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Do we know how much REACH has cost so far?

A recent study for the European Commission produced an estimate of the cost of registration during the first registration period that, on the face of it, is twice the estimate the Commission came up with before REACH was adopted – and almost as much as the estimate for the whole registration period through to 2018. But, as the study says, the picture is actually more complicated. Geraint Roberts reports.

Those who did not follow the slow development of REACH in the first half of the last decade may not be aware of the fierce debate that raged about the likely costs of the proposals. More than 40 impact assessments were conducted by national governments, the Commission, industry and environmental groups before a Commission press release in 2005 cleared by both the environment and industry directorates announced that "the costs and impacts of REACH are manageable" and the debate moved on to improving the proposals.

Worldwide interest

With REACH, or aspects of REACH, seen as a potential model for other countries, there is keen interest in whether these costs were underestimated or, for that matter, overestimated. In some cases industry groups are pointing to the seemingly higher than expected costs when lobbying against REACH-like legislation in other countries.

This debate has been stoked by a report written by consultancy CSES as part of the REACH review which assesses the "functioning of the European chemical market after the introduction of REACH". Published in April, following a workshop in December that presented its interim findings, it says the total cost for all firms involved in registration to the end of the first registration period is estimated at around €2.1bn. This is almost double the estimate of the Commission's 2003 impact assessment of €1.1bn (at 2011 values). And it represents three-quarters of the figure (again, at 2011 values) the Commission came up with in 2003 for the cost of the whole 11-year registration period.

Registration costs alone are significant, but are they greater than expected?

Of course, there are other costs associated with REACH compliance besides those connected to the registration of substances, such as costs related to other REACH processes, such as authorisation, or those stemming from strategic business decisions, but in many cases there are limited data available on these so far, and it is difficult to predict what these will be. As a result, when CSES looked at costs it limited its study to the costs of pre-registration and registration, along with human resources dedicated to REACH and information exchange activities along supply chains. But whatever the final number for the costs of complying with REACH up to 2018, it is clear that the costs to companies will be significant.

So why is there a significant difference between the Commission's estimate nine years ago and CSES's estimate today? And is it true that the cost of REACH so far is double the figure that was expected?

The CSES report gives two main reasons why it thinks its figure is so much bigger. The first, it says, is that the Commission's estimate back in 2003 was based on a study by consultants RPA which considered only the additional, new costs arising for industry from REACH. The consultants performed a "marginal analysis" that quantified the incremental changes in the direct costs to industry, and which excluded all of the key regulatory instruments, voluntary programmes and other activities that were already in place at that time.

Whereas RPA excluded the fees paid by firms for access to existing studies, CSES's average cost estimates include fees paid by firms to other Sief members to get such access or for letters of access. "In that respect", says CSES, "these are financial costs for firms resulting from REACH even if they are not additional costs for the industry". It was not possible for CSES to provide an estimate of the difference, "but clearly", its report says, "CSES estimates should be expected to be higher than those

contents

NEWS PAGE 1
The cost of REACH registration

EXPERT FOCUS PAGE 4
Implementing GHS in the US workplace

RISK ASSESSMENT P6
Version three of Ecetoc's risk assessment tool

RISK ASSESSMENT P9
TT21C: will it be the new paradigm?

EXPERT FOCUS PAGE 11
GLP: still vital but not a panacea

RISK ASSESSMENT P13
European research projects and nanosafety

NANOWATCH PAGE 16
Nanomaterials in food contact uses

EVENTS PAGE 18

JOBS PAGE 19

CLP CLINIC PAGE 20
Navigating a way through the guidance

REACH HUB PAGE 21
Conducting risk assessments

NGO PLATFORM PAGE 23
Knowledge sharing drives substitution

GUEST COLUMN PAGE 24
Mariann Lloyd-Smith, IPEN

of the RPA study as well as the subsequent Commission estimates based on them."

Unlike the final version of REACH, the initial draft required the registration of polymers and so RPA included polymer registration in its calculations. If its estimates of the cost of registering polymers are excluded, it came up with a cost of €2.1-2.2bn (in 2011 values) for registration and testing under the first registration period. And had RPA – which CSES stresses it is not suggesting made any mistake in its approach, but simply followed different parameters – taken into consideration the fees paid for access to existing data, the total cost estimate would have been higher.

QSARs have so far represented just 4% of the tests in registration dossiers, compared to the 30-60% assumed by the Commission

On the other hand, says CSES, the RPA study assumed there would be a large number of individual registrations (almost 70% of the total) and a smaller size of Sief and consortia, which means that it overstated the costs per registration and per firm.

"Ambitious assumptions"

The second reason why RPA's cost estimate was so much lower than its own, says CSES, is that the final estimates presented by the Commission that followed the consultation on the REACH proposals "made some additional rather ambitious assumptions concerning the use of QSARs in testing that led to significant reduction of the expected total costs". Whereas the Commission predicted savings of €1.3bn in comparison to RPA's initial estimates, CSES says "most, if not all" of this has not materialised because QSARs have so far represented just 4% of the tests included in registration dossiers, compared to the 30-60% assumed by the Commission.

CSES's report also concluded that "for the great majority of firms (close to 70%) registration costs did not exceed 1% of their annual sales in 2010, although for a small number (around 7%) they were above 5%". Interesting questions here are whether this represents too great a burden on firms, and whether companies have been able to pass these costs down their supply chains.

Commenting on the difference between the Commission estimate of €1.1bn in 2003 and CSES's recent estimate of €2.1bn, Erwin Annys, REACH director at the European Chemical Industry Council (Cefic) says the trade body does not have robust figures on the costs of REACH because it is difficult to obtain them from individual companies and such data are confidential. He repeated comments he first made at last December's Commission's workshop that his general impression is that "the €50,000 – 100,000 cost for a 2010 registration is clearly lower than the values we have in mind when talking about average costs for letters of access, which are much more in the order of €200,000 – 300,000". But he said there are "many potential explanations" for the differences, and "this needs further investigation to come to conclusions".

Importance of read-across

Mr Annys says his first impression is that "the difference in estimated and communicated cost has nothing to do with the acceptance of QSARs", and that Cefic believes read-across will play a much more important role than QSARs in potential cost reductions.

"The [CSES and Commission] figures have radically different parameters," says Axel Singhofen, environmental adviser to the Greens/EFA group in the European Parliament, "and unless you can dissect them so that they become comparable, it is just pointless number juggling." He also says the costs "have to be seen in relation to benefits, and unless any new study can prove (contrary to the many impact assessments done during the legislative procedure) that the costs of REACH outweigh the benefits, [the report] does not change anything."

The CSES report contains information that will have proved useful for the REACH review. But it remains very difficult to know what the costs of REACH to industry have been so far, and how much they will be by the time the final registration deadline is reached in 2018. It is also very difficult to know, if we want to compare like with like, if the costs so far are much more than was thought when the Regulation was proposed.

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COMMENT

Evolution rather than revolution?

At a lunch debate at the European Parliament in Brussels in May, the Centre for Alternatives to Animal Testing launched a bid to gain European buy-in for its ambitious and exciting project to map the pathways of toxicity in the human body – an endeavour dubbed the Human Toxome and likened to mapping the Human Genome in its scale and need for global interaction (*CW* **16 May 2012**).

The Human Toxome project stems from the groundbreaking agenda set by the US National Research Council five years ago with the publication of its report on "Toxicity Testing in the 21st Century, a Vision and Strategy" shortened to TT21C (**pages 9-10**)

Achievement of these aims would create the foundation for much faster and cheaper screening of the safety of many thousands of chemicals. It seems like a 'no brainer' and indeed research bodies in Canada, the US, Japan and China are wholeheartedly working on the concept alongside multinational companies and animal rights groups who quite rightly believe that this is the road to take to meet society's twin needs for safer chemicals without harming animals unnecessarily.

Yet in attending recent events in Europe, some key players have shown a reluctance to embrace the TT21C agenda with open arms. At one, industry representatives argued that the adoption of REACH in Europe, with its very specific data requirements, precluded them from going too far down another road. At the Brussels debate, speakers from the regulatory community raised further hurdles. They questioned how accurate the Human Toxome exercise could be and how sense could be made of the data that emerges. More than one person spoke of the "nightmare" of generating mountains of meaningless data. Another concern was how to handle conflicts between what the computational approach might tell us about the effects of a chemical and the earlier conclusions of traditional animal testing.

The point of TT21C and traditional testing approaches is to lead us to safer chemicals. If they are to make headway, TT21C initiatives also need to be guided to address the needs of regulatory toxicologists. Otherwise, as one industry speaker noted, the fear is that if a computational approach says a chemical has no effect, regulators may still ask companies to carry out further testing to prove it, so they may as well stick to the old approach.

In talking to some regulators in Europe, it's clear that they get the concept and buy in to the logic of improving the efficiency of toxicology by moving towards an "adverse outcome pathway" approach – hence the European Commission's backing for programmes such as Horizon 2020 and Seurat – but they are wary of the hyperbolic claims around the new mechanistic approaches. In other words, yes to trusting them in specific circumstances, no to wholesale replacement of traditionally derived data.

It seems what we need is evolution rather than revolution.

Mamta Patel, Editorial Director
Chemical Watch

US implements GHS in the workplace

In March the US Occupational Safety and Health Administration (Osha)* published its long awaited revision of its Hazard Communication Standard, aligning workplace rules on the classification and labelling of chemicals with those of the UN Globally Harmonized System (GHS). Michele Sullivan of consultancy MRS Associates explains the changes.

The revised standard (*CW* 20 March 2012), which is also called HCS 2012 or HazCom 2012, is based on the third revised edition of the GHS, and it aligns the Osha hazard communication standard with the UN system. Changes to the UN GHS are generally adopted on a biennial basis, but Osha has not indicated when it will address the fourth revised edition, or the fifth, which is expected in 2013. US Department of Transportation hazard communication provisions are aligned with the GHS under separate rule making.

HazCom 2012 will become effective on 25 May 2012, although it will not become mandatory until 1 June 2015 (see table). During this phase-in period, and to give industry enough time to produce labels and safety data sheets (SDS) consistent with the revised provisions, employers will be allowed to use at their own discretion the existing HCS, the revised one, or both.

HazCom 2012 maintains the framework of the current HCS and has six appendices where many of the technical requirements, based on the GHS, are to be found:

* Appendix A, health hazard criteria (mandatory);
* Appendix B, physical hazard criteria (mandatory);
* Appendix C, allocation of label elements (mandatory);
* Appendix D, safety data sheets (mandatory);
* Appendix E, definition of "trade secret" (mandatory); and
* Appendix F, guidance for hazard classifications Re: carcinogenicity (non-mandatory).

Scope and application

The HCS applies to any chemical which is known to be present in the workplace in such a manner that employees may be exposed under normal conditions of use or in a foreseeable emergency. The EU CLP Regulation, by contrast, applies to substances and mixtures "placed on the market".

The HCS has exceptions for containers labelled in accordance with other federal US labelling laws, for example on pesticides. The US Environmental Protection Agency (EPA) has not adopted the GHS for pesticides. So pesticides in production facilities will need an SDS and workplace container label based on HazCom 2012/ GHS (except when subject to labelling by the EPA under the Federal Insecticide, Fungicide and Rodenticide Act). The EPA has published a Pesticide Registration Notice (2012-1) to help pesticide registrants comply with both the Osha HazCom 2012 and the EPA requirements.

