

Annual Technical Meeting explores 'Science Concepts for Risk Assessment'

The 2013 Annual General Meeting and Annual Technical Meeting (ATM) were held on June 13 at Martin's Central Park Hotel, Brussels. The broad objective of the ATM was to present ECETOC's work over recent years on science concepts for risk assessment, and in particular on new technologies. The day started with the Annual General Meeting (for members only), followed by the Annual Technical Meeting (for members or by invitation only), which was attended by 40 participants from member companies, partner organisations and regulatory bodies.

After an introduction by Ben van Ravenzwaay (BASF), the newly appointed Chairman of the Scientific Committee, the presentations were divided into 2 sessions:

1. Developed Science Concepts for Risk Assessment - ECETOC Contribution and Leadership Role

Chris Money (ExxonMobil) kicked off with ECETOC's contribution and leadership role in science concepts for REACH.

Carlos Rodriguez (P&G) presented ECETOC



Professor Helmut Greim (Technical University Munich) addressed thresholds for genotoxic carcinogens

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activities on risk assessment of combined exposures to multiple chemicals.

Rémi Bars (Bayer CropScience) reviewed the past, present and future of endocrine disruption. He concluded that ECETOC was the first organisation to propose scientific criteria and still is actively contributing to the resolution of the ED debate. ECETOC's critical role on ED needs to be strengthened with the issues to come: low dose/threshold/non monotonicity/"inadequacy" of regulatory guidelines studies for ED/mixtures of ED.

2. Developing Science Concepts for Risk Assessment - ECETOC Contribution and Leadership Role

Helmut Greim (Technical University Munich) addressed thresholds for

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SG Corner

It is difficult to believe that it is just over a year ago that I became Secretary

General of ECETOC. During the year I have worn many hats as administrator, accountant, politician, scientist, mentor and leader. Some hats have fitted quite well while others been a bit of a stretch but hopefully none of them have looked ridiculous. As we all know, ECETOC is at the forefront of developing science and concepts to improve confidence in and reducing uncertainty around risk assessment of chemical substances. A cursory glance at events and output of ECETOC shows that we are still leaders in this area.

I have learned over the year that there are many demands on ECETOC and in order to continue with our Mission of promoting good science in human and environmental risk assessment we must continue to improve our clarity of thought, focus our activity and excel in communicating our achievements. In 2014 we will continue to focus on prioritisation and consolidation of activities and delivery of science in different ways to make it accessible and understandable at all levels.

To ensure we have a balanced, forward looking science portfolio, we will hold a workshop with our membership early in 2014 to increase membership governance and ensure the members play a pivotal role in setting the science agenda. We will continue to improve our science translation and delivery activities to increase the value of our output to all stakeholders.

Some may think these are bold goals in a time of continuing financial and resource constraints. I am however confident that these goals are achievable but will require continued efficiency improvements, focused activities and investment in different forms of communication and output in addition to the tried and trusted ECETOC reports.

Change continues, and in the New Year, we will be seeing the retirement of a senior member of the Secretariat, Ir. Hendrik (Henk) Vrijhof, chemicals programme manager since 2003. Henk joined ECETOC

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genotoxic carcinogens.

David Rouquié (Bayer CropScience) explored Mode of Action and risk assessment challenge, concluding that the general trend is to improve chemical risk assessment by using mechanistic information as proposed in the IPCS MOA framework. He also found that there is a need to build databases of known MOAs to make the best use of mechanistic information.

Saskia van der Vies (VU University Medical Center, Amsterdam) covered ECETOC's three workshops on Omics in Risk Assessment, the latest of which was held in February 2013 and published its findings as [Workshop Report No:25](#).

Johannes Tolls (Henkel) talked about increasing realism in environmental risk assessment, covering the EU Scientific Committees' view, ECETOC past and current contributions, and what needs to be done in addition.

Charles Eadsforth (Shell), in his speech on Bioavailability in Exposure Assessment, reviewed the work of three ECETOC task forces which were commissioned to address: 'Relationship between extraction technique and bioavailability' ([Technical Report No:117](#)), 'Develop interim guidance for the inclusion of NERs in ERA of chemicals' ([Technical Report No:118](#)) and 'Activity based relationships for aquatic ecotoxicology data' (Technical Report No:120 in Press, and paper in the open literature in preparation).

in 1988 as an environmental scientist having worked in national and international government. We wish him well in his retirement.

I must end on a sad note. Over the years, many of you will have come to know our human health sciences manager, Christa Hennes as a colleague and as a friend. It is with great sadness that we have to inform you that Christa recently passed away after a long and brave struggle with her health. She will be remembered for her professionalism, dedication and good-natured character, and also her bravery and fighting spirit. She will be missed very much by her colleagues and we send our deepest and sincerest condolences to her family.

