17th ANNUAL CEFIC-LRI WORKSHOP
"Non-animal –based Safety Assessment: Within reach or over-sold?"
18-19 November 2015
Le Plaza Hotel, Brussels

Executive Summary

The 17th Annual LRI workshop successfully addressed three main tasks: celebrating the 2015 LRI Innovative Science Award; reviewing a selection of current projects across LRI's four focus areas (intelligent testing, complex environments, acceptance of technologies and policy impact); and discussing the current status and future potential for integrating non-animal based safety testing into risk assessment and regulation.

The 2015 winner of the LRI Innovative Science, Dr Alice Limonciel of Innsbruck Medical University, received her prize at the workshop dinner. The award once again proved that it is a true win-win opportunity providing both a valuable career boost for an early career scientist and bringing new and disruptive ideas into the LRI research programme.

The project presentations highlighted the diversity of the LRI programme and its pragmatic approach providing a range of essential tools that the industry needs to fulfil and expand its risk assessment capabilities. All developed systems were freely available via the LRI Toolbox on the programme's website.

The panel discussion on the status of non-animal testing revealed disappointment with the overall progress in implementing animal alternative strategies. Several speakers felt that the focus on full animal replacement had sought to provide a 100% perfect alternative system when existing animal models themselves were not perfect. There was a call to stop developing more new methods and to start using what we already had: to "start to harvest" the LRI crops. The overall goal must be ensuring human (and environmental) safety, not looking for one-to-one replacements of animal tests.

There was a clear need for improved collaboration and coordination across non-animal testing to "break down silos" and embrace understanding from other science - areas where LRI surely had an important role. The requirements for methods that facilitated true risk assessment and not just identified potential hazard must be better understood.

The limitations of all the methods being developed (and already developed) needed to be understood; the key was to start using the new methods and not to continue to seek perfection. An important challenge will be developing and using exposure integrated risk assessment – potentially a method for rapid substance screening - but this could provide a way forward to greatly reducing animal testing.

All the presentations and other information on the 17th Annual LRI workshop can be found on the revised Cefic-LRI website at: http://cefic-lri.org/events/17th-annual-cefic-lri-workshop-2015/.

The 2016 annual Cefic-LRI workshop will take place on **16 &17 November 2016 in Brussels**.

LRI Innovative Science Award 2015

The 17th LRI Workshop opened on the evening of 18 November at Le Plaza Hotel in Brussels with a poster session and dinner during which the 2015 LRI Innovative Science Award was presented.

The poster session featured presentations by 10 LRI projects covering a wide range of LRI topics. Delegates and dinner guests were able to talk to the poster presenters over networking drinks. Brief details of the posters are given here: http://cefic-lri.org/events/17th-annual-cefic-lri-workshop-2015/ under the **Posters section**.

The LRI Award dinner session was chaired by **Yves Verschueren**, Managing Director of essenscia. In his opening speech he emphasised that substance safety is an international issue and his belief that chemistry is a fantastic science. He saw the role of LRI and the LRI Innovative Science award as helping policy makers to really understand the value of the chemical industry and highlight the benefits that the industry brings to everyone's quality of life. For the chemical industry even more value would be created in the future.

Mr Verschueren introduced the LRI Innovative Science Award. The winner of the 2014 LRI award was Portuguese researcher **Dr Alexandra Antunes** from the Centro de Quimica Estrutural, Complexo Interdisciplinar Instituto Superior Tecnico (CQE-IST) in Lisbon. She presented progress on her work to investigate if improvements can be made in the detection of early stage cancer. Her project entitled 'Covalent Modification of Histones by Carcinogens: a novel proteomic approach toward the assessment of chemically-induced cancers – CarcHistonOmic' is based on the concept that early stage cancer formation can be detected by studying the binding of chemicals substances to human proteins using mass spectrometry. This new compound specific biomarker has enormous potential to improve early detection and thereby the chances of successful therapy. For the first time ever, using a broadly available tool, this new methodology could quickly screen chemicals for their potential as carcinogens - in effect serving as an early warning system - and providing an invaluable new in-vitro approach.

