

Thinking ahead

Crine disrupters Animal alternatives QSAKS loxicity tess g KISK assessment methodologies Environment



K assessment methodologies Environmental databases PBT REACH Biomonitor Concernsus building Omics Intelligent testing Complex environments Society States Informed decision-making Inspectation nnovation Filling knowledge gaps Addressing societal concerns Validated decision-making Innovative science award Children's healt osals Chemical carcinogenesis Consumer exposure Environmental modeling Chemical industry's competitiveness Sustainable chemical industry Bettement Ecotoxicology Nanotechnology Testing strategies Innovation Endocrine Supplied Supplied SARs Toxicity testing Risk assessment memental databases PBT REACH Biomonitoring Human health Environment Male representative health Good programme Effective network Consensus buil nt testing Complex environments Societal acceptance of innovation ocietal concerns Validated methods Informed Fillion knowledge gans. A tricessing societal concerns. Validated methods. Informed Chemical calkings in Contumer exposure. Environmental modeling. Chemica Innovative science award Children's health Requests for proposals iveness Sustainable chemical industry Better chemicals management Ecotoxicology Nanotechnology Testing strategiesInnovation Endocrine disrupt ves QSARs Toxicity testing Risk assessment methodologies Environmental databases PBT REACH Biomonitoring Human health Environment Male re lobal programme Effective network Consensus building Omics intelligent testing Complex environments Societal acceptance of innovation Filling know ng societal concerns. Validated methods. Informed decision-making. Innovative science award. Children's health. Requests for proposals. Chemical car r exposure Environmental modeling Chemical industry's competitiveness Sustainable chemical industry Better chemicals management Ecotoxicology esting strategiesInnovation Endocrine disrupters Animal alternatives QSARs Toxicity testing Risk assessment methodologies Environmental databases oring Human health Environment Male reproductive health Global programme Effective network Consensus building Omics Intelligent testing Comple ocietal acceptance of innovation Filling knowledge gaps Addressing societal concerns Validated methods Informed decision-making Innovative scie 's health Requests for proposals Chemical carcinogenesis Consumer exposure Environmental modeling Chemical industry's competitiveness Sustainab Better chemicals management Ecotoxicology Nanotechnology Testing strategies Innovation Endocrine disrupters Animal alternatives QSARs Toxicity t ent methodologies Environmental databases PBT REACH Biomonitoring Human health Environment Male reproductive health Global programme Effecti is building Omics Intelligent testing Complex environments Societal acceptance of innovation Filling knowledge gaps Addressing societal concerns Valid rmed decision-making Innovative science award Children's health Requests for proposals Chemical carcinogenesis Consumer exposure Environment. Industry's competitiveness Sustainable chemical industry Better chemicals management Ecotoxicology Nanotechnology Testing strategiesInnovation rs Animal alternatives QSARs Toxicity testing Risk assessment methodologies Environmental databases PBT REACH Biomonitoring Human health En roductive health Global programme Effective network Consensus building Omics Intelligent testing Complex environments Societal acceptance of nowledge gaps Addressing societal concerns Validated methods Informed decision-making Innovative science award Children's health Requests fo carcinogenesis Consumer exposure Environmental modeling Chemical industry's competitiveness Sustainable chemical industry Better chemicals m ology Nanotechnology Testing strategiesInnovation Endocrine disrupters Animal alternatives QSARs Toxicity testing Risk assessment methodologies Env s PBT REACH Biomonitoring Human health Environment Male reproductive health Global programme Effective network Consensus building Omics complex environments Societal acceptance of innovation Filling knowledge gaps Addressing societal concerns Validated methods Informed decision-makes ience award Children's health Requests for proposals Chemical carcinogenesis Consumer exposure Environmental modeling Chemical industry's comp ole chemical industry Better chemicals management Ecotoxicology Nanotechnology Testing strategies Innovation Endocrine disrupters Animal alternat testing Risk assessment methodologies Environmental databases PBT REACH Biomonitoring Human health Environment Male reproductive hea me Effective network Consensus building Omics Intelligent testing Complex environments Societal acceptance of innovation Filling knowledge gaps concerns Validated methods Informed decision-making Innovative science award Children's health Requests for proposals Chemical carcinogenesis Environmental modeling Chemical industry's competitiveness Sustainable chemical industry Better chemicals management Ecotoxicology Nanotechn egies Innovation Endocrine disrupters Animal alternatives OSARs Toxicity testing Risk assessment methodologies Environmental databases PBT REACH an health Environment Male reproductive health Global programme Effective network Consensus building Omics Intelligent testing Complex environ ptance of innovation Filling knowledge gaps Addressing societal concerns Validated methods Informed decision-making Innovative science award for proposals Chemical carcinogenesis Consumer exposure Environmental modeling Chemical industry's competitiveness Sustainable chemical industry s management Ecotoxicology Nanotechnology Testing strategiesInnovation Endocrine disrupters Animal alternatives QSARs Toxicity testing Risk assessing s Environmental databases PBT REACH Biomonitoring Human health Environment Male reproductive health Global programme Effective network Conse s Intelligent testing Complex environments Societal acceptance of innovation Filling knowledge gaps Addressing societal concerns Validated method making Innovative science award Children's health Requests for proposals Chemical carcinogenesis Consumer exposure Environmental modeling s competitiveness Sustainable chemical industry. Better chemicals management. Ecotoxicology. Nanotechnology. Testing strategiesInnovation. Endocrine Iternatives QSARs Toxicity testing Risk assessment methodologies Environmental databases PBT REACH Biomonitoring Human health Environment Male th Global programme Effective network Consensus building Omics Intelligent testing Complex environments Societal acceptance of innovation Filling dressing societal concerns Validated methods Informed decision-making Innovative science award Children's health Requests for proposals Chemical of sumer exposure Environmental modeling Chemical industry's competitiveness Sustainable chemical industry Better chemicals management Ecotoxicolo Testing strategies Innovation Endocrine disrupters Animal alternatives QSARs Toxicity testing Risk assessment methodologies Environmental data siomonitoring Human health Environment Male reproductive health Global programme Effective network Consensus building Omics Intelligent testin nents Societal acceptance of innovation. Filling knowledge gaps. Addressing societal concerns. Validated methods. Informed decision-making. Innovat hildren's health Requests for proposals Chemical carcinogenesis Consumer exposure Environmental modeling Chemical industry's competitiveness industry Better chemicals management Ecotoxicology Nanotechnology Testing strategiesInnovation Endocrine disrupters Animal alternatives QSA lisk assessment methodologies. Environmental databases. PBT REACH. Biomonitoring Human health. Environment. Male reproductive health. Global program york Consensus building Omics Intelligent testing Complex environments Societal acceptance of innovation Filling knowledge gaps Addressing societ I methods Informed decision-making Innovative science award Children's health Requests for proposals Chemical carcinogenesis Consumer exposure El ling Chemical industry's competitiveness Sustainable chemical industry Better chemicals management Ecotoxicology Nanotechnology Testing strategie