Timelines for HCS2012 implementation

Effective completion date	Requirement(s)	Who
1 December 2013	Train employees on new label elements and SDS format	Employers
1 June 2015 1 December 2015	Compliance with all modified provisions of the final rule, except: distributors shall not ship containers labelled by chemical manufacturer or importer unless it is a GHS label	Chemical manufacturers, importers, distributors and employers
1 June 2016	Update alternative workplace labelling and hazard communication programme as necessary, and provide additional employee training for newly identified physical or health hazards. Includes the substance specific standard changes	Employers
Transition period to the effective completion dates noted above	May comply with HazCom 2012 (the final standard), or the current standard, or both	Chemical manufacturers, importers, distributors, and employers

Definitions

To align provisions with the GHS, many changes were needed to the Osha HCS definitions. It should be noted that in HazCom 2012 the term "chemical" is defined as any substance, or mixture of substances. HazCom 2012 also includes several Osha defined hazards that are not in the GHS, such as pyrophoric gas, simple asphyxiant and combustible dust.

There are several key definitions to consider in order to comply with HazCom 2012. The term "hazardous chemical" means any chemical which is classified as a physical hazard (Appendix B) or a health hazard (Appendix A), a simple asphyxiant, combustible dust, pyrophoric gas, or as a "hazard not otherwise classified" (HNOC). This is an adverse effect that goes beyond the GHS hazards and does not meet the criteria for the physical and health hazards in Appendices A and B. The reason for having the HNOC definition is to prevent HazCom 2012 from being less protective than the current HCS by picking up any hazards that are within the current HCS, but are outside the GHS. Such hazards do not have to be addressed on labels, but do have to be addressed on SDSs. The HNOC concept is found in several other systems globally where the competent authority retained non-GHS information when the GHS was implemented (for example, EU H statements, or use of the terms persistent, bioaccumulative and toxic, or very persistent and very bioaccumulative).

Hazard classification

The goal of the GHS is worldwide

**Chemical Watch's house style is to normally use all caps only for acronyms pronounced as individual letters*

harmonisation and the adoption of the same hazard classes and categories globally within each sector is encouraged. GHS hazards for the workplace sector are to some degree aligned globally. The unharmonised exceptions are often to maintain the current level of protection. In HazCom 2012 Osha sought to maintain or enhance the protection provided by the current HCS.

* **Physical hazards:** HazCom 2012 adopts all GHS revision 3 physical hazard classes and categories. To maintain protection Osha included GHS flammable liquid category 4.
* **Health hazards:** HazCom 2012 adopts all GHS revision 3 health hazard classes but not the lower level hazard categories. It does not include acute toxicity category 5, skin irritant category 3 and aspiration category 2, but does include eye irritant category 2B.

Osha HazCom 2012 adopted acute toxicity categories 1-4. The intention of the GHS Purple Book was to have one global acute toxicity estimate (ATE) calculation for mixtures. Osha included text for the acute toxicity mixture calculation to ensure that acute toxicity category 5 ingredients, which would not be classified under HCS2012, are included in the ATE mixture calculation.

Under HazCom 2012, the Report on Carcinogens of the US National Toxicology Program (NTP), the International Agency for Research on Cancer (IARC) monographs and the Osha carcinogen standards may be regarded as establishing that a substance is a carcinogen or potential carcinogen for hazard communication purposes in lieu of applying the GHS weight of evidence criteria. Osha provides an approximate equivalence or translation for these carcinogen classification schemes. HazCom 2012 also requires that if a substance is not classified as a carcinogen and there exists any positive studies performed according to good scientific principles with statistically significant results, then this must be noted on the SDS.

Osha generally adopted the lower, more protective mixture cut-off values/ concentration limits so that workers see the same information on labels and SDSs and so that workers are appropriately protected.

* **Osha Defined Hazards:**

HazCom 2012 includes several Osha defined hazards: pyrophoric gas, simple asphyxiant and combustible dust. These hazards have been assigned label elements.

Since Osha does not have the regulatory authority to address environmental issues, HazCom 2012 does not include the GHS criteria for environmental hazards.

Labels on shipped containers

A major change for US hazard communication is the switch from performance oriented labels on shipped containers to the GHS specified label elements. Per HazCom 2012, labels must be updated within six months of becoming aware of new and significant information regarding hazards. Pictograms must have a red frame, with a black symbol on a white background, for all shipped containers of hazardous chemicals regardless of destination. HazCom 2012 prohibits blank pictogram frames on the label. The standard does not specify specific size dimensions for either pictograms or labels, nor does it require hazardous ingredients to be disclosed on the label. There is no small package exemption but Osha will continue its practical accommodation approach. Labels must be in English. The signal word, hazard statement(s) and pictogram(s) must be located together on the label.

Safety data sheets

HazCom 2012 uses the term safety data sheet (SDS) instead of material safety data sheet (MSDS). It presents all 16 GHS SDS sections for consistency and harmonisation. Osha will not enforce information requirements in sections 12 through 15, as these areas are not under its jurisdiction; instead it encourages their inclusion on SDSs, so that the SDS is compatible with international GHS requirements.

HazCom 2012 Appendix D indicates that a subheading "within a section" needs to be marked when no relevant information is available. Osha does not consider the SDS subheading letters mandatory but the information in each subheading is required to be included. Hazards not otherwise classified and a statement that X% of the mixture consists of ingredient(s) of unknown acute toxicity are addressed in SDS section 2.

For mixtures, the chemical name and concentration of all ingredients which are classified as health hazards are required unless a trade secret claim can be supported.

SDS section 8 must include the Osha permissible exposure limits (PEL), American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLVs), and any other exposure limits used or recommended. In section 11, Osha has also maintained the requirement to note whether the hazardous chemical is listed in the NTP Report on Carcinogens or has been found to be a potential carcinogen in the IARC monographs or by Osha.

Any significant new information regarding the hazards of a chemical, or ways to protect against the hazards must be added to the SDS within three months. The SDS must be in English.

Trade secrets

Where a trade secret claim can be supported, the specific chemical identity, including the chemical name, other specific identification of a hazardous chemical, or the exact percentage of the substance in a mixture may be withheld from the SDS. When a trade secret claim is made for an exact percentage, a concentration range may be provided. However in this case, section three must indicate that a trade secret claim is being made and information has been withheld.

Other Osha standards

Osha also modified its other standards that contain hazard classification and communication provisions so that they will be internally consistent and aligned with the GHS modifications. These include the substance specific standards, and standards for flammable and combustible liquids, and process safety management.

GHS classification lists

HazCom 2012 does not have a list of chemicals classified according to the GHS criteria. It is unlikely that Osha will develop a GHS classification database but the issue of GHS classification lists is being discussed by the UN Subcommittee of Experts on the GHS (**CW Briefing, February 2012**). Osha is leading this effort and helping to form a consensus position in the Subcommittee on options to address the global GHS classification list issue.

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

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Ecetoc unveils version three of risk assessment tool

Companies gearing up to register substances for the 2013 REACH deadline should find their life made a little easier by changes to the Targeted Risk Assessment (TRA) tool, according to the European Centre for Ecotoxicology and Toxicology of Chemicals (Ecetoc), which developed and updated the model. Philippa Jones reports from a recent Ecetoc workshop.

Ecetoc's TRA tool has been a major contribution to the efficient risk assessment of substances under REACH. It was first launched in 2003, significantly revised in 2009, and at the beginning of May, a third version was introduced to users at a workshop in Brussels. "TRAv3 incorporates the experiences gained by users during the first registration phase," Chris Money, industrial hygiene adviser for Europe at ExxonMobil Chemical and a member of Ecetoc's scientific committee, told delegates. The updated tool "is not a radical departure, but rather a natural progression from TRAv2". It offers "increased flexibility and accuracy, gets rid of certain anomalies, and introduces certain process efficiencies".

Getting acquainted

The latest version has arrived well in time for 2013 registration activities, said Mr Money, but users should have a little practice to make sure they are fully happy with the new set-up before tackling risk assessments for the next deadline. It requires a little more thought than TRAv2, he said, but is supported by a new user guide, a set of frequently asked questions and an updated technical report. It will also be incorporated into the updated version of ECHA's Chesar tool (see box on next page) for generating exposure scenarios and preparing chemical safety reports.

Version 3 of the TRA is available in two forms: as an integrated exposure/risk assessment tool covering worker, consumer and environmental exposures; and as a stand alone consumer exposure estimation tool.

Dow's Dook Noij explained the changes made to the worker exposure assessments in TRAv3. The main difference is that they are "now fully integrated into the tool," he said, acknowledging that in previous versions "there was an integrated and a stand alone tool" that could be used to carry out these assessments. "We decided to ensure consistency as it was difficult for users to check whether the two tools were fully identical in the predictions generated," he said.

In general, said Mr Noij, updates to the worker exposure assessments were based on comments and requests for changes or new features made by users after the 2010 registration deadline. These were measured against four principles. "First, we did not want to move too far from version two of the tool for continuity; second, any changes needed a scientific basis; third, we had to keep in mind that we were talking about a tier-one tool that is conservative in nature; four, anything we implemented had to be universally applicable."

Noij: worker elements integrated

Frattini: TRAv3 to be plugged into Chesar

Consequently, he said, "we got rid of a number of anomalies". There is now consistency in the exposure predictions across process categories (Procs) for inhalation and dermal exposure. Also, some of the functionalities, such as inhalatory exposure, have been extended so that risk assessments for short-term exposure can be predicted and general ventilation can be used as a modifying factor. Extended functionality for dermal exposure has also been introduced so that users can differentiate between industrial and professional settings and include modifying factors for the duration of exposure, the concentration of a substance and the use of personal protection such as gloves.

Ecetoc has also opted to allow the use of gloves as a modifying factor. "This was used in almost all the registrations from 2010," said Mr Noij, "and so we decided to build this into the tool and ensure that it is being calculated in a conservative way." Unlike inhalatory exposure, the effect of duration of a work activity on dermal exposure is difficult to predict, he said, but "for certain types of substance, such as higher volatile liquids and low dusty solids, a conservative relation between duration and dermal exposure can now be applied."

A pragmatic approach

The worker exposure part of the tool has improved transparency concerning predictions, said Mr Noij. Users had highlighted the need for greater transparency on the application of ventilation in risk assessments and so TRAv3 uses an approach in line with tools such as the UK Health and Safety Executive's tool to for the assessment of repetitive tasks (ART). In this area, Ecetoc has taken such a "pragmatic and conservative approach" that its tool is "even slightly more conservative" than others used by REACH registrants. Mr Noij also highlighted the "addition of a look-up table for the prediction of exposure to liquids with very low vapour pressure" and the fact the tool is now capable of "providing messages to make the user aware of the limitations of an exposure prediction".

Procter & Gamble's Carlos Rodriguez, another member of Ecetoc's scientific committee, detailed the changes made to the consumer exposure estimation tool in TRAv3. It remains essentially "the same type of tool as v2", he said, in that it makes "tier one calculations, using simple models and limited data, is very conservative, very easy to use, very transparent and only needs a little data". But it has "improved considerably" he told the workshop, especially in terms of "flexibility" as the previous version offered "very little chance for the individual user to make any changes". In version three, he said, "users can choose to enter many of their own data and can justify their values and thereby improve the accuracy and relevance of the calculation for the specific user."