The 2015 LRI Innovative Science Award, worth €100 000, was presented to **Dr Alice Limonciel** of Innsbruck Medical University by Mr Verschueren.This year's winner responded to the theme 'Establishment of thresholds of activation of stress responses pathways and link to adverse outcomes for chemical classification and risk assessment'. Dr Limonciel's project proposal investigates cellular responses to the acceleration of chronic kidney disease progression due to chemical exposure. The project aims to identify the genes involved in cellular stress response pathways, quantify these responses in parallel with markers of cellular dysfunction and deliver a new generation of quantitative tools based on gene expression to evaluate the hazard linked to chemical exposure for use in risk assessment strategies. The project builds on technological advances and increased knowledge of molecular pathways that have created a paradigm shift in toxicology with the monitoring of molecular mechanisms as a driving force. In particular the focus will be on the characterisation and quantification of these mechanisms in in-vitro human renal cell cultures that will be integrated into a novel adverse outcome pathway linking cellular responses to the acceleration of chronic kidney disease due to certain chemicals.

LRI project impacts

The next morning (19 November) the delegates reconvened for the first main session of the workshop that took place in the impressive surroundings of theatre hall at Le Plaza Hotel. **Dr Stuart Marshall** of Unilever and Chair of the Cefic LRI Strategy Implementation Group welcomed delegates and reminded them of LRI's current four focus areas: intelligent testing; complex environments; acceptance of technologies; and policy impact. He also reminded his audience of the seven key questions that the research programme is seeking to address over the next ten years or so.

1. Omics / 21st Century Toxicology: How to link information at the molecular level to health impacts and interpreting results for meaningful decision making?

2. Predictive tools for health impact: What are pragmatic approaches for reducing complexity, whilst maintaining robust predictions of health effects?

3. Combination effects: How to identify combination effects scenarios of concern?

4. Eco-systems approach: Which new concepts enhance ecological relevance of risk assessment?

5. Real life Exposure: Which predictive, validated exposure scenarios apply to assessing environmental stressors?

6. Comparative assessment: How to interpret impact of health and environmental stressors?

7. Risk/benefit approaches: Can we understand societal drivers for public acceptance of innovation?

Nuts and bolts

The main morning plenary session was chaired by **Dr Bruno Hubesch**, LRI Programme Manager at Cefic, and covered the "nuts and bolts" of the programme: the impact that LRI projects made with a focus on environmental risk assessment, bioconcentration, chemo-informatics, exposure modelling, skin sensitisation, and acceptance of innovation. Today some 33 LRI projects in progress. The workshop session covered projects that had recently finished, while the poster session had described projects that are just starting.

ECO19: ChimERA: An integrated modelling tool for ecological risk assessment was described by **Prof Frederik De Laender** of the University of Namur in Belgium. ChimERA is effectively a network of models that integrates exposure and effect assessment to introduce dynamic effects within an ecosystem (such as predation and competition) and see how this affects the calculation of chemical exposure. ChimERA can predict how biomass dynamics affects chemical fate. The model predicts the influence of biomass on fate well, but there was a need to move from understanding of individual toxicity effects to population level effects and this was where species interactions came into play such as competition and predation. This is a complicated area that rarely gave a simple answer. However the ChimERA model had demonstrated a technically sound integration of fate, toxicity, population and ecosystem models that predicted bioavailable chemical concentrations and the response of species present. Output could also be tracked back from ecosystem to individual level in the model. Ongoing work includes scenario analysis to better understand how the model responds to changes in its parameters and further work to validate the model's results and analyse its output.

Regulatory and scientific interest in the bioaccumulation and ecological risk of ionisable organic chemicals (IOCs) is increasing, however most modelling tools were developed for neutral molecules. The second presentation outlined project **ECO21** that was looking to improve the performance and expand applicability of bioconcentration models for IOCs. **Dr Steven Droge** of Utrecht University described the challenges of the **BIONIC** project including the scarcity of empirical bioaccumulation data for IOCs, the need to include pH dependency for IOCs, biotransformation and the wide variety of compounds represented by IOCs. The project has produced new experimental data and developed QSAR (Quantitative Structure Activity Relationship) models to parameterise bioaccumulation for IOCs. Under the project some 50 key IOCs covering most classes of compounds have been tested using in-vitro biotransformation assays. Usually bioconcentration factor (BCF) can been predicted from K_{ow} (the water-octanol partition coefficient) however for IOCs this is a poor predictor. The project has focused on the use of K_M (membrane water partition coefficient) as a predictor with some success – the revised model is now within a factor of 5 for most compounds. The final activity for the project will be to put all the data together, use revised QSARs and compare the BCFs that the model predicts with the new experimental measurements. A continuation of the project might examine further

measurements to improve BCF predictions and look at covering additional data gaps that would allow for expansion of the chemical domains covered by the model.