Introduction

Anticipating and shaping After 10 years, LRI is adjusting focus to keep it in line with today's needs

Let's work together Forging links with academia and regulators is a prime goal for LRI

Timeline In its first decade, LRI has funded 120 projects involving over 300 scientists

Connecting with people

Three strategic research themes address the public's call for confidence

Vital support LRI's Innovative Science Award encourages young researchers to engage



LRI Annie Mutamba Avenue E Van Nieuwenhuyse 4, B-1160 Brussels, Belgium Tel: +32 2 676 7337 Fax: +32 2 676 7433 Email: lri@cefic.org Website: www.cefic-lri.org www.cefic.org

icis **Chemical** Business

Quadrant House, Sutton, Surrey, SM2 5AS, UK Tel: +44 20 8652 3187 Fax: +44 20 8652 3929 Email: icbeditorial@icis.com Website: www.icis.com

ICIS custom publishing Editor John Baker, global editor, custom publishing + 44 20 8652 3153 john.baker@icis.com Art and production Alexis Rendell **Subbing** Dan Bloch European sales manager

Maarten Dubbeld Commercial manager David Stanworth **Publishing director** Christopher Flook Repro Colour Systems - part of Fresh Media Group

Printing Fry

©2008 by Reed Business Information. All rights reserved. No part of this publication may be reprinted, or reproduced or utilised in any form or by electronic, mechanical or other means, now known or hereafter invented, including photocopying and record or in any information storage and retrieval system without prior permission in writing from the publisher.



Anticipating and shaping

Now 10 years old, the Long-range Research Initiative is responding to and shaping policy discussions on the safe use of chemicals and providing an early warning of upcoming issues

THE CHEMICAL industry's global initiative to support research into the health and environmental impacts of chemicals, the Long-range Research Initiative (LRI), will reach its 10-year milestone by the end of this year. With 120 projects now completed or underway, there can be no doubt that it has provided an improved basis for informed decision-making on the risks posed by the use of chemicals.

The International Council of Chemical Associations (ICCA) launched the LRI programme in January 1999, prompted by growing scientific and public concerns in the mid-1990s around endocrine disruptors. These concerns had been brought to a head by publication in 1996 of the book Our Stolen Future by Theo Colborn and others, with a foreword by then US vice president Al Gore.