Calculating values

The consumer exposure tool has also undergone a number of other refinements, "mainly on the inhalation side", said Mr Rodriguez. It now "takes into account

ventilation rates, which was not the case for TRAv2," although these have been "very conservatively introduced compared to those on the workers side". Another change is the way combined total risk characterisation ratios (RCR) values are calculated. In the TRAv2 tool, this was done by dividing the total exposure across all routes over a hypothetical "worst case reference value", whereas in version three, they are calculated by summing up individual RCR values from each exposure route. This change was made to fully match the methodology described in the REACH technical guidance documents.

Version three also offers users the capability to add specific product or article sub-categories. This means, for example, "if you know that oral exposure is not relevant, you do not have to calculate it," said Mr Rodriguez, and the feature is a "very powerful weapon to decrease any over-exaggeration in exposure estimations". Saturated vapour concentration has been set at the maximum possible inhalation exposure value considered for non-aerosols, whereas version two has no upper limit for inhalation exposure estimations. Likewise, for inhalation exposure, TRAv3 uses a default value of 0.6 as the number of air changes per hour. "This is still very conservative but better than before when it was not taken into consideration," stated Mr Rodriguez.

Greater flexibility

Explaining the changes made to the environmental exposure assessments, Johannes Tolls, environment safety assessment director at Henkel, said amendments were "mainly in the emissions estimation part" of the tool. "There have generally not been many changes in assessment science since we launched the model, but we have made some minor practical changes to the tool that will hardly be noticed by the user". These include, "improvements to the way risk management measures are used, making them specific for each emissions pathway". In terms of the actual emission assessment, Mr Tolls said there is now "more flexibility", and drew attention to the fact that the tool is aligned with Chesar.

Chesar 2.1, due for relase in early autumn, will include Ecetoc's exposure estimation tool for consumers

– Stefano Frattini ECHA

ECHA's Stefano Frattini reiterated the agency's commitment to release Chesar 2 at the end of June, and said the TRAv3 workers exposure tool will be plugged into it. Chesar 2.1, due for release in early autumn will include Ecetoc's exposure estimation tool for consumers. The third and final part of the ECHA tool, Chesar 2.2, should appear at the end of this year or the beginning of 2013 and add the generation of exposure scenarios for communication to its functions. Despite this staggered release, said Mr Frattini, "the application will remain stable" and each stage will "only add new functionalities".

Regarding the plugging of the TRAv3 consumer tool into Chesar, Mr Frattini said an exchange on the issue had already been initiated between ECHA and Ecetoc. This discussion should "become tighter over the next two months" and a final implementing brief should be ready at the end of June, said Mr Frattini, "after which, testing by ECHA will begin." However, "the TRAv3 consumer tool in Chesar will not include user definitions of new sub-categories," he said. This will only happen when the specific consumer exposure determinants (Sced) solution – the consumer equivalent of the specific environmental release categories (Spercs) that were widely used for REACH registration dossiers submitted for the 2010 deadline – "is sufficiently mature".

Timetable targets

This could take some time since, as Henkel's Mr Tolls explained, Sceds are being developed in a Downstream Users of Chemicals Coordination Group (Ducc) led project that only began at the start of 2012. "Currently Ducc is discussing with Ecotec the concept and the details for the development of Sceds," he said. "Ducc is striving to make sector conclusions and other deliverables available to Ecetoc by the summer. The aim is to make Sceds available for registrants for the 2013 deadline".

Companies involved in this process want Sceds to be able to "ensure consistency in the level of detail for refined consumer assessments," said Mr Tolls. They are being developed for a range of consumer products including washing, cleaning and maintenance products by the International Association for Soaps, Detergents and Maintenance Products (Aise), for hydrocarbons and products containing solvents by the oil industry trade association Concawe, for adhesives and sealants by the Association of European Adhesives and Sealants Manufacturers (Feica), for paints and coatings by the European Council of the Paint, Printing Ink and Artists' Colours Industry (Cepe), and for construction products by the European Federation for Construction Chemicals (EFCC).

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Assessing exposure

Targeted Risk Assessment (TRA)
Launched by Ecetoc in 2004, the TRA includes three separate models for estimating exposures to workers, consumers and the environment. Significantly revised in 2009, the recently launched third version is available in two forms: as an integrated exposure/risk assessment tool covering worker, consumer and environmental exposures; and as a stand alone consumer exposure estimation tool.

Chesar
Released by ECHA in 2010, this tool allows users to create chemical safety reports and exposure scenarios for extended safety data sheets. Chesar embedded two existing modelling tools, the TRA and the European Union System for the Evaluation of Substances (Euses) to carry out tier-one assessments. Chesar 2 will be launched at the end of June, Chesar 2.1 in early autumn and Chesar 2.2 at the end of 2012/ beginning of 2013.

Exposure Scenario Communication (ESCom)
The European Chemical Industry Council (Cefic) and the Downstream Users of Chemicals Coordination Group (Ducc) launched ESCom in May 2011 to facilitate the transfer of an exposure scenario between a supplier and the next player in the supply chain. ESCom uses the European Phrase Catalogue (Euphrac) to standardise information and will be compatible with Chesar 2.

CHEMICALWATCH Brussels workshop

13 June 2012, Brussels
REACH & CLP Enforcement Q&A workshop

Agenda
* 09.00 - 09.30 Registration, coffee and croissants
* 09.30 - 09.40 General welcome and introductions Mamta Patel, Editorial Director Chemical Watch
* 09.40 - 09.55 KEYNOTE: Latest Developments Towards Harmonised REACH and CLP Enforcement
* 09.55 - 10.15 How Companies Can Best Deal With Enforcement Authorities
* 10.15 - 10.30 Questions and Answers
* 10.30 - 11.00 Networking, refreshments
* 11.00 - 12.45 Panel discussion with Q&A
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TT21C: what does it take to become a new paradigm?

The US initiative TT21C has been receiving wide publicity. But what are its challenges and what lies ahead for this new approach heralded as having the potential to revolutionise toxicological assessment of chemicals? Sean Milmo reports.

PHOTO: courtesy of the EU Joint Research Centre. © EU 2010

The vision of TT21C: from in vivo tests to high-throughput in vitro tests.

Five years ago a toxicity testing committee set up by the US National Research Council (NRC) issued a report which proposed radical changes to the way risk assessments of chemicals are carried out. The committee, chaired by professor Daniel Krewski, director of the McLaughlin centre for population health risk assessment at Ottawa University, suggested an approach to safety assessment based on recent advances in molecular biology and biotechnology. Instead of relying on the 50 to 60 year old, and often inaccurate, system of conducting in vivo tests on laboratory animals, such as rats and mice, toxicological evaluation would be centred on in vitro studies of cells, cellular components and tissues. The objective would be to use these studies to track perturbations in the signalling pathways of cells in response to chemical exposures, and to link these disruptions to adverse effects on human health.

The ideas of the NRC committee's report, "Toxicity testing in the 21st century: a vision and a strategy", were given the label Tox21 by the US Environmental Protection Agency (EPA), which commissioned it, and TT21C by other organisations, and have been heralded as the beginning of a scientific revolution which will cause a paradigm shift in toxicology.

Winning support

In the history of science, new ideas tend to take over only when they have been acknowledged by the scientific community as having value. They become the new paradigm once enough evidence has been collected to show they have more validity than the older ones. The concepts behind TT21C have received widespread coverage in numerous presentations at conferences and in papers in scientific journals. They have received support from toxicologists in regulatory agencies, academia and industry and among NGOs and politicians.

"The interest has grown as the ideas have become a bit more mainstream and better communicated, and the concepts underlying the TT21C report better articulated and refined," says Mel Andersen, a prominent member of the NRC committee and associate director of the Institute for chemical safety sciences at the Hamner Institutes for Health Sciences. "Perhaps, the groups with the keenest interest in adoption are NGOs and consumer groups who simply want the backlog of untested materials evaluated in whatever manner possible."

Bridging the gaps

However the task of demonstrating that TT21C not only works, but is more effective and accurate than existing testing methods, could prove much harder. This is mainly because of the large gaps between the science underpinning the conventional and new methodologies. TT21C is about biological predictions, whereas existing techniques based on animal tests are about predicting disease. "The problem is that the science [behind TT21C] is only emerging," says professor Thomas Hartung of the Bloomberg school of public health at John Hopkins University in Baltimore, and director of the Centre for Alternatives to Animal Testing (Caat) in Europe.

If TT21C requires legislation in order to establish itself firmly as the new paradigm, particularly in North America and Europe, the challenge could be even more difficult. "If legislative changes have to be made, there will have to be a compelling case backing Tox21," says John Fowle, a retired EPA scientist who has recently written a paper on the use of Tox21 tools in the assessment of endocrine disrupters. "In the US, society will have to be convinced about it. Congress and the president will have to believe in it as well."

There is a divergence of opinion among TT21C supporters. Some think the initial aim, at least, should be to help prioritise chemicals for in vivo and other existing testing methods, while also providing data for weight of evidence or integrated testing assessments based on information from a range of sources. "As a prioritisation tool or component within an integrated testing system there will be no legal hurdles and a lot of flexibility in the way it is used," says Mr Fowle.

Others want to press on with achieving the ultimate objective of TT21C, replacing animal testing. "The vision of the TT21C report is that all testing should be done using in vitro systems," says Mr Andersen.

The less expensive option

TT21C methods are based on the high throughput assays derived from screening systems first developed by the pharmaceutical sector for rapid scrutiny of possible chemicals for new drugs. The programme is less expensive because it uses human cells in vitro, with the potential to be able to measure low-dose responses more accurately than in vivo techniques.

The NRC committee said a systems approach should be adopted to characterise toxicity pathways – which it defined as "cellular response pathways that, when sufficiently perturbed, are expected to result in adverse health effects". This approach would use the large amounts of molecular and cellular data generated by the high throughput processes to pinpoint toxicant-induced modes of action.

The cellular effects triggered by a chemical stem from its interaction with molecular circuits in the cell and subsequent changes in the behaviour of these circuits. These changes are reflected in the different shapes of dose-response curves with respect to various endpoints. "Identification and characterisation of these intracellular circuits associated with toxicity are central to the task of defining a new testing paradigm and have been recognised as a long-term goal by the NAS report," says a joint EPA/Hamner Institutes study.

Crucial advances

In overcoming initial scepticism, TT21C had possessed the advantage of being seen as at least a feasible solution to the problem of how to deal with the massive backlog of tens of thousands of chemicals on which there is little or no safety data. And its concepts are not based on a completely new science. Both the expertise and technologies are available to push it forward. "Advances in in vitro testing, measurement technologies such as the 'omics and image analysis, high throughput screening and others over the past decade have been crucial to its advance," says professor Hartung.

The US has been setting the pace in testing its concepts and starting the process of making them a central platform for risk assessment. The EPA uses its Toxicity Forecaster (ToxCast) programme, which in a first phase applied 500 tests to around 300 chemicals, and in its second phase is applying more tests to over 1,000 chemicals, in order to characterise the biological activity of substances across multiple cellular pathways. These methods of prioritisation have also been extended to the EPA's Endocrine Disrupter Screening Programme (EDSP) in which 2,000 chemicals are being evaluated in around 80 endocrine-related high throughput screening (HTS) assays.

White House pressure

The EPA is under pressure to make much more use of in silico models and molecular-based in vitro HTS systems. The Obama administration's 2012 budget tells the agency to make the EDSP "more efficiently use computational toxicology methods and high throughput screens that will allow the agency to more quickly and cost effectively assess potential chemical toxicity."

