

Joint ECETOC and WHO-IPCS workshop addresses 'Mode of Action'

This February in snowy Vienna, ECETOC brought together about 60 scientists from all corners of the world to discuss recent developments on the topic 'Mode of Action' and its application in risk assessment.

The objectives of the workshop were:

- To present the WHO-IPCS guidance on mode of action/human relevance analysis that has recently been revised to reflect increasing experience in integrating information from evolving technologies.
- To familiarise with and solicit input on envisaged implications for priority setting, risk assessment and testing strategies for both individual chemicals and groups, through consideration of case studies.
- To consider next steps for additionally addressing identified priorities in regulatory risk assessment such as category approaches.

Global initiatives to promote the use of mode of action (MOA) began around a decade ago and currently involve large numbers of scientists internationally.

In essence, MOA information on a chemical results from the use of good investigative science to ascertain the human relevance of findings in animal studies. Such information should form an essential and integral part of activities such as 'read across' and 'risk assessment'.

By way of background, a 2009 ECETOC / ILSI RF / HESI workshop exchanged views informally on conceptual approaches to the use of MOAs. The recommendations included:

- establishing an expert working group to oversee the creation of a repository or reference database of agreed MOAs;
- continuing and extending training and educational programmes based on risk assessment practices using MOA;
- changing the present risk assessment paradigm to encompass early focus on hazard characterisation including MOA versus hazard identification;
- providing guidance on the generation of information during standard toxicity tests that could be of value in MOA analysis;
- developing predictive methods for MOAs, focusing on key events;
- making optimum use of information from human studies;
- agreeing and harmonising MOA terminology on a global level.

These recommendations were helpful but not easy to put into practice.

As a consequence, WHO/IPCS formed a global Steering Group to co-ordinate implementation of an 'umbrella plan' of work. It comprises experts from ECHA, EFSA, Imperial College, JRC, OECD, University of Ottawa, US EPA, ECETOC, ILISI / HESI and WHO. It was further agreed that ECETOC / WHO would organise a workshop to review progress, hence this gathering in Vienna. The conclusions and recommendations are currently being summarised and will soon be published as a workshop report.



SG corner

As the new Secretary General of ECETOC, I would like to share with you how proud I am to have been invited to take on this role. It is also an opportune time to thank Neil Carmichael, the retiring SG, for the leadership and wisdom he has shown in guiding this organisation for the past 5 years. He leaves behind a great legacy as illustrated just this month, when I received news that the USA Society of Toxicology has awarded the scientific article by Bars *et al.*,^a 'Risk assessment of endocrine active chemicals: identifying chemicals of regulatory concern' as "Outstanding paper for advancing the science of risk assessment". In addition, the paper by Lavelle *et al.*,^b 'Framework for integrating human and animal data in chemical risk assessment' has been recognised as one of the "Top 10 best papers advancing the science of risk assessment" for 2012. Both of these papers were the product of work carried out by ECETOC task forces. Such awards are difficult to achieve and demonstrate the excellent scientific contribution ECETOC has provided, and continues providing, to help society make high quality, scientifically-based risk assessment and risk management decisions.

ECETOC can look back with pride on the outstanding contributions made to:

- The development of internationally agreed toxicology testing protocols;
- Developing concepts and application of risk assessment methodology and
- Applying scientific rigor to observational epidemiology studies.

Together, these activities have helped form the current concepts and application of scientifically-based risk assessment.

As you know, scientific methods and ideas are, however, always evolving and now we must look to the future and contemplate how the application of new tools, technologies and concepts can enhance current risk assessment procedures. For example, an Inter-Committee Coordination Group of Scientific Committees advising the European Commission has issued a discussion paper entitled "Addressing the new challenges for risk assessment". In summary, the document identified how the procedures currently used for both human and ecological risk assessment are anticipated to change over the coming years. Similar discussions on new concepts for hazard identification and risk assessment, involving integrated strategies, new tools and technologies, have been ongoing in the USA

Continued on page 2

Front page

- Joint ECETOC and WHO-IPCS workshop addresses 'Mode of Action'
- SG corner

Page 2

- Membership news
- Upcoming events

Page 3

- Recent events
- Scientific Committee news
- ECETOC report addresses dermal exposure to chemicals

Page 4

- Latest publications
- Future course mapped out for the EUROECOTOX project
- ECETOC report explores Categorisation methods, Read-across and (Q)SAR

Membership news



ECETOC welcomes Sumitomo Chemical as its latest member company. Established in 1913, Sumitomo Chemical Group includes over 100 subsidiaries and affiliates, and operates businesses in five sectors: basic chemicals, petrochemicals, IT-related chemicals, health & crop sciences, and pharmaceuticals.