The final presentation of the first morning session was given by **Dr Volker Koch** of Clariant and covered the **EEM9.3** project that is linking the LRI **AMBIT** chemoinformatic system with the **IUCLID** (International Uniform Chemical Information Database) substance database to support read-across of substance endpoint data and category formation. IUCLID is the key tool for the chemical community to fulfil data submission obligations under REACH. AMBIT is a component of the LRI toolbox of methods and instruments that is free to access via the LRI website. The inclusion of high quality substance data will enhance the predictive power of the AMBIT in-silico tool, the new version also implemented workflows for assessments and should minimise overall animal testing and resource costs. Dr Kock took delegates through AMBIT's capabilities working with IUCLID. One important feature is the automatic assignment of chemical structures from the AMBIT structure pool to the constituents, impurities and additives defined in an IUCLID substance. A search for a defined structure yields relevant substances and endpoint data that could be filtered as required by the user. AMBIT has several output options including the generation of an assessment report as a Word document that itemises justification/ validation of the approach taken. AMBIT is an open source application with many functions that can be further developed or customised. The project will be finalised on 8 December 2015 and then the new version of AMBIT would become a free, open, publically available tool. An AMBIT workshop was being organised for 21 January at Cefic in Brussels to allow users to gain "hands on" experience of the new system. Registration for the workshop was open now!

After a coffee break **Prof Denis Sarigiannis** of the Centre for Research and Technology Hellas (CERTH) described another linking project: **B11** on the Integrated External and Internal Exposure Modelling Platform (**INTEGRA).** This would also be available soon in the LRI toolbox to help users assess the source to dose continuum for the entire life cycle of a substance. Its applicability domain covers an extended chemical space. In the context of REACH the model can be used for internal exposure modelling and the output used to fill refined exposure estimates. Prof Sarigiannis called INTEGRA the first computational tool for risk assessment that allowed for biomonitoring data interpretation as well as risk characterisation based on in-vitro testing outcomes. In this way he felt it facilitated the shift from hazard based assessment to exposure based assessment. INTEGRA integrates exposures from several sources, pathways and routes, and translates external exposure estimates into actual uptake and internal dose. A key feature is the ability to reconstruct exposure starting from biomonitoring data using a complex exposure reconstruction optimisation algorithm. Linking emissions, concentrations, exposure and internal dose in this way allowed the coupling of environmental and biological processes in an approach that could also be validated at each step. Similarly the joint capture of toxicokinetics, toxicodynamics and exposure dynamics allowed the incorporation of mechanistic knowledge in exposure assessment and improved the validity and relevance of risk characterisation outcomes. Integrated external and internal exposure assessment with a particular focus on tissue dosimetry, also allowed the use of recent developments in high throughput toxicity testing and incorporation of other bio-chemical interactions.

Project **S3** covered the development of a robust participatory regulatory framework to enhance the **wider acceptance of innovative chemical technologies** and was described by **Prof Jason Weeks** of Cranfield University. This project followed two previous projects that had sought to map where 'hard' and 'soft' scientific disciplines met and map aspects of governance, however neither project had clarified what the drivers of acceptance of technology were. All three projects focused on nanotechnology. In recent years there has been a shift from only considering public attitudes

to an examination of the factors that influence those views. According to survey data the dominating factors are risks and benefits of the technology, the level of scientific knowledge, the influence of media, and trust in regulators, companies and scientists. The project had developed its own delphi-process involving a bias-less questionnaire that was presented to a wide demographic of adults from different cultural backgrounds. This multi-tiered PERFiCT (Participatory Engaged Regulatory Framework Innovative Chemical Technologies) framework was used to pull information together around the theme of what society needs to know to accept technology using specific case studies to communicate on risk issues. A set of recommendations have emerged from the study including the idea that wider society's opinion is often subjective (scientific evidence is often forgotten when debating ethical issues) and based on perception of risk. Prof Weeks highlighted that the key determinant is trust and confidence in government and regulations. Effective communication between policy-makers, scientists and the public can reduce uncertainty and allow specific technologies to be viewed with a higher level of understanding by the wider society. He felt it was important not to "force education" on the public, what was needed was an engagement process that understood public fears and worked with them.

