ecetoc

e-NEWSLETTER

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

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ECETOC and the Next Generation of Scientists

At the 2008 Annual General Meeting, we announced that the 2009 ECETOC work programme would place a special emphasis on young scientists. With this in mind, this year's Annual Technical Meeting held 9-10 June in Brussels, was programmed as a 1.5-day 'Young Scientists Event.'

In order to make this event both stimulating and participative, it included a poster competition. All participants were asked to vote for the best poster out of the 19 submitted by young scientists with up to 10 years of experience post-doctorate.

During the second day, while the votes were being counted by an independent voting committee, a variety of presentations were made by young scientists new to the ECETOC world. In the afternoon, break-out groups allowed for more in-depth discussion of questions relating to the perception of the health and environmental science by those just starting their careers in this area.

At the end of the day, results of the competition were announced. The best poster by a young scientist was won by Jillian Ross from CXR Biosciences in Dundee for her excellent poster on the use of transgenic mice to elucidate mode of toxicological action. The title of the poster was "'Human constitutive androstane receptor (CAR) supports the hypertrophic but not the hyperplastic response to the murine non-genotoxic carcinogen phenobarbital *in vivo*". As 2009 represents the 200th anniversary of the birth of Charles Darwin (who was only 22 years old when the Beagle voyage began), John Doe, Chairman of the ECETOC Scientific Committee, presented the winner with a copy of Darwin's book 'The Origin of Species.'

The event was a great showcase for the participants, many of them still studying for their doctorates. The quality of the posters and the presentations was uniformly high and the timekeeping immaculate. The feedback from the breakout groups is already providing valuable input to the draft programme of the 2010 Annual Technical Meeting, which will look at the future needs of ECETOC as its scientific strategy is refined. Hopefully, some of these young scientists will be able to participate in ECETOC's work to bring their fresh ideas and perspectives.

The winner Jillian Ross receives the ECETOC prize for her poster from John Doe

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Other Young Scientist Awards presented in 2009

In addition to the award given at the ATM, ECETOC presented its three regular awards to young scientists:

- The environmental science award was presented to Lucia Vergauwen of the University of Antwerp for her platform paper "An integrated study to the effects of temperature acclimation in zebrafish" which she had given at the annual meeting of SETAC Europe in May.
- The award on research on occupational health and exposure was presented to Craig Moore of Newcastle University for his platform presentation "The influence of everyday clothing on percutaneous absorption and distribution of model penetrants *in vitr*"' at the OEESC (Occupational and Environmental Exposure of Skin to Chemicals) 2009 conference in June.
- The third of these young scientist awards was presented at the EUROTOX 2009 meeting in September. It went to Katherina Sewald of the Fraunhofer Institute for Toxicology and Experimental Medicine for her poster presentation "Respiratory toxicology and immunotoxicology in human precision lung slices".

SG CORNER

Since I arrived at ECETOC, the development and implementation of ECETOC's "Science Strategy" has been the central theme of all we have undertaken. At the 2009 Annual General Meeting it was proposed that next year the AGM and ATM will be run as one meeting and that this meeting will be a major review of ECETOC's Science Strategy. Why so soon, you may ask? This review will be only 4 years after the 2006 ATM "futures workshop", from which the current strategy sprang.

The answer is threefold:

• Firstly, the environment in which ECETOC operates has evolved rapidly. REACH is no longer a prospect, it is operational. At a time when the industry was hit by recession in global markets, it had simultaneously to adapt to a quantum shift in regulatory requirements in Europe. This situation clearly affects the availability of industry scientists to participate in ECETOC activities.

• Secondly, the areas of science which we deal with are in a state of rapid transformation. Initiatives in the USA such as the National Academy of Sciences report "Toxicology in the 21st century" are resonating in Europe. Many of the approaches invoked in the NAS report, broadly grouped under 'systems biology', are seen in some quarters as the solution to many of the problems of accuracy and capacity for toxicology testing. New technologies are promoted as being the way forward for toxicology and ecotoxicology and, notably, in the replacement of in vivo testing. The area of cosmetics is immediately impacted as the use of animal data is phased out between 2009 and 2013, but the implications are potentially much broader.