Two other major TT21C research projects in the US are the Hamner Institutes' case studies of known pathways, and the Human Toxome Project, which is supported by a grant from the National Institutes of Health (NIH) and is mapping pathways of toxicity.

Europe has been much less active than the US in investigating the potential of TT21C – despite the long opposition among some groups to animal testing. "In Europe some people are taking up the vocabulary of [TT21C] but are not necessarily grasping the new approach," says Professor Hartung. "[TT21C] is not (as some think) an alternative method under a new name. However, interest in Europe is increasing." The seventh amended version of the EU's cosmetics Directive, which bans the marketing of cosmetics and cosmetic ingredients tested on animals from next year, has aroused interest in biological mechanisms in areas like genotoxicity and carcinogenicity so that in vitro tests do not need confirmatory animal studies.

Integrated approaches

The OECD, which publishes harmonised test guidelines, has started work on adverse outcome pathways (AOPs), linking cellular perturbations with adverse effects. By the end of this year it hopes to finalise an AOP on skin sensitisation and provide at least one AOP as a basis for quantitative structure activity relationships (Qsars). By 2016 the OECD hopes to introduce more AOPs into its Qsar Toolbox and to run a pilot for the development of integrated approaches for the testing and assessment of a number of hazard endpoints based on AOPs.

The EPA, other US agencies and the OECD seem to regard TT21C primarily as a means for the prioritisation of chemicals for testing and for providing data for integrated assessment systems. And ECHA allows data to be applied in weight of evidence methods for REACH risk assessments. As a result, TT21C assays tend to be validated for specific purposes within integrated systems, rather than for much wider applications. Validation needs to be "more case by case, to suit a certain purpose," says professor Hartung. "The variety of technologies we deal with make it necessary to stay very flexible."

Poor performances

However, other TT21C supporters want to create assays which are more formalised and which would not have to be validated, by demonstrating their ability to predict the results of in vivo animal tests. A team of researchers headed by Russell Thomas at the Hamner Institutes has found in a study, yet to be published, of over 600 in vitro assays used in the Phase 1 screening of the ToxCast programme, that they performed poorly in predicting the results of in vivo tests.

"My belief is that asking the question about predicting high-dose toxicity in animal tests is a bit of a red herring," says Mr Andersen. "We want to develop assays to insure regions of safety where effects do not occur and this redirection requires different analysis and quite different assays than those incorporated into the Phase I ToxCast programme."

Mr Andersen and other TT21C backers believe that by sticking to the clear objective of establishing a different paradigm, it could take over in a surprisingly short time, especially as the public and NGOs want data on multiple chemicals. "My view is that the genie of in vitro ToxCast-type testing is out of the bottle. Whether we want to move towards in vitro test methods or not is no longer the question."

This perspective seems ultimately to be similar to that of the EPA. With endocrine disrupters, it has set itself the intermediate goal of replacing current validated in vitro screening assays with validated high throughput assays in two to five years. But its long-term objective is to be able to consider after at least five years the full replacement of in vivo screening assays with validated in vitro high throughput assays.

Some scientists have said 20 years of research and development work would be needed before TT21C becomes the new paradigm, but others feel it may not take nearly as long as that.

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GLP: still vital but not a panacea

Criticism of Good Laboratory Practices (GLP) is miguided, say Jane Staveley and Wendy Hillwalker of Exponent. Instead the debate should be about the quality of a particular study, whether it was conducted under GLP or not.

Regulatory frameworks developed initially in North America and Europe, and which are being increasingly adopted by other geographies, rely on the use of standardised testing guidelines and Good Laboratory Practices (GLP) to generate reliable and valid data to protect human health and the environment. In recent years, these same regulatory frameworks have emphasised economy in use of resources for testing and mandate the use of existing data whenever possible, often in a weight of evidence (WoE) approach. This may include data generated from non-GLP, non-standard tests which have been published in peer-reviewed journals.

However, there is growing disenchantment among researchers, predominantly representing academic institutions, about the selection of critical data for risk assessments. They claim regulatory agencies are giving special prominence to industry-funded GLP studies over non-GLP studies conducted with government funding. A recent article in *Chemical Watch* (**CW Briefing, March 2012**) discussed this conflict and the effects it could have on the global adoption of GLP in chemical regulatory frameworks. We believe that the concerns raised about GLP studies are misidentified, and that the argument should really be about the suitability of the study design, transparency and access to raw data, and development of criteria for evaluation of all information that may be used in a WoE assessment.

Global acceptance of GLP and testing guidelines

Because regulatory risk assessment programmes rely on studies conducted according to test guidelines and under GLP, it is common (but incorrect) to equate the two. GLP is a regulatory mandate developed in the late 1970s by the US Food and Drug Administration (FDA) in response to misconduct by private research companies. It was later adopted by the US Environmental Protection Agency (EPA), Health Canada and the UK. The OECD included GLP in the framework for mutual acceptance of data (MAD) for the generation of data related to the safety of industrial chemical substances that could be shared between countries. The MAD harmonised testing requirements have since been adopted by Argentina, Brazil and India. Intergovernmental agencies, such as the American Society for Testing and Materials (ASTM), offer guidelines for incorporating GLP in laboratories, while the International Standards Organization (ISO) has developed an accreditation programme that parallels, but does not necessarily comply, with GLP.

The concerns raised about GLP studies are misidentified… the argument should really be about suitability of study design, transparency and access to raw data…

GLP encompasses many of the basic elements of conducting a sound scientific investigation. These include the training and qualifications of personnel, maintenance and calibration of equipment, handling of test and reference substances, written standard operating procedures, inspection by an independent quality assurance unit, detailed record keeping to allow reconstruction of the experiment, and archiving of all data. GLP allows for study transparency and access to raw data but it does not define the scientific question or the most appropriate methodology to answer it.

Significance of standardised test guidelines

The design and conduct of the study is critical if the data are to be appropriate for use in risk assessments. To that end, standardised test guidelines have been developed by various organisations, both governmental and independent. A test guideline describes the "methods and materials" for the experiment while GLP describes how the data will be generated and handled. For example, the test guideline specifies determination of weight while GLP assures that the balance used to make the measurement is calibrated.

There is significant value to the development and use of standardised test guidelines. These guidelines identify the study design to derive critical endpoints; for example specifying key organisms and developmental stages, exposure conditions, and the appropriate statistical approach. This standardisation minimises differences between testing laboratories and tests with different substances, allowing for comparative risk assessments. The evaluation of data for chemical regulation would truly be a nightmare in the absence of standardised test guidelines.

Test guidelines usually undergo thorough review and inter-laboratory validation and are subject to periodic updating as the state of the science advances. Legitimate concerns arise when investigators have to follow test guidelines that do not reflect best practices or have not been adequately validated. It is thus very important that all stakeholders involved in the development and use of test guidelines extend every effort to validate and update those guidelines. It is also important to recognise that inadequacy in a test guideline does not reflect on the application and adequacy of the system of GLP.

Non-standardised, Non-GLP studies

The debate over regulatory reliance on GLP over non-GLP studies is not only mislabelled, it is confounded by the dichotomy of the circumstances in which each type of study is typically performed.

Studies following standardised test guidelines are usually done under GLP in industry or contract laboratories and are funded by industry. The purpose of such studies is usually to fulfill a regulatory requirement for the approval of the use of the test substance, and the study design and endpoints have usually been validated through inter-laboratory testing. Adherence to GLP provides the documentation which allows the study to be independently reviewed by a third party. Few of these studies are published, as there are often issues of data ownership and compensation that preclude publication. In contrast, studies conducted in academic and government laboratories may follow a standard guideline but are much more likely to be asking new questions, attempting new techniques, and developing new endpoints. Few of these facilities operate under GLP, which adds an additional cost burden, however some do. The goal of these research efforts is publication, the constraints of which usually preclude the inclusion of sufficient details (let alone raw data) to allow an independent review at the level possible for a GLP study.

In summary, the objectives of each type of study are inherently different. Academic or government research institutions are engaged in ground-breaking research, while industry is conducting regulatory-driven studies to understand a chemical in the context of a specific regulatory paradigm. Although the latter is typically done using guideline studies under GLP, additional investigations may be done outside the realm of existing guidelines yet still under GLP.

The path forward

A WoE approach is increasingly being used by regulatory agencies to select appropriate data for purposes of assessment related to the protection of human health and the environment. The real issue of selecting critical endpoints for WoE decision making is about the quality of a particular study, not whether the study was conducted under GLP. GLP does not guarantee reliability or validity of study results, although it provides a sound framework for doing so. Reliability refers to the extent to which results are consistent over time and are an accurate representation of the total population under study, ie reproducible. Validity refers to whether the research measures what it was intended to measure, and valid findings are considered to be true. Each study, whether conducted under GLP or not, should be evaluated and weighed according to its scientific merit, ie are the data generated of high quality, valid and reliable?

The problem with WoE today is the uncertainty in the development of criteria for evaluating data quality in a way that goes beyond GLP compliance to allow use of "other scientifically relevant information" in risk assessment. Data generated from studies conducted according to an up to date, validated test guideline under GLP, are, and should be, considered the "gold standard" for regulatory risk assessment. But data generated by studies published in the peer reviewed literature have the potential to be an important element in the WoE approach. Researchers conducting non-GLP studies tout the scientific merit and validity of new endpoints and techniques that reach beyond the scope of cumbersome and out of date validated tests for identifying emerging concerns. However, data generated by non-GLP studies pose a greater challenge for acceptance by the regulatory community than data generated by GLP studies (either guideline or non-guideline studies). Researchers cite the peer review process as a valuable quality assurance tool for increasing the validity and reliability of non-GLP data. But the peer review process alone is insufficient for this purpose as it does not typically incorporate transparency of the study design or availability of raw data, which facilitates the reviewer's ability to come to a fully independent conclusion. There is progress towards transparency in the peer review process as more journals are allowing for supplemental material to be included for access on the internet.

Focusing on the dichotomy between industry-funded GLP studies versus government-funded non-GLP studies muddies the issue. GLP does not need to be "fixed"

Contract laboratories are an often under utilised partner in this discussion. They are staffed with experienced scientists and have significant institutional knowledge of the strengths (and weaknesses) of the test guidelines they are required to follow. They are independent of the sponsor, and their compliance with GLP provides up to 100% quality control checks by an independent quality assurance unit of the facility operations, protocol and SOP adherence, and data handling. Since the implementation of GLP, there is a long track record of consistent and high quality data resulting from these labs. Some countries certify contract labs; although this is not done in the US, labs are periodically subjected to an external audit by government agencies, such as the EPA, as well as the study sponsors to ensure GLP compliance.

In the long run, focusing on the dichotomy between industry-funded GLP studies versus government-funded non-GLP studies muddies the issue. GLP does not need to be "fixed"; emphasis on study design needs to be brought to the forefront for both GLP and non-GLP studies. It is likely that agreement can be reached on the following steps to improve the reliability and validity of all data used in regulatory risk assessments: timely revision of test guidelines to reflect scientific advances and development of new methods, with input from all qualified stakeholders; increased transparency of published studies, including access to raw data, to increase the viability of non-traditional methods and endpoints; and development of criteria for use in evaluation of all studies to be used in a WoE approach. The use of GLP, or at the very least, adherence to the spirit of GLP, is of continuing importance in generating critical data for risk assessment purposes, and "guideline" and "research" studies can co-exist in current and future regulatory decision-making paradigms.

