A review of REACH registration for petroleum substances in 2016

Ten years on—addressing the tensions that the REACH regulation has created for the regulatory compliance community.

The European Union REACH regulation was adopted 'to improve the protection of human health and the environment from the risks that can be posed by chemicals, while enhancing the competitiveness of the EU chemicals industry. It also promotes alternative methods for the hazard assessment of substances in order to reduce the number of tests on animals'.

Ten years after the REACH regulation came into effect, we are much more aware of the tensions that this regulation has created for the regulatory compliance community. This includes many experts within our industry, as well as in the regulatory bodies such as ECHA and the Member States competent authorities for REACH.

REACH is an evolving regulation and although our industry delivered compliant dossiers in 2010, new requirements are emerging which will require updates to the dossiers in order for them to remain compliant.

In 2015, Concawe met with ECHA to share the Concawe strategy and five-year plan for REACH, and to seek ECHA's critique of our plan. Concawe's strategy of supporting registrants of petroleum substances to comply with REACH at the lowest overall cost is consistent with the requirement in REACH to form Substance Information Exchange Fora (SIEFs), allowing registrants for the same substance to share information and costs of further work to fill in data gaps in their substance dossiers.

This article highlights some of the tensions created by these developments, and discusses ways in which they can be addressed.

Uses of petroleum substances

Following the launch of the Commission's 'Substance of Very High Concern (SVHC) Roadmap', ECHA published the 'SVHC Roadmap to 2020 implementation plan' in 2013. For practical purposes, this article refers to the Commission's SVHC roadmap and the ECHA implementation plan collectively as the 'SVHC Roadmap' except where it is necessary to distinguish them, when they are referred to specifically as either the Commission's SVHC roadmap or the ECHA SVHC plan.

Table 1 SVHC properties

CMR	Carcinogen, mutagen, toxic for reproduction
ED	Endocrine disruptor
PBT	Persistent, bioaccumulative and toxic
vPvB	Very persistent and very bioaccumulative

The goal of the SVHC Roadmap is 'by 2020, to identify all known SVHCs and add these to the candidate list for authorisation or restriction'. The SVHC Roadmap foresees the use of screening methods and risk management option analyses (RMOA) to identify the relevant SVHCs, using information from the ECHA registration database, other REACH and CLP databases and further available relevant sources.

The SVHC Roadmap lists, as groups of substances to be covered by the implementation plan, CMRs, EDs, PBTs, vPvBs and sensitisers, which are collectively SVHC properties (see Table 1). Petroleum and coal stream substances with CMR or PBT/vPvB properties are specifically mentioned due to their UVCB (substances of unknown or variable composition, complex reaction products or biological materials) nature and the very high volumes concerned.

The SVHC Roadmap prioritises substances with SVHC properties which are registered for non-intermediate uses within the scope of authorisation. Annex 6 of the ECHA SVHC plan explains that the focus for petroleum substance will be on the non-fuel uses of petroleum/coal stream substances.

Annex 6 demonstrates the need to understand the volumes going into different uses. From the 2013 'volumes and uses survey', Concawe was able to elucidate the breakdown of volumes by major use category. Using 2013 as a reference year, it was noted that 971 million tonnes of petroleum substances were manufactured or imported in the EU. The majority (933 million tonnes) were used as intermediates for processing into chemicals, or used as a fuel. This leaves 38 million tonnes for industrial, professional and consumer uses, which fall under the scope of the SVHC roadmap (Table 2).

A problem with our 2010 dossiers is that related substances were grouped into categories, and the volume for each substance was not broken down by use. Hence, the regulators were unable to distinguish between fuel uses, intermediate uses or non-fuel uses per substance. ECHA made it clear that, without such a breakdown, they would need to assume that the total category volume per substance may be used for non-fuel uses. ECHA have now accepted the summary of volumes provided by Concawe in 2015 for the purposes of the work of the Petroleum and Coal Stream Substances Working Group (PetCo WG), but it will be essential for registrants to clarify the different uses of each substance registered with updated dossiers.

The PetCo WG agreed that petroleum substances that have consumer or professional uses (widespread uses) should be given the highest priority, as these are the chemicals that workers and the general public can be exposed to, and are most likely to find their way into the environment. Industrial uses are also within the scope of the ECHA SVHC plan, although they are currently considered to be of medium priority, assuming that in these uses, adequate worker protection is applied, in compliance with the Occupational Safety and Health Framework Directive (89/391/EEC).

Chemical composition and substance identity

The ECHA website states that 'unambiguous substance identification is a prerequisite to most of the REACH processes'.

