

2011 ANNUAL TECHNICAL MEETING: "REACHing maximum impact"

This year's Annual Technical Meeting (ATM) was constructed around a simple idea: to showcase the efforts and products of ECETOC task forces. While many scientists have dedicated time and effort over the years to task forces in their area of special expertise, they may never have had the opportunity to see the bigger effort to which they are contributing. The Board and the Scientific Committee were keen to remedy this, by holding an ATM by the task forces, for the task forces.

The primary, and unifying idea, was to spread awareness of ECETOC's activities amongst the biggest contributors. With this in mind, all of our current or recent task forces were invited to present their products. In some cases this was a finished report in other cases it was interim findings.

The secondary objective was to highlight and discuss the impact of ECETOC's activities in the context of REACH. As member companies have now finished their first round of submissions, this is an excellent moment to review the extent to which our activities have been useful to member companies in fulfilling their obligations under the legislation.

The morning session started with environmental taskforces, with a review by Dr Jason Snape of ECETOC's activities and impact in the fields of environmental fate and persistence of chemicals. This was followed by a presentation from Dr Todd Guoin, of ECETOC's on-going activities concerning environmental risk assessment of pharmaceuticals.



Dr Jason Snape reviewed ECETOC's activities and impact in the fields of environmental fate and persistence of chemicals

The morning session was rounded off by Dr Kim Travis who presented the interim findings of the "low dose interactions" task force. This task force will be presenting more of their conclusions at the Berlin workshop on co-exposure in July.

There followed a working buffet lunch with posters attended by task force members. Ten excellent posters were on display from taskforces that were not making presentations. Although we allowed an hour and a half for this session, some people commented that it wasn't long enough. Clearly, this session was a great networking opportunity and much



SG CORNER

This summer sees the coming together of several linked activities which we, at ECETOC, have been working on for some time. These are the highly topical subjects of mixtures and endocrine disruptors.

The topic of mixture toxicity is not new, but because of linking to endocrine disruptors the subject has found a new momentum. Even the title is misleading, as the current interest is not so much in mixtures (preparations, formulations) but in adventitious co-exposure. The argument is advanced that co-exposure to more than one of these endocrine active substances at very low doses can have unexpected and magnified effects.

This is the so-called "cocktail effect". It is interesting for a moment to trace the history of this particular issue. A publication in 1996 in the Journal Science claimed a synergistic interaction between some oestrogenic chemicals in an *in vitro* system. This paper was subsequently withdrawn when the study proved to be impossible to duplicate. Nevertheless, the controversy about the phenomenon remains with many in the field convinced that the evidence supports these types of effect. For this reason ECETOC set up a task force last year to examine what evidence lay behind this belief.

ECETOC has been active in both mixtures and endocrine disruptors for some time, but has recently increased its efforts. This has been spurred on by a request in 2009 from Denmark that the European Commission re-examine whether existing measures in the area were sufficient, in particular with respect to protecting children. The European Commission is in the process of finalising its report on this subject.

From ECETOC's side we are also bringing our activities to a climax. In May we held a workshop in Florence on "the risk assessment of endocrine disrupting chemicals"; this was followed up by presentations at the European Environmental Mutagens Society in Barcelona in July. As this newsletter goes to press we will be holding a workshop in Berlin on co-exposure to chemicals. In this workshop, two ECETOC task forces will present their work. These are: "Low dose interactions" and "Mixtures in the aquatic environment".

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appreciated by the participants.

We started the afternoon with three topical task forces. Dr Remi Bars presented the proposals from the endocrine disruptors task force, which had been presented at a workshop in Florence the month before. Dr Johannes Tolls presented the current status of the Targeted Risk Assessment, which is now part of the official ECHA IT tool "CHESAR" and Dr Mark Pemberton presented the Results of the derived no-effect level (DNEL) task force, which has also been widely used by industry in their REACH submissions.



Dr Mark Pemberton presented the results of the DNEL task force



Lunchtime poster session

The final session was prospective in nature, with Mr Chris Money summarising an ECETOC internal brainstorming workshop on "REACH science needs" held in March. This workshop had been very popular and served to identify which ECETOC activities would be most useful in filling science gaps as REACH is implemented. This final ATM session was concluded via panel discussion led by Dr Fraser Lewis, chairman of the Scientific Committee. The ideas that have emerged were well received and will become the basis of the next years' program.