The ICCA's aim with LRI was to sponsor scientific studies that would address gaps in knowledge about how chemicals affect the health of humans and the environment and help industry and regulators understand the long-term impacts of chemical products and processes. The research would be peer reviewed and the results published openly in scientific periodicals, so as to be accessible by all.

Since its inception, LRI has focused not only on endocrine disruption, but more recently has provided significant proactive input to the controversial issue of biomonitoring of chemicals in the body. This has been driven in part by advances in science and detection techniques and the use of biomonitoring "trials" by environmental groups designed to create public anxiety over chemicals.

In Europe, the LRI programme is managed and funded at a level of €5m (\$6.6m)/year by the European Chemical Industry Council (Cefic). The US and Japanese trade bodies, the American Chemistry Council (ACC) and Japan Chemical Industry Association (JCIA), respectively, manage their own LRI programmes, but the overall effort is coordinated within the ICCA. In 2006, funding of some \$21m was committed by the three bodies to high-quality, peerreviewed academic research on topics selected by the industry.

The LRI initiative is now well established and has the active involvement of industry executives, academics and personnel from regulatory bodies in the three main regions that it covers. Regular meetings encourage networking and mutual understanding of the issues, and help set priorities for future research

VARIED APPROACHES

But there are some differences of approach between the regional programmes and the philosophy behind the EU programme has been changing in recent years, explains Cefic's director of research and innovation, Gernot Klotz.

"In the EU, in addition to scientific knowledge, we are more driven by the science/policy interface and a need to get a better balance between the two areas," he explains. In part, this has arisen from the intense discussions in Europe on science and its role in policy-making.

Cefic has been a major driver in regarding LRI in a broader context, as



[LRI] is now more forwardlooking, so it supports the competitive and innovative edge of the European chemical sector

> Gernot Klotz, director of Research and Innovation, Cefic

part of its overall innovation and sustainability strategy. "Two years ago, Cefic moved to fund LRI in Europe directly through its membership fees and so we decided to review it and revise it a little. It is now more forward-looking, so it supports the competitive and innovative edge of the European chemical sector and does not just react to short-term effects such as Reach legislation," says Klotz.

Originally focused on the industry's needs to be able to respond to public pressures with arguments based on good science, the audience for LRI in Europe is also subtly changing. Klotz sees LRI giving the industry a better basis for its overall advocacy efforts and helping its efforts to link with societal needs for safe and sustainable products. "LRI demonstrates the engagement of the industry on the topics of health and environment and shows that it is contributing to solving problems," he points out. "It complements other research and focuses on topics that

industry regards as crucial."

"LRI helps the industry in its own decision-making, especially during the innovation process," adds Klotz. Companies can better understand the issues around the introduction of new products, and may even decide not to go ahead with developments in the light of potential risks. The work of the LRI is targeted at generic questions, stresses Klotz, and is not product-oriented research for product evaluation. But, he adds, this can be done using the tools developed by LRI.

Cefic has identified three main strategic areas of research for the next four years: the development of intelligent testing, including alternatives to animal testing; understanding the effect of chemicals in complex environments, and the public acceptance of new technologies (see page 8).

This third thematic area of consumer and public acceptance of innovation is certainly a major one that needs to be addressed by the industry. David Duncan, head of consumer products research at Anglo-Dutch consumer products giant Unilever and a member of Cefic's Research and Innovation programme council, points out that consumers do not have a lot of confidence in innovation and the chemical industry as a whole.

"We have to crack this," he says. "And LRI has a positive role in supporting innovation." He warns that the industry has to make sure that it does not make the same mistakes with nanotechnology as it did with the introduction of genetically modified crops. "It's no use companies just insisting they are right on the science", he says.

Duncan advocates building consumer confidence and demonstrating that business is part of the solution to many of the problems facing the world today. "We need to engage through responsible communication about chemicals and about science and technology. That means we need to engage with stakeholders and society about chemicals of concern and educate people about areas like nanotechnology."

This also means, he adds, "engaging about risk and the balance between risk and benefit and how the chemical industry assesses that risk.... There just are no simple black and white answers. So don't be tempted to give them, or we will lose the credibility and trust in the long run."

An important aspect in consumer acceptance of innovation is collaboration, he adds. "One of the ways to reassure people that all the checks and balances are in place and all viewpoints are being considered is



LRI has a positive role in supporting innovation

> David Duncan, head of consumer products research, Unilever, and member of Cefic's Research and Innovation programme council

to be seen to be engaging widely with all opinion holders.

"Industry cannot act alone. To develop safety assessment procedures that do not involve animal testing demands extensive collaboration, across industries and regulators... to define research priorities and indeed, conduct leading-edge research, requires partnerships; and building consistent and effective responsible communication has to be done in partnership with many players."