The accepted way of identifying petroleum substances within the industry is by means of a summary of the relevant manufacturing processes and then physical parameters, including but not exclusively, boiling point range and any chemical specifications used to determine the substance. For many uses of petroleum substances a detailed chemical composition is simply not necessary. It is industry practice to market petroleum substances according to physico-chemical parameters specified in European Standards. Furthermore, petroleum substances are archetypal UVCB substances, making it impossible to determine the precise chemical composition to the

Table 2 Summary of volumes of petroleum substances by use category

Uses outside scope of the SVHC Roadmap	2013 volume in million tonnes
Fuels	618.0
Intermediates	315.0
Uses within scope of the SVHC roadmap	
Industrial	16.0
Professional	20.0
Consumer	1.5

Source: Concawe uses survey conducted in September 2015

Box 1 The PetCo Working Group

The PetCo (petroleum and coal stream substances) Working Group (WG), comprises representatives from ECHA, the Commission, Member States (currently Denmark, Estonia, Germany, France, The Netherlands and Poland) and industry stakeholders, including Concawe.

The mandate for the PetCo WG is to develop the approach for screening of PetCo substances for potentially relevant SVHCs.

level of each constituent. Examples of this are given in Table 3 on page 6, which shows that for one class of hydrocarbons only (the alkanes) any petroleum substance with a boiling point higher than 270°C (gas oils and heavier substances) will comprise at least 4,000 constituents. If olefins, naphthenics and aromatics are added, this number would easily exceed 5,000.

Informal feedback from ECHA on the chemical composition provided in the petroleum substances dossiers was that they did not provide sufficient detail on chemical composition for the regulators to be able to evaluate the hazards, or to determine whether the risk management measures in place for our substances were effective. ECHA also made it clear that there was inconsistency between registrants of the same substance, and suggested that some registrants had wrongly identified (a number of) substances.

Table 3 Petroleum substances are UVCBs

The predominant compounds are described by carbon number, boiling point ranges and hydrocarbon types. This table gives the number of isomers for one hydrocarbon class, the alkanes, and shows that the number of chemical compounds increases rapidly with carbon number.

	Carbon number	Boiling point (°C) (n-alkanes)	Number of isomers (alkanes only)
	3	-42.00	1
Gasoline and napthas	4	-1.00	2
	5	36	3
	6	69	5
	7	98	9
	8	126	18
	10	174	75
Gas oils	15	269	4,347
	20	343	366,231
Heavy products	25	402	36,777,419
	30	450	4,108,221,447
	35	490	493,054,243,760
	40	525	62,353,826,654,563

Thus, later in 2015, Concawe began the first phase of the petroleum substance identity programme. Concawe commissioned an analytical chemistry project in which detailed analyses were conducted on a sample of each of the 197 different petroleum substances registered under REACH.

However, given that petroleum substances are UVCBs, it is important to understand the range of composition for each substance. Therefore, in 2016 Concawe requested that each registrant provide the analytical data given in the registration dossiers for their substances. Concawe has to date received more than 2,800 data sets (representing ~70% of the active petroleum substance registrations) from registrants.

Concawe commissioned a consultant to conduct a statistical analysis of the data set for each registered petroleum substance, and to support Concawe's Substance

Identity Group in drafting Substance Identity Profiles (SIPs) for each petroleum substance.

The SIPs should provide sufficient information on chemical composition and composition range, to distinguish one petroleum substance from the next. This will allow Concawe to provide guidance to registrants, who will then be asked to confirm that they have registered with the correct European Community number.

This will address two of the concerns expressed by ECHA, that a number of registrants have incorrectly identified their substance, and that they (ECHA) observe a lack of consistency or even contradictory analytical information between different registrants for the same substance. In turn, this will justify the sharing of data generated on a substance between all registrants of the same substance.

Grouping of petroleum substances by chemical composition

Over many years, prior to REACH, scientists from industry developed rationales for read-across of data from one substance to related substances, based on chemical similarity, with the goal of minimising unnecessary animal testing. This was accepted on a global basis for different regulatory regimes, and the same approach was used to prepare the petroleum substance dossiers for REACH registration.

However, ECHA challenges this previously acceptable approach. In the draft and final decisions received so far on petroleum substances and reiterated in the 2015 meeting with Concawe, ECHA stated that they only accept the use of read-across from one substance to a different substance when there is clear justification to support it.

The primary goal of the substance identity programme is to understand the differences in chemical compositions, allowing us to distinguish one petroleum substance from another. A second, but equally important goal, is to demonstrate the similarity between different, but related petroleum substances. This second goal is fundamental to the use of read-across from one substance, for which experimental data has been generated, to chemically analogous substances.