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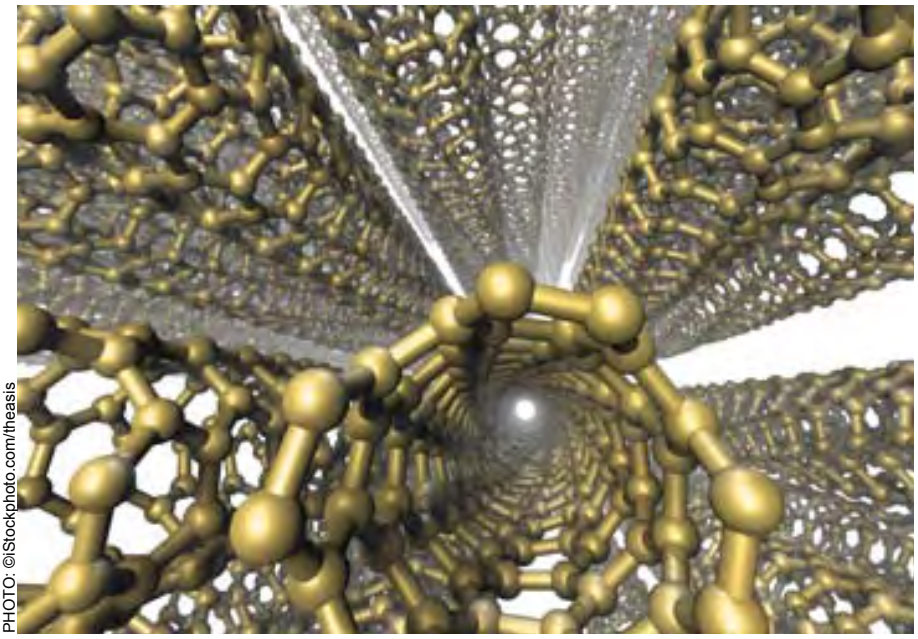
Jane Staveley (right) is a senior managing scientist and Wendy Hillwalker (below) is a senior scientist with Exponent, Inc, a consultancy providing scientific and regulatory expertise for the management of issues related to global stewardship of industrial chemicals, pesticides, personal care products, foods, and drugs.

European research funding: spotlight on nanosafety

Scientists and stakeholders recently met at an EU symposium in Spain to discuss safety issues and legislative challenges in light of current research findings in nanotoxicology. Laura Greenhalgh reports.

Over the last six years, the European Commission has invested €106m researching the safety of nanomaterials under its Seventh Framework Programme for Research and Technological Development (FP7). In recognition of the increasing use of nanomaterials across the market, over 25 collaborative projects have been launched under FP7 to address aspects including toxicology, exposure and risk assessment. In May 2012, the coordinators of four projects, Hinamox, Nanopolytox, Nephh and Enpra, and the European Commission's Joint Research Centre (JRC), hosted a symposium in San Sebastian where stakeholders discussed the latest research findings and challenges for the field ahead.



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Coating nanoparticles can reduce their immunotoxicity, researchers in Spain have found

Toxicity and hazard assessment

A project on the health impact of engineered metal and metal oxide nanoparticles (**Hinamox**), coordinated by CIC biomaGune in San Sebastian, was launched in 2009 to investigate the health risk of metal and metal oxide nanoparticles in consumer products, including titanium dioxide and zinc oxide in sunscreen, and copper oxide nanoparticles found in anti-fouling paints. The project is focused on monitoring nanoparticles in cells and whole animals, using novel bioimaging techniques to characterise particles and determine their biodistribution and fate in biological systems. This work includes the use of ion beam microscopy (IBM) and confocal raman microspectroscopy (CRM) to study cerium oxide nanoparticles in cells, and positron emission tomography (PET) to assess the inflammatory response to aluminium and zinc nanoparticles in mice.

The project also investigates the interaction of metal oxides with the immune system, and recent research by Africa González-Fernández from the Universidad de Vigo in Spain has found that coating particles can reduce their immunotoxicity. "For example, coating silicon nanoparticles with polyethylenglicol [PEG] reduces their toxicity to zero", she said. "In future it may also be possible to decorate nanomaterials with pathogen proteins to make them invisible to the immune system."

Life cycle assessment

Nanopolytox, (**Nanopolytox**) began in 2010 to investigate the environmental and health impacts of polymer nanocomposites. Coordinated at the Leitat Technological Centre in Barcelona, it aims to assess the toxicology of composite materials containing multi-walled carbon nanotubes (MWCNTs), three types of nanoclays and zinc, silicon and titanium metal oxide nanoparticles throughout their entire life cycle.

Over the last six years, the European Commission has invested €106m researching the safety of nanomaterials

"Nanoparticles used in composites in industry are commonly modified by the addition of functionalisation groups to their surface to enhance their embedding potential and convey other desired properties. In addition, transformation and ageing processes may also occur during their use and end of life phases," said Leitat researcher Gemma Janer. Therefore, they tested the effects of functionalisation and accelerated ageing on nanoparticle toxicity by measuring their effects on cell viability in vitro. "We showed that surface modifications can modulate cell toxicity and, in some cases, cell internalisation of nanomaterials," said Ms Janer. "The accelerated ageing process also causes some physiochemical changes, but in general, had little impact on cell toxicity." Nanopolytox ultimately aims to use these findings to develop predictive models on the biological and environmental fate of substances, and incorporate these into a theoretical life cycle analysis (LCA) to assess options for recycling and reusing polymer nanocomposites.

An LCA approach has also been used by the Nephh (**Nephh**) project to analyse the environmental and health risks of 12

silicon-based polymer nanocomposites used in the construction, automotive and aerospace industries and household usage. Huijun Zhu from Cranfield University in the UK described her work to determine the release of airborne nanoparticles under drilling, which found that polyamide composites reinforced with silica nanofiller release more nanoparticles than the equivalent polypropylene composite, generating up to 500,000 nanoparticles per cubic centimeter of air, but that the dust has low toxicity potential on human lung epithelial cells in vitro. Under collaboration with Jérôme Rose from the European Centre for Research and Teaching in Environmental Geosciences (Cerege) in France, the researchers are also examining the release of nanoparticles following impact between automotive vehicles using simulated crash tests. The Nephh project ends in August, and the results will be integrated into guides on procedures to ensure safe occupational use of nanomaterials, and the management of nanomaterial R&D waste by research entities and companies.

Focus on exposure

Progress under these projects largely reflects the wider state of nanosafety research under FP7. "Materials characterisation is well advanced for most common nanomaterials, and the hazards of these substances are mostly understood," said Georgios Katalagarianakis from the Commission's research and innovation directorate. However, significant progress is still needed in several other areas of research essential for risk assessment. "Research in ecotoxicity has suffered some delay," he said, "and while exposure monitoring is advancing fast to cover lost ground, there are still issues such as unclear metrics to quantify exposure." Faster progress, he said, is also needed for risk evaluation and risk communication.

The Enpra (Enpra) project was launched in October 2009 to develop a new approach for the health risk assessment of engineered nanoparticles that goes beyond traditional toxicology. Its approach is based on the exposure-dose-response paradigm, which states that exposure to nanoparticles via different routes of entry into the body is likely to lead to their distribution in other organs around the body, and that this cumulative dose in a target organ will eventually lead to an adverse response in a dose-response manner. The project aims to combine hazard identification and assessment of in vitro effects on the lungs, kidney, liver and cardiovascular and developmental systems with experimental data on exposure, to model exposure-dose response relationships using computation programmes. These include physiologically based pharmacokinetic (PBPK) modelling and quantitative structure–activity relationship (QSAR)-like methods, from which results will be extended into probabilistic models to estimate the risk posed by certain substances. Vicki Stone from Heriot Watt University in Edinburgh said the work's long-term goal is to develop systems that can be used as potential high throughput alternative toxicity tests, allowing determination of risk without the need for animal testing.

There is still a long way to go to actually quantify what exposure to manufactured nanomaterials is

– Derk Brouwer TNO

The successful development of such models requires validation of in vitro tests with the results from in vivo assessments of exposure. Professor Håkan Wallin from the Danish National Research Centre for the Working Environment (NRCWE) has carried out inhalation studies in rodents to determine the effects of various substances through this route of exposure, including sanding dusts from nanoparticle-containing paints and lacquers and glass coated with nano zinc oxide. However, he highlighted certain problems with particular nanoparticles such as zinc, which is difficult to identify in cells to determine dose levels due to high background levels and the effects of dissolving. In addition, he highlighted the complexity of lung physiology and toxicology. "It is not easy to substitute animal tests with in vitro assay, and we have a long way to go before we can eliminate animal testing in this area," he said.

Estimation of the health risks of these materials also requires accurate calculations of human exposure. "Factors such as breathing patterns and lung anatomy can affect the dose," said Derk Brouwer from the Dutch Organisation for Applied Scientific Research (TNO). In addition, problems with measurement devices, including coagulation processes and interaction with background aerosols, make it harder to estimate the number of particles. And there remains no agreement on the appropriate metric – number of particles or surface area – to estimate exposure. "There is still a long way to go to actually quantify what exposure to manufactured nanomaterials is, and to give an accurate value estimate of lung deposited dose. However there are promising developments with respect to measurement devices and strategies." These, he said, include the FP7 Nanodevice project, which is attempting to develop an easy to use, portable measuring device to characterise the number of engineered nanoparticles in workplace air.

Environmental exposure

Richard Williams from the UK Centre for Ecology and Hydrology has been investigating the environmental exposure from nanoparticles commonly used in consumer products, namely zinc oxide, silver and cerium oxide. Under the NanoFate (NanoFATE) project, Mr Williams has modelled the concentration of these substances following their entry into environmental water after use by consumers in cosmetics and personal care products. The model considers weather systems such as rainfall runoff and human land use of water, and also incorporates the effects of waste treatment on levels of nanoparticles and loss through sedimentation to predict river concentrations. To date, concentrations of zinc oxide and silver nanoparticles have been estimated for all European surface waters. These can then be combined with ecotoxicity values of effects in aquatic organisms for environmental risk assessment, and the project has produced an initial risk map for nanosilver based on its effects on the reproductive toxicity in daphnia magna.

"We now have a method for estimating spatial distribution across Europe," said Mr Williams. "However, our current studies are extremely provisional as they are based on a small amount of data. We need to increase our knowledge of how much is used across Europe, and also develop country and population-specific per capita loads rather than using uniform values... we are currently only calculating the concentrations of nanoparticles in water, but this doesn't say anything about the

bioavailability to organisms – what form they're in and how they behave in natural waters, and therefore whether they are actually accessible to the organisms or not."

Real life release

However, Richard Canady, director of the centre for risk science innovation and application (RSIA) at the ILSI Research Foundation, said these attempts to characterise nanoparticle exposure are insufficient, as a full understanding of the risks requires consideration of real life scenarios and the release of nanoparticles from real world uses. He said there is a significant dearth in scientific studies examining the release of nanoparticles from consumer goods, and that the few studies available often rely on qualitative rather than quantitative measures of release.

With funding from Canada's environment ministry, the RSIA is coordinating the NanoRelease (**NanoRelease**) project to produce a "state of the science" report on what is known and what needs to be known about detecting and measuring the release of MWCNTs from consumer products. The international collaboration involves representatives from industry, science and government and NGOs in the US, Europe, Canada and Australia. "The common language on how we understand release is not there," said Mr Canady. "Our goal is to develop methods for measuring release that we can all agree to, and to develop trust that these methods can be used to determine what is released."