Industry, regulators, academics and non-governmental organisations have to work together, he concludes, "to produce a robust enabling framework to build confidence in the industry, science and a risk-based approach to consumer and environmental safety."

In its first 10 years, LRI has begun to play its part. In the next 10, with its new, wider ambition in Europe, it should play an even bigger one. LRI has to move on from merely filling in those knowledge gaps, to using that knowledge to shore up public confidence in chemicals and innovation.



Forging links between the chemical industry and regulators on the one hand and the public on the other is a vital part of the LRI's job

Let's work together

NETWORKING BETWEEN industry and academia and close collaboration with regulatory bodies are key elements in the European Chemical Industry Council's (Cefic's) LRI programme. These links ensure it meets its aim of providing relevant scientific advice that industry and regulatory bodies can draw upon to address public concerns.

So, although the research projects that the LRI funds are the tangible manifestation of the programme, deliberations around what research to prioritise and the subsequent dissemination of the work are essential elements in the success of the initiative.

Every effort is made to build relationships with research programmes of high repute and with government agencies, notes Cefic, both to facilitate early awareness of issues that are critical to decision-making and to support the development of effective, science-based regulation for the sound management of chemicals.

The LRI participates in and provides input

into various government-led initiatives. For instance, it works in close partnership with the Organisation for Economic Cooperation and Development (OECD) on the development and screening of globally harmonised test methods to characterise and predict endocrine disruption in mammalian species and wildlife. It has also built up links and dialogue with the European Commission, both in Brussels and at its Joint Research Centre in Ispra, Italy.

One of the most visible aspects of LRI's networking is its annual LRI workshop, held by Cefic each year in November. Attended by a wide range of stakeholders, including policy makers, regulators, academics and NGOs, these provide not only the chance to catch up on the latest developments and better understand each other, but to engage in an evaluation of the LRI research agenda.

But behind this event, there is a systematic effort to make sure the work of the LRI is relevant to industry and regulatory needs.

The overall strategy is set by Cefic's LRI Strategy Implementation Group (SIG), which operates as part of its Research and Innovation Programme Council, headed by Cefic executive director of research and innovation Gernot Klotz. But much of the scientific expertise is provided through the External Science Advisory Panel (ESAP). The European Centre For Ecotoxicology and Toxicology of Chemicals (ECETOC), a chemical industry group, also provides science support and advice (see table and box).

ESAP helps shape the LRI programme and strategy by providing an analytical outside view of its activities to ensure it serves both industry and the public. The specialists on the panel are renowned independent scientists from across Europe and contribute to the scientific value and relevance of individual projects by providing expert advice and guidance on the research.

Dr Tim Gant of the Medical Research Council at the UK's University of Leicester, and until recently chair of ESAP, stresses that the body advises on science and not policy for the LRI programme. "We are drawn on largely as individuals, to provide advice on where there are good opportunities to use science."

There is now, he adds, less emphasis on the endocrine area and validation of testing, but more focus on a move towards development of test processes and more understanding of intelligent testing strategies.

Robert Visser, head of the environment health and safety division of the OECD's Environment Directorate, believes that the LRI is doing a lot of good work and "funds an impressive list of projects and validates a lot of our guidelines". Many of the LRI projects, he adds, are directly relevant to the work that the OECD carries out on validation of chemical testing to ensure globally harmonised techniques.

He cites work on quantitative structureactivity relationships (QSARs) and AMBIT, software developed for chemoinformatic data management, and points out that LRI projects in the areas of chemical carcinogenesis, human biomonitoring, human health and immunotoxicity and allergy feed into its own work areas.

INFORMAL INTERACTION

But the interaction is not on a formalised basis, and Visser believes that there could be more interaction between the two bodies. "I would like to see LRI work in a more systematic way with OECD.... Maybe the current projects are too academic and maybe we should talk on a more systematic basis to find out what the regulatory needs are, then balance applied and scientific work."

He points out that the OECD also talks directly to chemical companies to see what their concerns and priorities are - often in the areas of harmonisation of testing - and feels that these could also talk to the LRI to help set its agenda and assist the industry as a whole.

Bjorn Hansen, deputy head of the European Commission's D1 Chemicals unit in DG Environment, also affirms that LRI is regarded as "very useful". His unit has worked for many years with Cefic in its role of formulating EU chemicals regulations. Now, he explains, "LRI feeds into our work on guidance document development and our technical work, such as OSARs and IT tools."