• Thirdly, and more happily, ECETOC has made enormous progress in the 13 "Strategic Science Areas" it originally identified. Since the start of 2007 we have planned, run and reported eight workshops and another is in the final stages of editing. A tenth workshop on "Mode of Action in risk assessment" is taking place in November this year. It is now time to evaluate the progress made and to confirm the areas of greatest priority. It may be that some of these SSA's have been addressed and are no longer critical. Some may require redefinition and others may be re-confirmed.

The 2010 ATM/AGM will be held on the 8th of June; I hope you will put this date in your diaries already. The event will allow all interested parties the opportunity to contribute to the future direction of ECETOC's work. One of the starting materials to be used at this meeting will be the output from the 2009 ATM, our "Young Scientists Event". We will invite key individuals from our operating environment including academic, regulatory and industrial scientists. Your suggestions, in this regard, will be welcomed. In addition, we will solicit your input by a questionnaire early next year. In the end, ECETOC depends for its success on the way in which it meets the needs of its member companies by promoting good science. This makes participation at next year's event so important for ECETOC members; it will give all participants the opportunity to give feedback on how we have operated the Science Strategy up to now and to identify the issues we should be working on in the immediate future.

Neil Carmichael

Dr. Neil Carmichael
Secretary General

Strategic Science Area: Risk assessment of innovation

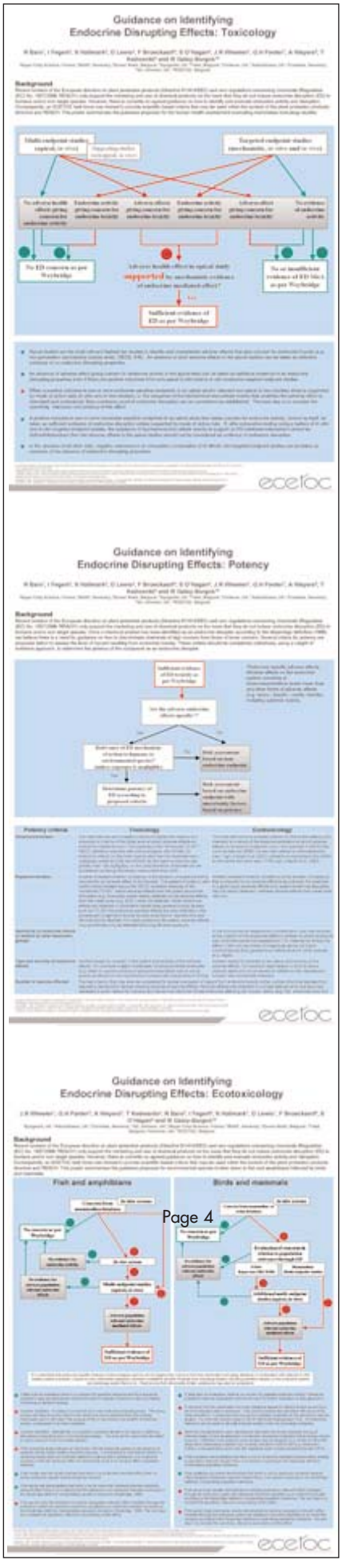
ECETOC AND EEMS JOINTLY ORGANISED SYMPOSIUM ON GENOTOXICITY OF ENGINEERED NANOMATERIALS

ECETOC and EEMS (European Environmental Mutagen Society) repeated their successful collaboration this year to organise a symposium and forum on the first day of the 10th International Conference on Environmental Mutagens (ICEM) which took place this 21-25 August in Florence, Italy. The aim of the symposium and forum discussion on the genotoxicity of engineered nanomaterials (ENM) was to review the biological significance of the available information on ENM and discuss approaches to identify and evaluate possible genotoxic effects. Knowledge of the mechanism of genotoxicity should support the rationale of genotoxicity testing of NM.