Regulatory progress

But despite significant progress under FP7 there is still a lack of scientific information to feed into regulatory decisions. "We now have to decide how to approach a field where we have limited information," said Marcello Cacace, from the Italian National Council of Research and advisor to the Commission's NanoSafety Cluster. He highlighted a need for greater research and a stronger sense of urgency because "there are too many unanswered questions pervading the nanosafety arena".

This was also acknowledged by Henrik Laursen from the Commission's environment directorate, who emphasised the difficulty in moving forward in a regulatory context without all the necessary information. "We have been struggling with the many unknowns surrounding the field of nanomaterials," he said. "Substance identification is one of the crucial areas – determining when a material is a material and when changes to that material mean it is no longer the same material in terms of a regulatory perspective." Further research and knowledge is needed, he said, to be able to discriminate between different substances, such as different forms of nanosilver.

This needs to be accompanied by approaches such as read across and substance grouping to enable the faster assessment of substances in risk assessment. "A case by case approach is not sustainable in the long term," said Mr Katalagarianakis. The next period of EU funding, under the Horizon 2020 programme, he said, will target large-scale regulatory testing of nanomaterialse in an attempt to provide the necessary mass of data to inform regulatory decisions. Significant progress in this area will be needed to ensure the continued economic development of the nanotechnology industry. "Safety concerns about some nanomaterials threaten to undermine the whole range of nanotechnology applications," he said. "Removing this barrier will be vital to encourage innovation."

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Regulation of nanomaterials in food contact uses: part 2

Following last month's article on the EU and US regulation of nanomaterials in food contact applications, Anna Gergely, Laurel Berzanskis and Mitchell Cheeseman of Steptoe and Johnson explain the policy approach and regulatory guidance of the EU and US regulatory agencies.

Nanomaterials are already specifically regulated in EU legislation covering cosmetics, food contact materials and biocidal products. These regulations, when relying on the use of positive lists, only allow the use of nanomaterials when specifically authorised. The European Commission has recently published a recommendation for a definition on nanomaterials to enable identification of nanomaterials and to create a baseline from which appropriate sector specific definitions may be drawn. Supporting the specific legislation are nonbinding guidance documents on nanomaterials, which have been issued in several sectors.

Unlike the EU, the US has issued neither specific regulations addressing nanomaterials, nor a precise regulatory definition of nanomaterials. Although this could change in the future, as both the Food and Drug Administration (FDA) and the Environmental Protection Agency have suggested including the evaluation of risks associated with nanomaterials in product approval procedures, currently there are only agency guidelines to assist industry in addressing safety issues.

PHOTO: ©iStockphoto.com/gbrundin

Some bottles are made from nanocomposites that minimise leakage of carbon dioxide

Risk assessment guidance

In 2011 the European Food Safety Authority (Efsa), on request from the Commission, issued guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. It takes a practical approach to assessing potential risks, covering food additives, enzymes, flavourings, food contact materials, novel foods, feed additives and pesticides.

The guidance, issued as a scientific opinion of Efsa's Scientific Committee, reinforced the 2010 opinion of the Commission's Scientific Committee on Emerging and Newly Identified Health Risks (Scenihr) from 2010, emphasising that "'nanomaterial' is a categorisation of a material by the size of its constituent parts and it neither implies a specific risk, nor does it necessarily mean that this material actually has new hazard properties compared to its constituent parts or larger sized counterparts."

Importantly, the guidance also confirms that the conventional risk assessment paradigm (hazard identification and hazard characterisation followed by exposure assessment and risk characterisation) is appropriate for the application of nanomaterials. On that basis it suggested that risk assessment can be carried out, provided the necessary data are available.

The guidance focuses on the assessment of engineered nanomaterials (ENM), ie those manufactured in a production process, and emphasises the need for adequate characterisation of the ENM in order to properly describe its identity as used in food/feed products and in the different tests. It acknowledges that the physico-chemical parameters of a nanomaterial may change depending on its environment; hence it is not sufficient to characterise an ENM by only describing its pristine state (as manufactured). It also recommends establishing the characteristics of the nanomaterial as supplied to the food/feed manufacturer, as present in the actual food/feed matrix and as present in biological fluids and tissues, and to compare these data with the characteristics of the form which was used in the toxicological test.

The Efsa guidance applies a weight of evidence approach

As a general principle, test requirements for nanomaterials should follow existing guidance for food and feed applications, it says, with additional considerations highlighted for case by case risk assessment. It also identifies situations under which some data requirements for the risk assessment could be waived (eg when an ENM is transformed in the food/feed matrix into an approved bulk substance).

The guidance applies a weight of evidence approach suggesting, in an essentially iterative process, that at each stage all available information should be evaluated and a decision taken on whether it is sufficient for risk assessment. Further decisions on which tests to conduct should depend on the amount and quality of all pre-existing information and the validity of tests used to generate data. If the information is considered insufficient, further testing would be required. The weight

of evidence approach takes into account all available sources of information and types of data. The guidance allows for less information to be provided when no exposure to the engineered nanomaterial is verified by data indicating no migration from food contact materials, or when complete degradation or dissolution is demonstrated with no absorption of engineered nanomaterials.

Importantly, the guidance also discusses how to handle uncertainties in the risk assessment protocol. It says the uncertainties inherent in the different risk assessment steps should be highlighted and quantified as appropriate. Estimation of uncertainties in experimental data should be handled by proper statistical analysis, but quantification of uncertainties in assumptions (eg extrapolation of data from animals to humans, or extrapolation from laboratory studies to complex systems) should also be highlighted and discussed. All in all, it should be clear from the assessment how the available body of information was taken into account when the final risk assessment was determined.

US guidance

In the US, the FDA's guidance and risk management strategy seek to safeguard its precious review resources and maintain the highest standard of safety assurance. The agency recognises that many substances used in food may include nanoparticles, even in their traditionally manufactured forms, and that review resources need not be spent on these uses. Consequently, it sees no purpose in quarantining such materials that have been shown to be safe for their use through a variety of methods.

Like its predecessor documents, the most recent FDA foods guidance encourages industry members to consult with the agency. The guidance does not represent a fundamental shift in the regulatory framework, and the agency is in fact proposing no such shift. Even though its guidance is less specific and provides far fewer details than the current Efsa guidance, the ability to work with FDA reviewers to vet testing plans and test results at each step of product development and adjust to specific input from the agency is a significant difference between it and its European counterparts. The FDA's ability to work with industry on a case by case basis is one primary reason for the difference in the approaches to guidance.

Although the FDA's guidance document says serious caution should be exercised regarding reliance on existing safety determinations, it does not rule out the possibility that materials authorised for use in a more traditional form may still be in compliance when produced using nanotechnology. The FDA's guidance document lays out factors that may be independently considered by manufacturers and a process whereby manufacturers may make compliance decisions regarding their own products when manufacturing changes are made. The general factors include whether "nanosizing" has a significant impact on the identity of the substance, on the technical effect/use of the substance or whether it raises new questions regarding the toxicity of the substance.

The document specifies that significant changes in the identity can include changes in physicochemical structure, purity or the nature of impurities. Such changes may affect the compliance of a substance with the terms of an existing authorisation or the applicability of a previous Gras (generally recognized as safe) determination, and may also change whether the substance is of appropriate food grade. In addition, the guidance says manufacturers should consider whether the use complies with an existing authorisation (food, colour additive, or Gras regulation or food contact notification), or is the subject of another Gras determination. In cases where nanosizing a material may include changes in identity or the creation of technical effects outside the scope of an existing authorisation or Gras determination, a new safety assessment and/or additional submission to the FDA may be necessary. Interestingly enough, the guidance says the administrative record for food and colour additive regulations, food contact notifications, and agency Gras determinations should be referenced in determining compliance. This contrasts with the FDA's long standing policy on the applicability of food and colour additive petition administrative records.

Assessing safety of significant manufacturing

A central recommendation in the guidance is for manufacturers to conduct an appropriate safety assessment for all significant manufacturing changes of food and colour additives, Gras uses and authorised food contact substances. The FDA's guidance recommends consideration of characteristic properties such as physicochemical structure and properties, as well as purity, impurities, bioavailability, or toxicity in such safety assessments. Interestingly, the Efsa guidance, as drafted, provides an excellent framework for manufacturers to make independent determinations of safety for food ingredient and food contact uses also applicable in the US for FDA purposes. In addition, the ability to interact with FDA review staff on a case by case basis means that manufacturers developing nanotech materials can stage environmental health and safety testing much more efficiently. Manufacturers who follow the principles in the Efsa guidelines and take advantage of the ability to consult with the FDA should have success in seeking authorisation through the FDA process.

Regulatory agreement

Whether manufacturers choose to consult with the FDA or develop their own assessments without its input, the acknowledgement that some nanomaterials may not require FDA authorisation is significant.

US and European regulators generally agree on the state of regulatory science regarding the assessment of food ingredients and packaging materials, and that the existing risk assessment paradigm is adequate for addressing the safety of nanomaterials in these applications. Both FDA and Efsa guidelines address the need to understand the form of the material produced by nanotechnology which consumers are exposed to, as well as the fate of those materials in the food matrix and then within the human body. But despite the general agreement regarding the scientific questions raised by nanotechnology, risk management approaches in Europe and the US are markedly different.

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

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*Nanowatch is a series of articles by Steptoe and Johnson LLP's transatlantic Nanotechnologies practice group (**www.steptoe.com**).*

This month's contributors are Anna Gergely (right), head of Steptoe's nanotechnologies group, Laurel Berzanskis (below left), a contract attorney at the firm's Brussels office and Mitchell Cheeseman (below right), managing director of the environmental and life sciences group in the firm's Washington DC office.

EVENTS

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www.chemicalwatch.com/events

Chemical Watch workshop

REACH and CLP enforcement

13 June 2012

Brussels

Expert panel: Ulrike Kowalski, ECHA Forum Secretariat; Szilvia Deim, ECHA Forum; Andrea Mayer-Figge, State of North Rhine Westphalia, Germany; Eugen Anwander, State of Vorarlberg, Austria; Uta Jensen-Korte, director general, European Association of Chemical Distributors (FECC); Peter Freunscht, Unilever; Steve Groome, Rhodia Novecare. Chaired by Mamta Patel, *Chemical Watch* and Ruxandra Cana, Field Fisher Waterhouse LLP

Website: Workshop details

26-27 June 2012

REACH: legal implications and supply chain strategies 2012

IBC Legal Conferences, Brussels

Website: Conference details

26-28 June 2012

4th European conference on standardisation, testing and certification in the field of OSH

Finnish Institute of Occupational Health, Helsinki (Espoo)

Website: Conference details

28 June 2012

Managing REACH for suppliers of articles: how compliant are you?