He sees LRI as useful in two ways. First, it provides the Commission with research that has been well funded and peer-reviewed. Second, it creates a forum for industry to

ESAP members	
Dr Timothy Gant	University of Leicester <i>UK</i>
Prof Herman Autrup (vice chair)	University of Aarhus Denmark
Prof Jurgen Brockmoller	University of Gottinger Germany
Prof Tom Burns	Uppsala University Sweden
Prof Guy Dirheimer	Federation of European Biochemical Societies France
Prof Lynn Frewer (chair)	University of Wageningen The Netherlands
Dr Bert Gordijn	Radboud University Nijmegen The Netherlands
Prof Bo Jansson	Stockholm University Sweden
Prof Colin Janssen	Ghent University Belgium
Prof Matti Jantunen	National Public Health Institute Finland
Prof lan Kimber	University of Mancheste UK
Prof Werner Lutz	University of Wurzburg Germany
Dr David Ray	Nottingham Medical School <i>UK</i>
Prof Anthony Seaton	Aberdeen University UK
Prof Paule Vasseur	CNRS - Metz University France

discuss issues amongst itself, thus providing a harmonising effect. But, like Visser, he believes the projects supported by LRI could be more geared to meeting the needs of the EU regulatory process.

A further vote of confidence in LRI comes from Sandra Coecke at the JRC in Ispra, where she is sector head of the European Centre for the Validation of Alternative Methods (ECVAM) to animal testing.

She points to several years of "fantastic liaison" between Cefic and LRI and ECVAM (and also the US-based Center for Alternatives to Animal Testing), through workshops and joint developments of mutual interest. The aim, she says, has been to develop new non-animal approaches to hazard and risk assessment based on the 3Rs (refinement, reduction and replacement) that can be used in international legislation.

The work has become increasingly important as the EU's Reach regulation and Cosmetics directive amendments come into

Support for implementation

The LRI programme is a member-led initiative that needs various bodies to provide additional expertise and to help shape scientific projects.

The boards, panels and teams that make up the initiative's organisational structure are composed of managers and scientific experts within the chemical industry or from independent organisations across Europe that share the LRI's aims and principles.

Since the establishment of the LRI programme, the European Centre For Ecotoxicology and Toxicology of Chemicals (ECETOC) has been an important partner.

In the early days, all requests for proposals (RfPs) were written following ECETOC state of the science (Stots) reviews. But as the LRI developed, so the role of ECETOC evolved. Today, its scientific input remains key to the programme's success.

Within the LRI, ECETOC has the responsibility of maintaining three "core teams" covering health effects, human exposure & risk assessment and the environment. These teams consist of industry scientists, who manage the scientific evaluation of applications for funding, recommend the best research proposals and monitor the progress of selected LRI projects the scientific quality and progress of the projects.

force, and feeds into the OECD's work on assessment strategies and alternative methods for assessing developmental neurotoxicity.

Cefic's Gernot Klotz stresses the role of networking in capacity building and learning across the relevant stakeholder groups. "LRI brings industry scientists in contact with academics and regulators, who need to network to learn. This also provides a better understanding on the industry side as a reliable basis for its advocacy efforts."

He adds that it also "demonstrates the engagement of the industry [and] makes it actively involved in science-based policy making." But ultimately, he concludes, the LRI has to network even further.

"Regulators and academics largely understand the issues, so LRI has to be part of the broader stakeholder discussion and link to the broader innovation issue around acceptance of new technologies." He sees LRI as a tool that can bring both sides together and help the public, as well as the industry.

Ten years to build on

The Long-range Research Initiative (LRI) is 10 years old. Already, it has funded 120 projects, involving more than 300 scientists in more than 50 universities or institutes in 15 countries in Europe and North America. It has brought better understanding of the potential impact of chemicals to both industry and regulatory bodies

State of the science white papers developed on:

- 1. Atmospheric chemistry
- 2. Chemical carcinogenesis
- 3. Ecosystem dynamics
- 4. Endocrine disruption
- 5. Environmental and human exposure assessment
- 6. Immunotoxicity and allergy
- 7. Neurotoxicity
- 8. Respiratory toxicity
- 9. Risk assessment methodology

Publication of final results becomes a condition of LRI contracting

- Topics of global importance harmonised under the International Council of Chemical Associations (ICCA) umbrella
- First projects reach fruition - LRI impact becomes visible
- Harvesting results: more than 50 papers on LRIfunded research are published
- Building consensus on testing methods: ICCA workshops on quantitative structureactivity relationships

1998 . . . 1999 . . . 2000 . . . 2001 . . . 2002 . . . 2003

- First requests for proposals published in an open tender process
- Creation of the External Science Advisory Panel (ESAP) to provide independent advice on the direction and scope of the LRI
- Members, ESAP and other stakeholders surveyed on future programme direction, leading to programme revision with higher priority for human exposure and renewed focus on endocrine issues
- LRI research recognised as highly relevant in political context of the EU's Chemicals Policy Review (later known as the Reach chemical regulation)