ECETOC is a flexible organisation and with the help of our Membership, and through leadership of the Science Committee and ECETOC Board, we will regroup to manage the loss of these key figures from our organisation, and continue to refresh our activities and approaches to sustain our Mission and support the aspirations of the Membership.

Dr Alan Poole
Secretary General

Dr Christa Hennes, ECETOC Health Sciences Manager



Over the years, many of you will have come to know our human health sciences manager, Christa Hennes as a colleague and as a friend. It is with great sadness that we have to inform you that Christa passed away earlier this month after a long and brave struggle with her health.

Christa joined ECETOC as Health Sciences Manager in October 2002 and was Scientific Secretary to the ECETOC Scientific Committee. Christa was a wonderful, kind and generous person to work with and will be remembered for her professionalism, dedication and good-natured character. She will be missed very much by her colleagues and we send our deepest and sincerest condolences to her family.

Many tributes have already arrived at the ECETOC secretariat from colleagues and friends of Christa; a small selection are shown below:

"I am deeply saddened by this news. Only last Friday I got the impression that she was responding well to the latest treatment. I know only too well, however, that things can take an abrupt turn for the worse in the battle against an aggressive cancer. Christa was a lovely person and she will be sincerely missed."

"Although I was basically aware of the very difficult situation of Christa and her lion-hearted fight against this life-threatening challenge it was a real shock for me to become aware of this big loss. Her dedication, her professionalism and her congenial character have always been a big asset for ECETOC. My deepest sympathy goes with her colleagues and especially with her relatives."

"I will remember Christa as a very intelligent, sweet and caring woman who just wouldn't give up. I'm honored to have been able to work with her so closely."

"I would like to express my sincere condolences to her family and to ECETOC on behalf of EUROTOX. We will remember Christa for ever ... giving the awards to young scientists ..and as a wonderful person and scientist."

"I am very, very sad to hear this bad news...The shock is deep and all my thoughts and sympathies are with Christa's family, friends and colleagues from the ECETOC family. We all will miss Christa dearly."

Scientific Committee News: Message from the Incoming Chairman

Cells and multicellular organisms strive for homeostasis. They do this to maintain themselves in an environment that is sometimes hostile for their own proper function. Homeostasis is mainly achieved by sensors of change, regulation of responses and feedback relating to the effectiveness of those responses. Similar concepts apply when organisations function well. Without knowing what is going on in the world, they will eventually get lost and lose track of their purpose, often becoming superfluous because the reason for their existence is no longer there.

I believe that ECETOC has shown that it has not lost its sensors and is, more than ever, able to respond to new challenges that are provided by (1) regulation, (2) new methods and (3) entirely new concepts (e.g. (1) endocrine disruption, the effect of mixtures (2) 'omics technologies (3) epigenetics). We do so through the input of our membership, the delegates and the members of the Scientific Committee. For an organisation such as ECETOC, a response to a particular demand needs to be appropriate. Overreaction has hardly ever solved any problem; however, taking a firm stand if backed up by solid science is appropriate and insisting on the use of good science in any area related to hazard identification and risk assessment is and will remain key to success. Our actions (workshops, technical reports and publications) do not remain unnoticed and we receive the necessary feedback with respect to the actions that we have taken, and sometimes also to those which we have not. As such, I believe that ECETOC is in a good shape to continue its work to improve processes leading to the assessment of chemical entities.

We all know that nothing is as perpetual as change. Change may be seen as the major challenge to homeostasis but this is not necessarily so. Profound changes that occur within a short period of time (let's call them revolutions) are indeed major disruptors. After a revolution things are very different, sometimes for the better, sometimes for the worse. In our society, very much adapted to homeostasis, revolution is often associated with fear and the sense of loss of direction. Being able to identify early indicators for a revolution is the only remedy against ending up in a chaotic situation. As a member of the Scientific Committee, I have seen over the past 13 years that ECETOC has the potential to identify these indicators of change. Under the leadership of Dr. Fraser Lewis, ECETOC Chairman from 2010 to 2013, we have organised workshops to address the state of the art in several of the early indicators of profound change (increased use of mode of action / adverse outcome pathways, assessment of endocrine disruptors, the significance of epigenetics). ECETOC changed to take on more willingly than in the past new areas, to assess the state of the art of the science. We have seen a shift towards an increased level of papers published in the peer reviewed literature, based on ECETOC's task forces and workshops. A further change to increase our impact on eco- and toxicological sciences is to provide all our reports for free in PDF format.