Dr Neil Carmichael
Secretary General

By the end of the year, we will see more clearly where these issues are going at the regulatory level and how much impact our activities have had. Hopefully, a broad consensus will have been reached by that time and the driving force in that consensus will be science and facts. In any event, ECETOC will have made its voice heard through these workshops and task forces, which are the culmination of several years of work from the scientists of member companies.

Neil Carmichael

Dr Neil Carmichael
Secretary General

Visit the ECETOC website at www.ecetoc.org for more information about ECETOC and to freely download its publications.

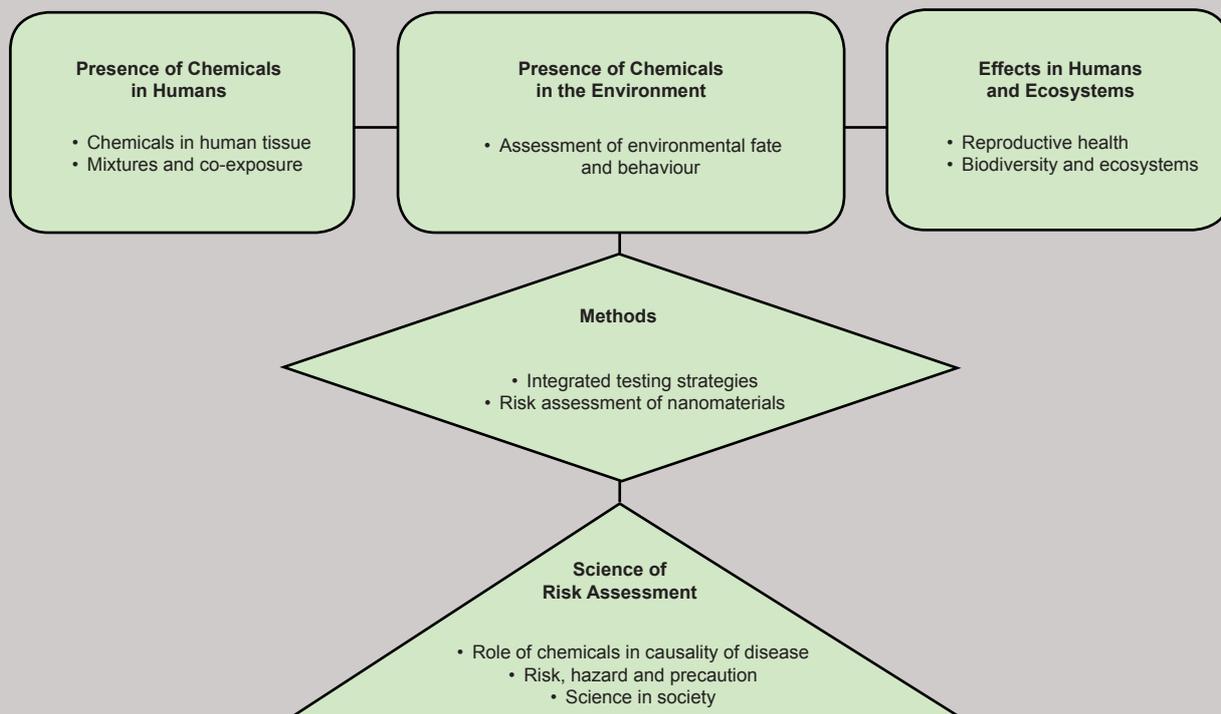
Please contact us at info@ecetoc.org with any enquiries

ECETOC REVISES ITS SCIENCE STRATEGY

The science strategy of ECETOC guides the development of its work programme and hence the specific activities that it undertakes. At last year's ATM, ECETOC member companies gave their input on current and future priorities, and this was subsequently evaluated by the Scientific Committee over the past year. The resulting revision includes 10 science areas grouped into 5 main themes as pictured below. Two science areas have been removed, i.e. on 'sensitive sub-populations' and 'indoor air', since there are no related activities at ECETOC for the time being. 'Integrated testing strategies' now includes the 'omics where ECETOC is active, in particular by organising specialised workshops. More detailed descriptions of the revised science areas with background, objective and desired outcome or impact can be found on the members' website. A printed brochure is available upon request.