- Second phase of research proposals: European Chemical Industry Council (Cefic) board renews LRI mandate and approves new funding, broadening its portfolio with additional research of relevance to the contemporary regulatory environment, including biomonitoring, alternative test methods and children's health.
- Geography referenced regional exposure assessment tool for European rivers (Great-Er) recommended for use in Reach
- The LRI-sponsored Great-Er II model is recommended by the German Federal Environmental Agency (UBA) for use in environmental exposure assessment of down-the-drain industrial chemicals and pharmaceuticals.
- First LRI Innovative Science Award goes to Roger Godschalk, Maastricht University, the Netherlands

- Launch of LRI Phase III and new research strategy
- ICCA LRI workshop sets industry action plan on biomonitoring and builds research agenda
- First endocrine screening test validated by OECD, co-funded by LRI
- LRI sponsors (through ECETOC) a workshop on testing strategies to establish the safety of nanomaterials
- LRI commits to characterising links between genotoxicity and chemical carcinogenesis
- ICCA LRI workshop on innovative approaches to toxicity testing. biomonitoring and risk assessment
- New Cefic LRI website launched
- Revised position paper on endocrine disrupters

. . 2004 . . . 2005 . . . 2006 . . . 2007 . . . 2008 . . .

- Offering guidance in Reach implementation: more than 20 LRI projects are cited in the successful Cefic proposal to lead on the key technical Reach Implementation Projects.
- Cefic takes the lead in the joint industry-European Commission initiative, the European Partnership to Promote Alternative Approaches to Animal Testing (EPAA)
- ICCA LRI workshop helps establish biomonitoring guidelines and shape priorities for ICCA work

- LRI teams up with stakeholders to identify research priorities that can best respond to society's real needs
- Refocuses to support innovation capabilities. Strategic value of LRI programme within the overall chemical industry's innovation strategy
- LRI teams up with more than 20 EU member states to form consortia for human biomonitoring
- LRI reaches the end of its first four-year mandate, marking completion of the majority of its existing projects
- Providing business tools: LRI conducts audit of the programme to evaluate the impact of its research
- Value of LRI is now clear in the processes that are shaping the EU's regulatory discussions, including Reach
- LRI's outputs, whether they are tools to predict the fate of chemicals, emissions databases or improved testing methods, begin to be recognised and used by international regulatory bodies
- Animal Alternatives Issue Management Team established
- LRI takes up the lead in developing methods for identification of respiratory allergens



Connecting with people

The European LRI programme is looking towards the future with its strategic research focused on three main areas, chosen to address key public concerns over the direction of scientific development

THE EUROPEAN Chemical Industry Council (Cefic) launched the third phase of its European LRI programme in November 2006, setting the focus for strategic research on three clearly defined priority areas. These are the thematic areas of intelligent testing and assessments, health impacts of complex environments and acceptance of new technologies and products.

These areas were selected as they are highly relevant to industry and society's real needs. Research projects within these thematic areas help address, for example, the public's concerns over animal testing, exposure to hazardous chemicals in the home

and the introduction of products incorporating nanomaterials. All of these are major concerns for society today.

This ongoing research programme, says LRI: "Reflects the industry's ambition to promote a stronger, sustainable link between science and society, in particular around issues of health and environment."

INTELLIGENT TESTING

Dr Tim Gant of the Medical Research Council at the UK's University of Leicester, and a member of LRI's External Scientific Advisory Panel (ESAP), explains that with recent rapid advances in genomics and

genetics, there is a real need to develop and validate better testing procedures and particularly to ensure that underlying mechanisms are, as far as possible, understood.

"We have ways of assessing potential hazard, but we now recognise risk is an individual characteristic - not all people react the same way [to the same exposure], but if mechanistic data are available, we can begin to understand how a chemical might differentially affect individuals."

The whole idea behind intelligent testing, he says, is to make sure the system you are using is relevant to the chemical under evaluation. "By understanding the mechanism, you have a chance of getting an intelligent risk assessment," he says.

Intelligent testing, explains Cefic, implies that different methods are applied in an integrated and complementary approach, focusing on the information needed from the testing. These tests can include improved animal testing (in vivo tests), test-tube techniques (in vitro), computational methods (in



silico) and high throughput assay methods. The goals are to get a better understanding of whether chemicals have any effect or not, and to make better use of resources.

But, as Gant points out, in order to develop suitable in vitro tests, you need to know the mechanisms by which the chemical poses a challenge to health or the environment. "This is putting an even greater strain on the need to understand mechanisms which is complex and potentially more expensive."

