

### ECETOC WORKSHOP LOOKS AT THE APPLICATION OF 'OMICS' TECHNOLOGIES IN TOXICOLOGY AND ECOTOXICOLOGY



*Intelligent Testing Strategies*   *'Omics' & related technologies*

**Within an 'Intelligent Testing Strategy' under REACH, new methodologies are needed to allow cost-effective evaluations of chemical risks. Toxicogenomics is an emerging discipline in toxicology that can be used for human and environmental risk assessment. It is expected to help in the prediction and evaluation of adverse effects of substances in the future.**

To review recent progress on the application of omics technologies to chemical safety and to assess their potential impact on the risk assessment of chemical substances, ECETOC organised a workshop in Malaga, Spain (6-7 December 2007).

The workshop addressed the following points:

1. Conditions to generate omics data relevant to toxicity (appropriate study design, quality control, exploitation and interpretation of data).
2. Usefulness of omics technologies in predicting toxicity in mammalian and non-mammalian models.
3. Usefulness of omics technologies in elucidating mechanism of action leading to toxicity.
4. Sensitivity of the omics technologies in detecting changes related to toxicity and comparison with sensitivity from more traditional methods (histopathology, enzyme assays, hormone measurements etc).

The 2-day workshop was limited to participation by selected industry experts, government agencies and invited external scientists (both toxicologists and ecotoxicologists), 29 people in all. The workshop reviewed 10 presentations on the above generic topics. In addition, 7 case studies were presented. Participants addressed specific questions in syndicate sessions and had a lively plenary debate.

The general conclusion among participants was that omics are now taking their place among other regular tools for hazard/risk assessment. However, the question remains whether the technology is ready to be incorporated into a regulatory setting. It was recognised that the pharmaceutical industry is more advanced at using omic data in the regulatory arena (e.g. US-FDA) and that mammalian models are more developed than those of environmental relevant species (e.g. US-EPA). For example, genome (DNA) sequence data for environmentally relevant organisms are still poorly described or non-existent.

The workshop firstly addressed the importance of using high quality study design and experimental controls (including quality controls). Good quality will improve confidence in the omics techniques and increase the likelihood of regulatory acceptance.

Interpretation of genomics data often proves to be a time consuming and challenging area of genomic science, but is a key factor to its successful application. The further development and implementation of guidance was found to be helpful, but it was stressed that full interpretation requires a refined and appropriate characterisation of the genes in the biological system as a whole.

### SG CORNER

So far this year ECETOC has been focussing on joint workshops.

For several years now, we have been developing the concept of 'strategic partnerships.' We have built on our relationships with many other organisations to increase our impact and widen our audience.

Already this year, we have co-hosted a workshop on fish embryo tests with ECVAM and HESI. In mid-April we have a joint workshop with ECVAM on refining reproductive toxicity studies. June will be a busy month with a workshop on biomarkers in epidemiology studies supported by ECPA and a workshop on probabilistic approaches for marine hazard assessment co-sponsored by the Environment Agency of England and Wales.

A long-term partnership with CEFIC LRI will allow us to organise our 9th consecutive EEMS symposium (this year on thresholds for genotoxic carcinogens). An ECETOC workshop on DNA adducts will be run as a satellite to this EEMS meeting, with the sponsorship of CEFIC and ACC. Then, in October ECETOC is organising two sessions at the EUROTOX meeting in Rhodes in October.

These joint events allow industry's scientists, via ECETOC, to have greater involvement and visibility than would otherwise be possible. More importantly, our willingness to partner gives ECETOC more opportunities to impact the scientific debates on a broader range of topics.

In addition, this broad range will include some new topics, as the forthcoming annual technical meeting will illustrate. This year the subject is: 'Counting the costs and benefits of chemical control: the role of environmental risk assessment in

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## SG CORNER continued..

socio-economic analysis.' This exploratory workshop will be the opportunity to discover what role ECETOC may eventually play in this debate if science has a role in the process. Member companies should be sure to send a representative to this exciting event.

Finally, some news of our window on the world, the internet.

ECETOC's website is in the process of being overhauled to make it easier and more attractive to use. Furthermore, it is our intention that our documents should be easier to find with search engines. We hope that this new site will be online by the end of May. Likewise, we have just agreed that members' site will be reviewed in order to facilitate improved internal interaction. This part should be completed by early next year.