The final project presentation of the morning was given by Dr **Dave Roberts** of the University of Liverpool on **B14: Skin Sensitization and the Chemical Applicability Domain of the Local Lymph Node Assay (LLNA)**. In order for a chemical to produce a sensitivity reaction it needed to directly or indirectly react with a skin protein. The LLNA protocol was the only extensive source of potency data for skin sensitisation against which new non-animal can be tested so it was important to fully understand its reliability and applicability domain. For most chemicals LLNA correlates well with human potency, however chemicals that are non-sensitizers but can be autoxidised to sensitising reaction products are often over predicted leading to false positives.

What Will Work in New Orleans?

The morning session was concluded with a summary from Dr **Alan Poole** of ECETOC on the **ICCA-LRI and US EPA workshop held in New Orleans in mid-June 2015** on the application of new approaches for chemical safety assessment. This was the fourth in a series of meeting discussing the promise of new technologies to rapidly and cost-effectively provide data for assessing chemical safety. The big questions were on the maturity of the new generation of 'omics' technologies and if they can support meaningful recommendations and decisions: has the time arrived to start harvesting these new techniques to help decision-makers? The workshop consisted of three sessions. The first addressed the use and applicability of the technologies. Around the world the use of the new technologies was advancing. In particular Dr Poole noted that the EPA's endocrine disrupting chemicals screening programme was now showing a 90% predictive output which was a breakthrough. However on QSARs generally there were still questions on confidence and predictability. The second workshop session focused on the issue of confidence. The goal was to use the technologies for identifying adverse outcome pathways (AOPs) that could link initial molecular-level events to an adverse outcome in an individual or population for use in regulation. At the moment no conclusion could be reached on confidence here. Similarly there was still a big question with respect to selecting the right predictive exposure model to get the best information rather than just 'some' information. In general there was a need for effective communication to the public on scientific confidence in the safety evaluations based on these new approaches. The final session looked at future promises and challenges. The new technologies are already being applied for chemical screening – especially in industry - and are catalysing the move away from traditional animal-based toxicity testing, but additional research and communication will be needed to ensure stakeholder confidence in their use for regulatory decision-making.

Non-animal testing
After lunch the afternoon session addressed the workshop's main theme: "Non-animal based safety assessment: within reach or over-sold? Do we need to set back expectations?" The session was chaired and moderated by **Prof Ian Kimber** of Manchester University.

Prof Kimber thought that the most difficult challenge is alternative methods for repeat dose systemic toxicity testing – how do you predict what is essentially unpredictable? Is it really impossible? Or if resourced properly is this challenge possible? He took the view that if society engaged its most eminent experts on these subjects and adequately funded the research then it could be done.

The stage was set for the main panel discussion by **Prof Jim Bridges** of the University of Surrey with a presentation entitled: 'Do we know where we are going and how to get there?' He set out four perceptions of the status of chemical safety testing based on the use of animals from a system that ensures human health protection, through a method that has shortcomings but for which only limited alternatives exist, to a growing inflexible system providing limited high level human health protection and, finally, a method we could easily ban very soon. He noted many reasons to move from the status quo including social-political, regulation, good corporate governance, ethics and cost and resource savings.

Prof Bridges felt that change was inevitable but we needed to understand what is the end goal? Essentially he saw the challenge as using laboratory, non-animal testing to fully understand "the significant changes (caused by individual stressors and combinations of stressors) in the highly complex systems of communication within and between cells in a single tissue and between different tissues that in combination preserve homeostasis in humans."

