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Review of certain provisions of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restrictions of Chemicals (REACH), as laid down in its Article 138

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS

Chemicals Strategy for Sustainability
Towards a Toxic-Free Environment

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1. Background

Regulation (EC) No 1907/2006 (hereinafter, REACH)[1] provides in its Article 138 for a number of reviews to be carried out by the European Commission. The objective of this Staff Working Document is to summarise these reviews, notably:

1. to assess whether or not to extend the application of the obligation to perform a chemical safety assessment (CSA) and to document it in a chemical safety report (CSR) for substances meeting the criteria for classification in the hazard classes carcinogenicity, germ cell mutagenicity, or reproductive toxicity[2], not covered by this obligation because they are not subject to registration or subject to registration but manufactured or imported in quantities of less than 10 tonnes per year" (Article 138 (1));
2. to assess whether or not to extend the scope of Article 33 to cover other dangerous substances, taking into account the practical experience in implementing that Article (Article 138 (8));
3. and to review, in accordance with the objective of promoting non-animal testing and the replacement, reduction or refinement of animal testing required under this Regulation, the testing requirements of Section 8.7 of Annex VIII (i.e. reproductive toxicity data requirements for substances that are manufactured or imported in quantities of 10 tonnes or more), Article 138(9).

These reviews are independent from each other. The following chapters are therefore also independent, with their own conclusions.

2. Review according to Article 138 (1)

2.1. Introduction

2.1.1. The Review

The main objectives of the REACH Regulation[3] are to ensure a high level of protection of human health and the environment, including the promotion of alternative methods for the assessment of the hazards of substances, as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation. The Regulation obliges manufacturers and importers to register their substances manufactured or imported in the EU above certain tonnage levels, and to provide a technical dossier for those registered substances. This dossier should include information on the physicochemical, toxicological and ecotoxicological properties of the substance, according to the standard information requirements of Annexes VII to X or the adaptation rules set out in Annex XI. For non-intermediate hazardous substances marketed above 10 tonnes per year, the manufacturer or importer needs to perform a chemical safety assessment (CSA) and document it in a chemical safety report (CSR).

[1] Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) OJ L 396, 30.12.2006, p. 1. Corrected version in OJ L 136, 29.5.2007, p. 3.

[2] The review of this provision for all substances not covered by this obligation because they are not subject to registration or subject to registration but manufactured or imported in quantities of less than 10 tonnes per year will be carried out and published at a later stage.

[3] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L396, 30.12.2006, p. 1).

Article 138 of REACH specifies a number of review obligations for the European Commission. Article 138(1) requires that:

> "*By 1 June 2019, the Commission shall carry out a review to assess whether or not to extend the application of the obligation to perform a chemical safety assessment and to document it in a chemical safety report to substances not covered by this obligation because they are not subject to registration or subject to registration but manufactured or imported in quantities of less than 10 tonnes per year. However, for substances meeting the criteria for classification in the hazard classes carcinogenicity, germ cell mutagenicity or reproductive toxicity, category 1A or 1B, in accordance with Regulation (EC) No 1272/2008, the review shall be carried out by 1 June 2014. When carrying out the review the Commission shall take into account all relevant factors, including:*
>
> > *(a) the costs for manufacturers and importers of drawing up the chemical safety reports;*
> >
> > *(b) the distribution of costs between actors in the supply chain and the downstream user;*
> >
> > *(c) the benefits for human health and the environment.*
>
> *On the basis of these reviews, the Commission may, if appropriate, present legislative proposals to extend this obligation."*

In this report SWD, the Commission addresses the obligation to perform a CSA and to document it in a CSR for substances marketed at less than 10 tonnes per year and meeting the criteria for classification in the hazard classes carcinogenicity, germ cell mutagenicity or reproductive toxicity, category 1A or 1B (CMR substances[4]). A review of this obligation for substances marketed at less than 10 tonnes per year but not meeting these CMR-criteria will be undertaken separately, together with the review obligation in Article 138(3) of REACH. For substances not subject to registration, such obligation is not considered useful, as there are no mandatory data to be reported in a CSA.

2.1.2. The objective of the action

According to the 2018 REACH Review[5], the main drivers of the REACH Registration process include improving the knowledge on the uses of substances and level of exposure, which in turn allows companies to decide on the most appropriate risk management measures to be put in place on site and to communicate these across the supply chain. The Chemical Safety Assessment and Chemical Safety Report (CSA/CSR) is a key instrument in communicating appropriate risk management measures in the supply chain. The REACH Regulation has not mandated the CSA/CSR for 1- 10 tonnes substances when it went into force, but it asked the Commission to review the benefits of extending this requirement to the low tonnage substances.

The objective of the action of requesting companies to provide a CSR also for 1 – 10 tonnes CMR substances would thus be, by increasing the level of information on substances, on their associated uses and their exposures, and by making this information available to all downstream users, to allow for the full achievement of the overall objectives of the REACH registration process.

[4] Where this report refers to CMR substances or CMRs, substances meeting criteria for CMR 1A/1B are meant.
[5] https://ec.europa.eu/docsroom/documents/28201

2.2. Reports collecting information on 1 – 10 tonnes CMR substances and consequences of requiring a CSA/CSR for those substances

The Commission put in place a study in 2014 ("Final Report on the extension of the obligation to perform a chemical safety assessment and to document a chemical safety report to CMR substances manufactured or imported between 1 and 10 tonnes per year")[6] to assess the benefits and costs of extending the requirement for a CSA/CSR to 1 – 10 tonnes CMR substances. A subsequent study in 2017[7] further elaborated that question in combination with increased information requirements for 1 – 10 tonnes substances. The outcome of those studies was reported in the second REACH review[8] that concluded that there was a need to assess affordability of additional registration requirements for the companies involved, especially given the number of SMEs who might be affected. That assessment should take advantage of the experience gained from the last registration deadline in 2018[9].

The two reports referred above pre-dated the June 2018 registration deadline for 1-10 tonnes substances and, since the registration information for low tonnage substances was then not yet available, it was necessary to apply a Monte Carlo simulation methodology[10] to develop virtual substance registration data and to estimate the associated costs. After the expiry of the 2018 registration deadline, the Commission contracted a third study[11] on the 1-10 tonnes substances requirements, which is using data on actual registrations submitted until 2018 and currently available from the REACH Registration database. Therefore, no simulation methodology is used in this last contract and the conclusions based on actual registration data is believed to be more robust. The 2020 study will be published in Q3 2020 but results on the 1-10 tonnes CMR substances could already be extracted for this report.

ECHA supplied detailed information on all 1-10 tonnes substances registered under REACH at the end of 2019. Some of these substances are only registered at the 1-10 tonnes level, others are registered at 1-10 tonnes and higher tonnages. For each registered substance (identified via EC number), ECHA's dataset provides information including the types of registration, the tonnage bands, the date of registration (anonymised), and information describing the type and role of each registrant. Alongside these data, for each substance, ECHA provided a separate dataset with the hazard classifications and labelling identified in the substance registration dossiers. These datasets allowed identifying:

- which substances would be required to undertake what level of assessment as part of a CSA and
- which (anonymised) registrants would incur the costs of providing this information.

[6] https://ec.europa.eu/environment/chemicals/reach/pdf/1-10t%20P2%201-10t.pdf
[7] https://ec.europa.eu/environment/chemicals/reach/pdf/phase-3-1-10t-main-report-final.pdf
[8] COM (2018)116 and SWD(2018)58
[9] The Commission has contracted out a study on the impacts of the 2018 REACH registration deadline, expected to be published early 2021.
[10] Monte Carlo methods, or Monte Carlo experiments, are a broad class of computational algorithms that rely on repeated random sampling to obtain numerical results. The underlying concept is to use randomness to solve problems that might be deterministic in principle. They are often used in physical, mathematical or economical problems and are most useful when it is difficult or impossible to use other approaches.
[11] No 07.0203/2019/8 M999/ENV.B.2,"Gather further information to be used in support of an Impact Assessment of potential options, in particular possible amendments of REACH Annexes, to modify requirements for registration of low tonnage substances (l-10 tonnes/year) and the CSA/CSR requirement for low tonnage substances with or without CMR properties in the framework of REACH", Phase 4, to be published in Q3 2020.

Information from ECHA's database of registered substances reveals that 9 520 substances are registered at 1-10 tonnes. Of these, 256 substances are registered only with physico-chemical data and 9 264 with full Annex VII data. Among these last ones, 3 520 are also registered above 10 tonnes and **209** of those are CMR-substances. 5 744 substances are fully registered at 1-10 tonnes only (i.e. not also at higher tonnages) and **85** of those are CMR-substances. Therefore, the total number of 1-10 tonnes CMR-substances in ECHA's database is **294**.

For the 1-10 tonnes only substances, no CSA is required at present and only general advice is provided to downstream users in the Safety Data Sheet (SDS). To comply with the risk assessment and risk management obligations under the parallel legislation[12] triggered by the classification as a CMR, manufacturers/importers (MIs) and downstream users (DUs) must rely on the general information presented in the SDS to complete their own in-house assessments of exposure and risk for their own operations.

Extending the CSA/CSR obligation to 1-10 tonnes CMRs would require MIs of such substances to complete the process established under Article 14 of REACH and the detailed requirements set out in Annex I of REACH. The elements to be documented in the CSR are listed in Annex I to this report. For DUs, the information in the CSA/CSR would greatly facilitate their own assessments of exposure and risk for their own operations and their compliance with other parallel legislation. This is because the exposure scenarios that would have to be included in the CSR and which describe operational conditions and risk management measures would facilitate compliance with the many regulatory instruments that are triggered by classification in accordance with Regulation (EC) No 1272/2008. This facilitation would result in a cost saving for the DUs. Those obligations in parallel legislation are summarised in section 2.3. The requirement for a CSR would also lead to the development of a more detailed extended Safety Data Sheet (eSDS). The importance of a good quality eSDS has also been identified in the REACH review actions 3 and 12[13], to ensure that the safe use information delivered via the SDS can be directly used by employers and site managers in terms of OSH and environment legislation. Improving the eSDS forms part of development work currently done by ECHA and the Commission.

Hence, the requirement for a CSA/CSR effectively moves some workload from each DU to the MI and is likely to benefit multiple DUs of each substance, thus reducing/eliminating duplication of efforts and leading to harmonisation of information.

The requirement for a CSR would also necessitate a PBT (persistent, bioaccumulative and toxic) - assessment. The purpose of the PBT/vPvB (very persistent, very bioaccumulative) assessment is to determine if the substance fulfils the criteria for PBT/vPvB given in Annex XIII and, if so, to characterise the potential emissions of the substance. For substances registered only at 1-10 tonnes, no PBT/vPvB assessment will have yet been performed because it forms part of a CSA/CSR that is not currently required by Annex VII of REACH.

For the 1-10 tonnes substances also registered at higher tonnages, a CSA/CSR already exists and will cover most uses, including the manufacturer's own use. For some substances, however, some of the uses registered only at 1-10 tonnes may not be covered by the existing CSA and additional exposure assessment and risk characterisation would be required. This would represent a cost of the CSA/CSR option for the substances.

[12] Worker health and safety regulation, general product safety requirements and waste legislation were considered.

[13] COM, General Report on the operation of REACH, SWD(2018) 58 final. Action 3 *Improving the quality & workability of the extended SDS*, and Action 12 *REACH-OSH interface* .

The assumptions concerning the numbers of 1-10 tonnes substances uses and the cost of the exposure assessments and risk characterisation are described further down.

2.3. Requirements under parallel regulation (from 2017 RPA study)

2.3.1 Overview

In the event that a substance is identified as meeting the criteria for classification as C, M, or R 1A/1B in accordance with Regulation (EC) No 1272/2008, the change in classification triggers actions on the part of manufacturers, importers and downstream users to comply with other pieces of community legislation covering areas including worker health and safety, product safety, and waste. Each area of regulation requires action to assess exposure and risks and to implement risk management measures.

For the purpose of this report, it is useful to recall what the obligations under parallel legislation are, as well as the associated costs. This will enable drawing a comparison with the costs from providing a CSR.

The key requirements are summarised below.

2.3.2 Worker Health and Safety Legislation

Key legislation and associated requirements in relation to worker health and safety include:

- **Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work (CAD)**[14]**–** which requires employers (i.e. manufacturers and downstream users) to determine whether any hazardous chemical agents are present at the workplace and assess any risk to the safety and health of workers arising from the presence of those chemical agents;

- **Carcinogens and Mutagens Directive 2004/37/EC (CMD)**[15] **–** which requires that, as a priority, workers' exposure must be prevented through substitution. If not possible, the employer shall use a closed technological system. Where a closed system is not technically possible, the employer shall reduce exposure to a minimum through a number of risk management measures specified in the Directive;

- **Pregnant and Breastfeeding Workers Directive 92/85/EEC**[16] **–** which requires that the employer shall assess the nature, degree and duration of exposure, assess any risks to the safety or health and any possible effects on the pregnancy or breastfeeding of workers and then decide what measures should be taken; and

- **Directive 94/33/EC on Young Workers**[17] **–** under which employers are obliged to assess the hazards to young people, generate new site-specific data on the nature, degree and duration of

[14] Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work, (*OJ L 131, 5.5.1998, p. 11–23)*
[15] DIRECTIVE 2004/37/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 29 April 2004 on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (OJ L 158, 30.4.2004, p. 50)
[16] Council Directive 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding, (*OJ L 348 , 28/11/1992, p. 0001 – 0008)*
[17] Council Directive 94/33/EC of 22 June 1994 on the protection of young people at work, (*OJ L 216, 20.8.1994, p. 12–20)*

exposure to chemical agents and adopt the measures necessary to protect the safety and health of young people.

At present, for substances for which there is no obligation to conduct a CSA under REACH, there is no obligation to provide exposure scenarios detailing the technical means to achieve risk management for identified uses in an extended SDS in relation to human exposures in the workplace. As such, under this parallel legislation, manufacturers and each downstream user must conduct their own bespoke assessments of exposure, risk and identification of risk management measures based on the general information provided in the SDS.

