anses
French agency for food, environmental and occupational health & safety

The Director General

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OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on the development of a method for identifying substances of interest for ANSES's REACH-CLP work programme

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are made public.

1. BACKGROUND AND PURPOSE OF THE WORK

Under a Memorandum of Understanding signed between ANSES and its supervisory Ministries, the Agency has been mandated by the French competent authority (Ministry of Ecology) to support implementation of Regulation (EC) No 1907/2006 (known as the REACH[1] Regulation). The Agency is therefore called upon to identify substances for which a hazard or risk to human health or the environment is suspected. Based on an assessment of these risks, the Agency may recommend management measures to the French authorities, such as classification/labelling, authorisation, or restriction.

In September 2011, more than 5000 substances were registered under the REACH Regulation. Many other chemicals are to be listed during the next registration phases planned for 2013 and 2018. Identifying substances of interest and priority in terms of public/environmental health is therefore a key challenge for the Agency's REACH and CLP[2] activities, against a background of limited resources.

Different organisations have undertaken a considerable number of studies on ranking, with varying aims. Since 1994, a review conducted on behalf of the US EPA has counted a total of 148 different methodologies[3].

[1] REACH: Registration, Evaluation, Authorisation and restriction of CHemicals

[2] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures (CLP Regulation)

[3] Davies G.A., Swanson M., Jones S. Comparative evaluation of chemical ranking and scoring methodologies. University of Tennessee, (1994)

The ANSES defined method aims to conduct an *a priori* analysis, with the aim of screening the thousands of chemicals placed on the European market, in order to identify candidates for management measures in the context of the REACH and CLP Regulations (i.e. harmonised classification, authorisation and/or restriction).

The work to identify candidate substances requiring management measures complements the actions being coordinated by the European Chemicals Agency, ECHA (e.g. the selection of substances for the CoRAP[4]) and the possibility of formal requests from different Ministries.

2. ORGANISATION OF THE EXPERT APPRAISAL

This expert appraisal was carried out in accordance with the French Standard NF X 50-110 "Quality in Expertise – General Requirements of Competence for Expert Appraisals (May 2003)".

ANSES entrusted examination of this request to the Expert Committee (CES) on Assessment of the risks related to chemical substances for the implementation of the REACH Regulation.

Seven CES members were appointed rapporteurs on this issue.

3. SUMMARY AND ANALYSIS OF WORK PERFORMED

3.1. Review of existing prioritisation methods

3.1.1. Score assignment methods found in the literature

Several methods for ranking substances by assigning scores were analysed[5]. While their goals are sometimes very different, they most frequently target the environment and exposure of the general population via the environment. Consumers, and especially workers, are relatively poorly considered in this type of exercise. Biases typically found concerned:

- the choice of inclusion list: substances from existing lists, exclusion of substances governed by sectoral regulations whose effectiveness may be limited.
- missing data: this type of method relies on having an identical data set for all substances on the inclusion list. However, some data may only be available for a limited number of substances, and substances with censored data may therefore be relegated to the bottom of the ranking list (a lack of information often equates to a score of zero).

[4] Community Rolling Action Plan: for substances that must undergo an in-depth risk assessment by a Member State

[5] **US EPA (2012)**, TSCA work plan chemicals: Methods document; **Hansen B. *et. al.* (1998)** Priority setting for existing chemicals: European Union risk ranking method, Environ Toxicol Chem, 18, 772-779; **Swanson M.B. *et al.* (1996)** A screening method for ranking and scoring chemicals by potential human health and environmental impacts, Environ Toxicol Chem, 16, 372-383; **Jouany J.M. *et al.* (1983)** Une méthode qualitative d'appréciation des dossiers en écotoxicologie: cas des substances chimiques, Sci. Vét. Méd. Com., 85, 3, 151-168; **Bonvallot N. *et al.* (2009)** Méthode d'identification et de hiérarchisation des substances reprotoxiques pour la construction de VTR, Environnement, Risques & Santé – 8, 119-131; **Snyder E. M. *et al*. (2000)** SCRAM: A Scoring and Ranking System for persistent, bioaccumulative and toxic substances for the North American Great Lakes, Env sci poll res, 7, 52-61; **Mitchell R.R. *et al.* (2001)** SCRAM: A scoring and ranking system for persistent, bioaccumulative and toxic substances for the North American Great Lakes – Resulting chemicals scores and rankings, Human and ecological risk ass, 8, 537-557

- the "black box" syndrome: the use of scores does not prevent certain ill-defined choices being made without explanation, making the methods involved less than transparent.

3.1.2. Review of methods used by the European Chemicals Agency (ECHA) under REACH

3.1.2.1. PBT Expert Group

This group, created to support ECHA's work (in particular that of the Member States Committee: MSC), is made up of representatives from ECHA, the Member States, NGOs and industry. Its mission is to provide scientific opinions on issues relating to identification of the PBT[6] and vPvB[7] properties of chemicals; these opinions are informal and non-binding. As part of its activities, potentially PBT/vPvB substances were identified and ranked primarily on the basis of their hazardous properties (screening was carried out by several Member States of potentially P (persistent) and B (bioaccumulative) substances based on data modelled using QSAR[8]). This selection was further refined by additional criteria on T (toxicity), as well as on exposure, data for which mainly came from the SPIN[9] database.
Substances whose PBT nature is proven may be proposed as candidates for authorisation. Those requiring a detailed analysis will be selected for evaluation. Those whose PBT nature is not proven will be removed from the list.
A member of ANSES represents France in this PBT expert group.