Dr Christa Hennes
Health Sciences Manager

Strategy Flow Chart



WORKSHOP ON RISK ASSESSMENT OF ENDOCRINE DISRUPTING CHEMICALS

9-10 May 2011, Florence

Science area:
Reproductive health



SCIENTIFIC COMMITTEE NEWS

A workshop was organised by ECETOC to discuss the 'Risk Assessment of Endocrine Disrupting Chemicals' and was held in Florence on the 9th and 10th of May 2011. Thirty-eight invited experts (from academia, regulatory bodies and industry) discussed approaches for the risk assessment of endocrine disrupting chemicals. The aims of the workshop were to evaluate emerging guidance produced by regulatory authorities, academic and industry scientists, identify areas of concordance and difference, consolidate the common scientific themes, provide a platform for constructive debate on areas of difference, and invite a wider critique of the proposed approaches.

The workshop consisted of a series of invited presentations. The first set of presentations dealt with human safety, whilst the second set of presentations covered environmental safety. German and British authorities (BfR and CRD respectively) initiatives and developments to define and test criteria for the identification of endocrine disrupting chemicals were presented. This was followed by presentations from the ECETOC Task Force on the ECETOC approach, which included refinements and further development of their original proposal 'Guidance on Identifying Endocrine Disrupting Effects (TR106)'.

The presentations were followed by four syndicate discussion sessions, which addressed four specific themes. Each theme was considered from both toxicological and ecotoxicological perspectives.

Theme I was concerned with the use of weight of evidence (WoE) for decision making. The participants concluded that a consistent approach for the WoE of endocrine disrupters is required, which would be applicable under various regulatory regimes. There was general support for requirement to demonstrate both an adverse effect in an intact organism (extended to population level impacts for the ecotoxicological assessment) and a plausible endocrine mode of action. For human health assessment there was general support for using the WHO IPCS mode of action framework. For ecotoxicological assessment it was acknowledged that no direct equivalent to the WHO framework exists, but several specific WoE frameworks for the evaluation of endocrine disrupting effects have been published. These should be evaluated and combined for the requirements under current legislation.

Theme II covered discussions on the human and population relevance of

endocrine related endpoints. It was noted that there were some rodent cases for which non-relevance to humans has been demonstrated, but that the number of such cases is low. The default position is to assume human relevance. Specific guidance was considered necessary to aid in the identification of endpoints in ecotoxicological studies that are of population relevance. Some endpoints are clearly directly population related, whereas others are more diagnostic in nature and are needed as parts of clusters of endpoints to infer population relevance.

Theme III dealt with the evaluation of lead toxic effects and the specificity of endocrine effects when identifying endocrine disrupters. While it was seen as scientifically sound, most participants thought that the application of this criterion would depend on the degree of separation between the (other) lead effect and the endocrine mediated effect. The acceptable degree of separation should be assessed on a case by case basis, and for EDs of very high concern a factor of 10 was suggested as a conservative starting point. This would result in a margin of exposure of at least 1,000. This could be a useful approach for the REACH legislation, which requires that individual exposure scenarios need to be addressed to guarantee safety for different uses of the same chemical. For ecotoxicological assessments, the participants felt that further work was required before an absolute value for the degree of separation could be recommended.

Theme IV was concerned with using potency to differentiate between endocrine disrupting chemicals. It was highlighted that the concept of potency assessment was introduced as a surrogate for risk assessment following the legislative introduction of a hazard based cut-off criterion for endocrine disrupters. Equivalent categories already exist for

In June, the Scientific Committee (SC) welcomed two new members from academia. Dr Lesley Rushton is an epidemiologist at the Department of Epidemiology and Public Health of Imperial College London, UK. Dr Kees van Leeuwen is an environmental toxicologist with broad experience in risk assessment of chemicals, who is at the KRW Watercycle Research Institute, Netherlands. Both their expertise will be a valuable addition to the broad knowledge base amongst SC members.

It was also decided to invite two more members from ECETOC member companies to the SC. Dr Marie-Louise Meisters of DuPont and Dr Jason Snape of AstraZeneca have accepted. They will bring expertise on mammalian toxicology, especially reproduction toxicology, and on environmental fate of chemicals, including pharmaceuticals, respectively.

Finally, Dr Ben van Ravenzwaay of BASF will become Vice-Chairman of the SC.