2.3.3 Product Safety Requirements

In addition to worker health and safety requirements, classification as C, M or R 1A/1B has implications in terms of safety of products. Annex XVII of REACH (entries 28 to 30) prohibits the placing on the market and the use of CMRs 1A/1B as substances or as constituents of other substances or mixtures for supply to the general public when the individual concentration in the substance or the mixture is equal to or greater to the generic/specific concentration limit of Regulation (EC) No 1272/2008. Consumer articles are not in the scope of the entries 28 to 30, but some specific legislation applies to some of these articles and all products in general. This includes:

- **Directive 2001/95/EC on General Product Safety**[18] **-** under Article 3 of the GPSD producers are obliged to place only safe products on the market. Assessment of the risk to consumers from the presence of a CMR substance in a product would be required where this would include consideration of human exposure to the substance due to the use of the product under reasonably foreseeable conditions;

- **Regulation No 305/2011 for the Marketing of Construction Products**[19] **-** all manufacturers of construction products containing substances identified with C, M or R properties must consider the implications of this in terms of risk and safety of their products; and

- **Toy Safety Directive 2009/48/EC**[20] **-** Article 18 of the Toy Safety Directive requires manufacturers, before placing a toy on the market, to carry out an analysis of the chemical, physical, mechanical, electrical, flammability, hygiene and radioactivity hazards that the toy may present, as well as an assessment of the potential exposure to such hazards. [21] To comply with their obligations, manufacturers of products containing 1-10 tonnes 'CMRs 1A/1B' substances would have to rely on the general information presented in the SDS to complete their assessments where this will not include detailed information on the technical considerations in relation to exposure, risk and safety (as no CSA is required).

[18] Directive 2001/95/EC of the European Parliament and of the Council of 3 December 2001 on general product safety, (*OJ L 11, 15.1.2002, p. 4–17)*

[19] Regulation (EU) No 305/2011 of the European Parliament and of the Council of 9 March 2011 laying down harmonised conditions for the marketing of construction products and repealing Council Directive 89/106/EEC, (*OJ L 88, 4.4.2011, p. 5–43)*

[20] DIRECTIVE 2009/48/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 June 2009 on the safety of toys, (OJ L 170, 30.6.2009, p. 1-37)

[21] The Toys Directive, in its Annex II, part III, also sets out particular safety requirements regarding the chemical properties of toys. In point 3, it refers to substances that are classified as carcinogenic, mutagenic or toxic for reproduction (CMR) of category 1A, 1B or 2 under Regulation (EC) No 1272/2008, which shall not be used in toys, subject to certain exceptions.

2.3.4 Waste Legislation

The Waste Framework Directive 2008/98/EC[22] defines hazardous waste as waste that fulfils certain properties, including carcinogenic, toxic for reproduction or mutagenic properties. This would apply to waste containing 1-10 tonne substances classified as C, M or R 1A/1B. This would require the determination of safe and environmentally preferred waste management options.

In relation to the 1-10 tonnes substances, the information provided in the SDS for waste management will be of a general nature with no specific quantitative analysis of risk and exposure in relation to the recommended risk management measures in relation to waste and the technical means to achieve this (as no CSA is required).

2.3.5 Costs of compliance with requirements under all parallel legislation described above

On the basis of the above, RPA have made an estimation[23] of the cost of compliance with parallel legislation in the absence of a CSA/CSR for 1-10 tonnes CMRs. The table below reflects those estimates for low, medium and high cost scenarios. These assume that assessments for compliance with parallel legislation (using the general information currently required to be provided in the SDS for a substance) would cost each downstream user between € 1 500 and € 3 500 for substances with 'CMR 1A/1B' properties.

Table 2.1 DU's costs to comply with parallel legislation (per use per substance)

	Low scenario	Medium scenario	High scenario
Number of uses per substance	1	2	5
Number of DUs per use	20	30	40
Cost for a DU to conduct assessments to comply with parallel regulation	€ 1 500	€ 2 500	€ 3 500

2.4. Costs of extending the CSA/CSR obligation to 1 – 10 tonnes CMR substances

2.4.1 Overview

The 2020 study by RPA[24] assesses options for possible amendments of REACH, modifying information requirements for 1-10 tonnes substances as well as the option of requiring a CSA/CSR for the 1-10 tonnes substances. The following REACH compliance costs have been identified as relevant and potentially significant for Manufacturers/Importers in relation to this:

[22] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives, (*OJ L 312, 22.11.2008, p. 3–30)*

[23] Estimations based on previous work in RPA (2017): Study to gather further information to be used in support of an Impact Assessment of potential options, in particular possible Amendments of REACH Annexes, to modify requirements for registration of low tonnage substances (1-10t/year) and the CSA/CSR Requirement for CMR substances in the framework of REACH, report prepared for DG Environment https://ec.europa.eu/environment/chemicals/reach/pdf/phase-3-1-10t-main-report-final.pdf and CSES (2015) Monitoring Impacts of REACH on Innovation, Competitiveness and SMEs, report prepared for DG Growth http://ec.europa.eu/DocsRoom/documents/14581/attachments/1/translations/en/renditions/native

[24] Phase 4 study of RPA on the 1-10 tonne substances and whether to increase information requirements and whether to expand the CSA/CSR requirement to them, to be published in Q4 2020.

- Cost of completing information on the substance, quantities and uses, classification and environmental fate;

- Cost of producing Robust Study Summaries;

- Cost of completing the physicochemical, human health and environmental hazard assessments;

- Cost of completing the human exposure assessment and risk characterisation where required by the outcome of the human health hazard assessment;

- Cost of completing the environmental exposure assessment and risk characterisation where required by the outcome of the environmental hazard assessment; and

- Cost of producing an extended Safety Data Sheet (eSDS).

The extension of the CSA/CSR obligations would also impact the downstream users' (DUs) compliance costs to comply with their duty under REACH to pass information up the supply chain (to the manufacturer/importer). Thus, for all of the 1-10 tonnes substances for which either or both the human and environmental exposure assessment are required, DUs would need to provide relevant information up the supply chain.

As with costs of information and dossier submission, in relation to each of these cost components there are differences in the type and nature of costs for substances registered only at 1-10 tonnes versus those also registered at higher tonnages. For 1-10 tonnes only substances, no CSA/CSR exists at present and, thus, they need to be developed. For 1-10 tonnes substances also registered at higher tonnage bands, CSAs/CSRs have already been produced by the registrants at above 10 tonnes and cover the manufacturing uses and those of the downstream users of those registrants. These CSRs are not available for any registrant in the range 1-10 tonnes only and they might not cover uses of their DUs.

For 1-10t substances also registered at above 10 tonnes, some components of the CSA are already complete and some of this can be used to complete tasks within the CSA for the 1-10 tonnes only registrants. These components include:

- **Hazard assessment and classification** – This will have already been completed for the initial registration at 1-10 tonnes. It will also have been completed by higher tonnage registrants as part of their CSA and published in the Chemical Safety Report (CSR). Further, 63% (130) of the 1-10 tonnes CMR substances also registered at above 10 tones have a harmonised classification. Regarding DNELs, the vast majority of the CMR substances will be non-threshold substances (for which no DNEL exists). For those that have a threshold, DNEL information can be extracted from the published CSR, as well as from other publicly available sources (without having to buy full access to the study/ies that the DNEL is based on). In the event that such data are not available to the 1-10 tonnes registrant, the CSA can 'default' to that for a non-threshold substance, as there is no requirement in Annex I to provide additional information for CSA over and above that required in the relevant Annex (Annex VII). With

all of these factors combined, the cost of completing hazard assessment and classification is zero or near zero for the 1-10 tonnes registrants.

- **PBT/vPvB assessment** – This section will have been completed by higher tonnage registrants and the outcomes been published in the CSR, as well as other publicly available sources. Thus, costs for entering the information for 1-10 tonnes registrants' CSA are zero or near zero.

- **Exposure assessment and risk characterisation** – for some, potentially all, of the downstream uses registered by 1-10 tonnes only registrants, a CSA will already have been completed. It is not known which of these uses will or will not have been covered in any existing CSA. The worst-case assumption that registrants would have to complete full assessments for their own registered uses has been applied. The number of uses to be assessed is calculated with reference to a percentage of all of the existing known uses. This percentage is given by the ratio of the number of 1-10 tonnes only registrants versus the number of all registrants. Thus, for example, for a substance with a total of 100 registrants and 10 1-10 tonnes only registrants, the percentage of uses that the 1-10 tonnes only registrants would have to assess is equivalent to 10% of all known uses. In reality, some of these uses will already have been covered in the existing CSA and, where this is the case, the cost for access to this is likely to be less than the costs for full assessment that have been assumed in the figures presented further down.

Regarding the issue of payments for access to information more generally, any payments made by 1-10 tonnes only registrants to other registrants at higher tonnages would represent so called 'transfer payments'. Such 'transfer payments' do not constitute an 'economic cost' when assessing the costs and the benefits of options for changed Annex VII requirements and, strictly, should not be considered. And even if one would want to consider it, it would not be practically possible, since the price of a Letter of Access is not regulated and that, consequently, companies can freely set it at their discretion. One can only assume that smaller companies will have more difficulties to afford it than larger ones. A more detailed assessment of affordability is presented further below. However, for the exposure assessment and risk characterisation elements, it is difficult to disassociate any such payments from the cost of full assessment and so the latter cost is assumed in the analysis (even though the cost of access to the relevant parts may be significantly less and some of these costs may actually represent transfer payments and not costs in the formal sense).

The sub-sections below discuss estimation of costs for each of the components and how they have been calculated for each of the two groups of substances.

2.4.2 Information on the substance, its uses, classification and environmental fate

Sections 1 to 4 of the CSR are to provide general information on the substance, its manufacture and uses, classification and labelling and environmental fate properties. The table below describes the sources of the required information in respect of the 1-10 tonnes substances. As can be seen, much of it is already provided according to the requirements of Annexes VI and VII of REACH. As such, in the analysis it is assumed that:

- The costs of completing CSR Sections 1-4 ranges between € 100 and € 250 per substance – an average of € 175 per substance.

- This cost applies both for substances registered at only 1-10 tonnes and also for substances registered at above 10 tonnes.

Table 2.2: CSR Reporting on the Substance, its Uses, Classification and Environmental Fate

CSR Section	Availability of information
1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES	Annex VI and VII information and summarised in Section 1 of the SDS: Identification of the substance/mixture and of the company/undertaking
2. MANUFACTURE AND USES	Annex VI information summarised in Section 1 of the SDS: Identification of the substance/mixture and of the company/undertaking/entity
2.1. Manufacture	
2.2. Identified uses	
2.3. Uses advised against	
3. CLASSIFICATION AND LABELLING	Annex VI and application of Annexes VII to XI. Summarised in Section 2 of the SDS: Hazards identification
4. ENVIRONMENTAL FATE PROPERTIES	
4.1. Degradation	Results from tests on ready biodegradation in accordance with Section 9.2.1.1 of Annex VII and summarised in Section 12.2 of the SDS: Persistence and degradability
4.2. Environmental distribution	Characterisation of possible degradation, transformation, or reaction processes and an estimation of environmental distribution and fate based on available data
4.3. Bioaccumulation	Results from tests on Octanol-water partitioning coefficient experimentally determined in accordance with Section 7.8 of Annex VII and summarised in Section 12.3 of the SDS: Bioaccumulative potential
4.4. Secondary poisoning	Based on analysis of composite and available information

2.4.3 Cost of upgrading to Robust Study Summaries

i. Substances registered at 1-10 tonnes only

In relation to substances registered only at 1-10 tonnes, study summaries produced for the current Annex VII endpoints provided as part of the registration would need to be upgraded to Robust Study Summaries. The table below provides the cost of study summaries for the Annex VII endpoints, the costs of upgrading these studies and the resulting total costs of Robust Study summaries estimated for each endpoint. Costs are based on estimated time for a toxicologist (whether in-house or consultant) at €1 000 per day and rounded appropriately.

Table 2.3: Cost of Robust Study Summaries

Section	Test	Study summary cost	Cost to upgrade to a robust study summary	Cost of producing a Robust Study Summary
8.1 Skin irritation	An *in vitro* study	€ 100	€ 50	€ 150
	An *in vivo* study	€ 100	€ 50	€ 150
8.2 Eye irritation	An *in vitro* study	€ 100	€ 50	€ 150
	An *in vivo* study	€ 100	€ 50	€ 150
8.3 Skin Sensitisation	Annex VII	€ 100	€ 50	€ 150
8.4 Mutagenicity	Ames test (VII)	€ 250	€ 50	€ 300
	MNT/CAB Vitro	€ 250	€ 50	€ 300
	Cytvivo	€ 500	€ 100	€ 600
Section 9.1 Aquatic Toxicity	Study on algae (Annex VII)	€ 100	€ 50	€ 150
9.2 Degradation	Ready biodegradability (Annex VII)	€ 100	€ 50	€ 150

Source: Phase 3 study and CSES study monitoring the impacts of REACH

ii. 1-10 tonnes substances also registered at higher tonnages

For the 1-10 tonnes CMR substances also registered at higher tonnages, robust study summaries will already be part of the existing CSA/CSR produced by higher tonnage registrants and there will be no need for upgrading, implying zero cost. However, the cost of access and administration of that is taken as being equal to the equivalent costs of upgrading. Thus, the costs set out in the previous table are also applied to registrants of 1-10 tonnes substances also registered at higher tonnages.

2.4.4 Cost of completing the physicochemical, human health and environmental hazard assessments

i. Substances registered at 1-10 tonnes only

For substances registered at 1-10 tonnes only, the following hazard assessments would be required as part of developing the new CSA/CSR:

- **Human health hazard assessment:** to determine the classification of a substance and to derive DNELs where possible using the available data;
- **Human health hazard assessment of physicochemical properties:** to determine the classification of a substance in relation to, as a minimum, explosivity, flammability and oxidising potential; and
- **Environmental hazard assessment:** to determine the classification of a substance and to identify the PNEC where possible using the available data.

It is noteworthy that there is no requirement in Annex I to provide additional information for CSA over and above that required in the relevant Annex (in this case Annex VII). If there is insufficient information to demonstrate 'non threshold' properties (and derive a DNEL) then, as noted above, risk management to eliminate exposure is the objective (as opposed to risk management to reduce

exposure to a certain threshold concentration). Additional information would not have to be generated or otherwise accessed[25].