3.1.2.2. Development of the CoRAP

Under Article 44 of the REACH Regulation, ECHA is required to develop the Community Rolling Action Plan (CoRAP) for substance evaluation, in agreement with the Member States. In accordance with Article 44.1, the European Agency therefore developed a screening method based on different risk scenarios (combinations of hazard and exposure criteria). ECHA computer applications were used to provide data for each scenario:

- CASPER (Characterisation Application for the Selection, Prioritisation, Evaluation and Reporting of REACH registration dossiers and other submissions) is used to exploit data recorded in the context of REACH;
- ProSP (Profiling Screening and Prioritisation Project) cross-references international databases containing predictive data (e.g. QSAR).

The criteria for the development of the CoRAP are based on the points listed in Article 44.1 of the REACH Regulation (information on the hazard, exposure, and tonnage aggregated according to the number of registrations).

3.1.3. Findings from the analysis of existing ranking studies

To ensure that its resources were optimised, ANSES (supported by its CES on Assessment of the risks related to chemical substances for the implementation of the REACH Regulation) sought to avoid duplicating existing work, especially that on identifying suspected PBT substances by ECHA's PBT Expert Group (environment) and on identifying candidate

[6] PBT Substance: persistent, bioaccumulative, toxic
[7] vPvB Substance: very persistent, very bioaccumulative
[8] QSAR: Quantitative structure-activity relationships
[9] Substances in Preparations in Nordic Countries

substances for assessment (development of the CoRAP), insofar as the Agency contributes directly to these actions.
ANSES's inclusion list focused on substances that have already been registered. Substances identified in the context of the CoRAP, suspected as PBT, managed by other Member States (listed in the Overview table) or already listed in Annexes XIV (authorisation) and XVII (restriction), were excluded.

Finally, efforts were made to ensure that the method was transparent and adaptable to changing knowledge and to the forthcoming increase in the number of substances registered under REACH, with the upcoming deadlines for registration (end of 2013 and end of 2018).

3.2. Method used

3.2.1. Drawing up the inclusion list

The inclusion list chosen for this exercise was the list of **substances registered under REACH in July 2011.** This concerns 4938 substances, corresponding to substances produced or imported in quantities over 1000 tonnes per year, substances classified as CMR[10] Category 1A or 1B (more than 1 tonne per year) and substances classified as very toxic to aquatic organisms (more than 100 tonnes per year).

To begin with, substances already being managed or having undergone preliminary work by a Member State or ECHA were removed from the list. This approach was adopted to optimise the work already conducted at European level, to avoid duplication:

- Substances covered by existing exercises under REACH were therefore removed from the inclusion list (delisted). These were: 84 substances registered on the list of candidate substances for authorisation, tens covered by the PBT Working Group's list and 90 substances registered for the CoRAP.
- On this last point, in order to prepare for updating the CoRAP in the coming years, the Member States and ECHA developed a method for identifying (screening) the most suitable candidates for this procedure (see Section 3.1.2.2). These candidate substances for the first update to the CoRAP were also delisted.
- There is an informal register enabling Member States to record early intentions to register substances that are shortly to be analysed, whether or not regulatory action is anticipated (assessment, harmonised classification, restriction, identification as SVHC[11], etc.). This register currently contains 480 substances that were also delisted.
- The 22 substances included in the list of persistent organic pollutants (POPs) from the Stockholm Convention were also removed during this first step, since these substances' conditions of use are already being managed.
- Finally, the 14 substances listed in Annex XIV (authorisation) and the 60 substances listed in Annex XVII (restriction) of the REACH Regulation were excluded.

At the end of this first filtering step, 4264 substances remained.

In a second step, several categories of substances initially regarded as lower priority were excluded to shorten the list:

[10] CMR: Carcinogenic, Mutagenic, Toxic for Reproduction
[11] SVHC: Substance of Very High Concern

- Intermediates, for which the exposure potential is reduced but cannot be ruled out entirely. This is a questionable choice because the collective risk (impact) is given priority over the individual risk. Exclusion of these substances is justified by the efficiency of the REACH Regulation for substance intermediates for which exemptions exist (e.g. authorisation) and whose requirements are less stringent than in the case of a full registration.

- Substances concerned by testing proposals. These are substances removed temporarily from the list, which will be reinstated once the tests have been performed and accepted by ECHA.

Finally, the petroleum derivatives on the list were retained for the first approach: although this group of compounds is often excluded by existing ranking exercises because they are complex substances more analogous to mixtures, the nature and use of such substances varies and can lead to significant exposure, particularly occupational exposure.

The working list therefore contained 2018 substances.

They can be broken down into:

- 1318 mono-constituents (the remainder being multi-constituents or UVCB[12]);
- 213 substances classified as CMR (1755 unclassified);
- 317 substances whose lead registrant is in France;
- 27 substances included in the NGO ChemSec's SIN[13] List, and 66 substances from ETUC-CES's[14] trade union priority list. A comparative analysis of the results of the exercise and these lists will be presented in the conclusions.
- 41 substances prohibited under the EU's Cosmetics Regulation.

3.2.2. Choice of ranking tool

The tool used for this exercise was the SIRIS method (System of Integration of Risk with Interaction of Scores), a mathematical multi-criteria decision support tool developed in the 1980s and used primarily for environmental risk assessments. This method has mainly been used to establish priority lists of substances to be screened for in water, and to classify plant protection substances based on the environmental risk they pose to surface waters. This tool was also used by AFSSET for ranking CMR substances to be substituted as a priority (for more information, visit the website www.substitution-cmr.fr).