Perceptions on the achievability of this varied widely, from impossible to readily achievable, but the political timescale was likely to be relatively short. He outlined a possible roadmap from the current in-vivo system to one based on in-vitro and in-silico only and the critical issues required to develop a successful strategy including criteria for testing – what will be the new 'gold standard' (animal or human) and what is the basis for selection of reference chemicals selection etc. – and what were the criteria for success. He estimated the likely realistic timescale for complete understanding at over 40 years. He saw the rate limiting steps in developing a coherent strategy to be inadequate progress in technology and understanding of the data, and delays due to lack of commitment or funding. Prof Bridges proposed a way forward to achieve risk assessments relying on non-animal testing that would need proactive dialogue and more understanding and use of developments in other relevant sciences including chemistry biology and medicine. There was also a need to recognise that for risk assessment purposes progress in scientific understanding must parallel technological developments and that understanding internal dose was key with developments in exposure science as important as developments in biological science to ensure replication of in-vivo studies in-vitro and in extrapolating from in-vitro to humans for which support to develop exposure science was crucial.

Panel discussion
An extensive panel discussion followed and addressed four principle questions covering the current situation in non-animal based safety assessment, objectives for the future, the expectations for such systems and the key challenges to be tackled. The panel line-up was:

- Dr Rick Becker, American Chemistry Council

- Dr Alan Poole, ECETOC
- Dr Karen Niven, Shell
- Dr Raffaella Corvi, JRC/EURL-ECVAM
- Dr Kirsty Reid, Eurogroup for Animals
- Dr Karel de Raat, ECHA
- Prof Jim Bridges, University of Surrey (part)

The session was moderated by Ian Kimber.

Q1. To what extent has the 'promise' of alternative methods in toxicology been realised – and to what extent over-sold?

Rick Becker thought that initially there had been too great a focus on getting a perfect animal replacement. The focus was on hazard identification – demonstrating an endpoint and effect. He felt exposure was just as important and that any framework must focus on hazard not risk. **Alan Poole** also worried about the emphasis on in-vitro perfection rather than pragmatism. Research had been too focused on replicating animal test rather than providing additional information that could enable reduction of animal use. **Karen Niven** agreed that despite a great deal of work non-animal testing had not yet delivered, but "the (scientific) fields were full of crops". We needed to start harvesting these crops and integrating results into our testing systems.

Raffaella Corvi agreed that progress had been made but what was needed was not just new methods but a change in mentality. Acceptance is the key. We were still struggling to replace animal test – still the golden standard – so she thought we needed to look more systematically at animal testing especially its variability. **Kirsty Reid** reiterated the need to ensure a high level of protection for the environment and human health. Lots of time and effort had been put into the development and validation of alternative testing and it must be implemented. However we should look for a viable overall strategy rather than focus on 1:1 replication of tests to move forward. **Karel de Raat** said this was a complex subject but there was no need to be pessimistic – great progress had been made! We needed to separate the aims of developing new regulatory techniques and gaining better understanding of toxicity. He reminded the audience that use of animal systems do not 100% guarantee protection of human health, but any alternative system must offer at least the same level of protection. **Jim Bridges** thought progress had been very disappointing. There had been too great a focus on low hanging fruit with poor coordination of dispersed efforts and we had not drawn enough on advances in biological and medical sciences.

Ian Kimber agreed: there had been enormous funding for relatively little result. He asked if alternative tests had to have the same sensitivity as animal testing. Delegates' questions and responses also called for greater use of biological data and wondered if slow progress had been due to an emphasis on a holistic approach that was over complex. The alternative approach to predict the potency of skin sensitisation worked well. It was also noted that developing new methods needed to assess a wide array of chemistries to clearly understand their limitations.

Q2. What new developments can realistically be achieved in the coming 5-10 years and is there any real prospect of developing anon-animal approach for assessing toxicity associated with repeat dose systemic exposure?

Jim Bridges thought the emphasis for 3Rs should be on 'rethink' not replace. He also thought that advances in organ transplantation would advance in-vitro systems and exposure science needed to be brought up to the same pace as the biological sciences. **Raffaella Corvi** stated that we needed to know the relevance of developments to humans: the aim must be to displace animal models with methods we understand, but we need to understand much more to do this.

Karen Niven called for people to “get out of our silos” to make progress we needed to learn from other disciplines and that outcomes were more important than publications. Communication was also very important to ensure mutual understanding between scientists. However, she also got the sense that this is not a linear process and perhaps we may be close to a tipping point or breakthrough.

