Directives: 96/82/EC, 2003/105/EC	Applies to storage of hazardous chemicals. Not in the scope of REACH
Medicinal products	Directive 2001/83/EC and Regulation (EC) No 726/2004	Applies to safety of active pharmaceutical ingredients and components of medicinal products. Not in the scope of REACH
Plant protection products	Directive 2009/128/EC	Normally exempted from REACH. PBT/vPvB assessment may differ from ECHA REACH guidance
Radioactive substances	Directive 96/29/Euratom	Not in the scope of REACH
Toys	Directive 2009/48/EC	CMR ingredients, allergenic substances are regulated
Trade (international)	Rotterdam convention and prior informed consent (PIC) – Council Decision 2006/730/EC and Regulation (EC) n° 689/2008	Applies to banned or extremely restricted and to extremely hazardous pesticides. Not in scope of REACH
Transportation	United Nations Orange Book, International Air Transport Association (IATA) , EU directive 2008/68 – inland transport of dangerous goods	Excluded from REACH
Waste	WEEE (Waste Electrical and Electronic Equipment) Directive 2012/19/EU, RoHS (Restrictions of Hazardous Substances) Directive 2002/95/EC, Landfill Directive	Waste is excluded from REACH

Table 1.2 *Examples of regulatory systems for hazardous chemicals outside EU.*

Region/ country	Scheme and/ or associated legislation	Regulator	Objectives	Scope	Comments
Europe (non-EU)					
Norway	Regulations relating to restrictions on the manufacture, import, export, sale and use of chemicals and other products hazardous to health and the environment (Product Regulations) (2004)	Klima-OG Forurensnings-Direktoratet	Human health and environment throughout life cycle	Restriction of manufacturing, supply and use of specified substances, substance types and chemical families	Same Regulator manages the Norwegian Product Register
Switzerland	813.11 Ordinance of 18 May 2005 on Protection against Dangerous Substances and Preparations (Chemicals Ordinance, ChemO)	FOPH; FOEN; SOCA		Notification of new substances; classification and labelling; SDS	
Middle East					
Turkey	Regulation on the inventory and control of chemicals (2008)		Notification of new substances and reporting data to an Inventory	All substances > 1 tonne	

(*continued overleaf*)

Table 1.2 *(continued)*

Region/ country	Scheme and/ or associated legislation	Regulator	Objectives	Scope	Comments
African nations					
	Little in the way of focussed legislation on supply		Many nations use, or are in the process of adopting, GHS or similar evaluation and/or apply occupational health and safety regulations		
Australasia					
Australia	National Industrial Chemicals Notification and Assessment Scheme (NICNAS); Industrial Chemicals (Notification and Assessment) Act	Australian Government Department of Health and Ageing		Regulation of industrial chemicals	2011 major review to make the scope more comprehensive Memorandum of Understanding established with the ECHA
New Zealand	Hazardous Substances and New Organisms (HSNO) Act (1996)	Environmental Protection Authority		Hazardous substances (physico-chemical, tox or ecotox)	

Asia					
China		Chinese Ministry of Environment Protection	New chemicals notification; classification and labelling		
Japan	Chemical Substances Control Law (2009)	MITI		All substances > 1 tonne (same as REACH)	Statement of Intent established with the ECHA
	Industrial Safety and Health Law (ISHL)		Workplace H&S		
South Korea	Toxic Chemicals Control Act (1991)	NIER			New legislation similar to REACH is expected soon
Taiwan	Occupational Safety and Health Act	Institute of occupational safety and health under council of labour affairs (CLA)			
India	No centralised scheme. Various pieces of specific legislation focussing on individual requirements			Manufacture and supply; use in industry and by consumers; covering health and environment	

(*continued overleaf*)

Table 1.2 *(continued)*

Region/ country	Scheme and/ or associated legislation	Regulator	Objectives	Scope	Comments
North America					
United States of America	Toxic Substances Control Act (TSCA)	EPA			A more comprehensive programme is expected to be brought in the near future, with similarities to REACH Statement of Intent established with the ECHA
	Chemicals 'Right to know' HPV programme (voluntary)	EPA	Collecting of hazard and use information for release in the public domain	Chemicals at high volume in USA	
Canada	Canadian Environmental Protection Act (1999)	Environment Canada	Management of new and existing chemicals and control of pollution		Memorandum of Understanding established with ECHA
	Government of Canada Challenge programme	Environment Canada; Health Canada	Risk assessment and management (in depth or screening)	Priority list (at time of writing, 200 substances) for in-depth assessment	