SIRIS is a scoring method that seeks to formalise the different stages of a logical process leading to a decision being taken based on data using a number of selection criteria. It can also be described as a 'downgrading' method because penalties are calculated starting from an ideal situation, with a score of zero, and substances are then downgraded based on criteria that appear increasingly unfavourable, and which are correspondingly penalised more heavily.

Prior to being applied in practice, the method requires three essential preparatory steps:

- selection of criteria to be taken into account;

- ranking of criteria in order of relative importance according to the desired objective;

[12] Substances of unknown or variable composition, complex reaction products or biological materials
[13] Substitute It Now!
[14] European Trade Union Confederation, 2011

- definition of conditions for each criterion.

Once these initial steps have been defined by the user, the SIRIS method can then be applied to calculate the score for each substance under study and classify them according to the defined objective. SIRIS Solution software (version 1.0) was used for this purpose, mainly to create a matrix of penalties based on the defined criteria, classes and conditions.

3.2.3. Choice of ranking criteria

There are many available criteria for estimating risk, under the first phase of REACH registration. They provide direct or indirect information on the physico-chemistry, hazards (environmental and to human health), exposure potential (occupational and environmental), etc.

The expert rapporteurs agreed that the number of criteria to be used in SIRIS must be limited. Some uncertainty remains about the completeness of the available data, and their discriminating potential. Initially, the following twelve criteria of interest were selected:

- *number of REACH registration dossiers;*
- *fish toxicity as predicted by ECOSAR[15];*
- *Daphnia toxicity as predicted by ECOSAR;*
- *green algae toxicity as predicted by ECOSAR;*
- *CMR classification;*
- *respiratory sensitiser (Cat. 1 Resp. Sens.);*
- *skin sensitiser (Cat. 1 Skin Sens.);*
- *'dispersive' use;*
- *consumer use;*
- *significant release into the environment;*
- *significant exposure of workers;*
- *annual production and/or import tonnage.*

Following an analysis of the degree of information provided and its statistical distribution (for continuous variables), the group adopted five criteria, with a choice of conditions for each one that would ensure their discriminating potential.

The criterion adopted in the first approach for the hazard level was the **CMR classification**, while those selected for potential exposure were **tonnage, consumer use, dispersive use and potentially significant exposure of workers.** It is important to note that the CMR classification includes the harmonised classification as well as the classification notified by registrants ("self declaration") in ECHA's notification register. In the event of disagreement between registrants, the worst case notification was used.

The second step prior to implementation of SIRIS's penalty calculation engine was to rank the criteria in order of relative importance, defined according to the determined objective.

This step is crucial in the SIRIS methodology, since the greater the importance of a given criterion, the higher the penalties assigned to each substance.

[15] ECOSAR: Ecological structure activity relationships

CMR classification and tonnage were the criteria typically found in the other exercises analysed, due to their discriminating potential and availability. These two criteria were therefore given predominance. The intensity of the diffuse nature of a substance will depend on its tonnage and how widely it is available on the market.

It was decided to combine these two criteria in the same class (Class 1) because they are regarded as having the same weight and a greater importance than the other three. In addition, there are no synergistic interactions between them, a requirement of the SIRIS method. These steps are summarised in Table 1.

Table 1: Classes, criteria and conditions chosen

Order of preference	**Class 1**		**Class 2**		
Criterion	CMR Classification	Tonnage	Dispersive use	Consumer use	Worker exposure
Modes	*o*: no *e*: 1 cat 2 *f*: 2 cat 2 *g*: 3 cat 2 *h*: 1 cat 1A ou 1B *m*: 1 cat 1A ou 1B + 1 cat 2 *s*: 1 cat 1A ou 1B + 2 cat 2 *t:* 2 cat 1A ou 1B *u*: 2 cat 1A ou 1B + 1 cat 2 *d:* 3 cat 1A ou 1B	*o*: 0 – 20 t *e:* 20 – 3 000 t *m:* 3 000 – 40 000 t *d*: > 40 000 t	*o*: no *d*: yes	*o*: no *d*: yes	*o*: no *d*: yes