In earlier studies, a 'first time' analysis for the hazard assessments was assumed to take between 1.5 and 3 days for an in-house or consultant toxicologist at € 1 000 / day. As such, costs were estimated at between € 1 500 and € 3 000, on average € 2 250 per substance. However, determination of classification of the substance will have already been completed as part of the original registration process. As such, costs for phase-in substances registered at 1-10t only likely to be minimal. For completeness, an estimated cost of € 225 per substance has been included based on 10% of the 'first time' assessment and determination of the classifications at € 2 250).

ii. 1-10 tonnes substances also registered at higher tonnages

For 1-10 tonnes substances also registered at higher tonnages, hazard assessments and determination of classification of the substance will also have already been completed as part of the original registration process but also will already have been developed as part of the existing CSA and communicated via an eSDS. In this study it was assumed that the cost paid by 1-10t registrants for this information to higher tonnage registrants is considered as kind of reimbursement of the cost already spent on the generation of this information. Therefore, the costs associated with the generation of information for the purpose of completing the physicochemical, human health and environmental hazard assessments are assumed to be zero.

2.4.5 Cost of undertaking PBT/vPvB screening and assessment

i. Substances registered at 1-10t only

The purpose of the PBT/vPvB assessment is to determine if the substance fulfils the criteria for PBT/vPvB given in Annex XIII and, if so, to characterise the potential emissions of the substance. The assessment is divided into a screening stage and an assessment stage.

PBT/vPvB screening

The procedures for PBT/vPvB assessment are set out in Annex XIII, Section 2.1, which identifies that, for substances with information from Annexes VII and VIII only "*the registrant shall consider information relevant for screening for P, B, or T properties in accordance with Section 3.1 of this Annex"*. There is no requirement to generate information for screening.

The screening applies to all substances and is assumed to cost € 750 per substance (0.75 days for an in-house or consultant toxicologist at € 1 000 per day).

PBT/vPvB Assessment

Continuing the requirements set out in Annex XIII, Section 2.1 :"*If the result from the screening tests or other information indicate that the substance may have PBT or vPvB properties, the registrant shall generate relevant additional information as set out in Section 3.2 of this Annex.[….].No additional information needs to be generated for the assessment of PBT/vPvB properties if there is no indication of P or B properties following the result from the screening test or other information*".

[25] Note that, in the case of the 206 CMR 1A/1B substances also registered at higher tonnages, 113 of these (55%) were originally registered in 2010 and, under the 12-year rule, any tox/ecotox information in those registrations would be free after 2022.

Following its Annex III screening exercise in 2016, ECHA suggested that Phase 3 should assume that 2.7% of all substances would be identified as potential PBTs/vPvBs by screening. Registrants of these substances would need to do one of the following:

- generate any selected information from Section 3.2 of Annex XIII sufficient to allow assessment;
- demonstrate that the process and use conditions of the substance meet the conditions as specified in Section 3.2(b) or (c) of Annex XI, and subsequently the substance is considered as if it is a PBT or vPvB in the registration dossier; or
- withdraw the substance from the market.

Regarding the first of these, the generation of additional information, Section 3.2 of Annex XIII identifies that the following information shall be considered for the PBT/vPvB assessment using a weight-of-evidence approach:

- **For assessment of P or vP properties:**
  - Results from simulation testing on degradation in surface water (OECD 309 = € 20 759)[26], soil (OECD 307 = € 60 804) and sediment (OECD 308 = € 55 217);
  - Other information, such as suitable and reliable information from field studies or monitoring studies
- **For assessment of B or vB properties:**
  - Results from a bioconcentration or bioaccumulation study in aquatic species (OECD 305= € 62 150);
  - Other suitable and reliable information on the bioaccumulation potential including results from a chronic toxicity study on animals (fish OECD 204 - € 59 754) or assessment of the toxicokinetic behaviour of the substance (€ 1 652);
  - Information on the ability of the substance to biomagnify in the food chain such as biomagnification or trophic magnification factors.
- **For assessment of T properties:**
  - Results from growth inhibition study on aquatic plants (Section 9.1.2 of Annex VII);
  - Classification for C or M 1A/1B, R 1A/1B/2 STOT RE 1 or 2;
  - Results from long-term toxicity testing on invertebrates and/or fish (Sections 9.1.5/9.1.6 of Annex IX (Daphnia OECD 211 = € 21 218 / fish (above) OECD 204 - € 59 754);
  - Results from long-term or reproductive toxicity testing with birds (Section 9.6.1 of Annex X OECD 205 = € 41 248); and
  - Other demonstrably suitably and reliable information.

It is not necessary to generate all of this information (which would cost in the region of € 261 000). ECHA Guidance[27] provides an Integrated Testing Strategy (ITS) that suggests a progressive route for the assessment of P, B and T properties. The outcome of the assessments is linked – a substance that can be established as not meeting criteria for P cannot be a PBT/vPvB and likewise for a substance where it is established that it is not B.

[26] All costs for OECD TG studies have been taken from a database of the consultant of the Phase 3 and 2020 study on the costs drawn from various studies, including from an authoritative industry association and have been updated to reflect 2020 prices.

[27] ECHA Guidance on Information Requirements and Chemical Safety Assessment - Chapter R.11: PBT/vPvB assessment, https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf

ECB (2002)[28] estimated that around 20% of the substances with potential PBT characteristics are actual PBT substances. As such, for around 20% of the 2.7% of substances for which the screening identifies potential PBT/vPvB properties, ECHA's ITS might lead to some (but not all) of the studies listed in Section 3.2 of Annex XIII being required to establish certainty on PBT/vPvB status. Assuming:

- For P/vP - one of the simulation tests on degradation in surface water (OECD 309 = € 20 759) or soil (OECD 307 = € 60 804) or sediment (OECD 308 = € 55 217) is carried out. The average of €45 593 is taken as the cost of this;
- For B –a chronic toxicity study on animals (fish OECD 204 - € 59 754) is carried out; and
- For T – the results of the chronic study on fish for B also provides the information for T.

This provides a total cost of € 105 347 for this 20% (of 2.7%) of substances. For the remaining 80% of substances that will be eliminated, it is assumed that the assessment costs € 10 000 on average. Thus, 20% at € 105 347 and 80% at € 10 000 suggests a cost of around € 29 000 when averaged across the 2.7% of substances identified as potential PBTs/vPvBs by screening and then required to undertake PBT/vPvB assessment.

ii. 1-10 tonnes substances also registered at higher tonnages

As with other parts of the CSA/CSR, for 1-10 tonnes substances also registered at higher tonnages PBT/vPvB assessment will already have been carried out by the higher tonnage registrants but the 1-10 tonnes registrants will not have contributed to the costs of that undertaking.

2.4.6 Cost of completing the environmental and human exposure assessment and risk characterisation

i. Overview

Application of Annex XIII of REACH requires that where human health and or environmental hazards have been identified in the hazard assessments, manufacturers and importers have to consider downstream uses of the substance in the CSA and conduct an exposure assessment and risk characterisation for each, and develop recommendations on risk management measures and the technical means to achieve them.

The hazard classifications of each substance registered at 1-10 tonnes are provided by the ECHA registration data post the 2018 registration deadline. For each substance, where the classifications identify human health and/or environmental hazards, human health and/or environmental exposure assessment and risk characterisation is required as part of CSA.

Such assessment is required for each use of a substance. The Phase 3 and CSES impact monitoring studies assumed that, in addition to the manufacturer's use, there are between 1 and 5 downstream uses for each substance registered at 1-10 tonnes (an average of 4 uses per substance including the manufacturer's own use). However, in the last study by RPA (Phase 4 study), these assumptions are substituted with actual data on the number of uses drawn from ECHA's registration database.

ii. Substances registered at 1-10 tonnes only

Paragraph 0.8 of REACH Annex I indicates that "e*xposure scenarios may describe the appropriate risk management measures for several individual processes or uses of a substance*". As such, one

[28] ECB (2002): Identification of Potential PBTs or vPvBs Among the IUCLID High Production Volume Chemicals (ECB 4/14/02 (PBT strategy – report)).

exposure scenario may be sufficient to cover multiple uses and processes and so, depending on the uses, multiple assessments covering each use may not be required.

However, the extent of overlap between the different uses of substances is difficult to estimate and so the analysis assumes that a separate assessment is required for each and every use. This very much represents a 'worst case/highest cost' assumption.

The estimated costs of undertaking exposure assessment and risk characterisation are drawn from Phase 3 and CSES impact monitoring studies and are provided in the tables below.

In relation to the number assessments that would be required for each substance, one exposure scenario may be sufficient to cover multiple uses and processes and so, depending on the uses, multiple assessments covering each use may not be required. At the same time, for a number of cases, the exposure scenario for one use may not cover other identified uses.

For the purpose of this analysis, it is assumed that the exposure scenario for the manufacturer's own use covers all downstream uses in 50% of cases. For the remainder it is assumed that the exposure scenario for a manufacturer's use does not cover any other uses and that an exposure scenario is required for each and every additional use. In reality, as per paragraph 0.8 of REACH Annex I, some grouping of uses will be possible. As such, this represents a 'worst case/highest cost' assumption.

The assumptions on the number of uses of each substance and the estimated costs of undertaking exposure assessment and risk characterisation are provided in the table below.

Table 2.4 Costs and assumption for Human Health and Environmental exposure assessments and risk characterisation

	Low	High	Average
Cost of Human Health Exposure Assess and Risk Characterisation per use	€ 1 500	€ 5 000	€3 250
Cost of Environmental Exposure Assess and Risk Characterisation per use	€ 1 000	€ 3 000	€2 000

Note: in these estimates it is assumed that for 50% of the substances, the exposure scenario of the MI's uses also cover the DUs' uses.
Source: Phase 3 and CSES impact monitoring studies

iii. 1-10 tonnes substances also registered at higher tonnages

For the 1-10 tonnes CMR 1A/1B substances also registered at higher tonnages, a CSA/CSR already exists and will cover most uses including the manufacturer's own use. For some substances, however, some of the uses registered at 1-10 tonnes may not be covered by the existing CSA and additional exposure assessment and risk characterisation would be required for these uses. This would represent a cost of the CSA/CSR option for the substances and not a 'transfer payment'.

Costs are calculated as follows:

- The percentage of the downstream uses of the 1-10 tonnes registrants that will already be covered by the existing CSA/CSR is assumed to be proportional to the percentage of the total number of registrants that have registered at above 10 tonnes. For example, if the total number of registrants (1-10 tonnes and higher) is 10 and 8 of those are registrants at above 10 tonnes, then 80% of the registrants are at above 10 tonnes. It is assumed that this equates to

80% of 1-10 tonnes uses already having been included in the existing CSA (and 20% not being included and requiring assessment).

The assumptions concerning the numbers of 1-10 tonnes substances' uses, the costs of the exposure assessment/risk characterisation are the same as those in the table above.

2.4.7 Communication with DUs

Undertaking the exposure assessments and risk characterisation requires communication with each of the DUs on all uses of a substance not already covered by an existing CSA.

In Phase 3 and CSES impact monitoring studies it was assumed that there were between 20 and 40 downstream users per use with this equating to between 20 and 200 downstream users per substance regardless of the number of manufacturers of the substance. This wide range of estimates produced problems with the estimates of both costs to DUs and also the benefits of the options.

To improve the assessment, a more realistic approach has been adopted based on the assumption that a substance with more manufacturers is likely to have more downstream users (and *vice versa*). The analysis now estimates that there are an average of between 1 and 10 (averaging 6) DUs **per MI** per substance.

Data from ECHA provide information on the number of manufacturers of each substance. For each individual substance, the number of DUs is calculated by multiplying the number of registrants by the average number of DUs per MI (6). This is then applied in the calculation of costs tailored to each substance. Whilst for 244 (82%) of the substances there are only between 1 and 5 registrants at 1-10 tonnes, there are three substances with more than 99 registrants. When combined with the average number of DUs per MI (6) this produces an extremely large number of assumed DUs for those substances with the highest number of registrants. This, in turn, translates into extremely high costs for only a few substances. Only a very small number of substances have a large number of downstream users. Only 10% of substances have DU costs above € 9 212, 5% above € 23 696, 1% above € 66 633. So the range of costs given in table 2.7 describes outliers in the extreme.

i. Substances registered at 1-10 tonnes only

The estimated cost of communication with each individual DU used in Phase 3 and CSES impact monitoring studies is provided in the table below.

Table 2.5 Cost of DU communications

	Human Health Exposure Scenario (per DU)	Environmental Exposure Scenario (per DU)
Low	€ 200	€ 200
High	€ 500	€ 500
Average	€ 350	€ 350

Source: Phase 3 and CSES impact monitoring studies

ii. 1-10 tonnes substances also registered at higher tonnages

For the 1-10 tonnes substances also registered at higher tonnages, as noted above, a percentage of uses will already be covered by the existing CSA and this is taken as being equal to the percentage of total registrants that have registered above 10 tonnes. This same percentage is applied to the total number of DUs to calculate the number of DUs needing to provide information to the exposure assessment and risk characterisation. As in the previous example, if 80% of the registrants have registered a

substance at above 10 tonnes, then 80% of uses are assumed to already be covered in the existing CSA. New assessments are therefore required for 20% of the uses of the substance, requiring communication with 20% of DUs of the 1-10 tonnes registrants.

2.4.8 Cost of producing an extended Safety Data Sheet (eSDS)

It is a requirement under REACH to provide an SDS for all substances and mixtures with hazardous properties (i.e. including those produced in quantities of 1-10 tonnes per year). The SDS must be consistent with the information provided in the registration generally. Where a CSA/CSR has been completed for a substance, the following additional requirements apply in respect of SDS to produce an extended SDS (eSDS):

- adding the results of the PBT/vPvB assessment to the SDS;
- expanding sections of the SDS in relation to, in particular, Sections 7 and 8 (Handling and storage; Exposure controls/personal protection) to reflect the relevant risk management measures and the technical means to achieve them; and
- including the relevant exposure scenario(s) in an annex to the SDS.

The estimated costs of these components used in Phase 3 and CSES impact monitoring studies are provided in the table below. To these costs must be added the cost of translation of the eSDS into different languages. As with Phase 3 and CSES impact monitoring studies, this is assumed to be required for 50% of substances for all uses and exposure scenarios with the number of language translations being between one and three (an average of two). Translation into other languages is assumed to cost of € 150 per language (as for previous studies).