Alan Poole didn’t see systemic non-animal testing being established in the next 10 years. He was not sure there was agreement on what success will look like and he reiterated that we should stop looking for perfection, start using the new techniques and gain a fuller, common understanding of what we already had. **Kirsty Reid** noted that despite all the tests that are being put forward few were coming through EVACM. There was a need to develop test on topics where hazard information is lacking. What we want are non-animal tests that can predict safety through systematic application of biological and exposure sciences said **Rick Becker**. Can we identify a system that allows us to understand biological activity to provide an indicator that is good enough to predict safety? It was also important to think about the short and medium term and also look at systems that aim to reduce the number of animals used in testing rather than completely replace them concluded **Raffaella Corvi**.

During audience questions the use of adult stem cells from adults was highlighted as a future important area and the point was made that most chemicals did not induce biological effects, however our new testing focused on this aspect. Overall there was optimism that the science would develop and that in the next 10 years or so and lead to a meaningful change in the toxicity paradigm.

Q3. What should be the promise for the future – matching realism with ambition?

After a short coffee break the discussion continued. **Rick Becker** stated that the majority of commodity and consumer chemical did not have biological function so he advocated turning the things around for the majority of the 15 000 or so chemical compounds. Given exposure and tools to understand potential biological activity would we need to do anything more? Thresholds of toxic concern (TTC) are indicators of safety, if we match TTC to exposure data and the exposure is orders of magnitude lower than TCC do we need to do more to prove safety? Omics can cover more of the biological space acting as surrogates for TTC with a next tier using animal testing for substances of concern. **Alan Poole** repeated the call to “harvest our current knowledge” to replace animals making practical use of the in-vitro techniques we have now. Product risk assessment was very different if it was part of R&D or product registration noted **Karen Niven**. There is phenomenal expertise in many industrial and pharmaceutical organisations in safety testing. It was important for industry and others to share their methods. She said that Shell has published full details of their animal testing data for the last eight years – 99% was used for product registration. She felt the medium term future could be more pragmatic if we can share how we make our products safe.

Raffaella Corvi agreed that industry has a lot of know-how. She felt we needed to be brave, use the methods developed so far and get confidence. But it was also very important to prepare a regulatory framework to embrace the new approaches. **Kirsty Reid** also agreed with previous views and she thought we were at a stage with new techniques and systems that could be used confidently in impact assessments. Work, such as that with the OECD, had produced lots of technical guidance documents on reduction and refinement of methods. We needed to start using this guidance. She thought ‘human on a chip’ technology was developing quickly and could help reduce animal use. It was also important to bring different sectors together to talk about differing

regulations and produce a horizontal approach involving other stakeholders such as CSOs and NGOs to get an outsiders view.

Karel de Raat stated that there was a real difference between replacing and adapting. Within REACH he thought there was ample opportunity to use new techniques, but this should be on a case by case basis and regulators would need to be confident that the new methods delivers at the same level as the current standard testing (the two-generation toxicity test). The new technologies allowed us to make the most of data we already have. He was optimistic that efficient and reduced use of animal testing was possible in combination with non-animal testing.

Some delegates were not convinced that exposure is the key, but **Rick Becker** said that exposure could be quantified for any scenario with an adequate margin of exposure.

Q4. What are the biggest challenges to making significant advances in the development of non-animal methods in toxicology?

Each panellist named their biggest challenge. **Karl de Raat** chose the inclusion of the level of the organism into alternative testing, while **Kirsty Reid** selected looking at the validity of existing animal models and how they can be improved. **Raffaella Corvi** looked to regulatory acceptance and to do more translational research. There was need to improve regulatory decision-making and case studies could help to develop confidence. She though it would be possible to gradually change regulations to accept animal alternatives. **Karen Niven** said that the main challenge had to be exposure in the context of risk assessment, which had to become the accepted norm. **Alan Poole** thought that the key was developing confidence in terms of laboratory efficiency and making sure we fully understood what we were measuring. **Rick Becker** agreed with Alan and Karen and wanted to focus on the chemical and biological spaces and what we already know.