Dr Fraser Lewis
Chairman of the Scientific Committee

TWO NEW TASK FORCES ESTABLISHED

In March, the SC agreed terms of reference for two new task forces:

'Practical guidance for the risk assessment of genotoxic carcinogens'

'Potency in carcinogenicity and reproductive toxicity classification'

Following approval of all nominations from ECETOC member companies, the SC in June formally established both TFs. First meetings have been set up for September. Details of these and other ongoing task forces are available on our website: www.ecetoc.org

repeated dose toxicity. The potency assessments proposed by the German and British authorities and ECETOC only apply to deciding whether substances of high regulatory concern are caught by the cut-off criterion and are therefore refused marketing authorisation. All other (less potent) endocrine disrupters would still undergo standard risk assessment.

Dr Malyka Galay Burgos
Environmental Sciences Manager

Science in Society at EUROTOX 2011



At the annual meeting of EUROTOX (European Societies of Toxicology) in 2008, ECETOC organised a workshop on 'Science in Society'. It explored the issues of conflict of interest and sources of funding in health and environmental science by presentations from eminent scientists in academia and industry, and was well received by the audience.

Hence, ECETOC's proposal for another session on the topic has been accepted by the programme committee of this year's EUROTOX congress (28-31 August, Paris). We have invited four speakers (Gerard Swaen, Dow Chemical; Peter Calow, University of Nebraska; José Tarazona, ECHA; Helen Håkansson, Karolinska Institute) to present their ideas on systematic improvement.

The session will take place on 29 August, 10:15-12:30, under the title 'Science in Society: Improving the credibility of research in health and environmental science'.

*Dr Christa Hennes
Health Sciences Manager*

www.eurotox2011.com/

Young Scientist Awards 2011

The ECETOC Best Platform Award is to honour the early career scientist with the best platform presentation at the SETAC Europe Annual Meeting. The award winner is invited to the SETAC Annual Meeting and is offered the opportunity to submit the manuscript for publication in Environmental Toxicology and Chemistry (ET&C) with the page charges paid by SETAC Europe. She/he also receives a free SETAC membership.

This year's Young Scientist Award at SETAC Europe has been awarded to Charles Hazlerigg from Syngenta for his platform presentation: 'The importance of density dependence and intra-specific interactions in population models for use in risk assessment'. The research has been carried out in collaboration with the Imperial College London and the University of Exeter.

*Dr Malyka Galay Burgos
Environmental Sciences Manager*

<http://milano.setac.eu/>



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ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) was established in 1978 as a scientific, non-profit making, non-commercial association and counts as its members the leading companies with interests in the manufacture and use of chemicals. An independent organisation, ECETOC provides a scientific forum through which the extensive specialist expertise of manufacturers and users can be harnessed to research, evaluate, assess, and publish reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

Agenda

Dates and times are subject to change. Please check our website for latest information: www.ecetoc.org

July

- 04 Exploring novel ways of using SSD to establish PNECs for industrial chemicals. TF meeting. Academy of Medical Sciences, London, UK.
- 06 Symposium at EEMS: Risk assessment of endocrine disrupting chemicals. Barcelona, Spain.
- 11-12 Workshop: Combined Exposure to Chemicals. Berlin, Germany.
- 25 Targeted Risk Assessment. TF meeting. ECETOC, Brussels, Belgium.
- 26 The application of critical body burden in risk assessment of SVHC. TF meeting. ECETOC, Brussels, Belgium.

August

- 29-31 EUROTOX Paris, France.

September

- 08 Understanding the relationship between extraction technique and bioavailability. TF meeting. ECETOC, Brussels, Belgium.
- 14 Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals. TF meeting. ECETOC, Brussels, Belgium.
- 20 Poorly soluble particles / lung overload scoping meeting. ECETOC, Brussels, Belgium.
- 21-22 Low-dose interactions. TF meeting. Syngenta, Jealott's Hill, UK.
- 22 Practical guidance for the risk assessment of genotoxic carcinogens. 1st TF meeting. ECETOC, Brussels, Belgium.
- 27 Exploring novel ways of using SSD to establish PNECs for industrial chemicals. TF meeting. Unilever, Bedford, UK.
- 30 Potency in carcinogenicity and reproductive toxicity classification. 1st TF meeting. ECETOC, Brussels, Belgium.

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

Avenue E. Van Nieuwenhuyse 4 Bte. 6, B-1160 Brussels, Belgium
Tel: +32 2 675 3600 Fax: +32 2 675 3625 VAT: BE 0418344469

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