There is, he says, a dearth of funding generally for projects to build bridges between basic molecular science and toxicology, but even so, there is some very significant work going on. He points to several recent LRI awards in epigenomics and the understanding of the transgenerational effects of chemicals as examples of how the LRI is helping to advance intelligent testing.

ACCEPTANCE OF TECHNOLOGY

The chemical industry places great emphasis on innovation and is continually bringing new products to market, as well as enabling its customers to do likewise. But it can only continue to do so if it has the trust of society. The furore over the introduction, or non-introduction as it turned out, of genetically modified crops into Europe provides

a salutary lesson in how public concerns can feed through into negative regulatory considerations.

Society's trust in science and technology has declined since the 1990s, says Professor Lynn Frewer, of the University of Wageningen, the Netherlands, an expert in food safety and consumer behaviour and current chair of ESAP. Indeed, she believes, it has been declining since the 1950s, when the environmental and health effects of chemicals began to be of public concern.

It is important to tackle this issue now, she says, especially as we are on the brink of several new emerging technologies, such as nanotechnology, which is already beginning to attract societal concerns. Frewer believes that several factors lie behind the lack of society's trust in new technologies.

One is that the industry has shown a lack of transparency on its research and decisionmaking in the past; another is that the public generally puts more weight on the risks rather than the benefits when considering the risk-benefit balance of new technologies and this drives their decision-making

The good news is that Frewer thinks the chemical industry has made progress. On nanotechnology, she says, the industry has made much more effort to understand consumer perceptions of the issues, through empirical investigation using both quantitative and qualitative analysis and by taking a psychological approach.

But there is still much more work to be done to understand how society weighs up and reacts to new technologies. She points to areas such as robotics, where there is a lot of societal sensitivity, and identification and biomonitoring technology, which brings with it privacy issues.

Cefic has started to fund research into this area and is looking to fund a project that is scoping the current range of methodologies that are available to measure societal responses and acceptance of new technology.

There is a huge literature about societal attitudes and it makes sense to scope what is currently available," says Frewer. "By understanding consumer concerns, industry can develop effective communication on things that are important to people, such as the uncertainties associated with various technologies and the safeguards that exist for consumer protection."

In the long run, such understanding should ultimately influence how industry goes about innovation and product development, so it can take public reactions

into account as it designs its research programmes and comes up with technologies and products that people actually want, rather than ones they are suspicious of, concludes Frewer.

Over many years, stakeholders have focused on developing testing methodologies to assess the hazards posed by specific chemicals. But the real world is much more complex. Individuals are continually exposed to mixtures of chemicals and other environmental stressors at varying concentrations as they go about their daily lives.

Understanding how to quantify the risk posed to the individual by such exposures is becoming more important, as the public and health and environmental groups become concerned over their effects.

COMPLEX ENVIRONMENTS

Herman Autrup, professor of environmental medicine at the University of Aarhus in Denmark, explains that there are two different problems to overcome in the assessment of complex environments: first, to understand how chemical compounds interact in their toxicological effects - do they, for instance have an additive effect, or not; and second, what is the effect of multiple dose exposures over time - does this build up to a toxic dose, or not?

"If the chemicals do not act though the same mechanism, but through differing pathways, this might lead to a toxic response. We simply do not know how such compounds are having an effect. They might be additive, or even protective." Many of the chemicals of concern are found, in food, or the air and indoors or outside, and it is difficult to assess the overall exposure levels to calculate the risks they pose.

For example, says Autrup, several major classes of organotin compounds are found everywhere, in food, consumer goods and textiles. "Each exposure may not exceed the level of concern, but add the effects up over all exposures and you might get concerns."

LRI is beginning to fund studies to help understand the action of complex environments. Projects have been studying potential effects on health (for example cancer, allergies, asthma) as well as the likelihood of exposure of consumers and workers.

As Autrup points out, there are emerging concerns as new scientific information shows new mechanisms for the development of cancer. This will mean industry can expect new regulatory requirements in areas that it does not yet know much about.

Vital support

The LRI's Innovative Science Award encourages young researchers to engage an new technologies and solutions to modern environmental and health challenges

EACH YEAR for the past five years, a young European scientist has won significant funding to pursue research into the environmental or human health effects of chemicals.

The prize of €100,000 (\$130,000) is awarded by the European Chemical Industry Council's (Cefic's) LRI programme and gives them the ability and confidence to pursue their ideas at an early stage in their careers. The award reflects the chemical industry's ambition to promote a strong link between innovation and society's expectations.

This year's winner of the LRI Innovative Science Award is Dr Emma Taylor from the MRC Toxicology unit of the UK's Leicester University. Her winning proposal is for a project on the transgenerational epigenetic effects of environmental chemicals on male fertility using in vivo and in vitro stem cellbased systems. Germ line toxicity, explains Taylor, is a profoundly important area of toxicology because it has the potential to affect not just the exposed population but also future generations.