Karen Niven also asked if the field needed a superstar to help communicate its messages and promote careers in the field to young people. **Rick Becker** agreed saying there was a need for a change management plan to ensure things continue to move forward.

One question asked if an annual cap on the use of animals would be useful to focus minds on reducing numbers. **Alan Poole** said that this might impact on advancing our understanding of the biology and therefore could be a bad thing. **Kirsty Reid** thought that a cap in Europe would just inspire companies to move out or share animals. The focus must be on developing alternatives and a cap would not help. **Karen Niven** concluded that companies are largely self-capping animal use as increasing use is seen to be bad, but she agreed that if animals are used in the cause of validating alternatives to animal testing then it was important not to reduce just for the sake of reducing. She noted that in the list of LRI projects there were few that used animals.

Conclusions and future perspectives

Dr Pierre Barthélemy, Executive Director, Research & Innovation at Cefic closed the workshop with some concluding remarks and future perspectives of the LRI programme. This was Dr Barthelemy's first LRI workshop and he had been impressed with the quality of the programme, the speakers and the organisation.

The LRI Innovative Science award on the first day of the workshop had shown again how this prize was a win-win situation providing both a valuable career boost for an early career scientist and bringing new and disruptive ideas into the LRI research programme.

The second day had highlighted the patchwork nature of LRI: its diversity and its pragmatic approach providing the tools that industry needs; tools from projects such as CHIMERA, BIONIC, AMBIT, INTEGRA, and PERFiCT. These were freely available in the LRI Toolbox to be found on the recently revamped LRI website.

From the panel discussion he noted the comments on the disappointing overall progress in implementing animal alternative strategies and the focus on full animal replacement that was, perhaps, seeking a too perfect strategy when existing animal models themselves were not perfect.

The second half of the discussion had called for improved collaboration and coordination across non-animal testing – an area where LRI surely had an important role. He also noted the need to understand the need for methods that facilitated risk assessment and not just identified potential hazard. We needed to understand the limitations of all the method we were developing and those already developed as well; the key was to start really using the new methods and not to continue to seek the perfect new method. An important challenge will be using exposure integrated risk assessment but this could provide a powerful way forward.

He thanked all attendees for their tangible interest in the LRI programme and looked forward to the 18th annual Cefic-LRI workshop that will take place in Brussels on **16-17 November 2016**.

Appendix - The 2015 LRI Workshop Poster Session

- AIMT6 – CON4EI: CONsortium for in-vitro Eye Irritation testing strategy
  - Dr An Van Rompay, VITO, BE
- B16 – External validation of Tier-1 workers dermal exposure estimates in ECETOC TRA
  - Dr Jody Schinkel, TNO, NL
- N5 – Pathological effects and biokinetics of life-time inhaled Barium Sulphate nanoparticles
  - Dr Dirk Schaudien, Fraunhofer ITEM, DE
- ECO27 – Chemicals: Assessment of Risks to Ecosystem Services (CARES)
  - Prof Lorraine Maltby, University of Sheffield, UK
- ECO28 – Modelling ecological scenarios for the assessment of chemical effects on aquatic communities
  - Dr Monika Hammers-Wirtz, Research Institute for Ecosystem Analysis and Measurement, Gaiac, Aachen, DE
- ECO29 – Does microbial adaptation through long term exposure lead to biodegradation of persistent pharmaceutical products?
  - Prof John Parsons, Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, NL
- ECO30 v1 – Expanding the applicability domain of the chemical activity approach for hazard and risk assessment
  - Dr Philipp Mayer / Dr Stine Nørgaard Schmidt, Denmark Technical University, DK
- ECO30 v2 – Linking algal growth inhibition to chemical activity
  - Dr Philipp Mayer, Denmark technical University, DK
- EMSG56.2 – Guideline Framework for the use of Univariate Analysis of 'Big Data' for Regulatory Use
  - Prof Tim Gant, Centre for Radiation, Chemicals and Environmental Hazards (CRCE), UK
- Q3 – Sound Science: Selective citation in science based decision-making
  - Miriam Urlings and Bram Duyxs, Universiteit Maastricht, NL

- S3 - Development of a robust participatory regulatory framework to enhance the wider acceptance of innovative chemical technologies
  - Prof. Jason Weeks, Cranfield Univ., UK