These changes were necessary, because without them ECETOC's work would not have received the attention required to make a lasting impact. These changes by themselves, however, will not be enough to maintain ECETOC's role as a leader in the field in the future. The national academies report on "toxicology in the 21st century" is another driving force for profound changes in the way toxicology may be done in the future. No more animal testing, reliance on adverse outcome pathways, the

use of human cells, physiology based pharmacokinetics, and mathematical modelling of interactions between chemicals and biological systems are only some of the challenges, or chances, we will have to face. At the same time, people raise doubt about our current risk assessment paradigm. There are discussions about low dose effects (effects below the commonly determined no observed (adverse) effect level), effects of mixtures (from additivity to synergism), foetal origins of adult disease and transgenerational effects. All of these issues will have to be dealt with and each single one is more complicated than most of the questions we had to deal with in the past. At the same time we observed a gradual reduction in the resources that industry can, and is willing, to provide to ECETOC. Therefore we need to focus on those issues where we can make an impact. We will need to be more careful with our limited resources, and at the same time look for opportunities to secure the financial interest of ECETOC as an organisation.

Which direction will we take? There are no definitive answers, but there are certainly concepts that should help us to be more effective. At the level of the Scientific Committee, we are reducing as much as possible lengthy protocols and unnecessary bureaucratic procedures. We will try to involve more of our membership in activities and will start new procedures in asking for each individual company's needs and options to assist ECETOC. We will need to be more selective in starting new task forces and other activities, and ensure that once they are started they finish their task on time, ideally resulting in papers published in the peer reviewed literature. The profoundness of the scientific challenges that lie ahead of us will require that ECETOC changes its working structure from a 100% on demand organisation, to one that maintains its flexibility to respond rapidly to the needs of our membership, while at the same time devoting a good part of its capacity to long-term projects. This will enforce the need to assess each proposal for a task force on the availability of resources, and strategic fit within the overall long-term strategy of ECETOC. This strategy needs to be defined by our membership and discussed with academia, and as far as possible with regulatory authorities. One of our wishes is to bring more regulators to ECETOC's table. Workshops appear to fare better than task forces in engaging regulators. We will need to extend our hands and ears to them, to increase our effectiveness. One of the most successful activities ECETOC ever engaged in was the Targeted Risk Assessment (TRA), because we were able to work on the needs of industry and regulators at the same time, bringing exposure science from the (ivory) tower into the offices of those who needed it most. We must try to extend this. If the general concept of toxicology in the 21st century is to work, then exposure science will have to play an essential role in this.

Finally, I would like to express my gratitude to Dr. Fraser Lewis on behalf of ECETOC's staff, the Scientific Committee and personally for his work as Chairman of the Scientific Committee over the last 4 years. I enjoyed his straightforward approaches and effectiveness as group leader. He will continue to work as a member of the Scientific Committee, and speaking for all, we are very glad that we can still rely on him. I hope that in some future time, he, and the others will be able to say similar things of me as the new Chairman of the Scientific Committee.

Ben van Ravenzwaay
Scientific Committee Chairman

New Task Forces

Following agreement of terms of reference by the Scientific Committee, the following task forces have recently been set up:

- Thresholds in Respiratory Sensitisation (First meeting held 23 July)
- Sufficiency of aquatic hazard information for environmental risk assessment (First meeting held 8th August)
- Chemical risk assessment - ecosystem services (First meeting held 4 October)
- Testing and Assessment of Nanomaterials by Criteria Related to Conceivable Risks (First meeting held 15 October)
- Guidance for Effective Use of Human Exposure Data in Risk Assessment of Chemicals (first meeting scheduled for 30 January 2014)
- Modelling Wastewater Treatment Plants (Call for nominations will be sent to member company Delegates shortly)

Details can be found on the ECETOC website <http://www.ecetoc.org/task-forces> and more detailed information on the Members' Website.

ECETOC Joins WHO Chemical Risk Assessment Network

Earlier this year, the World Health Organization (WHO) announced the launch of a network of leading risk assessment institutions from around the world to improve chemical risk assessment globally. The network will scale up action and facilitate sustainable interaction between institutions on chemical risk assessment and is a voluntary, collaborative initiative. ECETOC is delighted to announce that it will join as a Network Participant from 1 January 2014.

Upcoming Events

29-30 January 2014, Brussels, Belgium: 2014 Environment Progress Review

This scoping meeting aims to inform ECETOC member company scientists of progress in current and recently completed LRI projects, ECETOC task forces and workshops in the environmental sciences. The participants also identify ideas for consideration as new LRI projects or for ECETOC activities.