Table 2.6 Costs of Communication eSDS components

Cost of adding the results of the PBT/vPvB assessment to the SDS per substance	€ 10
Cost of expanding sections of the SDS in relation to Sections 7 and 8 (Handling and storage; Exposure controls/personal protection) per use	€ 50
Cost of including the relevant exposure scenario(s) in an annex to the SDS per use	€ 300
Percentage of substances where translation of eSDS will be needed	50%
Number of languages to translate into	Low=1 High = 3 Average = 2
Cost of translation per language	€ 150

Source: Phase 3 and CSES impact monitoring studies

These costs apply to both the substances registered only at 1-10 tonnes and the 1-10 tonnes substances also registered at higher tonnages (since all 1-10 tonnes registrants would have to update their current SDSs).

2.4.9 Number of substances and companies affected

i. Total number of substances in 'scope'

Information from the REACH Registration database reveals that a total of 294 substances are CMR substances registered at 1-10 tonnes. The table below provides a breakdown of these in terms of their exact C, M or R hazard, as well as in terms of their status of being a NONs or phase-in substance. This is of interest as the NONs registrations will already have an assessment similar to a CSA based on previous requirements.

Table 2.7 Breakdown of 1-10 tonnes CMRs 1A/AB

	NONs[29] 1-10t and above	NONS 1-10t only	Phase-in[30] 1-10t and above	Phase-in 1-10t only	Total
Number of CMRs 1A/1B	3	11	206	74	**294**
Number classified as Carc. 1A/1B	0	6	125	32	**163**
Number classified as Mut. 1A/1B	0	0	37	8	**45**
Number classified as Repr. 1A/1B	3	5	113	46	**167**
Phase-in CMR1/A/1B registered in 2010			113	25	**138**

As can be seen from the table:

- 206 of the CMRs fully registered at 1-10 tonnes are phase-in substances also registered at above 10 tonnes. For these substances, a CSA will have already been completed and exposure scenarios and risk characterisation will have been undertaken for the downstream uses connected with the higher tonnage registrants;
- 14 of the CMRs are NONs registrations under the older requirements of Directive 67/548/EEC which required a 'base set' of information (almost) equivalent to that in Annex VIII of REACH and assessments comparable to CSA under REACH;
- 74 CMRs are fully registered at 1-10 tonnes only (i.e. not also at higher tonnages). For these substances, no CSA will have been carried out to date and no exposure assessments and risk characterisation will have been undertaken for the downstream uses connected with the registrants market.

ii. Total number of companies in 'scope'

Information from the REACH Registration database reveals that a total of 929 companies would be affected by a new requirement to produce a CSA for 1-10 tonnes CMRs across 1 653 dossiers (of which 983 were submitted in 2010). The following table provides a breakdown of these and the final results provide costs of the CSA for CMR substances for each of these companies individually.

[29] NONs = substances previously notified under Directive 67/548/EEC (Notification of New Substances) and regarded as registered under REACH.

[30] Phase-in substances = substances that were already being manufactured or placed on the market before the entry into force of the REACH Regulation (i.e. 01 June 2007).

Table 2.8 Breakdown of registrants of 1-10 tonnes CMRs 1A/1B

	Number of companies	Number of CMR 1A/1B dossiers	...of which were submitted in 2010[1]
Large			
Importer	387	718	453
Importer, Only Representative	1	1	0
Manufacturer	58	96	41
Manufacturer, Importer	16	44	24
NA	1	14	1
Only Representative	303	571	355
Sub-total	***766***	***1 444***	***874***
Medium			
Importer	41	58	35
Manufacturer	4	4	0
Manufacturer, Importer	2	2	1
Only Representative	32	43	22
Sub-total	***79***	***107***	***58***
Small			
Importer	39	48	28
Manufacturer	12	12	4
Manufacturer, Importer	3	5	2
Only Representative	14	19	7
Sub-total	***68***	***84***	***41***
Micro			
Importer	12	14	8
Manufacturer	3	3	1
Only Representative	1	1	1
Sub-total	**16**	**18**	**10**
Grand Total	**929**	**1 653**	**983**

[1] Phase-in CMR substances had to be registered by the 2010 deadline. After 2022, any relevant data are expected to be free owing to the '12-year rule'. However, for 1-10 tonnes CMR substances the CSA can be based on Annex VII data as the exposure scenario and risk characterisation will be based on closed systems because all substances can be assumed to be non-threshold substances (i.e. there is no DNEL).

As is apparent from the table, large companies represent 82% of all registrants and 87% of all CMR dossiers registered, whereas small and micro companies constitute 7 and 2% of all companies and 5 and 1% of all dossiers, respectively, thus a very minor portion only. It is noteworthy as well that 90% of large companies are importers and/or only representatives, and that pure manufacturers represent only 7%.

Interestingly enough, importers and only representatives own 67% of all CMRs registrations (197 out of 294), which allows concluding that a large majority of the CMRs in the EU comes from outside the EU. This is a low bound figure, since it does not comprise ECHA's category 'manufacturer/importer', which covers manufacturing companies that are also importers of CMR substances.

2.4.10 The resulting costs of producing the CSA

The following table provides an overview of all costs described in the previous sections that have been considered for assessing the costs of expanding this obligation to produce a CSR.

Table 2.9 Summary of all costs considered for development of a CSA/CSR per substance

		Average cost 1-10 tonnes only	Cost range 1-10 tonnes only	Average cost 1-10 tonnes & higher	Cost range 1-10 tonnes & higher	Comment
2.4.2	Information on the substance	€ 175	€ 100 - 250	€ 175	€ 100 – 250	Documentation needed for each manufacturer.
2.4.3	Robust Study Summaries	€ 550	n.a.	€ 550	n.a.	Cost for generating these or buying access to them estimated to be equal.
2.4.4	Hazard assessment / classification	€ 225	n.a.	€ 0	n.a.	See explanation in Section 2.4. Overview why costs are zero for substances also registered at > 10 tonnes.
2.4.5	PBT/vPvB screening and assessment	€ 750 (screening) € 29 000[1] (assessment)	n.a.	€ 0	n.a.	See explanation in Section 2.4. Overview why costs are zero for substances also registered at > 10 tonnes.
2.4.6	Exposure assessment/risk characterisation	€ 11 506 (For all uses of each substance: Human Health = € 3 250 Environmental = € 2 000 Total € 5 230 Number of uses of each substance is from registration data. Average number of uses is 2.2 per substance)	€ 5 250 - € 52 500 (up to 10 uses per substance in registration data)	€ 8 400 (For all uses of 1-10t registrants: Human Health = € 3 250 Environmental = € 2 000 Total € 5 230 Number of uses per substance is from registration and adjusted. Average number of uses is 1.6 per substance)	€ 5 250 - € 63 000 (Up to 12 uses per substance need assessment)	For 1-10t and above substances, the number of uses for assessment is taken as (No. 1-10t registrants/ No. total registrants) x Total number of uses of substance.
2.4.7	Communication with DUs	€ 6 034	€ 700 - € 72 540	€ 6 063	€ 700 - € 279 300	Based on € 350 (€ 200 – 500) cost per

						DU for each of the two assessments (human health and environmental) The max. number of downstream users/substance in the data is 399 = 279 300)
2.4.8	Production of eSDS	€ 930 (€ 350 per use (average 2.2 uses = € 770) plus € 150 for translation and € 10 for adding PBT results)	€ 360 – € 3 810 Based on range of 1-10 uses from data on substances	€ 720 (€ 350 per use (average 1.6 uses = € 560) plus € 150 for translation and € 10 for adding PBT results)	€ 360 – € 4 510 Based on range of 1-10 uses from data on substances	Range reflects differences in numbers of uses and need for translation (range 1 – 3 languages)

[1] Costs for assessment occur only for est. 2.7 % identified in screening as requiring assessment.

This table illustrates that the most significant costs may come from the exposure assessment/risk characterisation (€ 11 500), from the PBT/vPvB screening and assessment (as high as € 29 000, although only in very few cases) and communication with DUs (€ 6 000, or higher in isolated cases). The rest of the costs are in the range of an average of € 225 (hazard assessment/classification) – € 930 (production of eSDS). The effective costs will though vary depending on the specific case.

The different cost elements and assumptions laid out above have been applied in the 2020 RPA study to the information available per substance in ECHA's database.

For our purpose, the main outcome of the table below is that the average cost of a CSA per substance is less than **€ 17 000**. Speaking of an average, one needs to bear in mind evidently that there are companies for which this cost would be higher, while it will be lower for others. The median value cost is € 11 943with a range of € 888 to € 293 000

Table 2.10 Numbers of 1-10 tonnes substances classified as CMR 1A/1B

	NONs 1-10t and above	NONS 1-10t only	Phase-in 1-10t and above	Phase-in 1-10t only	Grand Total
Number of CMRs 1A/1B	3	11	206	74	**294**
Number classified as Carc. 1A/1B	0	6	125	32	**163**
Number classified as Mut. 1A/1B	0	0	37	8	**45**
Number classified as Repr. 1A/1B	3	5	113	46	**167**
Phase-in CMR1/A/1B registered in 2010			113	25	**138**
Percentage of phase-in CMRs 1A/1B registered in 2010 [1]			55%	34%	**47%**
Average total cost of CSA per CMR 1A/1B substance	€ 20 114	€ 12 398	€ 16 193	€ 19 610	**€ 16 951**

[1] After 2022, any relevant data are expected to be free owing to the '12-year rule'. However, for 1-10 tonnes substances the CSA can be based on Annex VII data as the exposure scenario and risk characterisation will be based on closed systems because all substances can be assumed to be non-threshold substances (i.e. there is no DNEL).

It is to be noted regarding the percentage of phase-in CMRs 1A/1B registered in 2010 that, after 2022, any relevant data are expected to be free owing to the '12-year rule', which means that, from then onwards, companies will not be able to charge others for the Letter of Access. This will of course have a significant impact on these costs estimations. However, for 1-10 tonnes substances, the CSA can be based on Annex VII data, as the exposure scenario and risk characterisation will be based on closed systems because all substances can be assumed to be non-threshold substances (i.e. there is no DNEL).

The following table shows that the total costs, for MIs and DUs combined, is of less than **€ 5 million**, with DUs bearing slightly more than a third of them, the large majority of costs (64%) being on the side of MIs.

Table 2.11 Total cost of CSA

	NONs 1-10t and above	NONS 1-10t only	Phase-in 1-10t and above	Phase-in 1-10t only	Grand Total
Total costs of CSA for MIs (excluding further PBT studies)	€ 30 008	€ 101 968	€ 2 098 985	€ 972 730	**€ 3 203 691**
DU costs for CSA	€ 30 335	€ 34 410	€ 1 236 778	€ 478 440	**€ 1 779 963**
MI + DU Costs	€ 60 343	€ 136 378	€ 3 335 763	€ 1 451 170	**€ 4 983 654**
Percentage of total cost contributed by DUs	50%	25%	37%	33%	**36%**

Considering the total costs of a CSA/CSR for MIs and downstream users and dividing that total cost by the number of downstream users for the CMR substances, one arrives at a value that would justify the measure based on benefits for downstream users (DU's break even value, see table below).

Table 2.12 Number of uses and of DUs

	NONs 1-10t and above	NONS 1-10t only	Phase-in 1-10t and above	Phase-in 1-10t only	Grand Total
Total number of uses	8	14	1 267	177	1 466
Number of uses not covered by existing exposure assessments (and needing one)	5	14	329	177	525
Total number of DUs over all uses	120	102	8 520	1 176	9 918
Total number of DUs needing to contribute to new exposure assessments for their uses (a)	81	102	2 593	1 176	3 952
MI + DU Costs (b)	€ 60 343	€ 136 378	€ 3 335 763	€ 1 451 170	**€ 4 983 654**
DUs' 'break even' value (b/a)	€ 745	€ 1 337	€ 1 286	€ 1 234	**€ 1 261**

This value expresses that the action of having a CSR done and provided by the MIs is economically justified if it provides a break even value of minimum € 1 261 per downstream user. The value should be compared to the costs a downstream user incurs for compliance with parallel legislation (see section 2.3 for the different types of parallel legislation). In the 2017 study, those costs were estimated through expert judgment for a low, medium and high cost estimated scenario. The costs per substance

in the low estimate scenario were € 1 500 (and €2 500 and € 3 500 for the medium and high scenarios respectively), where € 1 500 corresponds to 1.5 days of work for a consultant toxicologist.

There are basically two different scenarios:

a) The **baseline** one, which reflects the situation as is at the moment, where no obligation exists for companies to provide a CSR, but where DUs need to comply with parallel legislation, by providing very similar information to that in the CSR.
b) An **alternative** scenario, which is the one this report focusses on, where companies would be requested to provide a CSR, consequently incurring costs, which they do not face at present. The cost of this scenario, according to the information available at the moment, thus in a retrospective manner, would have been of circa. €5 million in total, to be carried by MIs and DUs.

Under scenario a), the cost for a DU to generate the information is €1 500 as a lower bound, per substance per use (and € 2 500 and € 3 500 for the medium and high scenarios respectively). To be able to compare the two scenarios, one would assume under scenario b) that all costs would be borne by DUs solely.[31] Considering that there are 9 918 DUs and that the total cost is € 4 983 654, every DU would then need to incur € 1 261 costs per substance per use under b). This figure is then to be compared to that of scenario a), € 1 500. From this comparison, one can obviously conclude that there is a saving for DUs under scenario b) compared to a): all potential costs incurred by DUs above € 1 261 under parallel legislation imply a saving. Which is further underpinned by the fact that:

- The cost of a) is a lower bound, the saving is even bigger if one considers the medium or the high bounds.
- Under scenario b), most of the responsibilities would fall under the MIs, which are assumed to have better expertise than DUs on risk assessment and risk management.

Note that the cost figure under b) expresses a cost based on past data. It does not refer to what the actual cost would be, should the CSR obligation be imposed on companies from now onwards. But it helps having an indication of a potential future cost scenario, compared to the baseline scenario.