Less unfavourable

More unfavourable

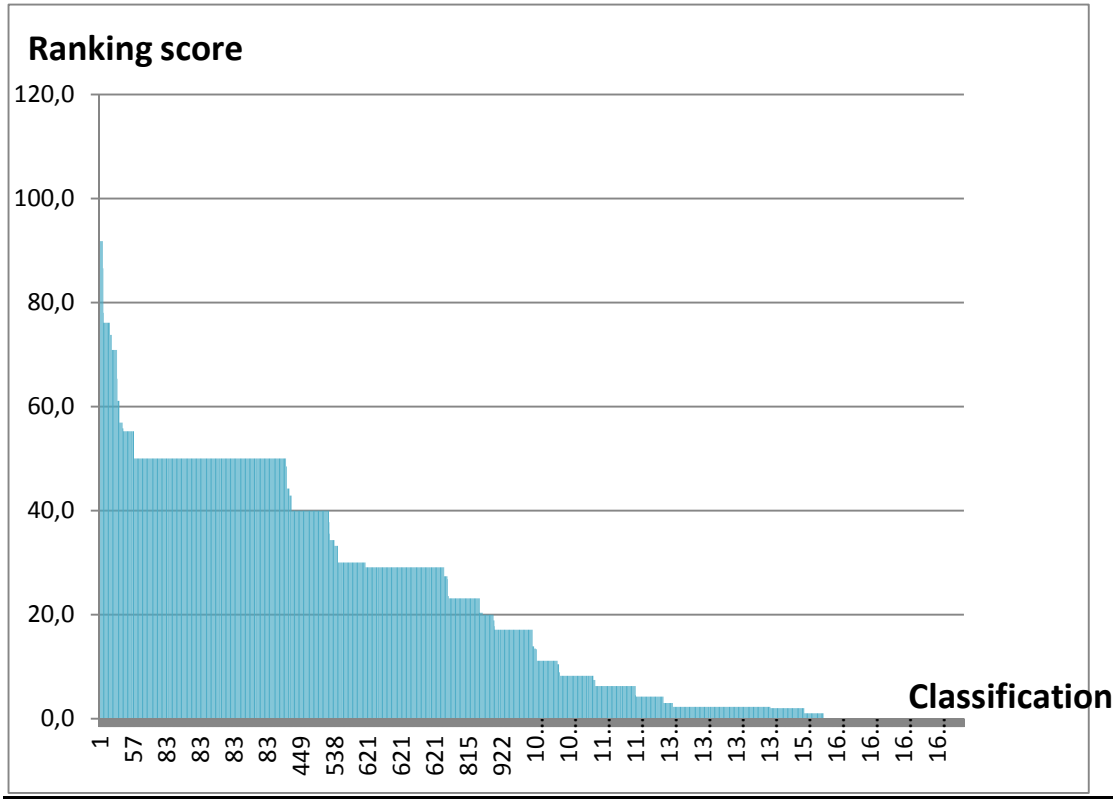
3.2.4. Discussion of the results

3.2.4.1. Distribution of the results and robustness of the chosen criteria

The results obtained by the SIRIS method indicate ranking scores ranging from 97 for the first substance (the most "risky" situation) to 0 for the last substance (the least "risky" situation).

The first 11 substances had 5 different scores (from 97 to 76.1) while the first 57 substances had 12 different scores (from 97 to 55.2). The method is therefore fairly good at discriminating the substances that *a priori* pose the greatest risk, according to the chosen criteria.

However, the method was less effective at discriminating between the remaining substances, with sometimes around twenty substances sharing identical scores, and in some cases even more, such as the substances from positions 83 to 436 (around 350 substances) that all have the same score (as shown in the graph below). This is probably an effect related to the limited number of criteria and conditions used.



An initial series of additional univariate analyses on the scores indicates that they reflect a multi-criteria judgment relatively well. The final scores are not strongly correlated with the Class 1 criteria identified as a priority that often "dominate" in other methods: these criteria influence the scores but do not explain them alone, justifying the merits of a mathematically developed method such as SIRIS. Similarly, the random selection of Class 2 criteria, instead of the information actually contained in the registration dossiers, changes the final ranking quite significantly for the first 50 substances, confirming that these criteria play a key part in the scores obtained by the SIRIS method. These advantages of the method are mainly related to the design of the score aggregation tool chosen (SIRIS): each criterion chosen by the experts can influence the final score. A consequence of this finding is that it will be

essential in subsequent use of the method to include complete and accurate data for all the criteria chosen, at the risk of significantly changing the final ranking and, in a context of limited resources where only a few substances will be further investigated, not selecting the substances which should have the highest priority.

Finally, and more generally, scores were only calculated for substances on the final candidate list, from which many substances had been removed through the delisting process described above. One of the variables contributing significantly to this delisting was the identification of a substance as an "intermediate", and it is worth reiterating that the extreme sensitivity of this classification merits special attention to avoid abusive use of this "regulatory shortcut".

3.2.4.1. Further analysis of the first 50 substances

Additional data were sought on the first 50 substances on the list obtained: data on composition and exposure scenarios published on ECHA's website.

- **The vast majority of the first substances appearing on this list belong to the family of petroleum derivatives (hydrocarbons),** regarded as UVCB in the context of REACH. Assessing the risks associated with these types of compounds is considered difficult (there are many substances of complex and variable composition), which may explain why the ranking exercises found in the literature do not take them into account.

  This systematic exclusion is however questionable given the different categories and uses that can be defined for these compounds: a distinction can in fact be made between petroleum gases, tars/bitumens, petroleum solvents, mineral oils, etc.

  Analysis of the registration dossiers shows some inconsistency depending on the level of classified impurities. Some exposure scenarios distinguish between professional use of CMR substances and consumer use (non-classified substances). However, a substance's purity profile according to its use cannot always be deduced from the composition data in the dossier. Doubts were also raised about the effectiveness of the assaying methods employed. The INRS[16] recently published the results of a study[17] comparing three methods for determining the carcinogenic potential of a mineral oil. It showed in particular that the regulatory IP346 method is not protective enough with regard to regenerated oils/oils containing additives (varying levels of benzo[a]pyrene were identified in oils found on the market).

  In addition to mineral oils, the expert rapporteurs drew attention to solvents and degreasers such as white spirit: although they are dearomatised, they can still contain other classified impurities. N-hexane is of particular concern (neurotoxic).