REACHReady, Derby, UK

Website: Event details

2-3 July 2012

Registering agrochemicals in the EU

Pharmaceutical Training International, Edinburgh

Website: Course details

2-5 July 2012

X2012 – 7th International conference on the science of exposure assessment

The British Occupational Hygiene Society, Edinburgh

Website: Conference details

4-5 July 2012

Module 7 basic CHIP classification and module 9 advanced CHIP classification and labelling

Chemical Hazards Communication Society (CHCS), London

Website: Event details

9-13 July 2012

Risk assessment week

ReachCentrum and TNO Triskelion, Brussels

Website: Course details

11-13 July 2012

2nd INACHEM – Indonesia international chemical expo

inaChem, Jakarta Convention Centre, Indonesia

Website: Event details

1-2 August 2012

REACH and CLP USA

Informa Life Sciences, Raleigh, North Carolina

Website: Conference details

5-6 September 2012

CIR – Chemical industries regulation 2012

Informa Life Sciences, Barcelona

Website: Forum details

5-6 September 2012

Nanomaterials: regulations, risks and rewards

Informa Life Sciences, Barcelona

Website: Conference details

5-7 September 2012

Safer consumer products summit

Infocast, San Jose, California

Website: Summit details

10-11 September 2012

Global chemical industry sustainability summit

Chemical Industries Roundtables, LLC, Brussels. Website: Summit details

19-23 September 2012

SCHC 2012 Fall meeting

Society for Chemical Hazard Communication, Arlington, Virginia

Website: Meeting details

1-3 October 2012

3rd Annual global petrochemicals technology conference

Fleming Gulf Conferences, Doha, Qatar

Website: Conference details

11-14 October 2012

Turkchem Chem Show Eurasia 2012

Artkim Group, Istanbul

Website: Event details

16-18 October 2012

EFIB 2012

EuropaBio and Smithers Rapra, Dusseldorf, Germany

Website: Event details

16-19 October 2012

European Society of Toxicology in vitro 2012 international conference

Portuguese Toxicology Association (AP Tox), Lisbon, Portugal

Website: Conference details

8-9 November 2012

Biocidal Products Directive (98/8/EC)

Pharmaceutical Training International, MWB Victoria, London

Website: Course details

12-14 November 2012

SCMchem 2012

Worldwide Business Research, The Wigwam, Phoenix, Arizona

Website: Event details

Chemical Watch webinar

Korea, developing a new chemicals regulation

26 June 2012

Speakers:

* Dr Hyunpyo Jeon, senior researcher and regulatory affairs, KIST-Europe
* Kyun Woo Chang, team leader – marketing team, Samsung Fine Chemicals
* Dr Sanghee Park, Chemtopia

3pm Brussels, 2pm London, 9am New York, Seoul 10pm. Duration: 90 minutes

Website: Webinar details

Job title	Location	Summary	Organisation
Regulatory and product applied toxicology specialist	Seneffe, Belgium	Within our product safety and regulatory compliance department, the candidate will bring their expertise to the assessment of the toxicological and regulatory related profile of Dow Corning's products and to the implementation of new regulation requirements in Europe. **Closing date: 10-Jun-2012**	DOW CORNING
Product stewardship officer/ MSDS officer	North England/ Midlands	As an MSDS/ Product stewardship officer you will be working within an established team for a leading speciality chemicals company who offer the job security that comes with the wide range of industries they service. In a temporary role, you will compile MSDSs as well as check and review them. **Closing date: 15-Jun-2012**	NonStop RECRUITMENT
Registration specialist – crop protection	North East, UK	A unique opportunity to join an industrial agrochemical company, where you will have a broad and wide ranging regulatory role. Our client is a globally recognised company with a growing pipeline. **Closing date: 15-Jun-2012**	NonStop RECRUITMENT
Senior regulatory affairs specialist	Rhineland-Palatinate, Germany	Excellent opportunity to take a senior role in the EU regulatory affairs team of a leading plant protection product company. It has a wide range of pesticide and herbicide products developed for a diverse range of applications. **Closing date: 2-Jul-2012**	vrs regulatory
SDS author	East Midlands, UK	We are looking for a chemical industry professional with experience of SDS authoring, hazard classifications and a strong interest in chemical legislation/regulatory affairs. You will join an established team and provide regulatory/ legislative support in the areas of SDS compilation, hazard classifications, labelling, transport regs, CLP and REACH. **Closing date: 2-Jul-2012**	vrs regulatory

Navigating a way through ECHA's guidance documents

ECHA does a lot of things well, but the approach chosen for the website design makes it hard to find the extensive guidance on CLP. For the CLP novice it's a challenge to sort and prioritise the many documents. In this briefing, REACHReady's Bob Warner gives tips to those who are new to CLP and who may be daunted by the task of finding a way through this maze of many hundreds of pages.

Let's be clear from the beginning: to advise business on CLP compliance demands a wide range of knowledge and skill. It is probable that few of us will have what is needed. And while we can use the ECHA guidance to build our knowledge, we can't be considered to be competent without core professional expertise and practical experience.

For example, advising on the obligations in CLP may demand skill in the interpretation of confusing legal text, and for this you will almost certainly need formal training in law. Classifying on the basis of toxicity data will often require expertise in dealing with the interpretation of studies and their relevance for people. This task can only be done if you are competent in the scientific area in question. So one of the keys to managing CLP is to recognise your limitations, and to be able to identify when you need expert advice.

Where do you start to learn?

We suggest the best starting point is the Questions and Answers on CLP (**Questions & answers**), a little known but very useful document which is an excellent primer. After that, you will be ready for the longer and more detailed ECHA introductory guidance on CLP (**Introductory guidance**). This is a solid, rather pedestrian introduction, accessible to those with a general regulatory background and familiarity with chemicals. It is generally well written but some of the links don't work and there are some parts where the text will add little (for example the advice on Article 45 of the Regulation). You could have a copy of the CLP Regulation (**CLP Regulation**) to hand at the same time, but we suggest you defer studying it at this stage.

As a follow up the helpful CLP frequently asked questions (**CLP FAQs**), which is regularly updated, should be read.

And then?

The above documents, which will probably take about five hours to work through and understand, should enable you to scope your needs. You will know what you have to do and whether you have the resources and expertise to proceed. If so, and particularly if your interests take in mixtures where you may need to develop labels based on your suppliers information, then the next step is probably the guidance on labelling and packaging (**Guidance**). At this stage you will almost certainly need a copy of the Regulation, particularly Annexes I, VI and VII. It is possible this will be all you need to deliver a compliance plan in your business.

More detail?

The next big step is the challenge of practical classification based on data. This is often the point at which expert advice is needed. Updated in May, the guidance on the application of the CLP criteria is a massive and highly technical publication written by experts for experts. Do not approach it lightly. But even if you plan to use an expert, we suggest you find time to read through the first 70 or so introductory pages. You will then be well placed to consider critically some of the difficult issues in CLP, for example the question of the relevance of physical form, the usefulness of Annex VII, and some of the issues surrounding data acceptability.

Getting the job done

We have argued before that complying with CLP is not a simple matter. It's a major cross-functional task with implications for purchasing, marketing and customer relations. It will cost a good deal of money – probably far more than you expect. There is no upside, you probably won't gain more sales, or save any people, or help the planet. So remember to use all the opportunities in the Regulation to minimise cost. Doing so means a good basic understanding of CLP and we hope this article will get you to that position. If not there are some good service providers who can help so long as you know the right questions to ask!

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

*Bob Warner is a member of the CLP team at REACHReady (**www.ReachReady.co.uk**), one of the leading REACH & CLP advisory services.*

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The risk assessment labyrinth: reaching a sensible outcome

Under the previous registration deadline, many risk assessments were conducted too late and in too little time. This time around registrants should make sure they are better prepared, says Vincenzo Girardi.

If the facts don't fit the theory, change the facts. It is perhaps wise advice when discussing a football match with friends, or economics with colleagues, but can it be applied to risk assessment? The theory of REACH says you need to arrive at a risk characterisation ratio of less than one to prove that the risks of using the chemical substance are under control. If the basic facts don't give this result, why not change them?

But when thinking about risk assessment under REACH, one must bear in mind questions such as: what do you change? Can I change the derived no effect levels (Dnels) or predicted no effect concentrations (Pnecs) from hazard assessments, or do I modify the exposure assessments? Which facts don't fit the theory? And who makes that decision, and on what basis? If I change some hazard assessments and some exposure assessments, do I satisfy concerns from all sides? This is an interesting conundrum: How do you practically, sensibly and realistically arrive at the final outcome?

When REACH came into force in 2007 attention focused on registration and the collection of data, working in Siefs, cost sharing and data sharing. The technical guidance documents came out fast and furious to help us all understand how to deal with its different components. All was going well until the documents were published for the chemical safety assessment: not just one document, but a whole series was produced – a real test of dedication and tenacity. Many companies have contributed to making things clearer about how to carry out the assessment. The famous diagram (**ECHA diagram**), to the right, which sticks in my mind, has certainly been an effective communication tool to breakdown how to deal with the suite of documents dedicated to this subject.

For many it soon became apparent that the workload behind any risk assessment was not going to be easy. It was clear that experts had to be involved to make sure the results were at the very least of a reasonable quality ranging to very high quality.

There has been controversy about what is expected to be carried out, most notably whether a complete assessment for both human health and environment is required or just one or the other. If one was not done, who would challenge this? Here the jury is still out. With the number of assessments carried out so far, the final results speak for themselves.

Too little, too late

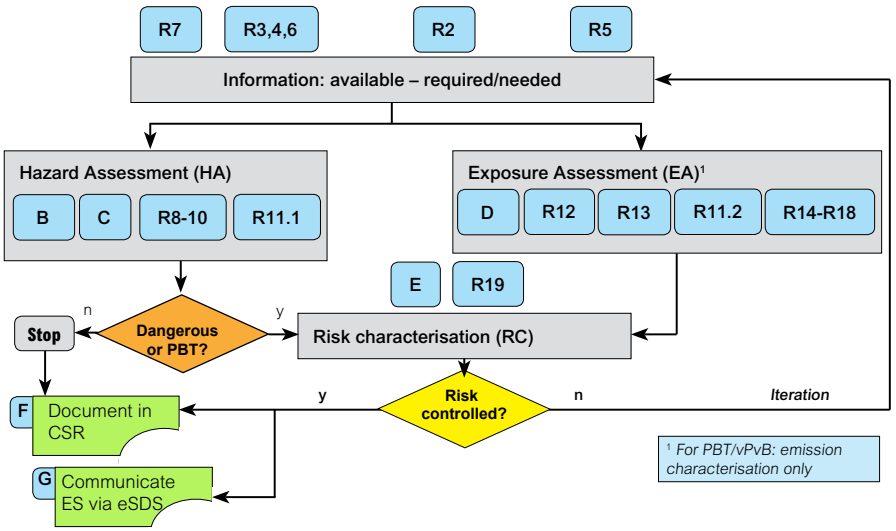
Based on the experience gained from the 2010 registrations, consortia will probably agree that the time dedicated to carrying out risk assessments was not enough, and they were done too late. We should learn from this in 2013. We should begin sooner, take more time and bring in the experts to produce something that is useful and accurate.

So what is the risk assessment really all about? Is it proving that you can achieve a risk characterisation ratio (RCR) less than one, or that in reality, the chemicals are being handled and dealt with safely in the workplace? How should one go about making the iterations in the assessment until the appropriate RCR is achieved?

In the technical guidance documents, Part E and R19 refer to the calculation of the RCR and uncertainty analysis. As pointed out at the beginning of this article (even if it was tongue in cheek), there are several ways to change the RCR. Starting with the hazard assessment to derive the Dnels/Pnecs, if there is a need to obtain more accurate values then more testing may be required, which in turn implies making testing proposals before actually obtaining any values to then continue with the assessment. Therefore, dragging out the conclusions could prove to be a downside of doing this. From the exposure assessment, relying on the risk assessment models for the answer may prove too conservative, making measured exposure data the better approach to take. One can immediately imagine the disadvantages of this approach such as time, resources, and effort. Could it be considered though to be the best approach to take (although for 2013 registration maybe it is too late to put into action)? This leads me to consider then that the most practical approach is to review, and to potentially increase or improve, the risk management measures and operational conditions in the workplace. Is this a price worth paying to achieve the objective set in the assessment of a RCR below one? I would not attempt to advocate one solution above the others, but simply wish to highlight that the decisions to be made cannot be taken lightly.