2.4.11 Affordability

From the previous calculations, one can conclude that savings for a downstream user are lower than the estimated costs for compliance with parallel legislation. Put differently, it suffices that each downstream user spends a minimum of € 1 261 in contributing to a CSA/CSR, or a minimum of 1.26 days of work, for the measure to be justified for the purpose of complying with parallel legislation.

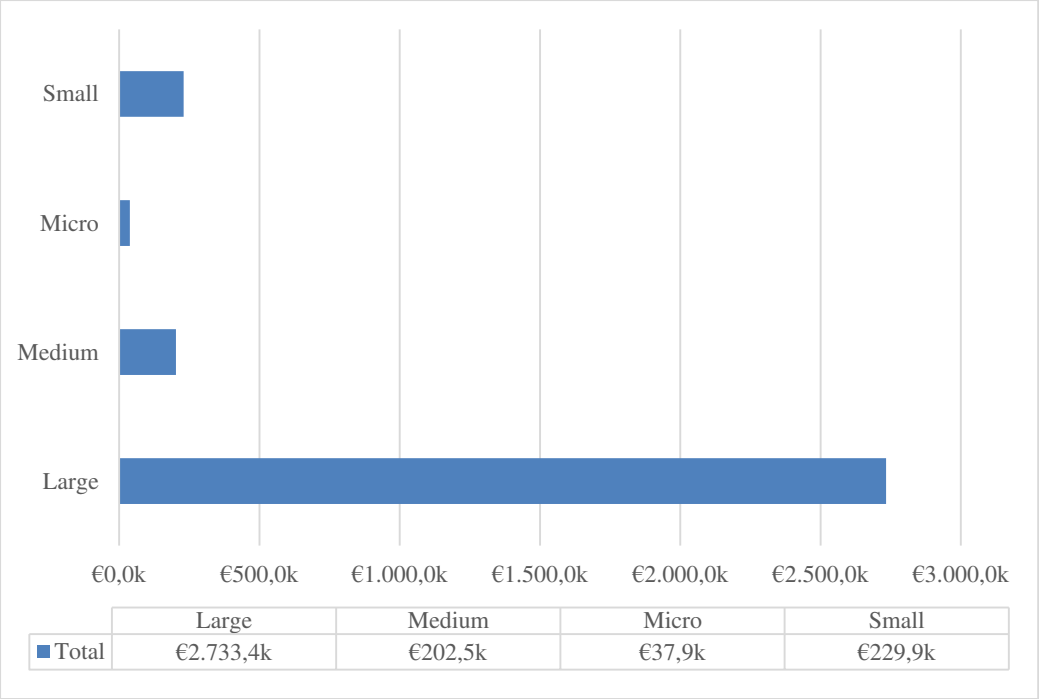
Table 2.13 Savings to contributing DUs to 'breakeven'

€s per DU	Expressed as working days @	€ 1.000	per day
€ 1 261	1.26	days saved on each DU workplace assessment to breakeven	

The figure below shows graphically that most of the costs of the measure would be borne by large companies (circa. 83% of the total) and only a very small portion by SMEs (circa. 17%).

[31] This is not realistic, since the cost under b) is to be borne by both MIs and DUs, but it helps for the purpose of a theoretic comparison.

Fig. 2.1 Total cost of CSA to MIs



The tables below provide a more disaggregated distribution of costs incurred by companies of different sizes.

For the purpose of the assessment, it is useful to look at the distribution of costs on a per substance per company basis. The first table shows that large companies are the ones incurring the highest costs of CSA per substance. All other three company sizes are below the average, with micro companies being the least impacted ones of the three and small ones the most.

Table 2.14 Distribution of costs incurred by different company sizes of the MI

	Cost of CSA per registrant across all of the CMRs registered by them		
	Average	**Median (50 percentile)**	**90 percentile**
Large	€ 3 568	€ 933	€ 7 974
Medium	€ 2 564	€ 1 276	€ 6 283
Small	€ 3 380	€ 1 293	€ 6 489
Micro	€ 2 371	€ 714	€ 8 212
Grand Total	**€ 3 449**	**€ 1 050**	**€ 7 694**

The following table informs on the number of companies carrying different magnitudes of the total costs. For example, at the 50%-ile, 50% of the companies incur costs below the percentile value (€ 1 050). 95% of companies bear costs of less than €12 000 and 50% of less than €1 100. Of those spending more than €100 000, only one is a small company, all the others being large ones. And, among the top 10%, who spend more than €8 000, only 6% are small and micro companies.

Table 2.16 Number of companies with different magnitudes of total costs (percentile ranges)

Percentile	Percentile value	Large companies	Medium companies	Small companies	Micro companies	Total
5,0%	**€ 94**	71	3	0	1	**75**
10,0%	**€ 137**	17	2	1	0	**20**
20,0%	**€ 232**	93	4	4	2	**103**
30,0%	**€ 425**	69	9	6	2	**86**
40,0%	**€ 714**	73	10	3	3	**89**
50,0%	**€ 1 050**	74	6	9	3	**92**
60,0%	**€ 1 504**	67	10	15	1	**93**
70,0%	**€ 2 726**	79	8	4	1	**92**
80,0%	**€ 4 803**	74	13	6	0	**93**
90,0%	**€ 7 694**	67	9	16	1	**93**
95,0%	**€ 11 993**	39	4	2	1	**46**
99,0%	**€ 37 678**	34	1	1	1	**37**
99,9%	**€ 103 410**	8	0	1	0	**9**
100,0%	**€ 115 053**	1	0	0	0	**1**

The very low values on the top part of the table can be explained by the fact that several companies have undertaken the registration of one single substance. In this manner, the overall cost is distributed among all contributing parties, thus reducing the individual share. For instance, 188 companies have participated to the registration of the substance with EC number 200-849-9, which explains why the cost for the 5%-ile is only €94[32].

The three parameters above - i) the savings to contributing DUs and ii) the distribution of costs per substance and iii) per size of registrant - allow concluding that the measure should be considered as affordable for a large majority of companies.

On the side of the uncertainties, it was not possible to assess what cost a MI would have to incur in order to decide that he would rather withdraw his substance from the market than bearing the cost. This could be a potential consequence of the measure, especially if the added costs would fall only upon a single MI.

2.5. Benefits of extending this obligation (not quantified)

The expected non-quantifiable benefits include:

2.5.1. Implementation of consistent and adequate risk management measures in relation to worker exposure

The extension of the CSA/CSR obligation to 1-10 tonnes CMRs would, for each substance, result in the identification of consistent and robust risk management measures for implementation by DUs and manufacturers alike and communication of these and other important information to all multiple DUs of the substances. Under the current regulatory regime, each individual manufacturer and downstream

[32] To avoid confusion, please note that of those 188 companies, 75 have that substance as the only one they have registered, which is the figure that the table shows (73 large, 3 medium and 1 micro), whereas the other 133 have registered 2 or more substances.

user is required to assess their own situation individually with the aid of only the general information provided in the SDS (as opposed to that of an extended SDS including DNELs where they have been established for substances). This is a duplication of effort, and with the more limited information available to conduct assessments, the result may be the implementation of a range of different risk management measures by different manufacturers and different downstream users. Some of these may provide adequate control and some may not.

2.5.2. Adequate risk management measures in relation to articles

In the case of 1-10 tonnes CMRs used in articles, there is currently no obligation to perform a CSA/CSR and whilst the safety of the article may be considered under specific product legislation where it is applicable to the article and its use, it is otherwise only a consideration under the general product safety regulation, which may be insufficient.

If the CSA/CSR obligation were to be extended to 1-10 tonnes CMRs, the use of a substance in an article above 1 tonne per year would have to be included in the CSA/CSR. This would facilitate identification and the recommendation of consistent and robust risk management measures or, where the use cannot be supported 'for reasons of protection of human health or the environment', risk assessors including ECHA and policy makers would be alerted to this fact and action concerning these articles on the market or about to be put onto the market could be implemented. Consequently, more information on hazardous substances in articles would become available.

2.5.3. Control of environmental risks

Extending the CSA obligation to 1-10 tonnes CMRs would require consideration of environmental exposure, its likely effects, and appropriate risk management for identified uses. Under the current requirements, this would not otherwise be considered for these substances other than when action was identified as being required by Member States or the Commission under Union legislation.

2.5.4. Benefits for Member States and the Commission

Extending the CSA/CSR obligation to 1-10 tonnes CMR substances and the subsequent consistent documentation of appropriate risk management measures for the concerned substances would simplify and improve the control on safe handling of substances in the workplace under all applicable legislation enforced by all relevant authorities. This is because there would only be one set of RMM as described in the CSR, and not potentially differing ones proposed by the DUs themselves in their individual CSRs. It would also facilitate the identification of cases for which the Commission or Member States would consider that the manufacture, placing on the market or use of a substance, on its own, in a mixture or in an article poses a risk to human health and for which a restriction procedure should be initiated, or where consideration could be given to risk management measures in product-specific legislation.

In addition, the extended CSA/CSR obligation would further ensure the generation of robust study summaries on selected human and environmental health endpoints. Currently, these robust study summaries must be generated by Member States during the development of a harmonised classification and not by MIs (as they would, were the CSA obligation to be extended).

2.5.5. Comparison of the total CSA/CSR costs to health benefits of avoided CMR risks

In addition to the benefits described until now, one could consider how the total costs for developing a CSA/CSR for 1-10 tonnes CMR substances compare to the benefit estimates for avoiding one or more of the health risks associated with the respective classifications by using the willingness to pay (WTP) values that the Committee for Socio-economic Analysis (SEAC)[33] determined for monetising chemicals health impacts.

From the ECHA database, the following distribution of Carcinogenicity, Mutagenicity, or Reproductive toxicity hazard category 1A/1B for the 1-10 tonnes CMRs could be extracted:

Table 2.15 Distribution of Carcinogenicity, Mutagenicity, or Reproductive toxicity hazard of 1-10 tonnes CMRs

Number of substances	CMRs (1A/1B)	C 1A/1B	M 1A/1B	R 1A/1B	R 1A/1B but not C or M
At 1-10 tonnes only	85	38	8	51	44
At 1-10 tonnes and higher	209	125	37	116	83
Total	294	163	45	167	127

The SEAC document provides the following willingness to pay (WTP) values for avoiding the morbidities that are most likely to be linked to CMR hazards listed in the table below:

Table 2.18 WTP values for morbidities relevant for CMR substances

	Lower	Upper	Average
Premature Death	€ 3 500 000	€ 5 000 000	€ 4 250 000
Cancer morbidity	€ 410 000	€ 410 000	€ 410 000
Statistical pregnancy	€ 22 000	€ 41 000	€ 31 500
Very low birth weight	€ 126 000	€ 405 000	€ 265 500
Minor birth defect	€ 4 300	€ 43 000	€ 23 650
External birth defect	€ 26 000	€ 330 000	€ 178 000
Internal birth defect	€ 128 000	€ 712 000	€ 420 000

Dividing the total costs of requiring a CSA/CSR for 1-10 tonnes substances registered at this and at higher tonnage levels (€ 4 983 654) by the WTP values above, one can consider how many morbidity incidences avoided would justify the cost of requiring CSA/CSR (see the table below). While also parallel legislation will provide health protection benefits with respect to substances carrying these classifications, it was considered when REACH was drafted that the CSR can aid in realising these health benefits, and can help DUs that normally have lower expertise than the MI for risk assessment and risk management. The obligation to develop a CSR also aimed to ensure a better communication

[33] Willingness-to-pay values for various health endpoints associated with chemicals exposure https://echa.europa.eu/documents/10162/13637/seac_reference_wtp_values_en.pdf/403429a1-b45f-4122-ba34-77b71ee9f7c9

in the supply chain on the most relevant Risk Management Measures that are also communicated via eSDS.

This argument further strengthens the conclusion that there are benefits from MIs generating a CSR under REACH for CMRs in the 1-10 tonnes tonnage band. This does not imply that parallel legislation does not work, but that if implemented, the obligation to generate a CSR would contribute to the general REACH objective of protecting human health.

The benefit is as well that the effort would not be only on DUs, as is the case at the moment under parallel legislation, but mostly on MI, who have better expertise on risk assessment and risk management than DUs do.

Furthermore, this exercise serves as a means to put into perspective the € 5 million cost of the action.

Table 2.19 Comparison of total CSA/CSR costs with the WTP values from table 2.18

	Total Nr of cases to avoid for all 294 CMR substances to break even	Nr of cases to avoid per CMR substance to break even
Premature Death	1.17	0.0040
Cancer morbidity	12.16	0.0413
Statistical pregnancy	158.21	0.5381
Very low birthweight	18.77	0.0638
Minor birth defect	210.73	0.7168
External birth defect	28.00	0.0952
Internal birth defect	11.87	0.0404

This table provides the number of morbidity cases that would need to be avoided at the minimum to breakeven with the costs of the CSA/CSR. It shows that action could be considered "economically justified" if only ONE of these figures is within the bounds of probability (the figures are not additive), e.g. if only by implementing this amendment two premature deaths or 13 cancer cases are avoided, the action could be considered justified. This is of course not a central argument to justify the action, but a supporting one, to contextualise the cost impact of the action compared to the benefits in terms of protection of human health it will provide.

2.6. Conclusion

Based on the analysis presented in section 2.4, the costs for manufacturers and importers of drawing up the chemical safety reports for 1-10 tonnes CMRs is estimated at € 3 203 691, whereas that for downstream users is € 1 779 963, for **a combined total of € 4 983 654**.

On the basis of this cost estimate, it was calculated that if the fact of having MIs performing the CSA/CSR provides a break even value of a minimum of **€ 1 261 per downstream user**, the measure can be considered economically justified. This value need to be compared to the cost a downstream

user incurs today for complying with parallel legislation, which is estimated to be **€ 1 500** (lower bound). So, this comparison confirms that the measure is economically justified. The measure can also be considered affordable, both for larger and smaller companies. Large importers and only representatives would bear most of the costs. However, it cannot be excluded that the costs carried by a manufacturers or importer could be impacting competitiveness, especially if a substance is marketed only by one or few registrants. Thus, withdrawal of some substances from the market can not be excluded.