Speakers at the symposium explained that the major target organs of NM exposure are the lung, the central nervous system, and the cardiovascular system. An important point is the physico-chemical characterisation of the test material according to the endpoint studied (e.g. inflammatory response, DNA damages). Furthermore, it is essential to clarify whether NM induce primary genotoxicity (as a result of direct interaction with the DNA and/or spindle apparatus or indirectly as a consequence of oxidative stress and interaction with a non-DNA target), or cause secondary effects (as a result of inflammation). For example, DNA damage, as determined by the Comet assay, and micronucleus production are indicators for genotoxicity but as endpoints incapable of differentiating between a primary or secondary mechanism. In vitro studies need to be conducted using p53 proficient cell lines [Note: p53 is a transcription factor which regulates the cell cycle and thus functions as a tumour suppressor]. In all studies, the human relevance of effective doses seen in experimental studies needs to be evaluated. Particularly with aerosols, agglomeration and aggregation of NM makes it difficult to define the actual concentration at the target.

The forum expanded on the problems associated with genotoxicity testing of nanomaterials, and elucidated possible genotoxic mechanisms to support improved test strategies. In the ensuing discussion the audience addressed four questions, whether: (i) current OECD tests are appropriate and sufficient, (ii) NM found systemically are biologically relevant, (iii) there is a minimal set of parameters to be reported in a study, and (iv) which NM material can be used as a reference?

A set of articles will be published as a Special Issue of Nanotoxicology (Prof. V. Stone, Napier University, Editor-in-chief). Guest Editors overseeing the peer review process will be Prof. Stone and Dr. M. Donner (DuPont Haskell Laboratory).



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Website

Be sure to visit www.ecetoc.org to download any of our publications

Strategic Science Area: Risk, hazard & precaution

Strategic Science Area: Reproductive health

ECETOC WORKSHOP BRINGS TOGETHER EXPERTS TO DEBATE PROPOSED GUIDANCE ON INTERPRETING ENDOCRINE DISRUPTING EFFECTS

This 29-30 June in Barcelona, Spain, ECETOC convened a workshop to discuss 'Guidance on Interpreting Endocrine Disrupting Effects'. Fifty-five invited experts (from academia, regulatory bodies and industry) debated an approach developed by a related ECETOC task force published earlier this year in the form of an ECETOC Technical Report no. 106. The proposed approach provides guidance in the form of flowcharts that could be used as a decision tree for the identification of endocrine disrupting effects in human health (toxicology) and environmental assessments (ecotoxicology). The aim of the workshop was to assess the suitability of such an approach and to open a forum for critical analysis. It also provided an opportunity to propose improvements to the scheme.

Format

The workshop consisted of a series of invited presentations: The first of which outlined the regulatory background to the issue, the second reported on German national initiatives to develop toxicology criteria for endocrine disrupters. This was followed by presentations from the ECETOC task force introducing the ECETOC approach, including detailed explanations (with case studies) for its application in the toxicology and ecotoxicology fields. The presentations were followed by four syndicate discussion sessions, each addressing specific issues.

Feedback on the proposed guidance

Overall the ECETOC evaluation framework was considered scientifically sound and was viewed as a valuable contribution to the definition of specific scientific criteria that are required for the determination of endocrine disrupting properties. However, whilst it was acknowledged that the ECETOC framework was particularly suited for chemicals with comprehensive toxicology and ecotoxicology databases, it was lacking guidance for those chemicals with poor databases. In particular practical guidance is lacking with respect to what data needs to be generated for chemicals with partial or significant data gaps (in respect to the ECETOC scheme). To this end, it was recommended that additional case studies should be included in the ECETOC evaluation framework using both data poor and data rich chemicals.

To refine further the ECETOC evaluation framework, Workshop participants recommended to include the systematic and structured approach of the WHO/IPCS conceptual framework for evaluating the mode of action for cancer and non-cancer endpoints. This conceptual framework is part of a large project on the harmonisation of approaches for the assessment of risk from exposure to chemicals.

It was also agreed that approaches for determining endocrine disrupting properties should be consistent and harmonised for the three inter-related pieces of EU legislation that concern chemicals under REACH, biocides and plant protection products directives.

Break-out sessions

Several conclusions also arose from the break-out group sessions. These can be summarised as follows:

First, it was considered inappropriate to introduce a new class of chemical toxicity specifically for the endocrine disrupters given that the adverse effects resulting from endocrine disruption can be detected in apical studies (reproductive, development and chronic toxicity studies as well as the cancer bioassays) and they are, therefore covered by the existing EU or GHS classifications.