Sumitomo Chemical's Delegate to ECETOC, Dr Tokuo Sukata, explains:

"In order to play a significant role in building a sustainable society, Sumitomo Chemical is promoting sustainable chemistry by contributing to both the solution of problems facing our environment and

society, and the betterment of people's lives. Taking into account the increased globalisation of our company's business, we are very pleased to engage for our expertise as a member of ECETOC, so as to enable the benefits of chemicals to be realised while protecting human health and the environment.

In the activities of ECETOC, we are willing to contribute to the emerging issues and to dedicate to the development of concepts, data and positions, which can underpin the use of scientific principles in the translation of policy into legislation especially in Europe."

Upcoming events

Date announced for 2013 AGM and ATM

The 2013 Annual General Meeting and Annual Technical Meeting (ATM) will be held on June 13 at Martin's Central Park Hotel, Brussels.

The broad objective of the ATM will be to present ECETOC's work over recent years on science concepts for risk assessment, and

in particular on new technologies. The day will start with the Annual General Meeting (for members only), followed by the Annual Technical Meeting (for members or by invitation only).

More information will be announced shortly on the ECETOC website.

Two ECETOC sessions at EUROTOX 2013

For this year's annual meeting of EUROTOX (European Societies of Toxicology), ECETOC builds on the work of recently completed task forces and workshops by organising two sessions for the programme.

- *Tiered approaches to assess complex mixtures* to be chaired by Heli Hollnagel (Dow Chemicals) and Martin van den Berg (University Utrecht)

- *New developments in 'omics for use in risk assessment* to be chaired by Bennard van Ravenzwaay (BASF) with additional sponsoring by ECPA (European Crop Protection Association)

EUROTOX 2013 1-4 September 2013, Interlaken, Switzerland
<http://www.eurotox2013.com>

ECETOC-EEMS symposium on applied 'omics at 11th ICEM, November 2013

ECETOC and EEMS, the European Environmental Mutagen Society, have jointly organised a symposium on Applications of proteomics & metabolomics in (eco)toxicological and biomedical research. The symposium is scheduled to take place on

Tuesday 5 November as part of the 11th International Conference on Environmental Mutagens (ICEM).

This is a global scientific event to be held from 3 to 8 November 2013 in Foz do Iguassu, PR, Brazil.
<http://www.icembrazil.org/icem>

SG Corner continued from front page...

for a number of years.

Under my leadership, ECETOC will anticipate and respond to the new scientific methodology as it evolves, ensuring good science remains the platform underpinning hazard and risk assessment. This is not to say our current tools and methodologies are redundant. In fact, quite the opposite: as the new concepts and technologies mature, they will enhance our current knowledge and understanding, and help remove some of the uncertainties and resulting criticism surrounding risk assessment.

With the acceleration of information and knowledge, there is uncertainty about what the next development in the scientific process applied to hazard and safety assessment will look like. The certainty is that, with your support, ECETOC will be there to interpret and organise the avalanche of new ideas and concepts that will shape the future of scientific risk assessment.

Dr Alan Poole
Secretary General

^a Bars R, Fegert I, Gross M, Lewis D, Weltje L, Weyers A, Wheeler JR, Galay Burgos M. 2012. *Regul Toxicol Pharmacol* 64(1):143-154.

^b Lavelle KS, Schnatter A, Travis K, Swaen G, Pallapies D, Money C, Priem P, Vrijhof H. 2012. *Regul Toxicol Pharmacol* 62:302-312.

ECETOC establishes 3 new task forces

The Scientific Committee has agreed the terms of references for 3 new task forces. The respective calls for nominations were answered positively, and the groups will soon start their work.