In addition, benefits are also expected for human health and the environment, as of all 294 1-10 tonnes CMR substances (registered at this tonnage band and higher), 163 are carcinogenic, 45 substances are mutagenic and 167 substances are toxic for reproduction[34]. Due to upgraded risk management measures, the extension of the requirements are expected to lead to benefits in terms of reduced morbidity, only from CMR-related health effects. The number of adverse human health events that would need to occur to offset the costs of registering these substances is admittedly low (e.g. the avoidance of 2 premature deaths or 13 cancer morbidities).

In light of the above, the introduction of a CSA/CSR requirement for the MIs for all 1-10 tonnes CMR substances seems justified, even if only considering the quantifiable costs and the unquantified benefits. It seems therefore highly recommendable to extend the obligation to develop a CSA/CSR to 1-10 tonnes CMR 1A/1B substances.

In order to implement an extension of the obligation to provide a CSA/CSR also to 1-10 tonnes substances that are CMR 1A/1B would require amending Article 14 of REACH.

[34] Numbers do not add up because one substance can have more than one classification

3. Review according to Article 138 (8)

3.1. Introduction

Article 33 of the REACH Regulation sets up a duty to communicate information on articles containing substances of very high concern (SVHC) identified pursuant to Article 57 (and as a result listed in the Candidate List)[35] in a concentration above 0.1 % weight by weight (w/w).

In accordance with Article 33(1), the supplier of an article is required to provide to its recipient sufficient information, available to the supplier, to allow safe use of the article including, as a minimum, the name of the SVHC present in the article. Consumers can also request that same information in accordance with Article 33(2). When this occurs, the supplier of the article is obliged to provide such information free of charge within 45 days.

The inclusion of these provisions in the REACH Regulation aimed to ensure safe use of articles by end-users, including consumers. In this regard, the Court of Justice has further clarified the scope and objectives of Article 33 in its Judgment in Case C-106/14[36]. In particular, the Court has stated that this obligation, read together with recitals 56 and 58 of the REACH Regulation, is aimed to enable '*all operators in the supply chain to take, at their stage, those risk management measures which follow from the presence of [SVHC] in articles in order to guarantee their completely safe use*'. The Court has also considered that '*the duty to provide information is aimed indirectly at allowing those operators and consumers to make a supply choice in full knowledge of the properties of the products, including those of articles forming part of their composition*'.

In its judgment, the Court has also clarified the scope of the obligations on information on SVHC in articles, by still considering components of complex products as individual articles if they fulfil the definition of an article under the REACH Regulation. Consequently, the Court has considered that '*the supplier of a product one or more constituent articles of which contain(s) a substance of very high concern* [...] [must] *inform the recipient and, on request, the consumer, of the presence of that substance by providing them, as a minimum, with the name of the substance in question*'.

In view of the above, the purpose of this review according to Article 138 (8) of the REACH Regulation is to consider the practical experience in implementing this Article in order to assess whether or not to extend its scope to other dangerous substances. Based on the review, the Commission may, if appropriate, present legislative proposals to extend that obligation.

3.2 Reviews and reports on the implementation of Article 33 of the REACH Regulation

Since the entry into application of Title IV, and consequently Article 33, of the REACH Regulation in June 2007, several reports and initiatives have assessed the level of implementation of this Article, focusing on both the supply chain and consumer angles of the communication obligations. This section aims at summarising the views of the Commission, Member States and relevant stakeholders with a view to assess the current level of implementation of Article 33.

[35] Further information can be found on ECHA website.
[36] Judgment of the Court (Third Chamber) of 10 September 2015, Case C-106/14.

3.2.1 Reports on the operation of REACH

In 2011, the European Chemicals Agency (ECHA) submitted the first report on the operation of REACH in accordance with Article 117(2)[37]. In this report, ECHA considered that diverse legal interpretations of Article 33 were causing business uncertainty and hampering its implementation.

Subsequently, '*effective communication through the supply chain of information on substances and how to use them safely*' was listed as one of the three main areas for improvement in the first General Report on the operation of REACH adopted by the Commission in accordance with Article 117(4)[38] – the first REACH review. This report also mentioned the challenging nature of these provisions for industry, which had to develop new tools and information management systems.

The next ECHA report on the operation of REACH in 2016[39] found that companies had commenced to document and communicate their use of substances in articles. However, despite the increasing availability of tools (e.g. the IUCLID 6 release) to generate and transmit information on the presence of chemicals in articles, the overall quality of such information remained very limited. ECHA called on all actors involved with substances in articles to '*become active and allocate more resources for real progress to be achieved in this field. Increased enforcement efforts could activate companies to improve their knowledge on substances in articles and, where relevant, take action to ensure safe use or look for safer alternatives'.*

In 2018, the second 'General Report on the operation of REACH and review of certain elements' adopted by the Commission (the second REACH review)[40] still reflected difficulties for actors of the supply chain to fulfil the obligations on the presence of substances of very high concern in articles (Articles 7 and 33 of the REACH Regulation).

Among the key findings, the second REACH review noted the development of information management tools by companies promoted by EU projects or activities of some Member States. It also stated that '*however, it remains difficult for actors in the supply chain to retrieve, verify and communicate information on SVHCs in articles'.* This is still the case despite the fact that stakeholders consider the efficient functioning of these obligations as '*necessary for economic operators to implement appropriate risk management measures and to make informed purchasing decisions as well as for the ability of suppliers to respond to consumer requests'*. Finally, it was stated that '*the information generated in the supply chains through Article 33 is not available for national or EU authorities.* [...] *The information communicated following consumer requests is not centrally collected and accessible, thereby potentially increasing the burden for suppliers by repetitive consumer requests*'.

The second REACH review also identified areas for future action, in particular better tracking of chemicals of concern in products to '*facilitate recycling and improve the uptake of secondary raw materials'.*

[37] ECHA, The operation of REACH and CLP, 2011.
[38] COM(2013) 49 - first REACH review.
[39] ECHA, Report on the operation of REACH and CLP, 2016.
[40] COM(2018) 116 and accompanying Staff Working Documents – second REACH review.

3.2.2 The findings of pilot projects on enforcement

ECHA FORUM[41] organised in 2019[42] a pilot project on enforcement of Articles 7(2) and 33 of REACH in 15 Member States, targeting a few candidate list substances in about 700 high-risk products or materials. While 12 % of the articles contained candidate list substances in a concentration above 0.1 % w/w, the project showed that for about 90 % of these articles containing candidate list substances, suppliers were found to have missed their information obligations laid down in Article 33(1). In addition, about 55 % of the 400 inspected companies were unable to provide the requested information to consumers in accordance with Article 33(2). The pilot project found a big gap in communication throughout the supply chain, partly attributed to the location of many of the suppliers outside the EU. The report recommends companies that buy products to ask actively their suppliers for the information on the presence of candidate list substances, thus ensuring the flow of information in the supply chain.

Further findings of this report indicate that about 30 % of the inspected companies were not aware of the actual list of the Substances of Very High Concern (SVHC), the Candidate List. In many cases, the lack of compliance with Article 33 happened in SMEs, less aware of their legal obligations, more reliant on the information received from their suppliers and with less capacity to perform their own chemical analyses.

The '*first and most important suggestion to ECHA, COM, and National helpdesks'*, given by the FORUM pilot project, was to organise a comprehensive awareness-raising campaign on the duties related to substances in articles. As another recommendation to improve the situation, the pilot project of the FORUM suggested ECHA to '*develop more guidance on what specific information to provide in the supply chain beyond the name of the substance(s) and when*'.

Another study prepared by the Swedish Chemicals Agency and published in May 2020[43] reached similar conclusions, showing that recipients of articles have generally no information on the presence of substances of very high concern in the articles supplied to them. The situation is even more challenging when it comes to e-commerce, where a recent study from the Nordic Council[44] has exposed a lack of information on the presence of substances of concern in products, with non-compliance rates varying between 20 % and 60 %. It has to be noted, however, that this project was not exclusively focused on compliance with Article 33 of REACH.

3.2.3 Other projects

In 2017, the Commission launched a study to review tools to track hazardous substances in articles[45]. The study provided an overview of the different types of available tools that support the tracking and communication of hazardous substances in articles in supply chains and to consumers, and evaluated them with regard to their ability to support the implementation of Article 33 of REACH and their potential contributions to the circular economy and a non-toxic environment. The results showed that there was noticeable progress over time in data management and development of supporting tracking tools; and that companies used a wide range of tools to ensure compliance with legal requirements.

[41] The Forum for Exchange of Information on Enforcement.
[42] FORUM - Substances in Articles. Pilot project report. Harmonised Enforcement Project.
[43] KEMI Enforcement 9/20: Information on hazardous substances in articles.
[44] Nordic Council of Ministers: project on enforcement of internet trade.
[45] Publications Office of the EU, Scientific and technical support for collecting information on and reviewing available tools to track hazardous substances in articles with a view to improve the implementation and enforcement of Article 33 of REACH, 2016.

These tools vary with regard to the information content and the means of conveying such information, spanning from product marking through compliance declarations, restricted substance lists, third party certification and generic material databases to complex IT-tools. The study also pointed to sector-specific differences in the implementation of these tools, depending on the complexity of products, degree of supply chain control and extent of overall regulatory requirements for technical aspects.

The EU-funded Life project AskREACH[46] also referred to similar concerns about the compliance with the Article 33(2) provisions. The surveys on consumer awareness and communication on SVHCs in articles done in the context of this project found that awareness of the 'right to know' was low among respondents. The survey results showed that '*only in three of 14 countries were a majority of respondents aware of their 'right to know'; and that of the few respondents who were aware of this right, the majority had never sent a request of information to a company*'. On the other hand, there are indications that the awareness by consumers about their "right to know" may be slowly increasing. In a 2016 Eurobarometer survey[47], 66 % of EU citizens said that they are aware that '*if you ask whether a product contains particularly hazardous chemicals, the seller is required by law to provide you with this information*'.

The surveys carried out in the context of the AskREACH project also confirmed that a large proportion of companies are not well prepared to respond to consumers 'right to know' requests. About 40 % of the about 200 consulted companies had received at least one request from consumers, and about half of these companies did not have the information needed to respond to consumers without consulting their suppliers. About 40 % of the companies surveyed did not have any IT-solution in place to collect and manage information on SVHCs in articles, depending on the information sent by their suppliers on paper or within the product information. Around half of the companies also considered that it is technically difficult to comply with the legal obligations laid down in Article 33.

On a more positive note, a majority of companies considered the current provisions on communication through the supply chain as an incentive to substitute SVHCs with less hazardous alternatives.

Stakeholders, and particularly consumer associations, have also developed their own projects on Article 33. All of them highlight severe compliance issues with regard to consumer enquiries. As an example, a French consumer association in 2018 found that almost 70 % of the selected companies provided incorrect or incomplete information[48]. A Danish consumer association had found a similar pattern in 2017, with several companies replying that articles did not include SVHCs although they did[49]. The European consumer organisation (BEUC) already presented similar results in a transnational study back in 2011[50].

Business associations have shared at many occasions their view on the lack of an efficient implementation of Article 33, pointing at low enforcement of imports as one of the main factors[51]. Despite these problems, the European industry is contributing to a better implementation of these

[46] The project LIFE AskREACH (No. LIFE16 GIE/DE/000738) addresses the 'right to know' pursuant to Art. 33(2) of REACH, providing a claim for consumers to ask companies about substances of very high concern (SVHCs) in articles. The Commission is co-funding AskREACH, together with the German Environmental Agency, the Baltic Environmental Forum and the Administration of the Latvian Environmental Protection Fund.
[47] European Commission, Special Eurobarometer 456.
[48] Que choisir - Substances toxiques : Nos analyses sur 39 produits du quotidien (available only in French).
[49] Kemi - Test: Plastic products contained unwanted phthalates (summary in English, text in Danish).
[50] BEUC – How much are we told?
[51] Not exclusively regarding Article 33 of REACH, but also for the chemicals legislation in general. See e.g. 'More than 90% of all chemicals in consumer products non-compliant with REACH come from outside of the EU'.

provisions. The European Chemicals Association (CEFIC) committed in 2018 to work together with ECHA to improve the means of communication of safety information in the supply chain[52].

3.3 The current level of implementation of Article 33 and ongoing actions to put it more efficiently into effect

The documentation and projects summarised in the previous section allow the conclusion that the challenges to meet the obligations laid down in Article 33 of REACH remain for suppliers of articles, as compliance with the communication duties vis-à-vis recipients of those articles and consumers is limited throughout the Union.

The reports and reviews summarised in the previous section can help explain why there has been little improvement in the implementation during the last decade. These include lack of awareness of duty holders, absence of adequate information management systems in certain companies, technical difficulties derived from the complexity of articles and their chemical content and scarce information on imported articles.

The situation varies depending on the nature of value chains, companies' size or the existence of stable relationships with suppliers. Many companies are well aware of their legal obligations regarding Article 33 and can more easily adapt their information systems in order to comply with them. Other companies focus on the import of low-value/high-volume products, have limited contact with chemical regulations and requirements, and are therefore less aware of obligations such as those laid down by Article 33. They generally also have limited control over their supply chains.

To address the issues identified, the Commission, ECHA and stakeholders have already been working on possible solutions to improve particularly the awareness of duty holders and consumers.

For instance, the Life project AskREACH has developed a mobile application to check the presence of SVHCs in products. The Scan4Chem[53] App was launched at the end of 2019. In its six first months of implementation it has been downloaded more than 35 000 times, with 66 000 barcodes scanned in 12 countries. More than 17 000 products such as clothing, sports equipment or toys have been registered in the application database, from hundreds of producers and importers. Under the same project, a supply chain tool[54] is being developed to help companies fulfil their supply chain communication duties. Suppliers of the selected companies will receive training and case studies for real articles from various sectors will be prepared.

The recent revision of the Waste Framework Directive may also bring further changes for the implementation of Article 33 of REACH. Pursuant to Article 9(1)(i) of Directive 2008/98/EC on waste[55], Member States shall take measures to '*ensure that any supplier of an article as defined in point 33 of Article 3 of* [REACH] *provides the information pursuant to Article 33(1) of that Regulation to the European Chemicals Agency as from 5 January 2021*'.