- **Lead compounds:** the four lead-derived substances on the list have similar uses, and although they are not all covered by a specific classification in Annex VI of the CLP Regulation, they may be classified under the generic entry Index No. 082-001-00-6 (Repr. 1A). For this type of compound, a "grouping" approach should be considered. Indeed, an analysis of the exposure scenarios shows for example that three lead derivatives are used in the manufacture of PVC[18] materials. As part of

[16] INRS: French National Research & Safety Institute
[17] Champmartin C., INRS. Hygiène et sécurité du travail – 2ème trimestre 2012. ND 2356-227-12.
[18] PVC: Polyvinyl chloride

ECHA's preparation of the SVHC dossier at the request of the European Commission, ECHA's departments are currently preparing a Best-RMO[19] for several lead compounds including the four substances identified in this ranking exercise, which were added to the list of candidates for authorisation in December 2012. In addition to the four substances studied, the working list contained 11 other lead-derived compounds, of which 10 have also been included on the list of candidates for authorisation on the Commission's initiative. As there was no prior communication about this initiative from the departments of the Commission or ECHA, these compounds were not delisted for this year's exercise, which is why they appear in the final results. This finding again highlights the importance of advance communication by the various Member States, ECHA and the Commission, about their current intentions and work on chemicals, and about any Best-RMO analyses conducted prior to management decisions involving authorisation or restriction.

In this regard, it should be recalled that Sweden is currently preparing to restrict lead in articles intended for consumer use (dossier scheduled for submission in April 2013).

- **Boron compounds:** In addition to the two substances studied, one of which is classified as Category 1B toxic for reproduction and the other which is currently the subject of a proposal for classification as Category 1B toxic for reproduction by the Netherlands, the working list included seven other compounds derived from boron. Harmonised classification for these compounds should 7also be investigated initially. Depending on the uses of these substances, a Best-RMO analysis could be conducted for this group to the exclusion of substances already managed under REACH.

- **Two other emerging substances:** Copper sulphate (CAS No. 7758-98-7) was notified by some registrants as a Category 1A carcinogen and Category 1B reproductive toxicant. Copper compounds are being evaluated by France (namely ANSES) in the context of the Biocide Regulation. Many other uses have also been reported. In addition to biocide data, a thorough analysis of the toxicological data from the registration dossier(s) is under way to clarify the reasons for these notifications. Chromium(III) oxide (CAS No. 1308-38-9), which is not listed in Annex VI of the CLP Regulation, has been reported by some registrants as a Category 1B reproductive toxicant. An analysis of the toxicological data in the registration dossier would be required to confirm or refute these classification statements and take appropriate action.

[19] Best-RMO: Best Risk Management Option: a comparative analysis of the best risk management options available

3.2.4.2. Comparative analysis with the list produced by the European Trade Union Confederation (ETUC-CES)

The purpose of the Trade Union Priority List is to contribute to the practical implementation of REACH, in particular the authorisation procedure by proposing substances of very high concern (SVHC) which, from a trade union perspective, should have priority for inclusion in the candidate list and potentially in the authorisation list.

Based on the criteria for identifying substances of very high concern under REACH (Article 57), chemicals regarded as being of very high concern in the trade union priority list are CMR substances, Categories 1A, 1B or 2 listed in Annex VI of Regulation (EC) 1272/2008, carcinogens classified Category 1, 2A or 2B by the International Agency for Research on Cancer (IARC), PBT/vPvB substances listed in the framework of the OSPAR Convention and by the European Technical Committee for New and Existing Substances, known and suspected endocrine disruptors listed in the Community Strategy for Endocrine Disruptors, neurotoxic substances listed by Vela *et al.* (2003), sensitisers listed in the Annex VI of Regulation (EC) 1272/2008 and the "REACH allergens" listed by Friedhelm *et al.* (2006).

The trade union list includes 568 substances grouped into 334 entries ranked by score, all of which are chemicals produced in large quantities and/or identified in the context of a Substance Information Exchange Forum (SIEF)[20]. 209 entries relate to substances or groups of substances listed as agents responsible for recognised occupational diseases and 63 entries relate to substances or groups of substances causing diseases whose occupational origin is suspected.

Only 59 substances from the ETUC-CES list were found in the working list, the others having been delisted. This means that most of the substances highlighted in the ETUC-CES list are already being managed or the focus of interest by a Member State or ECHA.

Of these 59, only 22 are found among the first 100 substances in our ranking. This can be explained by the fact that the priority criteria from our list and the ETUC-CES list are different.
However, all the substances from the ETUC-CES list are found in the first half of our ranking.

[20] For more information on the Substance Information Exchange Forum, consult the FAQs on the ECHA website: http://ECHA.europa.eu/web/guest/support/faqs/frequently-asked-questions/frequently-asked-questions-about-reach

