

14th Annual Cefic-LRI Workshop
Evolution or revolution:
What Research Priorities for Future Risk Assessment?
14-15 November 2012
The Square Brussels Meeting Centre

Summary

Cefic-LRI 2012 Workshop provides food for thought

Opening the main workshop sessions on November 15 Chair of the LRI SIG **Dr. Stuart Marshall** of Unilever argued that human health and environmental risk assessment paradigms – the ‘meat and drink’ of LRI - had remained fundamentally unchanged for decades. However some recent drivers were bringing change to provide better assessments with minimal animal testing. The big question was how can LRI continue to effectively add to these developments?

Pierre Joris of Solvay and member of the Cefic R&I Programme Council emphasised that high quality science was the basis of the LRI programme. The robust science of LRI was also a basis for competitiveness and positioned Cefic as a recognised supplier of quality science for input to decision making.

Trust is key

Effective risk assessment is at the heart of LRI’s work and **Prof. Colin Janssen** of Ghent University emphasised the need to put ecological realism into environmental risk assessment (ERA) procedures arguing that more than just technical progress on risk assessment is needed to advance ERA – in particular there is a need to ‘mind the gap’ between what we want to do (prevent adverse effects on populations or ecosystems) and what we do do (measure effects at cellular or individual animal level). He argued that an ‘improved’ ERA approach that combined current exposure and effect assessment with an ecosystem assessment is needed. He also called for a greater communication effort and dialogue with users of risk assessments.

Cefic Executive Director for R&I **Dr Gernot Klotz** gave the industry perspective on research priorities for future risk assessment also as the basis for acceptance of innovation. The key question for the workshop was what research is needed for future risk assessment? Science-based decision making is essential but the focus must be on a balanced benefit and risk discussion on a societal basis. What was needed was greater focus on the science discipline of interpretation: what does the data mean in terms of real impact?

This is the big challenge for all decision makers: too high a level of safety towards potential risks will put people out of work, but if the risk is high and proved we must act quickly on issues. Within the EU there are currently around 150 regulations using risk assessment. There is a clear need to improve assessment, to look into exposure data and see where in-vitro data can contribute. However, the question” what does it mean in real life” has to be at the centre of all efforts. Gernot also encouraged people to reach out to other scientific disciplines that could help to interpret the data and help understand its impact such as social sciences.

Dialogue and debate

The call for greater dialogue and communication with decision-makers, regulators and the public was a theme for many speakers during the workshop. At the evening reception on 14 November that marked the start of the workshop **Ms Sile Lane** of the UK-based organisation Sense about Science had discussed the organisation's work to boost public confidence in science and bring more science-based evidence to bear on policy-making. She advised "making more of your scientists" to talk about issues and engage with the public.

This call was reflected by **Dr Jan Staman** from the Rathenau Instituut who encouraged scientists to 'rebrand' as experts to help build trust. Policy-makers and the public need experts who are not afraid of grand societal challenges: who know who they are, what their role is and what they can contribute.

The media perspective was also discussed by **Erika Widegren** of Atomium Culture who considered the changing media eco-system. She also emphasised the need to engage directly with the public as public attitudes to news access changed – mainly due to the rise of social media. Not all scientists can be good communicators but media shapes opinions about new technologies. So there was a need to consider how to use new media to help us.

Nanoparticles: first results

The workshop featured the results from the first LRI studies on nanoparticle toxicity. The N1 project was presented **Dr. Otto Creutzenberg** of Fraunhofer ITEM. The test materials for both studies were ZnO nanoparticles used in cosmetic materials and 'nano' silica used in the food sector. A combination of in-vitro and in-vivo testing was used and proved complementary. Inhalation, dermal and genotoxicity testing for both substances showed low or no adverse effects – and no addition effects due to particle size.

The second project described looked at reproductive toxicity of the same two nanoparticle materials. The LRI-N3 project was described by **Dr. Andre Wolterbeek** from TNO. The study used the same ZnO and silica samples used in N1 for prenatal developmental toxicity studies (both ZnO and silica) and a two generation reproductive toxicity study (silica only) on Wistar rats. Again no significant adverse effects were observed except in mothers subjected to a high dose (7.5 mg/m³) inhalation group. It was noted the choice of vehicle and method of dispersion influenced the size distribution of the nanoparticles and characterisation of size distribution was important but resource consuming.

These initial tests for nanotoxicity showed no significantly unusual or additional effects, but **Dr. Tom van Teunenbroek** from the Dutch Ministry of Environmental and Spatial Planning described the very large nanotechnology safety project NANoREG that will cover all safety aspects from hazard identification to risk assessment, followed by risk management, mitigation and avoidance for e route for manufactured nanomaterials (MNMs). The project will not only consider safety but also what has nanotechnology has got to offer. It will analyse the critical characteristics of MNMs that need to be considered to develop safer substances.

