

Long-range forecasts

Cefic wants its flagship research programme to deliver 'science for policy impact'



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The European Chemical Industry Council (Cefic) is putting to good use scientific knowledge accumulated from its contributions to the international chemical industry's scientific research programme, the Long-range Research Initiative (LRI). It is working with ECHA to develop read-across guidelines for chemical safety assessment ([GBB Dec 2012/Jan 2013](#)), and its findings are feeding into the European Commission's work to set criteria to identify endocrine disrupting chemicals; its endocrine modulation steering group (EMSG) recently submitted documents to DG Environment on criteria for categorising endocrine disrupters ([CW 6 December 2012](#)). And with the latest set of Cefic-LRI research projects soon to be allocated funding, the [programme](#) will continue to inject science into chemicals policy debate.

"The collaboration with ECHA [on read-across] comes from the fact that we have done a lot of work in the past on projects with read-across," says LRI programme manager, Bruno Hubesch. "One quarter of all filings with REACH contain a read-across argument, but their success rate is close to zero. Now we are talking to ECHA to figure out why, in their view, they don't fly."

The EMSG research goes back two decades, and the LRI has funded research for 15 years (see box). Dr Hubesch is currently selecting academic research projects for the next round of funding. A new three to four-year ecotoxicological research project, focusing on the environmental impact of chemicals on a whole ecosystem rather than on a single species, will be one of the longer and larger projects to be funded. The project aims to explore the value of "ecological realism" – a concept backed by scientists at last summer's Setac world congress ([GBB July 2012](#)) and at Cefic-LRI's [annual workshop](#) in November, as well as by the Commission's scientific advisory committees and by chemical industry research body Ecetoc, the European Centre for Ecotoxicology and Toxicology of Chemicals ([CW 20 December 2012](#)).

Current regulatory studies typically follow population changes in a single species, such as the daphnia water flea, following chemical exposure. "The question that ecotoxicologists are raising now is: do population changes matter?" says Dr Hubesch. "What matters is the impact on the ecosystem."

At Cefic-LRI's workshop, Colin Janssen, a member of the EU's Scientific Committee on Health and Environmental Risks (SCHER), made an urgent plea for more "ecological realism" in



Photo: Cefic-LRI

LRI workshops aim to bring together scientists and policy makers

risk assessment. Professor Janssen also belongs to the working group responsible for the Commission's discussion paper on how to address the new [challenges](#) for risk assessment.

The paper said the main challenge for ecological risk assessment is managing to develop tools that take account of the complexity of potentially exposed ecosystems and enable assessment of site-specific effects. "The EU's risk assessment paradigm is a prescription science," said professor Janssen. "There is a clear disconnect between what we want to do and what we are actually doing."

Professor Janssen stressed the importance of establishing close cooperation between regulatory authorities and industry on what is needed for appropriate risk management. Improved communication between scientists and risk assessors is critical, he added, referring to the opinion paper on "Improvement of risk assessment in view of the needs of risk managers and policy makers" issued by the EU scientific committees just over a year ago ([CW 21 December 2011](#)).

A key conclusion of the risk assessment discussion paper, said professor Janssen, was that risk should be expressed in terms of likely impacts on human health and ecosystem services "rather than in terms of the more prevalent risk characterisations. The output of risk assessment needs to be more policy and management relevant, something that they [risk managers and policy makers] can understand and relate to other risks."

Also speaking at the workshop, Gernot Klotz, Cefic executive director for R&I, called for greater focus on the science discipline of "interpretation", saying it frequently ends up as a "half-sentence" at the end of a research document. He encouraged the

LRI scientists to reach out to other disciplines that could help to interpret risk assessment data and to communicate its impact.

A crucial part of such communication is explaining research uncertainties. "Uncertainties are very important but they are rarely quantified," said professor Janssen. "We need to quantify them so that we can inform other parties that have to deal with the data."

Protein push

Meanwhile, Andreas Bender, from Cambridge University, has come up with a clever way to integrate exposure data (for which he received the 2012 LRI Innovative Science Award). His group, he said, is "exploring ways to integrate data from different sources to understand bioactivities and to design novel chemistry." This, he said, involves a "magic triangle" of data on molecular structure, phenotype, and mode of action. "We can synthesise nearly every molecule we want – that's the independent variable that gives us a lot of power." When it comes to mode of action, Dr Bender focuses on the interactions of chemicals with proteins, anticipating the protein pathways based on chemical structure. "We have a molecular structure and we know what the phenotype is and then we try to incorporate the mode of action," he said.