Table 2: Substances from the ETUC-CES list that were found on our inclusion list

Ranking	CAS No	EC No	Substance name
30	11138-47-9	234-390-0	perboric acid, sodium salt
42	1306-19-0	215-146-2	cadmium oxide
57	5064-31-3	225-768-6	trisodium nitrilotriacetate
57	1333-86-4	215-609-9	carbon black
57	556-67-2	209-136-7	octamethylcyclotetrasiloxane
57	96-29-7	202-496-6	butanone oxime
83	9014-01-1	232-752-2	subtilisin
83	7785-87-7	232-089-9	manganese sulphate
83	7727-21-1	231-781-8	dipotassium peroxodisulphate
83	7439-96-5	231-105-1	manganese
83	1163-19-5	214-604-9	bis(pentabromophenyl) ether
83	793-24-8	212-344-0	N-1,3-dimethylbutyl-N'-phenyl-p-phenylenediamine
83	111-30-8	203-856-5	glutaral
83	111-76-2	203-905-0	2-butoxyethanol
83	108-78-1	203-615-4	melamine
83	101-72-4	202-969-7	N-isopropyl-N'-phenyl-p-phenylenediamine
83	105-60-2	203-313-2	caprolactam
83	100-97-0	202-905-8	methenamine
83	100-42-5	202-851-5	styrene
83	95-33-0	202-411-2	N-cyclohexylbenzothiazole-2-sulfenamide
83	78-93-3	201-159-0	butanone
83	67-63-0	200-661-7	propan-2-ol
436	106-93-4	203-444-5	1,2-dibromoethane
438	1309-64-4	215-175-0	diantimony trioxide
438	98-01-1	202-627-7	2-furaldehyde
438	88-12-0	201-800-4	1-vinyl-2-pyrrolidone
444	126-99-8	204-818-0	2-chlorobuta-1,3-diene
444	68-12-2	200-679-5	N,N-dimethylformamide
449	63449-39-8	264-150-0	paraffin waxes and hydrocarbon waxes, chloro
449	13048-33-4	235-921-9	hexamethylene diacrylate
449	10325-94-7	233-710-6	cadmium nitrate
449	10108-64-2	233-296-7	cadmium chloride
449	2855-13-2	220-666-8	3-aminomethyl-3,5,5-trimethylcyclohexylamine
449	1344-43-0	215-695-8	manganese oxide
449	552-30-7	209-008-0	benzene-1,2,4-tricarboxylic acid 1,2-anhydride
449	110-65-6	203-788-6	but-2-yne-1,4-diol
449	100-37-8	202-845-2	2-diethylaminoethanol
449	98-83-9	202-705-0	2-phenylpropene
549	110-85-0	203-808-3	piperazine
549	108-05-4	203-545-4	vinyl acetate
549	106-88-7	203-438-2	1,2-epoxybutane
557	8006-64-2	232-350-7	turpentine, oil
557	4719-04-4	225-208-0	2,2',2''-(hexahydro-1,3,5-triazine-1,3,5-triyl)triethanol
557	822-06-0	212-485-8	hexamethylene diisocyanate

Ranking	CAS No	EC No	Substance name
557	75-05-8	200-835-2	acetonitrile
621	5392-40-5	226-394-6	citral
621	603-35-0	210-036-0	triphenylphosphine
621	109-87-5	203-714-2	dimethoxymethane
621	102-77-2	203-052-4	2(morpholinothio)benzothiazole
804	123-91-1	204-661-8	1,4-dioxane
815	9032-08-0	232-877-2	amylase, gluco-
815	7440-41-7	231-150-7	beryllium
815	5468-75-7	226-789-3	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]
894	51000-52-3	256-905-8	vinyl neodecanoate
922	34090-76-1	251-823-9	tetrahydro-4-methylphthalic anhydride
922	25013-15-4	246-562-2	vinyltoluene
922	19438-60-9	243-072-0	hexahydro-4-methylphthalic anhydride
922	11070-44-3	234-290-7	tetrahydromethylphthalic anhydride
922	1304-56-9	215-133-1	beryllium oxide
922	97-77-8	202-607-8	disulfiram
1010	7758-01-2	231-829-8	potassium bromate
1018	74-88-4	200-819-5	iodomethane
1020	142-47-2	205-538-1	sodium hydrogen glutamate

3.2.4.3. Comparative analysis with the Substitute It Now! (SIN) List

Version 2 of this list consists of 378 substances (updated in May 2011). These are substances identified by ChemSec[21] as meeting the criteria for substances of very high concern (SVHC) as defined in the REACH Regulation. Of these, 311 substances are carcinogenic, mutagenic and toxic for reproduction (CMR), 17 are persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB), and 50 are of equivalent concern (e.g. endocrine disruptors).

Only 20 substances from the SIN list were found on the inclusion list, the others having been delisted to obtain the working list. This means that most of the SVHC highlighted in the SIN list are already being managed or the focus of interest by a Member State or ECHA.

Few are found among the first 100 substances in our ranking.
This can be explained by the fact that the SIN list only takes into account hazards to human health or the environment (CMR, PBT and vPvB substances and those of equivalent concern) in its classification, and not criteria for estimating exposure.
However, all the substances from the SIN list are found in the first half of our ranking.

Table 3: Substances from the SIN list (V2) that were found on our inclusion list

Ranking	CAS No	EC No	Substance name
30	11138-47-9	234-390-0	perboric acid, sodium salt
42	1306-19-0	215-146-2	cadmium oxide

[21] Non-profit organisation founded in 2002 by four environmental organisations whose aim is to promote application of the key principles of precaution, substitution, polluter pays and right to know.