- *Chemical Risk Assessment - Ecosystem Services* (to investigate a new risk assessment paradigm based on a structured framework for identifying which ecosystem services might be affected by chemicals, setting protection goals and then assessing relevant risk assessment schemes)
- *Thresholds in Respiratory Sensitisation* (to elaborate a broad scientific review on available evidence on thresholds in respiratory sensitisation that would support discussions by risk assessors and risk managers on how to assess and regulate respiratory sensitisers)
- *Considerations for use of additional information in assessing the PBT properties of chemicals under the 2011 Amendment to Annex XIII of REACH* (to address a recent change on PBT chemicals under REACH)

Details can be found on the ECETOC website under 'Ongoing Task Forces'.

The latest information on ECETOC events can be found on the ECETOC website:
<http://www.ecetoc.org>

Recent events

Workshop: 'Omics and risk assessment science 25-26 February 2013, Málaga, Spain

30 experts representing industry, academia and regulatory bodies met in Málaga to review the progress made since the previous workshop in 2010 on the application of 'omics technologies to chemical safety and assess the potential impact of these new technologies on the risk assessment of chemical substances.

In particular the workshop addressed the following points:

- Case studies of the application of 'omics data for risk assessment & regulatory (eco)toxicology.
- Guidance to help to increase the intrinsic value of 'omics data and stimulate its use in (eco)toxicology.
- Impact of 'omics sciences on the risk assessment process.
- Can 'omics data contribute to the elucidation of (1) life stage / subpopulation sensitivity, (2) low dose effects and (3) the effects of mixtures?

A workshop report will be published in due course to share the findings of the meeting.

Environmental progress review 28-29 February 2013, Brussels, Belgium

Early in February, ECETOC hosted its annual 2-day scoping meeting to inform member company scientists of progress in current and recently completed environmental Cefic LRI projects, ECETOC task forces and workshops. The first day, with the largest turn out to date of 30 participants, reviewed existing and recent activities whilst the second day focussed in identifying new ideas for ECETOC or Cefic LRI activities.

Workshop: Assessing environmental persistence 6-7 November 2012, Paris, France

This two-day workshop, sponsored and organised by ECETOC, the UK Environment Agency and the Federal Environment Agency of Germany, took place at Les Salons France-Amérique, Paris, France on the 6th and 7th November 2012. This is a follow up of an initial 2007 workshop which ECETOC which was held to assess areas of research required to help develop the scientific understanding of factors that affect the persistence of chemicals in the environment. In the 2007 workshop, ECETOC and the Environment Agency (EA) of England and Wales co-hosted a Workshop on "Biodegradation and Persistence" at Holmes Chapel in the United Kingdom. Attendees, from academia, regulatory agencies and industry discussed the challenges and uncertainty faced with persistency assessments at the screening and confirmatory testing level.

The primary aim of the 2012 workshop, which was attended by 45 people from academia, industry and the regulatory community, was to:

- Identify whether / how the programmes initiated as a consequence of the Holmes Chapel Workshop have helped further the understanding of biodegradation / persistence related issues,
- Identify and prioritise key areas for further future research.

A Workshop Report on the outcome of the discussions will shortly be published.

Scientific Committee news

Scientific Committee membership

The following changes occurred:

- Dr David Farrar, Ineos ChlorVinyls, retired from his company and thus also from the committee.
- Dr Gerard Swaen, Dow Chemicals, resigned whilst retaining close ties with the University of Maastricht.

ECETOC would like to acknowledge their long-standing contributions over many years.

- Dr Peter Boogaard, Shell, joined as a new member. Peter is a toxicologist with broad experience; he is already well known to ECETOC where he participated in and chaired several task forces.

ECHA Workshop on: Scientific adequacy of *in vivo* mutagenicity assays, the transgenic rodent gene mutation assay (TGR) and the unscheduled DNA synthesis assay (UDS)

Last October, ECHA held a workshop to discuss the above topic. Invited participants came from industry, member states competent authorities, academia, and one NGO. As ECETOC representative, Dr Ewan Booth, Syngenta, was able to give industry's perspective on TGR vs. UDS in mutagenicity testing.