For this, ECHA is required to establish a database containing the information provided by suppliers of articles, making it available to waste operators and, upon request, consumers. By using the database as interface, communication by companies through the supply chain may be facilitated, as it could, among others, reduce the need for individualised IT systems for many SMEs. In the long-term, this

[52] ECHA-CEFIC: Joint statement of 14 June 2018.
[53] LIFE AskREACH, Scan4Chem app.
[54] LIFE AskREACH, Supply chain tool for communication on SVHCs in articles.
[55] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives: consolidated text.

may also contribute to ensuring better control of incompliant imports of products, as it will allow to concentrate enforcement activities on articles suspected to contain SVHCs, but not notified to ECHA.

Communication of information through the supply chain and to waste operators on the presence of SVHCs and other substances of concern will also require other efforts, using mechanisms such as those explained in the recently adopted study on 'Information flows on substances of concern in products from supply chains to waste operators'[56].

3.4 Conclusion

Although the implementation of Article 33 of the REACH Regulation has gradually improved in the last decade, overall it remains limited. This low level of implementation is affecting the achievement of the main objectives of these provisions, making it more difficult for operators further down in the supply chain to take the necessary risk management measures.

The situation is particularly worrying for imported goods and articles placed on the market via e-commerce, where there is a general lack of information on the presence of SVHCs.

In view of the challenges with its implementation and the low level of compliance with Article 33, as it stands now, the benefits of any extension of its scope to cover other dangerous substances are questionable. The extension of obligation would rather result in additional challenges, adding burden on companies and not further contributing to the objectives of REACH.

The Commission and stakeholders should continue working together to improve the implementation of the provisions already in force. Recent regulatory developments in the context of the waste legislation (particularly, the development of the ECHA SCIP database[57]) could also improve the general implementation of Article 33 in the coming years.

4. Review according to Article 138 (9)

4.1. Introduction

Section 8.7 of Annex VIII of REACH concerns screening-level information on reproductive toxicity for substances manufactured or imported in quantities of 10 tonnes or more per registrant. The only sub-point of section 8.7 in Annex VIII, point 8.7.1. (see Annex II to this report), lays down, as the standard requirement for such substances, a screening study for reproductive and developmental toxicity in one species, according to either Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 421 or 422. OECD TG 421 is for a reproduction/developmental toxicity screening study, while TG 422 is for a combined repeated dose toxicity 28-day study with the reproduction/developmental toxicity screening. The screening study is only required in the absence of evidence from structurally related substances, (Q)SAR estimates or *in vitro* methods that the substance may be a developmental toxicant.

However, column 2 of point 8.7.1. sets out specific rules for adaptation of the above requirement and specifies that the study does not need to be conducted if the substance is known to be either a genotoxic carcinogen or a germ cell mutagen and appropriate risk management measures are implemented. It also does not need to be conducted if relevant human exposure can be excluded in accordance with Annex XI, section 3, or if a higher tier (i.e. according to Annex IX) pre-natal developmental toxicity study or reproductive toxicity study is available.

[56] European Commission, Information flows on substances of concern in products from supply chains to waste operators, 2020.
[57] ECHA, SCIP database website.

Furthermore, if the substance meets the criteria for hazard classification as toxic for reproduction category 1A or 1B for effects on sexual function and fertility, and the available data are adequate for a robust risk assessment, the study does not need to be conducted but testing for developmental toxicity must be considered. Likewise, if the substance meets the criteria for hazard classification as toxic for reproduction category 1A or 1B for developmental effects, and the available data are adequate for a robust risk assessment, the study does not need to be conducted but testing for effects on sexual function and fertility must be considered.

Annex VIII does not explicitly prescribe further testing on reproductive toxicity to follow-up on effects seen in the screening study. Further information on reproductive and developmental toxicity is obligatory according to Annex IX and X for substances registered in the higher tonnage bands (≥ 100 tonnes per year). However, Annex VIII, section 8.7.1. provides that in cases where there are serious concerns for adverse effects on development or reproduction, a prenatal developmental toxicity study (according to Annex IX, section 8.7.2; TG 414) or an Extended One-Generation-Reproductive Toxicity Study (EOGRTS; TG 443) may, as appropriate, be proposed by the registrant instead of conducting a reproduction/developmental toxicity screening test.

Reproductive toxicity refers to adverse effects on sexual function and fertility in adult males and females, as well as to adverse effects on the development of the offspring. According to ECHA's endpoint specific guidance[58], the purpose of the reproduction/developmental toxicity screening tests (OECD TGs 421 and 422) is to provide initial information of the effects on male and female reproductive performance such as gonadal function, mating behaviour, conception and parturition and histopathological information on reproductive organs. Initial information on the offspring is limited to mortality, abnormal behaviour and body weight of pups after birth, a macroscopic examination and additional parameters for detection of possible endocrine disrupting modes of action as given in the revised TGs (2016). These screening tests do not provide complete information on all aspects of reproduction and development.

To clarify the legal text and improve the effectiveness of the compliance check in REACH, the data waivers and triggers of point 8.7.1 in Annex VIII are currently under revision. Possible amendments and their potential impact on the animal testing are discussed in a sub-group to the CARACAL expert group dedicated to the update of information requirements in the REACH Annexes.

4.2. State of development of alternative test methods for reproductive toxicity

The test methods used to fulfil regulatory requirements, including the standard information requirements under REACH, are generally based on internationally agreed standard protocols. In the area of test methods for human health, such standard protocols are laid down in test guidelines developed and adopted by the OECD, and, according to Article 13(3), the test methods applicable for the purpose of REACH are included in Regulation (EC) No 440/2008[59] or otherwise recognised by the Commission or ECHA.

For the assessment of reproductive toxicity for human health, OECD test guidelines addressing effects on sexual function, fertility and development of offspring currently only include *in vivo* studies (TG 421: Reproduction/Developmental Toxicity Screening Test, TG 422: Combined Repeated Dose

[58] https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf/e4a2a18f-a2bd-4a04-ac6d-0ea425b2567f

[59] Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). OJ L 142, 31.5.2008, p. 1

Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, TG 414: Prenatal Developmental Toxicity Study, TG 443: Extended One-Generation Reproductive Toxicity Study, TG 416: Two-Generation Reproduction Toxicity Study). No test guidelines for alternative (non-animal) methods that directly address sexual function, fertility or developmental effects have as yet been adopted by OECD. Two projects related to reproductive toxicity are currently included in the OECD work programme, a feasibility study for an embryonic stem cell assay for cardiotoxicity and a guidance document on *in vitro* assays for developmental neurotoxicity. Several TGs are available for *in vitro* tests addressing possible endocrine modes of action that are i.a. relevant for reproductive toxicity, like (anti)oestrogenicity (TG 455, TG 493), steroidogenesis (TG 456) and (anti)androgenicity (TG 458). Methods for identifying chemicals with thyroid activity are undergoing EURL ECVAM (EU Reference Laboratory for alternatives to animal testing) validation.

Recognising the importance of reliable alternative methodologies for the assessment of reproductive toxicity, the European Commission has funded a number of research projects to develop such tools under past and ongoing framework programmes. Projects with a particular focus on reproductive toxicity are listed in Annex III to this report.

Given the diversity of physiological processes associated with the mammalian reproductive cycle and the complexity of the underlying regulatory networks, it is currently not possible to model chemical effects on the whole cycle with a single or limited number of non-animal approaches. Therefore, research in the area has aimed at identifying the main biological processes and improving mechanistic understanding, in order to develop mechanistically-based *in vitro* tests. A comprehensive review of the state-of-the-art in the development of alternative methods for all toxicological endpoints, including reproductive and developmental toxicity, has been published in 2014 by JRC (European Commission's Joint Research Centre)[60]. According to the report, the available *in vitro* models cover only a small part of the reproductive cycle, with many steps of the cycle not yet addressed at all. The existing *in vitro* tests include cell-based models (primary cultures and stem cells), organ cultures and whole embryo cultures. Some non-mammalian models for developmental toxicity are being developed using zebrafish embryos or the nematode worm *C. elegans* as model organisms, but have not yet reached the stage of validation. A recent workshop report[61] reviewed the available models and acknowledged their potential as screening tests, but also highlighted the need of understanding better the advantages and limitations of these tests before they may be considered suitable to replace mammalian test systems.

According to the JRC report, most of the methods that have been developed are not (yet) used in the regulatory assessment of reproductive toxicity. *In vitro* models like primary cell or organ cultures have mainly been used for mechanistic research and have not been optimised for toxicity testing. Three *in vitro* methods for embryotoxicity, the mouse embryonic stem cell test, the micromass test and the whole embryo culture, have been scientifically validated and endorsed by the ECVAM Scientific Advisory Committee (ESAC)[62]. However, the participants of a workshop on their practical application identified limitations and considered them not ready for regulatory use[63]. These limitations

[60] http://publications.jrc.ec.europa.eu/repository/bitstream/JRC91361/echa_jrc_sla_report_public_05-09-14_withcover%20ipo.pdf

[61] Solecki R, Rauch M, Gall A, Buschmann J, Kellner R, Kucheryavenko O, Schmitt A, Delrue N, Li W, Hu J, Fujiwara M, Kuwagata M, Mantovani A, Makris SL, Paumgartten F, Schönfelder G, Schneider S, Vogl S, Kleinstreuer N, Schneider M, Schulze F, Fritsche E, Clark R, Shiota K, Chahoud I (2019). Update of the DevTox data database for harmonized risk assessment and alternative methodologies in developmental toxicology: Report of the 9th Berlin Workshop on Developmental Toxicity. Reproductive Toxicology 89:124-29

[62] https://tsar.jrc.ec.europa.eu/test-method/tm1999-01; https://tsar.jrc.ec.europa.eu/test-method/tm1999-02; https://tsar.jrc.ec.europa.eu/test-method/tm1999-03

[63] The Practical Application of Three Validated In Vitro Embryotoxicity Tests. ATLA 34, 527–538, 2006

concerned i.a. difficulties of the three tests to discriminate between weak and non-embryotoxicants and uncertainties over the applicability of the tests for a broad range of chemicals (important chemical classes were not included in the validation, the chemicals tested covered only a limited number of mechanisms of toxicity and only 20 chemicals were tested during the validation).

With respect to QSAR (quantitative structure-activity relationship) models for developmental toxicity, the JRC report points to the limited availability of models due to the inherent difficulty to relate chemical structures to complex toxicological endpoints and to the lack of high quality data sets to train the models. It refers to an earlier JRC study done for EFSA (European Food Safety Authority) (published in 2010[64]) which had evaluated several available models and found them potentially useful for supporting hazard identification and prioritising substances for further assessment, but not for predicting the absence of developmental toxicity. While QSAR models may not be able to completely replace in vivo testing, a range of structural features have been associated with developmental and reproductive toxicity[65], and could be used as supporting evidence in the context of priority setting, as well as providing elements for chemical grouping, read-across, and weight of evidence assessments.

The focus in recent years has been on connecting different types of data within testing strategies and weight of evidence approaches to support hazard and risk assessment. This has been formalised within the OECD's programme on Integrated Approaches to Testing and Assessment (IATA). Underpinning the IATA approach are Adverse Outcome Pathways (AOPs) which capture mechanistic knowledge by describing how a chemical interacting at molecular and cellular level can ultimately lead to adverse effects at the organ and organism level. This mechanistic knowledge can be used to develop relevant *in vitro* assays or *in silico* models addressing specific key events within different AOPs, which can be combined in testing strategies or used to support weight of evidence approaches within IATAs.

With regard to reproduction and fertility, the focus of AOP development within the OECD has mainly been on fish-specific pathways related to endocrine disruption, with two AOPs endorsed by the OECD. For developmental effects in mammals, AOPs exist for adverse effects on brain development (three AOPs endorsed by the OECD) and vascular effects (one AOP endorsed)[66]. Moreover, many other AOPs within the field of reproductive toxicity are currently under development. In addition there is an ongoing OECD project (4.124) co-led by the European Commission, Denmark and USA on assessing the performance of a range of different *in vitro* assays related key events relevant to developmental neurotoxicity with the objective of developing an OECD guidance on how the assays could be used within different IATAs.[67]

While there are examples of promising AOPs concerning developmental and reproductive toxicity, these focus on specific mechanisms and cannot, individually, be used to prove the absence of relevant toxicity through other mechanisms. Before such approaches are suitable for regulatory use, further development will be needed to develop sets of tests covering all relevant developmental pathways, as well as defined approaches[68] to allow their use for hazard identification and risk assessment. Information from internationally accepted AOPs or other *in vitro* and non-animal data, however, can already be valuable in supporting read-across or weight of evidence assessments.

[64] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2010.EN-50

[65] Wu S, Fisher J, Naciff J, Laufersweiler M, Lester C, Daston G, Blackburn K. (2013). Framework for identifying chemicals with structural features associated with the potential to act as developmental or reproductive toxicants. Chem Res Toxicol. 26:1840-61.

[66] http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm

[67] https://www.oecd.org/chemicalsafety/testing/TGP%20work%20plan_September%202018.pdf

[68] As described in OECD guidance document 255: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)28&doclanguage=en

With regard to the information on reproductive toxicity to be provided in REACH registration dossiers, ECHA's endpoint specific guidance[69] provides a comprehensive overview of the available testing methods, as well as other information sources that can be used in the evaluation of reproductive toxicity in the context of read-across or weight of evidence assessments.

In addition, a 2017 report by ECHA[70] describes in detail the current status of non-animal approaches and their regulatory applicability for REACH and other chemical-related EU legislation. The report states that presently there is no animal-free/*in vitro* method that can provide information equivalent to the information generated by the reproduction/developmental toxicity screening test. It points out that, in cases where information on both repeated dose toxicity and reproductive toxicity needs to be generated, registrants can reduce the number of animals needed by performing a combined study according to OECD TG 422, instead of two separate studies. According to the ECHA report, current *in vitro* and *in silico* methods investigate only partially the embryonic development (e.g. rodent *in vitro* cultures) or part of the potential mechanisms/MoA. Likewise, with respect to (Q)SAR models, the report states that not all the necessary aspects for reproductive toxicity can be covered by a QSAR prediction. Thus, information from these prediction methods is not appropriate to establish the absence of an effect, but may be used as supportive evidence to strengthen read-across, substance categories and weight of evidence.