"There is already evidence that common environmental chemicals can induce harmful inheritable changes. Thus, further research is vital in order fully to assess transgenerational toxicity, understand how such effects are induced, set safety guidelines, and promote the development of solutions and strategies to combat harmful inheritable phenotypes," explains Taylor.

She comments that the award looked very exciting when she saw the call for entries. "It provided significant financial support, particularly for a personal award, and was very flexible in terms of how the budget could be used. It was also perfect for the toxicogenomic work we do in our lab."

The award will provide a significant part of her salary for two years and still fund a large consumables budget and money for travelling to conferences. But it is not just the financial benefit, she adds. "This is a



Taylor by Evonik's Michael Droeschei

prestigious award and will greatly benefit my personal career. And, it gives me an insight into Cefic and the chemical industry in

Each year, the award alternates between environmental and human health projects, and is funded jointly by Cefic and the Society of Environmental Toxicology and Chemistry (SETAC) or the Federation of European Toxicologists and European Societies of Toxicology (EUROTOX).

Previous winners are:

- Dr Roger Godschalk, University of Maastricht, the Netherlands (2004)
- Prof Dr Paul van den Brink, Wageningen University, the Netherlands (2005)
- Dr Ellen Fritsche, Heinrich-Heine University, Germany (2006)
- Dr Roman Ashauer, Swiss Federal Institute of Aquatic Science and Technology (2007).

SIGNIFICANT FUNDING

Most agree that the value of the prize represents "significant funding" and stress the freedom and confidence it gives them to carry out their research.

Roger Godschalk says winning the prize also helped his career, as the award was

recognised in the talent planning programme of his institute. He is using the prize money, and a matching sum provided by the Netherlands' National Institute for Safety and Environment (RIVM), to investigate germ line mutations caused by exposure to carcinogenic chemicals, notably polycyclic aromatic hydrocarbons.

He is looking for answers to how these chemicals affect DNA in sperm and if mutations can be transferred to subsequent generations. "We started the project from scratch, but have a lot of data coming in now. We have published one review article and have three papers almost complete and we will publish them soon," he says.

Paul van den Brink agrees, noting that the prize is "a lot of money for a scientific award." And it's not just the money, he says. "It brings recognition and the freedom to spend it on what you think is important... and accelerate work."

His work is focusing on the sensitivity of different aquatic species to pesticides, depending on their characteristics, such as size and lipid content, and aims to give an understanding of why some species are more sensitive than others. The project requires a lot of complicated experiments and is assessing no fewer than 15 species.

Last year's winner, Roman Ashauer is working on a related topic, developing measurements and models for a better understanding of toxic effects on aquatic organisms over an extended period. These can help assess the ecotoxicological effect of untested compounds as well as improve the risk assessment of chemicals through a better understanding of how mixtures act over time. Ashauer is able to work with one colleague and two part-time students as a result of the award. "We are up and running and generating data and expect results over the next two to three years."

Ellen Fritsche's project is looking into the validation of a human in vitro model for testing developmental neurotoxicity, in an effort to substitute for animal testing, which has ethical, cost and time issues.

Gernot Klotz, Cefic's director of research and innovation, says that Cefic's continued support to young scientists "helps broaden our knowledge for developing innovative technologies and products. The winners' vision and enthusiasm reaffirms industry's belief that technology leadership and innovative solutions can help face many challenges of our society today and tomorrow in a responsible way."

Highlights of current LRI activities

Intelligent testing & assessment

Develop alternative approaches to animal testing (replacement, refinement, reduction)

Develop and validate testing and assessment strategies for endocrine disruption

Computational tools to prioritise and group chemicals (incl. USRA)

Risk assessment of PBTs (Persistent, Bioaccumulative, Toxic chemicals)

Tier approaches for aquatic toxicity testing

Health impact of complex environments

Better understanding of HBM data

Harmonisation of HBM approaches

Validated test methodologies for developmental neurotoxicity

Refinement of risk assessment through modern technologies, e.g.. toxicogenomics, epigenetics

Societal acceptance of innovative technologies & products

Tier approaches for safety of nanomaterials

Impact of nanomaterials on eco-systems

Societal acceptance of new technologies

LRI-sponsored workshops to frame emerging issues together with regulators, academia, NGOs and industry



For more information, contact:

Annie Mutamba, Research and Innovation Communications Cefic - the European Chemical Industry Council Avenue E Van Nieuwenhuyse 4 B-1160 Brussels Belgium

Tel: +32 2 676 7333 Fax: +32 2 676 7433 email: lri@cefic.org

www.cefic.org www.cefic-lri.org