Most other models, said Dr Bender, look at a chemical structure and associate it with toxicity. But the problem with this is that if the toxicity is protein-mediated, as it so often is, the chemical sub-structure causes the toxicity by binding to a protein. "You only focus on a part of the problem if you look solely at the chemical structure," he said. "I propose to pool information to look simultaneously at chemical structure, protein bioactivity and gene expression data."

Some other LRI-funded projects focus on "tiered testing". For

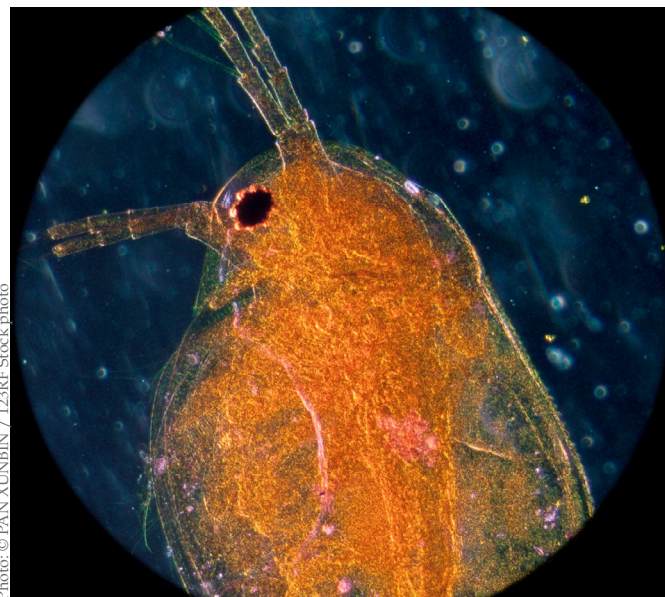


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Are single species tests, such as those on daphnia, hogging the limelight?

example, Bas Blaauboer, from Utrecht University, told the workshop that he has made *in silico* predictions using *in vitro* data on metabolic fate, health effects and biokinetics, and compared the results with *in vivo* data for a wide range of compounds from different substance classes. He suggested that future risk assessments could be approached via *in silico* and *in vitro* studies if validated against existing *in vivo* data. "We're not there yet," he said, "but I think we're on the right track."

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Cefic's LRI programme

The Long-range Research Initiative (LRI) programme has been running since 1997, providing scientific advice on chemicals and risk assessment to industry and regulators and providing the chemical industry with a credible voice in the debates, such as that on "gender-bender chemicals", which were springing up at that time. It emerged soon after Cefic's Endocrine Modulation Steering Group (EMSG), which brought "science-based knowledge into the discussion," says programme manager, Bruno Hubesch. "Cefic started the LRI programme to tackle any science issue that the chemical industry may have that forms part of a policy or regulatory discussion," says Dr Hubesch. "LRI is not science for science – it's science for policy impact."

The LRI is a global programme under the auspices of the International Council of Chemical Associations (ICCA), bringing together Cefic, the American Chemical

Council and the Japan Chemical Industry Association. "We coordinate this programme globally and have a bi-yearly meeting to align what the needs are," says Dr Hubesch. In future the LRI programme may broaden to include other countries, he adds.

The programme is 100% industry-funded and Cefic allocates Dr Hubesch some €4m annually, 80% of which goes on research. The US LRI has a similar budget, while that in Japan equates to about €1m.

The main research areas are health and environment, exposure science and emerging technologies. Deciding how to allocate funds is not easy. Dr Hubesch first seeks input from company experts in his LRI strategy implementation group to find out which subjects are of interest to them. The European Centre for Ecotoxicology and Toxicology of Chemicals (Ecetoc) is closely allied to the LRI and plays an

important role in coming up with new project ideas.

An academic [advisory panel](#) also helps the decision-making process, and is particularly helpful in identifying longer-term projects that merit funding. Many LRI research projects, despite the "long" in the title, need to be completed quickly in order to address immediate policy issues, such as an emerging regulation. "If we find that a project idea is very interesting from a science point of view, but will take too long to carry out and miss a regulatory deadline, we will not do it," says Dr Hubesch.

He and his advisors then make a "priority call" to whittle down the annual shortlist from 25–30 to about seven projects. "We look for the science quality of the project, then we put it through another discussion on when and where it will have a policy impact."