Risk assessment is also expected to be understood by all the registrants as they will be expected to provide extended safety data sheets (eSDSs) to their downstream users. Without the basic understanding of what this entails, miscommunication can filter down. Bear in mind too that if a chemical safety report

ECHA guidance and the CSA process Source: European Chemicals Agency, http://echa.europa.eu/



(CSR) is not totally accurate, the subsequent eSDS cannot be expected to be any better, as the source (the CSR) is already inaccurate.

Take just one issue surrounding risk assessment – the appropriate interpretation of use descriptors. When trying to work with the use descriptors, there are so many different options that can be used, with different consequences. If companies from the same sector use different use descriptors the results will not be aligned, and downstream users receiving eSDSs from different suppliers have to deal with this misalignment and the actions they need to take. Who is best positioned to determine objectively which descriptors are more appropriate for the different industry sectors?

This brings to the forefront the work carried out by industry trade and sector groups to draw up standard generic exposure scenarios that can be incorporated into the risk assessment of substances. The European Chemical Industry Council (Cefic), the Downstream Users of Chemicals Coordination (Ducc) group, the European Association of Chemical Distributors (FECC) and other trade associations soon realised that the communication of risk assessment needed to be done in a systematic manner. They took it upon themselves to set this in motion with their generic exposure scenarios and Excel sheets on specific exposure scenarios. This work covered the exposure assessment at the workplace. However, this must be combined with the hazard assessment based on the studies to derive the appropriate Dnels and Pnecs. Not only were these two sides considered separately, they must be drawn together somehow to arrive at the famous RCR. This is another reason why there is a need for experts to step forward and prove themselves.

If companies from the sector use different use descriptors the results will not be aligned

Companies need to grasp the fact that even if they are going to outsource work to others, they should, as a minimum, continue to hold basic knowledge of what will be delivered, and what they need to check and verify to be compliant. The same can be true for downstream users when they receive an eSDS because they need to extract the essential data relevant to them and accurately discern what needs to be implemented and why.

Whether a registrant is an expert or not, the REACH legislation does require it to be better educated in the workplace assessment to ensure the risk of danger is reduced or is under control to the best of its ability. Workers want to be reassured that the risk assessment being carried out is not merely a desk-based, number-crunching exercise, but does reflect reality and ensures safety measures can be practically applied without putting their lives – and their livelihoods – in jeopardy.

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

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Knowledge sharing drives substitution

Substitution of hazardous chemicals is encouraged by European chemicals regulation, but so far it has only been required for a few substances, says Anna Lennquist of ChemSec. Where regulation is slow, many companies have found it advantageous to move ahead of it. Subsport (Subsport), the Substitution Support Portal, is a platform where companies and organisations share their substitution experiences for others to build upon.

The lack of information on safer alternatives is often identified as a barrier when dealing with substitution of hazardous chemicals. In response to this, the Subsport project was formed to set up an online, state of the art resource on safer alternatives. It has been developed, with the help of EU funding, by four partners: the German consultancy Kooperationsstelle Hamburg IFE; the Spanish technical trade union foundation Istas; the Danish consultancy Grontmij and the Swedish NGO ChemSec. Although from different backgrounds, all the partners have experience in building databases on hazardous chemicals or safer alternatives.

Shared experiences

Subsport aims to support anyone taking on the matter of substitution through systematic approaches and tools for substitution, along with providing well documented case stories as practical models (*CW* 2 April 2012).

Substitution may be a complex issue that can be time, and financially consuming. It requires knowledge of both the toxicological and technical aspects of chemicals and production processes, as well as detailed supply chain communication. But, it can also be relatively quick and easy, if you are inspired by what someone else has already done.

The case stories presented in Subsport have been given by a wide range of stakeholders, from large multinationals to small companies, trade unions, hospitals and universities, through to public procurement departments. The nature of the case stories ranges from very quick and simple solutions, to describing years of complex product redevelopment. The case story database currently consists of 100-200 substitution examples, and is growing.

In the past, finding companies willing to share experiences on substitution has been one of the challenges for the Subsport team. Lately however, attitudes have changed. More and more companies realise that they need to share information in order to comply with the future demands on chemicals management, and also that this does not threaten their competitiveness – but rather the opposite. Being visible in the Subsport case story database could be a way of being recognised for the substitution efforts already performed and finding new customers or suppliers and gaining economies of scale.

Substitution and regulation

REACH aims at eventually substituting all substances of very high concern with safer alternatives whenever possible. During the authorisation process, applicants are required to make an analysis of available substitutes, and third parties may contribute with information on alternatives. This process has already started, with the first deadlines for applying for authorisation for specific uses coming up in early 2013. Subsport is set up to be able to play a role in this process, by providing information on alternatives. However, for third parties to be able to provide relevant information during the authorisation process, it is important that ECHA makes detailed information on the uses applied for publicly available.

Online resource

Subsport has been online for two years and is continuously updated with information to support substitution. It is set up to be the primary online resource on substitution and its various levels of information have been identified specifically to fulfil the needs of a broad range of stakeholders, from companies and authorities, to research and public interest groups.

The portal provides information on international regulations and their respective requirements for substitution. It gives information on available methods and tools to work with substitution and alternatives assessment. The tools are described so that it is easy to find the most suitable one for the specific user or situation. The portal also provides basic information and a step-wise approach to getting started with substitution. Besides this information, there is also a search function allowing access to a large number of other available databases on alternatives to hazardous chemicals.

And last but not least, Subsport holds a database of lists of restricted and priority substances. The lists are from authorities, stakeholder organisations and companies. There is also general information on how to identify chemicals of concern.

Workshops

Apart from the internet-based Subsport resource, the project also provides training on alternatives identification and assessment. The content and materials are developed to be adaptable to the experiences of the participants, and include discussions and work in small groups. Information on upcoming sessions can be found on the Subsport website (Subsport).The portal is free of charge and currently available in four languages: English, Spanish, German and French. The project is funded by the EU Life+ Programme, the German Federal institute of Occupational safety and Health (BAuA) and the Austrian environment ministry.

We are confident this is a valuable tool for anyone interested in substituting hazardous chemicals with safer alternatives and we would like to invite companies with case stories to please share them in Subsport – the more is shared, the larger the impact towards a toxics-free future.

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

Anna Lennquist (anna.lennquist@chemsec.org) is a toxicologist at ChemSec, which was founded in 2002 by four Swedish environmental groups. ChemSec lobbies for changes in chemcials legislation and works with companies to reduce their use of hazardous substances. In 2008 it published the first version of its SIN (substitute it now) list of chemicals.

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The future we want from Rio+20 and ICCM3

Two decades ago, the international community met at the first Rio Earth Summit; expectations were high and much was achieved. The important principles of precaution, intergenerational equity, right to know, participation and polluter pays were established, becoming the international tenets of sound chemical management.

At the 2006 launch of the UN's Strategic Approach to International Chemicals Management (Saicm), the International POPs Elimination Network (Ipen) joined with governments, industry, workers and other civil society groups to declare that sound management of chemicals was essential for sustainable development, including the eradication of poverty and disease. Six years later, "Chemical safety for sustainable development" is the theme for the third International Conference on Chemicals Management (ICCM3), for despite the global consensus, sound chemicals management has not been fully integrated into development agendas. To address this in the lead up to this year's UN Conference on Sustainable Development (Rio+20), Ipen is calling for a global recommitment to Saicm.

The UN Human Rights Council warns that basic human rights to life and health are "threatened by exposures to toxic chemicals, hazardous wastes, and contaminated drinking water and food". Chemical contamination affects us all, with the worst impacts experienced by the most vulnerable; children, indigenous peoples, peasant farmers and workers in many hazardous industries. Children are exposed to toxic chemicals before they are born, while cancer, heart disease, reproductive and developmental disorders, asthma, diabetes and mental illnesses, have links to the pollution of air, water, food and consumer products, and wastes.

Clearly, fundamental change is needed in the way we design, use, manage and dispose of chemicals and Rio+20 must reflect this. While most governments maintain the risk management approach to regulation of chemicals, Saicm acknowledged that many chemicals are simply unmanageable and their hazards cannot be controlled over their life cycle. Rio+20 must result in a global phase out of unmanageable chemicals, including highly hazardous pesticides, persistent bioaccumulative toxins (PBTs), genotoxins, carcinogens, endocrine disrupters and substances that undergo long-range transport. Global phase-outs are essential to avoid banned chemicals from one country being sold or dumped in another, particularly in those that do not have the capacity to enforce sound management of chemicals. The costs of not taking action are substantial. The World Health Organization conservatively estimates that industrial and agricultural chemicals are responsible for 1.2 million deaths per year and at least 1.7% of the global burden of disease.

The world desperately needs leadership to move the global community to more sustainable patterns of consumption, production and extraction. Rio+20 must address urgent and serious chemical issues such as marine plastic debris, dumping of electronic wastes, the impacts of mining, its wastes and pollution, and the ever-increasing volumes of waste generated. Rio+20 should acknowledge the impact climate change is having on chemical releases, exposure and toxicity; and help the move internationally to green design, green chemistry and sustainable procurement.

A sustainable chemical industry is essential to the future we want; one that pays the true cost of its products throughout their life cycle, while striving to eliminate all pollution. Rio+20 should revisit Principle 16 of Agenda 21, which promotes the internalisation of environmental costs and the use of economic instruments to ensure polluters take responsibility. Now more than ever, a polluter pays approach is crucial as countries cannot afford the burgeoning externalised costs of chemical damage to their people and environment, nor can they cope with the economic imposts on the public purse of these pressures.

To achieve chemical reform, Rio+20 needs to encompass a global recommitment to Saicm and its goal of a toxic-free future, as well as ensuring the financial means and resources to further implement it. There is an expectation that Rio+20 will set the tone for ICCM3 later this year, where the serious under-resourcing of Saicm will have to be addressed. Saicm needs a long-term, substantial, global financial mechanism to support sound chemicals management. These are issue of international concern that Saicm must address; for example, ICCM3 needs to develop the international framework that ensures public access to information on chemicals in products.

The summit must also initiate work on hazardous substances in electrical and electronic products and help ensure their safe alternatives are identified and substituted. Further policy options to combat the trade in near-end-of-life electronic products need to be developed, as well as model legislation for extended producer responsibility and manufacturers' financial responsibility for electronic wastes.

ICCM3 will need to initiate new activities around nanotechnology, including life-cycle assessment, product and material registers, regional pilot projects, and measures to address worker health and safety concerns. And as an emerging global issue, endocrine disrupting chemicals (EDCs) must be accepted as a priority and a global watch list of EDCs established.

Ipen has released a global common statement (**IPEN statement**) for a toxics-free future. It urges all of us to commit to a future where people have the right to enjoy healthy, sustainable livelihoods that do not harm their bodies or the environment. We have a right to safe and secure communities and workplaces that are free from toxic threats to people, surrounding environments and to future generations. This is the future we want.

The views expressed in our contributor columns are those of the authors and not necessarily shared by Chemical Watch.

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