Last but not least, improved technology means that visitors to the ECETOC offices can now catch up on their e-mail (or the football results) by using our wifi network (not during meetings of course)!



Dr. Neil Carmichael  
Secretary General

### Environment programme review

This January, ECETOC environmental scientists came together in Brussels to review and to prioritise the ECETOC environmental programme, review progress of existing LRI projects and prioritise new projects.

More information is available on the password protected ECETOC members' site.

### ECETOC YOUNG SCIENTIST Awards 2008

This year, ECETOC will sponsor two awards for young scientists and is looking forward to seeing the entries:

The ECETOC **environmental science related** Young Scientist Award (YSA) will be presented for the **best platform presentation** at the 2008 Society of Environmental Toxicology and Chemistry (SETAC) Europe Annual Congress (Warsaw, Poland, 25-29 May 2008).

The ECETOC **human health related** Young Scientist Award will be presented for the **best poster** at the 2008 European Societies of Toxicology (EUROTOX) Annual Congress (Rhodes, Greece. 5-8 October 2008).

## OMICS WORKSHOP continued..

Participants agreed that in future, genomics will change the current paradigm of toxicology and environmental science. As regards human health, the general consensus was that toxicogenomics will have value in providing supportive evidence for toxic mechanisms but should not necessarily be expected to be a definitive endpoint in a regulatory setting of drug/chemical risk assessment. With more toxicogenomic tools becoming available and users gaining more experience, it is most likely that environmental science will increasingly witness the application of genomic tools in chemical hazard/risk assessments.

Concerning the predictability of toxicogenomics, chemical class-specific molecular signatures were identified in several of the case studies presented. By selecting the DNA/genome sequences that were altered in the same direction (following exposure to a chemical having the same presumed mode of action), distinct cellular pathways can be identified. The pathway associated with a particular set of gene expression profiles may then be used to predict the genotoxic or non-genotoxic (i.e. carcinogenic) action of a chemical. Nonetheless, due caution is required when choosing a relevant biological model. Information on the toxic mechanism (mode of action) of the selected biomarkers, and on their stability, will be improved by new developments i.e. systems biology and careful validation based on independent chemical/drug class.

For prospective ecological risk assessment, understanding species diversity is still paramount. It is necessary to discriminate the effects of chemicals in the environment from the compensatory homeostatic

response at organism level in the presence of a toxicant and the compensatory dynamics of the population as a whole. High levels of conservation between species, means that micro-organisms (e.g. E.coli), nematodes, earthworms and fish could be useful as indicators for higher organisms.

In summary, workshop participants concluded that the omics technology is here to stay and is becoming less expensive. Regulators do not require omics data as yet, but the available data can already be included in dossiers. It will be a long term process to address all these issues, but science and industry will profit in the future from the effort made. It was recommended to anticipate for further omics guidance updates from regulatory bodies in Europe (ECHA) and USA (EPA/FDA).

In his summing up, Dr Carmichael (ECETOC Secretary General) suggested giving quality standards and guidance for regulatory purposes (e.g. biomonitoring) and developing a (mechanistic) NOTEL indicative of early patterns of change. In case of ecological change, the NOTEL (no observed transcriptional effect level) should allow extrapolation from individual to population.

An ECETOC Workshop Report is being prepared by the organisers, along with a paper for publication in the open literature. Speakers and other participants are contributing to the process.

### ECETOC co-organises fish embryo workshop with ECVAM and HESI



Biodiversity and ecosystems

**ECETOC cooperation with ECVAM (European Centre for the Validation of Alternative Methods) and HESI (ILSI Health and Environmental Institute) resulted in the organisation of a fish embryo workshop this 4-6 March in Aulnay-sous-Bois, France on the application of the fish embryo test as an animal alternative method in hazard and risk assessment, and scientific research.**

The workshop focussed on the development of the technical basis that is needed for embryonic fish tests as an alternative to standard fish toxicity test procedures around the globe. It sought to coordinate the ongoing debates on emerging practices of the fish alternatives and animal model development sciences to meet the scientific, regulatory and biomonitoring needs.

Participants at the workshop reviewed the state of the science regarding investigation of fish embryonic tests, pain and distress in fish, emerging approaches utilising fish embryos, and the use of fish embryo test data in hazard and risk assessment, effluent assessment, and international classification and labelling of chemicals.