Tiered testing

A tiered approach to aggregating exposure assessment for indoor environments was presented by **Ir. Rudi Torfs** of VITO covering two LRI projects on exposure assessment and

aggregated exposure (B4-CERTH and B5-THL). Aggregated exposure assessment (AEA) is an assessment of exposure to a single agent from all potential sources and pathways and related and all related exposure routes and is a dauntingly complex task. However AEA is needed to develop a pragmatic and realistic framework for risk assessment and achieve a better representation of exposure. The TAGS (Tiered Aggregate Exposure Assessment) approach provides a decision structure within an exposure scenario and can help decide if you need simple/ single exposure assessment (SEA) rather than aggregate exposure assessment (AEA).

More development was required including better and more integrated tools for tiered AEA, more data for model parameterisation, research to differentiate exposure assessments for adults and children and in the longer term all knowledge and tools must be integrated into an overall framework that can characterise the full 'exposome'.

Integration of metabolic fate, health effects and biokinetics predictions in an in-silico - in-vitro - in-vivo approach to a tiered testing strategy was also the subject of the presentation from **Prof. Dr. Bas Blaauboer** of Utrecht University. The LRI project HBM3-IRAS used a variety of models to make in-silico predictions of metabolites, toxicity and target tissues using only in-vitro toxicity, kinetic and metabolism data. The results of this modelling were the compared with in-vivo data for a wide range of compounds from different substance classes. The project showed that future risk assessments could be approached via in-silico and in-vitro studies (where available) if the in-vitro studies were validated against in-vivo data. Such an approach would help reduce the need for animal testing for risk assessment.

Evolution or Revolution?

Prof. Michael McLachlan, University of Stockholm described some innovative techniques for assessing bioaccumulation factors (BCF) undertaken in LRI ECO-14 project using novel techniques for passive dosing (with constant concentrations of test substance in the dissolved phase) and sampling (using acupuncture needles) to allow kinetics in an individual fish to be studied. The procedure also used internal benchmarking of chemicals to improve precision and information content. Passive dosing and sampling were seen as evolutionary developments but the use of benchmarking to measure relative bioconcentration could be revolutionary in terms of simplifying test design, reducing animal use and reducing the time taken (80% or more) to achieve results.

Work on endocrine disruption has been a significant part of the work of LRI since its early days and recent industry workshop outcomes and key on-going LRI research efforts were described by **Dr. Steffen Schneider** of BASF. The cross industry workshop had looked at health effects and possible new endpoints, however evidence was not robust. The LRI EMSG 56 was a project designed to generate data to fill information gaps on endocrine effects via a complicated study involving prenatal and postnatal observations. The results had seen effects where effects were predicted but also observed effects at 'no effect' levels. Some studies were being repeated to confirm these observations.

Cefic-LRI Innovative Science Award

The annual LRI Innovative Science Prize is one of the highlights of the year. The 2012 winner is **Dr. Andreas Bender** of the University of Cambridge. He was formally presented with his prize by Pierre Joris.

Andreas is a chemist by training and will use the prize to determine biologically relevant effects of exposure by chemical, biological and phenotypic data integration. He described the 'Magic triangle' of molecular structure, phenotype data and protein or mode of action. Currently each was used separately to make predictions but through integration of information joint modelling was likely to significantly improve predictive results, which was the goal of the project.

Earlier the workshop got a progress report from the 2011 LRI Prize winner, **Dr Thomas Preuss** of RWTH Aachen University, who is looking to improve mechanistic understanding of population recovery for aquatic macro-invertebrates. He studies population sustainability and the impacts of toxic effects. The essential parameter is the time for a population to recover (time to recovery – TTR). Recovery of a population within 56 days is deemed acceptable pesticide guidance. However there is uncertainty so there is need to develop a science-based mechanistic model. Thomas described his individual-based Daphnia population model (IDamP) that had been validated for various conditions and inputs. The model is used as a virtual laboratory to analyse influence of ecological scenarios on recovery time and showed great power to improve environmental risk assessment.

Challenges in the future of Risk Assessment were discussed by **Prof. Corrado Galli** of the University of Milan. He posed the question: do we want to continue with a hazard based criteria or move to a scientific-based logical step-wise approach? He argued for the latter approach via a bottom up approach that could introduce greater flexibility. Such a dynamic model for future human risk assessment should consider exposure early as if there was no exposure route then there was no need to test!

The contribution of epidemiological research and its quality was assessed by Prof. Dick Heederik of Utrecht University. A major issue in epidemiological research is the role of various form of bias. Studies can suffer from various forms of bias and bias should be controlled for or quantified so that the influence on associations between exposure and risk is known. However, application of quality criteria to evaluate the epidemiological evidence helped to select high quality studies, which are less prone to the effect of various biases. It also helps to improve transparency in risk assessment, and gives insights on uncertainties, helps providing evidence-based transparent decision-making and led to improvement of the quality of future research.

Summing up the workshop **Stuart Marshall** said that there had been much food for thought to feed the next LRI programme. New paradigms were being proposed that dealt with greater complexity and integration of data. At the same time there was a clear need to engage with the media and public partners which required the right communications.

In terms of future perspectives LRI was working in both revolutionary and also evolutionary ways – the key thing is to get the balance right! All the presentations given at the workshop



and posters displayed will be made available on the LRI website and the fuller Proceedings of the 14th Workshop will be available to download in the near future.