Commenting on a report from the DG SANCO Scientific Committees

In November, ECETOC, through experts in its membership, provided detailed comments on the discussion paper 'Addressing the new challenges for risk assessment' that was published for public consultation by SCENIHR, SCCS, SCHER. Overall, the paper was considered a comprehensive thought starter in developing a road map to address the challenges of toxicology testing in the 21st century.

New ECETOC reports

ECETOC report addresses dermal exposure to chemicals

Exposure to chemicals can occur through the mouth, nose or the skin. While a lot of work has been done studying health risks of chemicals taken up through the mouth and nose less has been done on health risks caused by chemicals getting into the body through the skin. Chemical legislation, most notably REACH, does however require information on possible health risks from dermal exposures. This ECETOC Report has therefore been developed to provide a step wise approach for assessing and understanding health risks of substances that get onto the skin either as a solid, a liquid or when sprayed as an aerosol.

The value of the ECETOC document is that it uses a decision tree type approach that can be used by both, experienced or less experienced, scientists to provide relatively simple or if necessary refined estimates of health risk. Several examples are provided guiding the reader through the step wise approach. While the document is mainly for skin exposures occurring in the work place it can also be used for those scientists interested in assessing risks from skin exposures in other settings.

Published in March 2013 as ECETOC Technical Report 119: *Evaluation of Systemic Health Effects Following Dermal Exposure to Chemicals*, the Summary and link to download the report free of charge are available via <http://bit.ly/ecetoc-tr119>

Latest publications

All ECETOC reports are freely available from our website:
www.ecetoc.org/publications

Technical Reports

TR 116: Category approaches, read-across, (Q)SAR
(Published November 2012)

TR 117: Understanding the relationship between extraction technique and bioavailability (In Press)

TR 118: Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals (In Press)

TR 119: Evaluation of Systemic Health Effects Following Dermal Exposure to Chemicals (Published March 2013)

TR 120: Activity based relationships for aquatic ecotoxicology data: use of the activity approach to strengthen MoA predictions (In Press)

Workshop Reports

WR 24: Assessing Environmental Persistence
6-7 November 2012, Paris (In Press)

Scientific Articles

Weltje L, Wheeler JR, Weyers A, Galay Burgos M. 2013. Refinement of the ECETOC approach to identify endocrine disrupting properties of chemicals in ecotoxicology. *Toxicology Letters*. doi: 10.1016/j.toxlet.2013.02.019
In Press, Uncorrected Proof

ECETOC at a glance

Established in 1978, ECETOC is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals, biomaterials and pharmaceuticals.

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ECETOC report explores Categorisation methods, Read-across and (Q)SAR

Categorisation, read-across and (quantitative) structure-activity relationships are alternative approaches to fill data gaps, for example, in chemical safety dossiers for REACH. They are, in principle, accepted by regulatory authorities but difficulties remain in practice. Technical guidance is available and there are a plethora of models and tools. Guidance, however, on applying them in practice is still missing. This task force had the objective of summarising guidance and tools available, reviewing their practical utility and providing recommendations and learning. A number of case studies were added for illustration.

This ECETOC report was developed within a few months only, thanks to the hard work by the task force members. It was shared in time with the participants of a workshop by ECHA (with the active support from Cefic-LRI) on 'Read-across assessment' held last October.

Published in November 2012 as ECETOC Technical Report 116: Category approaches, Read-across, (Q)SAR, the Summary and link to download the report free of charge are available via <http://bit.ly/ecetoc-tr116>

Final EUROECOTOX project meeting maps out future course for the network

The consortium of the European Network for Alternative Testing Strategies in Ecotoxicology (EUROECOTOX) FP7 project, held the final project meeting last October in Brno (Czech Republic), hosted by partners from the Masaryk University.

The meeting provided a forum for discussion and work on the final project deliverables, and the possibilities for the management of the EUROECOTOX network once the FP7 funding finished at the end of November 2012.

It was decided that from December 2012 the network would be administered by the EUROECOTOX partner ECETOC, which



has a proven track record in the use of alternatives to animals for environmental assessments since a task force in 2003. Apart from running the network, ECETOC, with the help of Cefic LRI funding, will be updating and widening the scope of the mapping of relevant new alternative projects in the EU.

Website link: <http://www.euroecotox.eu>

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