Human health risk assessments.

Prior to REACH, reprotoxicity tests were only required for substances that were suspected to be CMRs, or for chemicals that were designed to be biologically active. REACH was the first chemical regulation in the world to make reprotoxicity data a standard requirement. In the EU, reprotoxicity testing which involves vertebrate species cannot be conducted without permission from ECHA.

By the 2010 deadline, 207 petroleum substance dossiers had been registered for REACH, using a category approach that distinguished 20 different petroleum substance groupings. For six of the category dossiers it was evident that there was insufficient reprotoxicity information available. Therefore, these dossiers contained proposals for two reproductive toxicity studies, one studying prenatal development and another studying development after delivery.

These six testing proposals were for one substance targeted in each category where it was clear that there were information gaps and where read-across was considered to be justifiable to the other substances within the category. The principle was that since the whole substance is tested, the result can be extrapolated to all substances showing a similar composition.

ECHA has challenged our read-across rationale within the six categories, on the basis that the chemical similarity of the substance category members was not sufficiently substantiated. Unless we develop stronger justification for read-across, it is highly likely that the regulators will require additional animal testing for reprotoxicity and prenatal developmental toxicity, even beyond these initial six categories.

During the main registration phase of REACH, the accepted standard test for reprotoxicity was the 'two-generation reprotoxicity test' (OECD 416)[1]. Until 2015, all registrations that included a testing proposal were for the standard two-generation test. The REACH regulation was amended in 2015, when the two-generation reprotoxicity test was replaced by the Extended One-Generation Reproductive Toxicity Study (EOGRTS) (OECD 443). However the Commission suspended decisions on all reprotoxicity testing until consensus on the required technical scope of the EOGRTS was achieved. The Commission sent out letters requiring updated testing proposals in the final quarter of 2016.

A different tension is related to the regulatory requirement for prenatal development toxicity tests (PNDT) to be conducted on two species. Previous practice was to use a single species, typically the rat, for the PNDT work, but in 2015 the requirement for a second species was confirmed by ECHA. This requirement alone would require significant additional testing for petroleum substances, unless an acceptable alternative can be developed.

This is in line with a goal we have in common with ECHA and also with the anti-animal testing lobby, which is to develop alternatives that will minimise the requirement for additional animal testing. In 2016 Concawe initiated a new research programme known as CAT-APP (category approaches and read-across in regulatory programmes). The goal of this research is to improve our understanding of the relationship between chemical composition and biological response to exposure to different petroleum substances. In turn, such information together with the improved chemical composition data will allow us to group petroleum substances for different human health end points, allowing a scientifically-sound justification for read-across between members in the same grouping. The CAT-APP programme is discussed further in a separate article on pages 10–13 of this edition of the Concawe *Review*.

Environmental risk assessments

The approach developed by Concawe's Ecology Group (EG) for environmental risk assessments has its origin in the early 1990s when Concawe was developing approaches to enable responses to potential prioritisation of petroleum substances under the Existing

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[1] More information on OECD testing guidelines can be found at www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788

Substances Regulation[2], the predecessor of the REACH Regulation. Given the complexity of petroleum substances and the fact that the environmental fate and effects properties of their constituents are predictable using Quantitative Structure Activity Relationships (QSARs) that correlate with physical-chemical properties, the EG developed the Hydrocarbon Block (HCB) Method (HCBM)[3]. In principle, such an approach could also be applied to health hazards. However, the range of effects (end points) under consideration is much larger and the data are not as widely available as they are more difficult to generate by block.

The HCBM takes a petroleum substance and divides it into blocks that represents the constituents present on the basis of chemical classes (e.g. paraffins, olefins, naphthenics, aromatics) and carbon number distributions. Originally, these blocks covered ranges of three carbons for each of the then defined 16 chemical classes. Today these blocks are only one carbon number for 16 redefined chemical classes.

For the purpose of an environmental risk assessment the predicted environmental concentrations (PECs) and predicted no-effect concentrations (PNECs) are established for each HCB that is identified in the petroleum substance under assessment. Obtaining the overall perceived environmental risk (ER) is then calculated by adding all the identified HCB-risk ratios or PEC/PNEC-ratios (see equation below).

Calculating the perceived environmental risk

$$ER_{ps} = \frac{PEC_{HCB1}}{PNEC_{HCB1}} + \frac{PEC_{HCB2}}{PNEC_{HCB2}} + \frac{PEC_{HCB3}}{PNEC_{HCB3}} + \frac{PEC_{HCB4}}{PNEC_{HCB4}} + \ldots\ldots \frac{PEC_{HCBn}}{PNEC_{HCBn}}$$

This process is automated in the PETRORISK model which is capable of establishing the ER originating from manufacturing the petroleum substance and each identified use at a local, regional and continental scale, taking into account the volumes and perceived release fractions for each of these.