05-06 February 2014, Brussels, Belgium: Science Scoping Meeting on Human Health & Human Exposure in Risk Assessment

A scoping meeting to validate and agree science programmes for ECETOC and CEFIC LRI in areas of Human Health and Human Exposure. This is the opportunity for member companies to be heard, to put ideas forward and to provide input directly into ECETOC and CEFIC LRI Research Programmes.

11-13 February 2014, Amsterdam, Netherlands: Estimating toxicity thresholds for aquatic ecological communities from sensitivity distributions

The workshop will discuss and report current thinking on when and how species sensitivity distributions, SSDs, should be used and how the methodology might be further developed. A workshop report will be published to disseminate the findings of the meeting.

12 June 2014, Brussels, Belgium: Annual General Meeting followed by Annual Technical Meeting

The 2013 Annual General Meeting and Annual Technical Meeting (ATM) will be held on June 12 at Pullman Brussels Midi Hotel, situated next to the gare du Midi in Brussels. 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.



Keep up to date with the latest ECETOC news by following us on Twitter, LinkedIn, Research Gate or RSS news feed.

Recent Events

22 April 2013 : Expert Panel to better understand Endocrine Disrupter Low Doses Effects

An Expert Panel workshop was organised by ECETOC to discuss the controversy of the so-called low dose effects of endocrine disrupting chemicals, and to propose a possible research programme to throw more light on this area. The panel agreed that the only practical way to support or refute the proposed hypotheses is through the use of mechanistic mode of action, MoA/AOPs models focusing on key events, their quantitative description and dose-response characteristics. The concept here is to identify the key events of the mode of action of chemicals for which low-dose effects have been reported.

These key events will need to be characterised for a large range of doses, and the resulting datasets integrated through the use of mathematical modelling using a system biology approach. Such models would then be interrogated to investigate whether or not low dose effects could indeed be occurring. Adverse outcome pathways, need to be integrated using an understanding of relationships between the ultimate adverse effect, key events, the site of possibly multiple action and the exposure. This is in agreement with the WHO-IPCS MoA/ AOPs concept (see for example ECETOC / WHO Mode of Action Workshop Report no.26, available via: <http://bit.ly/ecetoc-wr26>). It was recognised however, that as a first step there was a need to have an extensive review of the data already published. The outcomes of these discussions are compiled in ECETOC Workshop Report no.27 available via: <http://bit.ly/ecetoc-wr27>.

May 2013: Young Scientist Awards: Environmental science related award

The ECETOC Best Platform Award honours the early career scientist with the best platform presentation at the SETAC Europe Annual Meeting. The award winner receives a free registration to the next SETAC Europe Annual meeting and travel and accommodation support. She/he also receives a free SETAC membership. This year's Best Platform Award has been awarded to Julita Stadnicka-Michalak, Eawag, Switzerland, for her talk entitled: "Predicting toxicity to fish based on in vitro data". Download Abstract PDF: <http://bit.ly/ecetoc-ysa-Stadnicka-Michalak>
<http://glasgow.setac.eu>

July 2013: ECETOC's Work Recognised By Regulators

According to the findings of a survey conducted by ECETOC earlier this year, representatives from the EU and national regulatory bodies, as well as other key stakeholders see ECETOC's contribution to the chemical regulation assessment field as very positive. The survey shows that the European regulatory science community recognises and appreciates the support ECETOC gives to science-based regulation. According to the survey, ECETOC should continue to play a key role in assisting with the regulation of chemicals, biomaterials and pharmaceuticals. ECETOC should retain its focus on evaluating the latest developments in testing methods and risk assessment in (eco)toxicology and on developing pragmatic approaches to regulatory requirements. ECETOC would like to thank all who took part in this survey. The results of the stakeholder survey are available at <http://bit.ly/ecetoc-2013imagesurvey>

September 2013: ECETOC sponsored two sessions at EUROTOX 2013 - Tiered approaches to assess complex mixtures and New developments in "omics" for use in risk assessment

The sessions included presentations highlighting the deliverables from various ECETOC Task Forces and ECETOC Workshops. These presentations will be published in the meeting proceedings.