Ranking	CAS No	EC No	Substance name
55	7718-54-9	231-743-0	nickel dichloride
57	556-67-2	209-136-7	octamethylcyclotetrasiloxane
83	1163-19-5	214-604-9	bis(pentabromophenyl) ether
83	100-42-5	202-851-5	styrene
436	106-93-4	203-444-5	1,2-dibromoethane
438	1309-64-4	215-175-0	diantimony trioxide
444	18718-11-1	242-522-3	nickel bis(dihydrogen phosphate)
444	13770-89-3	237-396-1	nickel bis(sulphamidate)
444	10028-18-9	233-071-3	nickel difluoride
444	126-99-8	204-818-0	2-chlorobuta-1,3-diene
444	68-12-2	200-679-5	N,N-dimethylformamide
449	63449-39-8	264-150-0	paraffin waxes and hydrocarbon waxes, chloro
449	10108-64-2	233-296-7	cadmium chloride
557	373-02-4	206-761-7	nickel di(acetate)
557	88-85-7	201-861-7	dinoseb
815	5571-36-8	427-230-8	cyclic 3-(1,2-ethanediylacetale)-estra-5(10),9(11)-diene-3,17-dione
815	7440-41-7	231-150-7	beryllium
815	605-50-5	210-088-4	diisopentyl phthalate
919	3724-43-4	609-368-2	chloro-N,N-dimethylformiminium chloride
922	1304-56-9	215-133-1	beryllium oxide
922	79-16-3	201-182-6	N-methylacetamide
922	57-57-8	200-340-1	propiolactone
1010	7758-01-2	231-829-8	potassium bromate

4. CONCLUSIONS AND DISCUSSION

Given the many substances registered since the introduction of the REACH Regulation, a method was developed to identify candidate substances for management under the REACH and CLP Regulations. **This "reasoned approach" complements the existing exercises led by ECHA,** in particular those aimed at identifying candidate substances for evaluation (for inclusion in the CoRAP), and the work of the working group dedicated to substances suspected of being PBT (PBT Expert Group).
The resulting actions will therefore be different: primarily analyses such as Best-RMO (which aim to document and recommend risk management options, mainly through restriction or authorisation) or proposals for harmonised classification.

The distribution of the results shows that the criteria chosen are relatively selective for the top-ranking substances, but less discriminating thereafter.

The CMR and tonnage criteria are expected to be less operational for the second phase of registration scheduled for the end of 2013. Moreover, the tonnage criterion is not suitable for identifying substances in the form of nanomaterials, given their lower production volumes compared to more traditional substances (in "bulk" form).

However, the findings of the evaluation procedures and the substances for which testing proposals are to be validated by ECHA should lead to the inclusion list being supplemented by substances characterised by high tonnages and/or a CMR classification.

The process implemented does have limitations, some of which are typically found in similar exercises:

- The use of the tonnage parameter alone is limiting when it comes to understanding a substance's exposure potential, which varies according to the physico-chemical properties of the substance, the number and type of uses, etc.
- The tonnage data are not specifically related to the different uses reported: the relative importance of one use compared to another is therefore difficult to assess.
- Susceptible populations cannot easily be targeted even though consumer use was considered in the exercise.
- Distinguishing substances with a collective risk (impact) from those posing an individual risk presents a major difficulty. For an equivalent level of tonnage the management measures are not in fact identical: in one case a small population may be exposed to high doses, while in another, a large population may be exposed to lower levels.
- Finally, many of the initial data have not been verified and/or validated: these are raw data, taken from declarations in registration applications.

Among the positive points of the exercise, it is worth noting the large size of the inclusion list (almost 5000 substances). The choice to keep petroleum derivatives (hydrocarbons) is new compared to existing methods.

The SIRIS tool was also able to propose a list of substances that were all placed in relative order: the other exercises of the same kind (list of candidate substances for the CoRAP, SIN list, etc.) are not based on a downgrading method and propose lists of hundreds of unranked substances.

Management of petroleum derivatives (hydrocarbons) has also been discussed at European Commission level: the Roadmap defined through to 2020, mainly for the identification of SVHC, includes this family of substances. ECHA is seeking to establish a working group dedicated to this family of substances, and although its mandate remains to be defined, it already seems useful for ANSES (on behalf of the French competent authority) to take part in this work, considering that hydrocarbons emerged as a priority from the exercise performed.

The results confirm the benefit of grouping substances. There are many advantages to considering several substances from the same group with the same hazardous properties:

- Gain in efficiency with respect to protection of public health and/or the environment. A single dossier can cover several substances with potentially similar uses, and a greater combined tonnage;
- Possibility of preventing a substance undergoing a management action being substituted by another with the same profile but that has escaped the regulatory provisions.

This grouping can be done in different ways: through a hazard approach (with a view to harmonised classification) and/or by uses (to avoid substitution by another substance of equivalent hazard level, for example, lead compounds in PVC).

Finally, an analysis of the results showed that some substances without specific harmonised classification and not covered by a generic entry were classified as CMR by some but not all registrants: it would be interesting to establish the causes of such heterogeneity among

registrants in the classification and labelling notifications, despite the possibility of communication in the SIEF.

The conclusions of this work will be presented and discussed with ECHA.

Marc Mortureux

KEY WORDS

REACH, chemicals, ranking.