As all petroleum substance constituents are susceptible to distribution over the four environmental compartments, air, water, sediment and soil, as well as being prone to environmental degradation processes, PETRORISK models these environmental fate processes when estimating the PECs for each use and environmental compartment.

The distribution is a function of physical chemical properties including water solubility, vapour pressure and environmental partitioning constants that are either measured or derived by quantitative structure activity relationships (QSARs). However, the environmental degradation rate constants of many constituents are estimated to obtain the environmental half-lives used in the PEC-derivation. To decrease the uncertainty in these bio-degradation fate QSARs, the EG is currently supervising three projects that will look into constituent removal from the environment by biodegradation.

Regarding environmental effects, the required PNECs for simple one- to three-constituent HCBs can easily be established on the basis of ecotoxicological testing. However, many of the HCBs have too many constituents to establish the ecotoxicological data by testing each constituent. In this respect it has to be noted that testing on fish falls under the EU Directive[4] on vertebrate animal testing, which requires Commission consent.

In view of this, and the huge amount of testing that would be required for the derivation of the PNEC for each HCB, the EG has supported academia to develop the Target Lipid Model (TLM) a QSAR effect model that estimates the concentration of any substance that is protective of 95% of the species in a given ecosystem. The EG considers that, given the conservative nature of this model and the large amount of real test data on which it is based, this 95% protection level is equal to a PNEC. The TLM is embedded in the PETROTOX ecotoxicological prediction model which estimates the observed ecotoxicity when a test solution is made by exposing water to a specific amount of the petroleum

[2] Council Regulation (EEC) No 793/93 on the evaluation and control of the risks of existing substances (March, 1993).

[3] Concawe report 96/52: *Environmental risk assessment of petroleum substances: the hydrocarbon block method*.

[4] Directive 2010/63 of the European Parliament and of the Council on the protection of animals used for scientific purposes.

substance. In laboratory testing this is known as the water-accommodated fraction (WAF) and is currently the only way of performing ecotoxicological tests on petroleum substances.

In 2013, ECHA issued compliance checks to the lead registrants of 36 petroleum substances which challenged the validity of the TLM and concluded that the petroleum substances registration dossiers lacked valid PNECs. In response, throughout 2014 and 2015, the EG performed additional ecotoxicological testing on aquatic plants and blue-green algae to strengthen the species distribution of the TLM, and contracted a further review of the literature to find additional data for this purpose. The results of this work led to a refinement of the TLM that is now embedded in the PETRORISK 7.04 version of the model.

In 2016, the EG then used the new version of the PETRORISK model to update the environmental risk assessments in the dossiers for the categories covered by the ECHA compliance checks.

Another aspect of the environmental hazard assessment required for REACH is the need to determine whether a substance or constituents are persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances. This concept was developed by competent authorities in response to the conclusions of Rachel Carson's book, *Silent Spring*, and led to the creation of a list of 12 persistent organic pollutants (POPs). Today, the authorities are expanding this concept to include PBT and vPvB substances, with the aim of avoiding potential environmental and health issues in the future. As a result, any substance that is considered to be either PBT or vPvB is likely to be added to the SVHC list.

The criteria for determining whether a substance should be classified as PBT or vPvB are stringent and based upon laboratory experimental data and a conservative theoretical interpretation that does not always reflect the environmental reality. Therefore, Concawe is active in the ECHA /industry PBT expert group and the EG is considering further work to develop data that tests the hypothesis that the theoretical approaches are sufficiently protective of the environment.

Conclusions

Due to the UVCB nature of petroleum substances, the interpretation of the REACH regulation has resulted in the need for scientific dialogue with the regulatory authorities, and within ECHA and the competent authorities in Member States. These regulatory authorities are challenging many of the approaches adopted by our industry. REACH requires actual data to be provided to substantiate each effect, which is challenging for complex substances such as petroleum substances. Where the criticism is valid, Concawe has responded by conducting scientific programmes to provide additional data and improve our understanding. However, where we felt it was merited, Concawe has, and will, continue to challenge the regulatory community. The result is that the information in the petroleum substance dossiers will require significant updates over the next few years, to facilitate the evaluation of petroleum substances and ultimately to assure our customers, and society in general, that we understand the hazards and have effective risk management measures in place to manage the exposure.