It was also recognised that there was no scientific reason to approach the toxicity resulting from an endocrine mode of action differently to other types of toxicity (e.g. neuro-, immuno-) resulting from non-endocrine modes of action.

Overall, there was a general consensus that European regulatory decisions to authorise or not authorise chemicals purely on the basis of hazard in the absence of proper risk assessment was not scientifically justified and contradicted approaches taken by other authorities outside Europe. However, it was recommended that appropriate risk assessment should be performed which takes into account a number of issues i.e. threshold of biological responses, potential 'low dose' effects and mixtures of chemicals acting by similar modes of action.

WORKSHOP LOOKS AT THE ENHANCEMENT OF THE SCIENTIFIC PROCESS AND TRANSPARENCY OF OBSERVATIONAL EPIDEMIOLOGY STUDIES

Strategic Science Area: Role of chemicals in the causality of disease

Environmental epidemiology studies are often treated with scepticism, even by the general public. In the past, scare stories based on findings from such studies, have turned out to be without foundation. There are many reasons for this, among them a pressure to have positive findings that can be published. This is compounded by the non-publication of negative findings and the difficulty to have such studies accepted for publication by high impact journals.

In view of these recurrent issues, ECETOC organised a workshop in London this 24-25 September at the Royal College of Physicians. Among the participants were leading experts from North America and Europe, from academia, government, science journals and industry.

The situation with such 'observational studies' was compared with that which previously existed with clinical trials. In this case, it was shown that the trials showing a beneficial effect were more likely to be published than those which did not. One major step was the setting up of 'clinical trials registries' which are open to the public and which provide a record of clinical trial designs and outcomes. These are supported by the editorial policies of key journals which only accept manuscripts if they were previously registered in these databases. In addition, the availability of the study protocol allows the results reported to be compared to the outcomes which were planned to be measured.

The workshop reached a consensus that it would be worthwhile to extend this approach to observational epidemiology studies. This approach was not considered to be a panacea, but would lead to improvements in the areas of ethics, transparency and universality (the availability of all data). As the existing databases hosted by the US NIH and the WHO were already suitable for this purpose, it was proposed that they be used, rather than starting a new system.

LATEST Publications

Technical Report 105	Evaluation of Cardiac Sensitisation Test Methods (published October 2009)
Workshop Report 15	The Probabilistic Approaches for Marine Hazard Assessment (published June 2009)
Technical Report 106	Guidance on Identifying Endocrine Disrupting Effects (published June 2009)
Monograph 38	Toxicity of Engineered Nanomaterials (published May 2009)
Workshop Report 14	Use of Markers for Improved Retrospective Exposure Assessment in Epidemiology Studies (published February 2009)

ECETOC In Brief

ECETOC, **E**uropean **C**entre for **E**cotoxicology and **T**oxicology **o**f **C**hemicals, was established in 1978 as a scientific, non-profit, non-commercial association, financed by 50 of the leading companies with interests in the manufacture and use of chemicals. A stand-alone organisation, it was established to provide a scientific forum through which the extensive specialist expertise in the European chemical industry could be harnessed to research, review, assess and publish studies on the ecotoxicology and toxicology of chemicals.

FORTHCOMING Meetings

November

02-3 Using Mode of Action Information to Improve Regulatory Decision Making - workshop
City Presentation Centre, London

04-05 Guidance on Assessment Factors to Derive DNELs TF - editing team meeting
ECETOC, Brussels

07 Carcinogenicity of Formaldehyde - 2nd task force meeting
ECETOC, Brussels

December

02 183 Scientific Committee Meeting
ECETOC, Brussels

04 Risk assessment approaches for PBT/vPvB chemicals or persistent organic pollutants (POP) - 5th task force meeting
ECETOC, Brussels

10 LRI Health effects monitoring team (HEMT) - monitoring team meeting
ECETOC, Brussels

January

14-15 Linear Polydimethylsiloxanes - 3rd task force meeting
ECETOC, Brussels

Next Edition ...

We will provide details We'll be feeding back on the Toxicology Forum.

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