ANNEXE(S)

Annex: Table of data entered into the SIRIS software for the first 50 substances

ANNE entered i

Classif.	EC No	NAME	CLASS 1		
			CMR classification		
			C	M	R
1	268-629-5	Gases (petroleum), C3-4	1A or 1B	1A or 1B	1A or 1B
2	305-586-4	Distillates (petroleum), cracked, ethylene manuf. by-product, C9-10 fraction	1A or 1B	1A or 1B	2
2	292-694-9	Aromatic hydrocarbons, C8	1A or 1B	1A or 1B	2
2	271-213-6	Alkenes, C9-11, C10-rich	1A or 1B	1A or 1B	2
2	270-737-2	Distillates (petroleum), steam-cracked, C8-12 fraction	1A or 1B	1A or 1B	2
2	270-728-3	Distillates (petroleum), cracked stripped steam-cracked petroleum distillates, C8-10 fraction	1A or 1B	1A or 1B	2
2	270-727-8	Distillates (petroleum), cracked steam-cracked petroleum distillates	1A or 1B	1A or 1B	2
2	265-048-9	Natural gas (petroleum), raw liq. mix	1A or 1B	1A or 1B	2
9	231-847-6	Copper sulphate	1A or 1B	no	1A or 1B
10	270-689-2	Hydrocarbons, C2-4, C3-rich	1A or 1B	1A or 1B	1A or 1B
11	309-877-7	Lubricating oils (petroleum), C24-50, solvent-extd., dewaxed, hydrogenated	1A or 1B	no	2
11	309-874-0	Lubricating oils (petroleum), C>25, solvent-extd., deasphalted, dewaxed, hydrogenated	1A or 1B	no	2
11	297-474-6	Lubricating oils (petroleum), base oils, paraffinic	1A or 1B	no	2
11	295-394-6	Foots oil (petroleum), hydrotreated	1A or 1B	no	2
11	292-660-3	Slack wax (petroleum), clay-treated	1A or 1B	no	2
11	273-563-5	Gases (petroleum), crude distn. and catalytic cracking	1A or 1B	1A or 1B	1A or 1B
11	272-883-2	Gases (petroleum), straight-run stabilizer off	1A or 1B	1A or 1B	1A or 1B
11	271-624-0	Gases (petroleum), C1-5, wet	1A or 1B	1A or 1B	1A or 1B
11	270-752-4	Gases (petroleum), catalytic-cracked gas oil depropanizer bottoms, C4-rich acid-free	1A or 1B	1A or 1B	1A or 1B
11	270-670-9	Fuel gases, crude oil distillates	1A or 1B	1A or 1B	1A or 1B
11	265-156-6	Distillates (petroleum), hydrotreated light naphthenic	1A or 1B	no	2
11	265-098-1	Distillates (petroleum), solvent-refined light naphthenic	1A or 1B	no	2
11	265-176-5	Paraffin oils (petroleum), catalytic dewaxed light	1A or 1B	no	2
11	265-174-4	Paraffin oils (petroleum), catalytic dewaxed heavy	1A or 1B	no	2
11	265-097-6	Distillates (petroleum), solvent-refined heavy naphthenic	1A or 1B	no	2
26	292-699-6	Aromatic hydrocarbons, C7-8, ethylene-manuf.-by-product	1A or 1B	1A or 1B	2

Classif.	EC No	NAME	CLASS 1		
			CMR classification		
			C	M	R
26	292-697-5	Aromatic hydrocarbons, C6-10, C8-rich	1A or 1B	1A or 1B	2
26	273-266-0	Distillates (petroleum), light thermal cracked, debutanized arom.	1A or 1B	1A or 1B	2
26	271-726-5	Gasoline, pyrolysis, debutanizer bottoms	1A or 1B	1A or 1B	2
30	309-867-2	Extract residues (coal), light oil alk., acid ext., indene fraction	1A or 1B	1A or 1B	2
30	308-733-0	Residues, steam cracked, thermally treated	1A or 1B	1A or 1B	2
30	295-434-2	Naphtha (petroleum), hydrodesulfurized light, dearomatized	1A or 1B	1A or 1B	2
30	292-966-7	Fatty acids, C16-18, lead salts	no	no	1A or 1B
30	270-729-9	Distillates (petroleum), cracked stripped steam-cracked petroleum distillates, C10-12 fraction	1A or 1B	1A or 1B	2
30	270-093-2	Distillates (petroleum), light distillate hydrotreating process, low-boiling	1A or 1B	1A ou 1B	2
30	235-702-8	Dioxobis(stearato)trilead	no	no	1A or 1B
30	235-252-2	Trilead dioxide phosphonate	no	no	1A or 1B
30	234-541-0	Disodium octaborate	no	no	1A or 1B
30	234-390-0	Perboric acid, sodium salt	no	no	1A ou 1B
30	215-235-6	Orange lead	no	no	1A or 1B
30	215-160-9	Chromium (III) oxide	no	no	1A or 1B
42	215-146-2	Cadmium oxide	1A or 1B	2	2
43	310-162-7	Pitch, coal tar, high-temp., heat-treated	1A or 1B	1A or 1B	1A or 1B
43	298-754-0	Residual oils (petroleum)	1A or 1B	no	2
43	271-763-7	Residues (petroleum), topping plant, low-sulfur	1A or 1B	no	2
43	272-180-0	Extracts (petroleum), solvent-refined heavy paraffinic distillate solvent	1A or 1B	no	2
43	270-674-0	Fuel oil, residues-straight-run gas oils, high-sulfur	1A or 1B	no	2
48	604-314-4	not technically possible following IUPAC rules	1A or 1B	no	no
48	310-012-0	Hydrocarbons, C3-6, C5-rich, steam-cracked naphtha	1A or 1B	1A or 1B	2
48	295-762-6	Hydrocarbons, C5-8	1A or 1B	1A or 1B	2

Substances in gray do not have harmonized classification with regard to CMR effects (carcinogenic, mutagenic and / or toxic for reproduction). However they present classifications CMR reported by notifiers ("self classification") in the C&L inventory of ECHA. In case of disagreement between notifiers, the most penalizing notification was retained for the present work.