September 2013: Human health science related award at EUROTOX 2013

This is a Best Poster Award for toxicological research into mechanisms and risk assessment, selected by a panel in which ECETOC participates. The winner receives a monetary prize and a free invitation to the following year's EUROTOX meeting. This year's Young Scientist Award on human health sciences, presented at the EUROTOX annual meeting in Interlaken, Switzerland, has been awarded to Olesja Bondarenko of the Estonian National Institute of Chemical Physics and Biophysics for her poster presentation on 'Biological effects of nanoparticles of silver, gold, TiO₂ and nanoporous silica to selected invertebrate species and bacteria: FP7 project NanoValid.' Download PDF from <http://bit.ly/ecetoc-ysa-bondarenko>
EUROTOX 2013 website: <http://www.eurotox2013.com>

November 2013, Symposium at ICEM 2013: Applications of proteomics & metabolomics in (eco)toxicological and biomedical research

The symposium was jointly organised by ECETOC and EEMS, the European Environmental Mutagen Society, as part of the 11th International Conference on Environmental Mutagens (ICEM) held from 3 to 8 November 2013 in Foz do Iguassu, PR, Brazil. There presentations on (i) the use of proteomics for the identification of compounds inducing reproduction toxicity, (ii) the sensitivity of metabolomics; a comparison of metabolomics and regulatory NOEL and LOEL values in 28-day rat studies, (iii) a stem cell based metabolomics approach to detect embryotoxicity in vitro, and (iv) 'omics sciences in (regulatory) toxicology: conclusions from ECETOC's 3rd 'omics workshop.

For more information, visit the ICEM web site: <http://www.icembrazil.org/icem/>

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

Latest publications

All ECETOC reports and related explanatory science newsflashes are freely available from our website: www.ecetoc.org/publications



Technical Reports

- [TR 117:](#) Understanding the relationship between extraction technique and bioavailability (Published May 2013)
- [TR 118:](#) Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals (Published May 2013)
- [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)
- [TR 121:](#) Efficacy and safety of antidotes for acute poisoning by cyanides (Published November 2013)
- TR 122: Poorly soluble particles / lung overload (In Press)
- TR 123: Environmental risk assessment of ionisable compounds (In Press)

Workshop Reports

- [WR 24:](#) Assessing Environmental Persistence, 6-7 November 2012, Paris (Published December 2013)
- [WR 25:](#) 'Omics and risk assessment science 25-26 February 2013, Málaga (Published September 2013)
- [WR 26:](#) Mode of Action: Recent Developments, Regulatory Applications and Future Work 21-22 February 2013, Vienna (Published June 2013)
- [WR 27:](#) Expert Panel to better understand Endocrine Disrupter Low Doses Effects 22-23 April 2013, Barcelona (Published October 2013)

Scientific Articles

- van Ravenzwaay B, Dekant W, Vrijhof H. 2013. Risk Assessment of Endocrine Disrupting Chemicals – Introduction to this Special Issue. *Toxicology Letters* 223(3):269-270. Doi 10.1016/j.toxlet.2013.10.006
- Lewis RW. 2013. Risk Assessment of 'Endocrine Substances: Guidance on Identifying Endocrine Disruptors. *Toxicology Letters* 223(3):287-290. Doi 10.1016/j.toxlet.2013.09.001
- 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* 223(3):291-294. Doi: 10.1016/j.toxlet.2013.02.019
- Fegert I. 2013. ECETOC Florence Workshop on Risk Assessment of Endocrine Substances, Including the Potency Concept. *Toxicology Letters* 223(3):310-314. Doi: 10.1016/j.toxlet.2013.03.027
- Moore N, Boogaard PJ, Bremer S, Buesen R, Edwards J, Fraysse B, Hallmark N, Hemming H, Langrand-Lerche C, McKee RH, Meisters ML, Parsons P, Politano V, Reader S, Ridgway P, Hennes C. 2013. Guidance on Classification for Reproductive Toxicity under the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). *Critical Reviews in Toxicology* 43(10):850-891. Doi:10.3109/10408444.2013.854734
- Scholz *et al.* 2013. A European Perspective on Alternatives to Animal Testing for Environmental Hazard Identification and Risk Assessment. *Regulatory Toxicology and Pharmacology* 67(3):506-530. Doi 10.1016/j.yrtph.2013.10.003.
- Patlewicz G, Ball N, Booth ED, Hulzebos E, Zvinavashe E, Hennes C. 2013. Use of Category Approaches, Read-Across and (Q)SAR: General Considerations *Regulatory Toxicology and Pharmacology* 67(1):1-12. Doi 10.1016/j.yrtph.2013.06.002

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

Avenue E. Van Nieuwenhuysse 2 Bte. 8, B-1160 Brussels, Belgium
Tel: +32 2 675 3600 Fax: +32 2 675 3625 VAT: BE 0418344469

Visit www.ecetoc.org or e-mail info@ecetoc.org for more information about ECETOC and to download ECETOC reports free of charge