In principle, the available non-animal approaches thus could be used to detect a potential to cause adverse effects and conclude on the presence of a hazard if supporting information is available. However, as these methods do not provide information on maternal toxicity or allow to deduce at which doses the effects would occur in an *in vivo* test, it is challenging to establish whether relevant effects could occur in humans. Moreover, non-animal predictive methods do not provide information for risk assessment (e.g. NOAEL value) and toxicokinetic information would be needed to support the dose level considerations.

In line with the above assessments of the state of alternatives to animal testing by JRC and ECHA, the Report from the Commission to the European Parliament and the Council on the development, validation and legal acceptance of methods alternative to animal testing in the field of cosmetics (2018)[71] concluded that, while considerable progress is being made in the development, validation and legal acceptance of alternative methods, the current level of alternative methods does not yet make it possible to fully replace in vivo (animal) tests for all toxicological endpoints in the safety assessment of cosmetic products, and that challenges still remain for the most complex endpoints, where more research is needed.

4.3. Information on reproductive/developmental toxicity submitted for REACH

The fourth edition of ECHA's report (2020) on the use of alternatives to testing on animals for the REACH Regulation[72] provides an overview of the studies and alternative data that have been submitted by registrants in order to fulfil the information requirements of Annex VIII, section 8.7.

[69] https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf/e4a2a18f-a2bd-4a04-ac6d-0ea425b2567f

[70] https://echa.europa.eu/documents/10162/22931011/non_animal_approcches_en.pdf/87ebb68f-2038-f597-fc33-f4003e9e7d7d

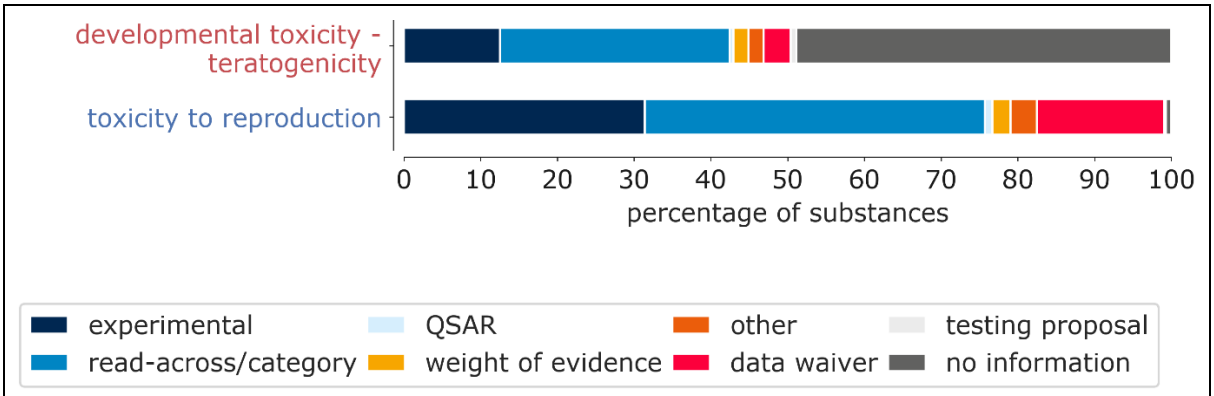
[71] https://ec.europa.eu/transparency/regdoc/rep/1/2018/EN/COM-2018-531-F1-EN-MAIN-PART-1.PDF

[72] https://echa.europa.eu/documents/10162/0/alternatives_test_animals_2020_en.pdf/db66b8a3-00af-6856-ef96-5ccc5ae11026

For substances manufactured or imported in quantities of 1-100 tonnes, the final registration deadline was in June 2018, so a large number of registrations were submitted only after the cut-off date for the previous, third report in March 2016. The fourth report therefore provides, for the first time, a comprehensive coverage of data used in registration dossiers across all tonnage bands. ECHA performed, for the purpose of this report, an analysis covering 12184 substances for which registration dossiers containing toxicological data had been submitted before 31 July 2019, including 2642 substances manufactured or imported in quantities of 10-100 tonnes, which have to fulfil the requirements of Annex VIII. ECHA examined, on a per substance basis, which approaches registrants used to fulfil the information requirements. The distribution of the use of various approaches, i.e. the use of experimental studies, submission of testing proposals, read-across and weight of evidence assessments, (Q)SAR-based conclusions, data waiving and others, is shown in Figure 1.

For the endpoint of reproductive toxicity, for ca 31% of substances an experimental study was available. For ca 44% of substances, registrants performed a read-across assessment. For ca. 17%, registrants waived the data requirement. For the remaining substances, registrants provided information based on QSAR, Weight of Evidence assessments or other type of information. While a separate developmental toxicity study is not a standard information requirement at Annex VIII level, for ca 50 % of the substances, registrants also submitted information for this endpoint. This comprised experimental studies for 12% of the substances, read-across for ca 30%, and other approaches for ca 8% of substances.

Fig. 4.1 Relative proportions of the options used by registrants to cover REACH information requirements for reproductive toxicity for substances manufactured or imported in quantities of 10-100 tonnes.



information requirements	experimental	read-across/category	QSAR	weight of evidence	other	data waiver	testing proposal	no information
toxicity to reproduction	31.4	44.3	0.9	2.4	3.4	16.6	0.2	0.7
developmental toxicity	12.5	29.9	0.5	2.0	2.0	3.5	0.8	48.8

From these analyses, it is evident that registrants have made extensive use of adaptation possibilities following the provisions in column 2 of Annex VIII, section 8.7. or in Annex XI. Read across is by far the most frequently used adaptation, followed by data waiving. Weight of evidence assessments and other approaches play a rather minor role for this endpoint and tonnage level.

From these analyses, it is evident that registrants have made extensive use of adaptation possibilities following the provisions in column 2 of Annex VIII, section 8.7. or in Annex XI. Read across is by far the most frequently used adaptation, followed by data waiving. Weight of evidence assessments and other approaches play a rather minor role for this endpoint and tonnage level.

The experience of ECHA in general when evaluating compliance of registration dossiers for different information requirements and across all tonnage levels is that adaptations can have quality deficiencies. In particular, read-across adaptations frequently suffer from poor documentation and shortcomings in the data used as well as the scientific justification. It is currently difficult to estimate whether or to what extent this is also the case for the information on reproductive/developmental toxicity submitted for substances in the tonnage range of 10-100 tonnes per year. However, it is possible that additional studies will have to be requested for those substances if adaptations are found to be inadequate.

Concerning the type of test submitted for substances at Annex VIII level, 529 (20%) had been tested in a combined repeated dose toxicity 28-day study with the reproduction/developmental toxicity screening (OECD TG 422), and 309 (11.7%) had been tested in a reproduction/developmental toxicity screening study (OECD TG 421). Furthermore, for some substances, higher tier studies for reproductive toxicity or developmental toxicity were available (2.5% or 4.9% respectively).

Fig. 4.2: Percentage of substances for which guideline studies were used to fulfil the standard information requirements for each information requirement at different tonnage levels.

Of the screening tests according to OECD TG 421 and 422 that were available across all tonnage levels, the majority have been performed after REACH entered into force. Of the combined repeated dose toxicity 28-day study with the reproduction/developmental toxicity screening according to OECD TG 422 (or equivalent), 432 of the submitted studies date from before 2009 ("old studies"), 1640 are "new" studies, performed from 2009 onwards. Of the reproduction/developmental toxicity screening study according to OECD TG 421 (or equivalent), 181 were "old" and 678 "new" studies. These analyses indicate that, when new studies are needed for both repeated dose toxicity and toxicity to reproduction screening, data was frequently generated using the combined repeated dose toxicity

study with the reproduction/developmental toxicity screening test (OECD 422). This significantly reduces the number of animals and costs.

4.4. Conclusion

Despite vast research efforts undertaken in the EU and internationally, and the development of some alternative approaches that model individual parts of the reproductive cycle, there are currently no alternative test methods or other non-animal approaches available that could fully replace the required screening test for reproductive/developmental toxicity in REACH Annex VIII, section 8.7.1. However, the mechanistic understanding of reproductive toxicity has increased in recent years and a range of alternative methods and approaches has been developed based on this knowledge. Such approaches can be, and are being, used on a case-by-case basis as elements in the assessment of a chemical's potential to cause reproductive toxicity effects, e.g. in the context of read-across or weight of evidence assessments. REACH already contains extensive provisions for the flexible use of such approaches in adaptations to the standard information requirements based on Annex XI. The possibility to use a combined screening study for repeated dose toxicity and reproductive/developmental toxicity in order to reduce the number of animals needed is already foreseen in the current requirement in REACH Annex VIII, section 8.7.1, and this combined screening study is widely used by registrants. Therefore, a revision of this section with the aim to introduce alternative test methods or approaches as the standard information requirements is currently not warranted.

5. Annex I: Elements of a CSA/CSR

5.1. The Chemical safety assessment (CSA)

1. **Human health hazard assessment:** to determine the classification of a substance and to derive levels of exposure to the substance above which humans should not be exposed;

2. **Human health hazard assessment of physicochemical properties:** to determine the classification of a substance in relation to, as a minimum, explosivity, flammability and oxidising potential;

3. **Environmental hazard assessment:** to determine the classification of a substance and to identify the Predicted No-Effect Concentration (PNEC);

4. **PBT and vPvB assessment:** to determine if the substance fulfils the criteria for PBT/vPvB (given in Annex XIII of REACH) and, if so, to characterise the potential emissions of the substance;

5. **Exposure assessment:** quantitative or qualitative estimation of the dose/concentration of the substance to which humans and the environment are or may be exposed. This considers all stages of the life-cycle of the substance resulting from its manufacture and identified uses and covers any exposures that may relate to the hazards identified in the above hazard and PBT/vPvB assessments;

6. **Risk characterisation:** for each exposure scenario, this step considers the human populations (exposed as workers, consumers or indirectly via the environment and if relevant a combination of those) and the environmental spheres for which exposure to the substance is known or reasonably foreseeable. Characterisation assumes that the risk management measures described in the exposure scenarios have been implemented. In addition, the overall environmental risk caused by the substance is reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

5.2. The Chemical Safety Report (CSR)

The CSR documents the CSA and also provides a summary of all the relevant information used in addressing each of the aspects of the CSA.

5.3. The Extended Safety Data Sheet (eSDS)

Where a CSA/CSR has been completed the following are added to the SDS to form an extended SDS (eSDS):

- SDS made consistent with the information in the CSA;
- results of the PBT/vPvB assessment must be reported; and
- the relevant exposure scenario(s) must be included in an annex to the SDS.

6. Annex II

Information requirements for reproductive toxicity in REACH Annex VIII

COLUMN 1 STANDARD INFORMATION REQUIRED	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
8.7. Reproductive toxicity 8.7.1. Screening for reproductive/ developmental toxicity, one species (OECD 421 or 422), if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from in vitro methods that the substance may be a developmental toxicant	8.7.1. This study does not need to be conducted if: — the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or — the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or — relevant human exposure can be excluded in accordance with Annex XI section 3, or — a pre-natal developmental toxicity study (Annex IX, 8.7.2) or, either an Extended One-Generation Reproductive Toxicity Study (B.56, OECD TG 443) (Annex IX, section 8.7.3) or a two-generation study (B.35, OECD TG 416), is available. If a substance is known to have an adverse effect on fertility, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage fertility (H360F), and the available data are adequate to support a robust risk assessment, then no further testing for fertility will be necessary. However, testing for developmental toxicity must be considered. If a substance is known to cause developmental toxicity, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered. In cases where there are serious concerns about the potential for adverse effects on fertility or development, either an Extended One-Generation Reproductive Toxicity Study (Annex IX, section 8.7.3) or a pre-natal developmental toxicity study (Annex IX, section 8.7.2) may, as appropriate, be proposed by the registrant instead of the screening study.

7. Annex III

Projects funded by EU research framework programmes with a particular focus on developing methodologies to test for and assess reproductive toxicity

- The FP6 ReProTect project (2004-2009) aimed to integrate existing and newly developed in vitro models into a testing strategy that could provide detailed information about the potential hazard of compounds to reproduction[73].
- The FP6 NHR DEVTOX project (2005) performed a prospective analysis of the mechanisms of nuclear hormone receptors and their potential as tools for the assessment of developmental toxicity[74].
- The FP7 ESNATS (2007-2013) project developed a battery of tests based on embryonic stem cells, in particular human embryonic stem cells[75].
- The FP7 ChemScreen (2010-2013) project aimed to generate a simple, rapid screening system for reproductive toxic chemicals, integrating in silico and in vitro methods as a means to identifying potential reproductive toxicants[76].
- The FP7 COSMOS (2011-2015) project built a freely accessible database with information on a range of toxicological endpoints, including reproductive-developmental toxicity of cosmetic ingredients and other substances[77].
- The Integrated European 'Flagship' Programme EU ToxRisk (2016-2021) under the Horizon 2020 programme aims to advance the mechanism-based toxicity testing and risk assessment and to enable the move towards a toxicological assessment based on human cell responses and a comprehensive mechanistic understanding of causal relationships of chemical adverse effects. The focus of this project is on two areas: repeated dose systemic toxicity, using the lung, kidney, liver and nervous system as examples of potential target organs; and developmental and reproductive toxicity[78].
- The H2020 EURION project 2019 - 2024[79] is a cluster of 8 projects for endocrine disruption testing. Amongst them, the FREIA project[80] focuses on female reproduction, and includes animal and non-animal methods, the ATHENA project[81] concerns brain development in relation to thyroid toxicity and the project ENDpoiNTs[82] addresses developmental neurotoxicity.

[73] https://ecvam-dbalm.jrc.ec.europa.eu/projects-and-studies/eu-integrated-projects/eu-integrated-project/eu-integrated-project-reprotect-development-of-a-novel-approach-in-hazard-and-risk-assessment-for-reproductive-toxicity-by-a-combination-and-application-of-in-vitro,-tissue-and-sensor-technologies./key/eup_102
[74] https://cordis.europa.eu/project/rcn/74090/factsheet/en
[75] https://cordis.europa.eu/project/rcn/87281/reporting/en
[76] http://chemscreen.eu/
[77] https://cordis.europa.eu/project/rcn/97712/factsheet/en
[78] http://www.eu-toxrisk.eu/
[79] http://www.eurion-cluster.eu
[80] http://freiaproject.eu/wp/about/
[81] https://cordis.europa.eu/project/rcn/219094/factsheet/en
[82] https://endpoints.eu/