Readers can anticipate the publication of the outcome of the workshop as a report and a series of peer reviewed publications. It is hoped that this event has laid the groundwork for future research, method development and subsequent workshops in this area.

## Marine hazard workshop coming up in Oslo



Biodiversity and ecosystems



Intelligent Testing Strategies



Risk, hazard & precaution

**This 18-19 June, an ECETOC workshop on probabilistic approaches for marine hazard assessment will take place in Oslo, Norway.**

Organised with the collaboration of the Environmental Agency of England and Wales and hosted by the Norwegian Pollution Control Authority, this workshop will focus on *evaluating the applicability of probabilistic methods in marine hazard assessment* as alternative to the deterministic methodology laid down in the EU-Technical Guidance Document marine paragraph, i.e. the application of assessment factors. It also aims to provide an overview of required data and extrapolation techniques in the form of an ECETOC report and a peer-reviewed manuscript. The results will be disseminated through presentations at scientific meetings.

## In memory of Gauke Veenstra

It is with great sadness that we learned that Gauke Veenstra had died on Good Friday. Many people will remember him as a friend, a family man, a colleague or whatever role he played in their lives. In my case, he was one of my first colleagues after I joined Dow Chemical in 1982; a relationship which developed into a personal friendship. His Shell colleagues in more recent years also thought equally highly of him as a person of knowledge, commitment and integrity.

On this page, I would like to remember his contributions to and on behalf of ECETOC. We first learned of Gauke's illness when he was unable to come to a meeting of a task force of which he was chairman. It is not the intention to make a list here, but to recognise the many contributions Gauke made.

Gauke's contributions to ECETOC spanned many years. He was a member or chairman of several task forces, monitoring teams, REACH ad-hoc groups and had many other roles. His versatility and willingness were assets to us right up to his final illness. Everyone here at the secretariat and those who knew him through these activities remember a wise and thorough professional. They also remember a gentleman in the old sense: polite, modest, humorous and kind. All these qualities will be recalled when we think of Gauke and he will be sorely missed.

Dr. Neil Carmichael  
Secretary General

## LATEST Publications



Technical Report No. 102

Intelligent Testing Strategies in Ecotoxicology: Mode of Action Approach for Specifically Acting Chemicals  
Published December 2007

Document No. 45

Triggering and Waiving Criteria for the Extended One-Generation Reproduction Toxicity Study  
Published March 2008

Be sure to visit [www.ecetoc.org](http://www.ecetoc.org) to download any of our [publications](#)

## ECETOC In Brief

**ECETOC**, European Centre for Ecotoxicology and Toxicology of Chemicals, was established in 1978 as a scientific, non-profit, non-commercial association, financed by 51 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

### May

- 21 Potency values from the LLNA: Application to classification, labelling and risk assessment task force meeting  
ECETOC offices, Brussels
- 22 LRI HETRA monitoring team  
Fraunhofer ITEM, Hanover

### June

- 3 Scientific Committee meeting  
ECETOC offices, Brussels
- 4 Annual Technical Meeting  
'Counting the costs and benefits of chemical control: The role of environmental risk assessment in socio-economic analysis'  
Martin's Central Park Hotel, Brussels
- 5 (morning)  
Board meeting  
Martin's Central Park Hotel, Brussels
- 5 (afternoon)  
Annual General Meeting  
Martin's Central Park Hotel, Brussels
- 10 Guidance for classification of carcinogens under GHS task force meeting  
ECETOC, Brussels
- 18 Potency values from the LLNA: Application to classification, labelling and risk assessment task force meeting  
ECETOC, Brussels
- 18-19 Probabilistic approaches for marine hazard assessment workshop  
Oslo, Norway
- 24-25 Use of markers for improved retrospective exposure assessment epidemiology studies workshop  
Sodehotel la Woluwe, Brussels

### July

- 18 Cyanides antidotes task force meeting  
ECETOC, Brussels

### September

- 4 Board meeting  
ECETOC offices, Brussels
- 23 Scientific Committee meeting  
ECETOC offices, Brussels
- 25 Thresholds for genotoxins and their application in risk assessment symposium  
During EEMS Annual Congress  
Cavtat, Croatia
- 25-26 The biological significance of DNA adducts: Part II workshop  
Post-EEMS Annual Congress  
Cavtat, Croatia

### Next Edition ...

There'll be a report on ECETOC's triggering and waiving criteria for the extended one-generation reprotoxicity study workshop

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