	Pest Control Products Act, the Canada Consumer Product Safety Act and the Food and Drugs Act	Health Canada	
South America			
Uruguay	No centralised scheme. Various different specific items of legislation		GHS and SDS; restriction of specific dangerous chemicals
Venezuela	No centralised scheme. Various different specific items of legislation		CLP and SDS; restriction of specific dangerous chemicals
Peru	No centralised scheme. Various different specific items of legislation		CLP; restriction of specific dangerous chemicals
Colombia	No centralised scheme. Various different specific items of legislation		CLP and SDS; restriction of specific dangerous chemicals
Paraguay	No centralised scheme. Various different specific items of legislation		CLP and SDS; restriction of specific dangerous chemicals

(*continued overleaf*)

Table 1.2 *(continued)*

Region/ country	Scheme and/ or associated legislation	Regulator	Objectives	Scope	Comments
International programmes					
	UNECE (United Nations Economic Commission for Europe) Protocol; Stockholm Convention		Identification, monitoring and strategic long term control of persistent organic pollutants	Operates through a candidates list process with separate final lists of substances banned; restricted; or for which unintentional production must be avoided	
	ICCA (International Council of Chemical Associations)/OECD HPV programme (voluntary)	OECD with substance specific 'sponsorship' by a national authority	Collecting of hazard and use information for release in the public domain	Chemicals at high volume in any global region	
	Globally Harmonised system (GHS) for classification and labelling. Enacted into law (fully or partially), through various locally applying regulations, for example CLP 2008 in EU	UN (UNECE), administrated where applicable by local regulators, for example the ECHA	Identification and clear communication of chemical hazards in the supply chain		

International Programme on Chemical Safety	IOMC (Inter-Organization Programme for the Sound Management of Chemicals) (international cooperation between WHO ILO OECD UNEP FAO UNIDO UNITAR and Canadian COHS)	Communication of data by inter-governmental organisations	
OECD MAD (mutual acceptance of data)			Basis of international acceptability for non-clinical data sharing

gathering information on properties and use pattern of substances manufactured and supplied in large volumes.

This section briefly summarises these regimes as they stand at the time of writing, though it does not attempt to be comprehensive, especially with regard to laws and programmes at Member State (e.g. the UK) or national (e.g. England/Wales, Scotland and Northern Ireland) levels. Such legislation continues to develop, and global regulation and safety standards for chemicals in supply can be expected to harmonise increasingly in future. Many commentators have noted that existing regulatory systems are beginning to move towards approaches similar to those used in REACH, as countries seek to avoid becoming the default market for certain chemicals that are deemed unsafe in other areas where more stringent standards are applied.

1.2.10.1 Risk

Under REACH, in many circumstances, risk must be assessed.

In this context, risk can be summarised as the likelihood of the undesirable property being expressed under foreseeable circumstances. Under REACH it is necessary to give consideration to the normal life cycle of industrial chemicals carried out in EU, from manufacturing to processing of end-of-life wastes. Major industrial accidents and misuse of substances are outside the scope.

Assessment of risk is not always required as part of the REACH submission. There are often misunderstandings surrounding whether or not an assessment of risk is necessary. The following questions are pertinent:

- Does the substance have any identifiable hazard(s)?
- What is the tonnage?
- What is the pattern of use? Could the foreseeable life cycle of the substance lead to exposure of humans or the environment?
- Are any reasons associated with limited exposure used as part of waiving for any of the property data endpoints?

Assessment of exposure and risk is necessary when a substance has any identifiable hazard (see above), has a tonnage of at least 10 tonnes/year, and is used in any application not operated under ‘strictly controlled conditions’ (an exceptional level of control which, if demonstrated to specified standards, can mean a reduced registration package is possible) and in the event that exposure-based adaptation is used in data waiving anywhere in the technical dossier.

1.2.10.2 Qualitative versus Quantitative Approaches

In the case of many hazards, a quantitative approach to assessing risk is possible. This is normally the case for human health short-term and long-term exposure and for environmental effects.

In the case of human health, the effects data are used to derive an estimated safe dose (derived no-effect level or DNEL – for various exposure pathways and types of user). The exposure modelling leads to an estimated dose to humans associated with workplace or consumer use, or exposure via the environment. The risk is then characterised by taking

the ratio of estimated exposure/DNEL, leading to a RCR. A value of RCR < 1 indicates that the risk is acceptable.

In the case of the environment, the estimated safe dose for an ecosystem is called the predicted no-effect level (PNEC – for various environmental compartments, e.g. aquatic organisms, soil organisms). Exposure modelling leads to predicted environmental concentrations (PECs) for the equivalent compartments. The risk is then characterised by taking the ratio of PEC/PNEC, leading to a RCR (occasionally referred to as risk quotient). A value of RCR < 1 indicates that the risk is acceptable.

1.2.10.3 Management of Risks if RCR Is Equal to or Greater Than One

It is important for registrants to be aware that if any RCR ≥ 1 is found, indicating an unacceptable risk, then further work is needed on the part of the registrant. The RCR must be refined to give a value less than one, before the registration can be made. This would usually be done by adapting the exposure assessment to take account of additional measures to restrict the relevant exposure. Some tips are presented in this book in Chapters 8 and 10, discussing exposure assessment and refinements, and in Chapter 11 on managing risks.

1.2.10.4 Test Proposal Rule

For chemical properties that are required under Annexes IX–X of REACH, new testing must not be conducted without the permission of the ECHA. If the endpoint applies at the tonnage band for the substance, and no existing data (including prediction) are available, the registrant must include a testing proposal in the registration. The ECHA will review the testing proposals as part of its evaluation process (Section 1.2.3 in this chapter). For any proposed test in vertebrates, a public consultation procedure is additionally undertaken as part of the evaluation, to establish if any studies already exist and invite comments on the proposal. See Example 1.1 and Case Study 1.1.

Example 1.1

The registrant has no information regarding the 90-day repeated dose toxicity.
The registrant proposes a study.
The ECHA conducts a public consultation, stating that the registrant proposal appears correct in the light of the available data.
Other industry bodies and commentators review the proposal.
A non-governmental organisation is aware that there is relevant data held in the database of a non-EU country.
The registrant gains access to that data and therefore proposes to not test.
The ECHA considers that the study is not compliant and insists on a test.
The registrant appeals.
The Member States and the ECHA review the information, including further representations from all stakeholders, and a final decision is reached. No appeal is possible.

Case Study 1.1 Test proposal procedure

The Lead Registrant of a substance (requiring an Annex IX-compliant data set) has evaluated the available data. The SIEF members own several studies and two of the three substances are well described in the published chemical literature; also the substances are within the applicability domain of established (Q)SARs. The registrant concludes that the physico-chemical, environmental and parts of the mammalian toxicity data sets are adequately covered but that the substance lacks subchronic repeated dose toxicity data and sensitisation and eye irritation data. The registrant concludes that testing of these three endpoints is necessary to complete the hazard assessment and risk characterisation.

1. The registrant has already established that no such data exist already within the SIEF or in the public domain.
2. The sensitisation study is required at Annex VIII, so the registrant proceeds and commissions a suitable laboratory to undertake the test using the method recommended in Guidance part R7a, following the Guideline in Regulation EC 440/2008.
3. Eye irritation data are required at Annex VII. For eye irritation a stepwise approach is necessary, because it is required to initially assess the effect in an *in vitro* test. An *in vivo* test may need to be conducted afterwards, depending on the outcomes. Since the *in vivo* eye irritation test is required at Annex VIII, the registrant may also proceed and commission the test providing this stepwise approach is followed.
4. The 90-day repeated dose test is required at Annex IX, so the registrant must not proceed to undertake this test. The registrant includes a Testing Proposal in the IUCLID dossier in the relevant endpoint section, including details of the substance identity to be tested and the guideline method to be used.
5. Following registration, the ECHA evaluates the Test Proposal. The ECHA publishes on its web site the substance identity with the study that has been proposed, and a data holder for a structurally similar substance comes forward with an existing study which can be read-across.

1.2.10.5 Availability of Existing Data and Rights of Access

In the course of preparing a dossier, it is often discovered that there are a lot of useful data already in existence. While ‘completeness’ is highly desirable, the rights and investments of each data owning organisation must be respected. Copyright must also be held for published data. It is very important to ensure appropriate rights of access are put in place between the registrant and the data owner before the registration is made. A fee is normal, and is generally in proportion to the typical cost of the test in question. This also applies to data originating from regulatory authorities and published data. Some publishers require a fee or impose terms and conditions.

Table 1.3 *Definitions of the Klimisch reliability codes.*

Klimisch	Definition	Comment
1	Reliable	Compliant with the required test guideline, test conducted with no significant shortcomings and in compliance with Good Laboratory Practice (GLP).
2	Reliable with restrictions	Close to Klimisch 1 but with a shortcoming, such as a departure from the guideline, incomplete reporting, or the result is a prediction rather than a measurement. Scientific papers in journals can meet these requirements, if exceptionally well documented.
3	Not reliable (also Invalid)	Definitely unreliable due to a deficiency in acceptable scientific practice; such data are usually of no worth.
4	Reliability not assignable	Uncertain reliability, but insufficient information available to resolve the uncertainty; this can include reports of uncertain origin or poorly-reported scientific papers. If the origin of the data is unknown, then Klimisch 3 might be more appropriate. These results could be useful as part of weight of evidence, but are usually of no worth.

Example 1.2

For example, if a measurement of water solubility is made, but for reasons of analytical difficulties a definitive result cannot be calculated, the study could still be Klimisch 1 or 2. The uncertainty in this case is due to a technical limitation rather than the study being poorly executed or reported. However, this should not become an excuse for work falling short of widely-accepted quality criteria.

1.2.10.6 Data Reliability

When a study report is reviewed for inclusion in a registration data set, a Klimisch code should be assigned. These codes are summarised in Table 1.3.

Some degree of expertise should be applied.

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