ecetoc

e-NEWSLETTER

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

No. 17, July 2010

ECETOC STRATEGY REVIEWED AT THE 2010 ANNUAL TECHNICAL MEETING

The ECETOC Science Strategy was launched in 2007 based on input given by our Member Companies and other interested parties at the Futures Workshop held the previous year. It is an issue-based approach broken into 13 science areas that are grouped under 5 themes:

- Presence of chemical in humans
- Presence of chemicals in the environment
- Effects in humans and ecosystems
- Methods
- Science of risk assessment

This strategy has served us well over the last years, and we have been able to use it as a guide for discussing our work programme within the Scientific Committee and with our Member Companies. Since then, new challenges have come up for the chemical industry, both on science and on the regulatory front. Issues are becoming increasingly more complex but, at the same time, we are confronted with a diminishing resource of specialists in the industry that can address them. Therefore the Board and the Scientific Committee already decided last year that this annual technical meeting should review our strategy and our ways of working.

The day started off with stimulating presentations by:

- Bjørn Hansen (DG Environment) on the regulatory landscape in Europe with emphasis on REACH, for which he pointed out the need for better category approaches.
- Bob Diderich (OECD) on the very topical subject of systems biology approaches and non-animal methods.
- David Owen (Scientific Committee Vice-Chairman) building on the previous speakers' points by offering his views on the vision for 21st century toxicology.
- John Doe (outgoing Scientific Committee Chairman) providing an overview on the ECETOC Strategy and the feedback we had received by preparatory meetings and surveys.
- Neil Carmichael (Secretary General) presenting our most recent activities, particularly those where we had the largest impact.

These presentations provided a good basis for discussion in the subsequent breakout groups that were charged to discuss:

- Developing the future science strategy.
- Maintaining access to intellectual resources in a cost-neutral environment.
- Making ECETOC more attractive to broad membership from the chemical industry.

Many insightful and helpful suggestions were made by the 40 or so participants.

The outcome is currently being evaluated by a group of the Scientific Committee and will be presented to the Board in September.

Inside this issue

SG CORNER

At the ECETOC Secretariat, the summer got off to a flying start with the annual meetings. This year was particularly intense with a board meeting, the annual general and technical meetings and a scientific committee all in the space of three days! Despite the logistical strain, it all held together and was beneficial in allowing participants to combine these activities in one trip. Further, as the annual meetings were focussed on updating the strategy, it allowed continuity of thought from one meeting to another. The outcome of these deliberations will go through a final refinement process by the ATM organising committee before being presented to the board in September.

Part of our ongoing science strategy will be to continue the development of the initiatives concerning pharmaceuticals in the environment, as described in the previous newsletter. These initiatives have attracted enthusiastic support from the pharmaceutical industry and I am delighted to announce that the world's largest research based pharmaceutical company, Pfizer, has become a member of ECETOC. At the same time, I am equally delighted to welcome another new member company, Johnson & Johnson who are a more diversified company, being a major player in consumer products as well as health care. In both cases, access to the expertise of these two giants will be a great asset to ECETOC.

Martin Kayser presents John Doe with his retirement present

As all of you reading this will know, the engine room of ECETOC is the Scientific Committee. This is where the continuity of the program is ensured and the quality of the product is controlled. Chairing this eminent group is a challenging task; not for the faint hearted. John Doe has been the Chairman for 4 years and has contributed great energy and vision to ECETOC in the fulfilment of this role. The strategy review has been led by John since the beginning and though he retired from his company at the turn of the year, he stayed on at ECETOC to see the baby born.

John will be missed by all the Scientific Committee and by me personally as I have worked with him in many capacities for

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Task force to evaluate low dose interactions

Science Area: Mixtures

Much attention is being given to the so called 'cocktail effect' which is hypothesised to occur due to simultaneous exposure to low levels of environmental chemicals. According to this theory, unexpected effects can occur due to interaction in the body between these chemicals even though the levels would be below the threshold of toxicity for the individual chemicals or their breakdown products. It is claimed that these interactions at low-dose levels may be greater than additive.

Consequently, ECETOC has formed a task force to review relevant literature and known examples, and to evaluate whether the evidence on low-dose interactions demonstrates any effects that are 'unexpected' in light of current toxicology theory; should this be so, they will determine if specific modes of action are frequently associated with this. Finally, they will evaluate the adequacy of current risk assessment practice in light of the conclusions drawn. The task force will hold it's first meeting in September.

SG Corner (continued)

nearly 20 years.

Taking over the chair of the Scientific Committee will be Dr Fraser Lewis. Fraser is an environmental expert and a skilled leader of meetings, who was also highly instrumental in developing the strategy review. Over the last 3 years we have re-invigorated the portfolio of environmental projects and Fraser's expertise will be invaluable in guiding these activities to a successful conclusion.

To round off the changes that took place at the AGM, Dr. Hans-Juergen Bender of Procter & Gamble stepped down from the Board of Administration due to his other commitments. We are sorry to see him go and thank him for his valuable input to the Board since 2008. He was replaced by Dr. Petra Hanke-Baier, also of Procter & Gamble, whose International background in Product Safety & Regulatory Affairs will be a welcome addition to the fields of expertise of our Board members.

Neil. Carmichael

Dr. Neil Carmichael
Secretary General

Calls for nominations for two new task forces

Two task forces are being organised as a result of the findings of an ECETOC workshop 'Significance of Bound Residues in Environmental Risk Assessment' which was held on 14-15 October 2009 in Brussels (see ECETOC Workshop Report No. 17).

The first, **Understanding the relationship between extraction technique and bioavailability,** has been commissioned to develop a framework for intelligent extraction strategies. Submissions should be received by Company Delegates, preferably by 23rd July 2010.

The second, **Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals,** has been commisioned to evaluate the proposed risk assessment framework developed following the ECETOC workshop and to assess its utility as an interim approach for regulatory assessment of chemicals. Submissions should be received by Company Delegates, preferably by 11th August 2010.

Full details can be found on the Members' Website (http://members.ecetoc.org) or by contacting your Company Delegate.

MÁLAGA WORKSHOP REVIEWS THE PROGRESS MADE IN 'OMICS IN (ECO)TOXICOLOGY

Science Area: 'omics' and related technologies

In 2007, ECETOC organised a Workshop on the application of 'omics technologies in toxicology and ecotoxicology. This year a workshop was held in Malaga on 22 and 23 February to review the progress made since then 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.

Attended by selected industry experts and invited external scientists, seven case studies were presented as well as sessions on future perspectives, system biology and modelling. These were followed by syndicate discussions on baseline, new descriptors, adverse effects, identification of mode of action and its qualitative application to risk assessment.

The following conclusions were drawn in a final plenary session:

- 'Omics data are particularly valuable for understanding modes of action (MoA) via underlying molecular patterns and by exploring responses to model compounds in highly standardised systems.
- Novel patterns or biomarkers (e.g. gene signatures, metabolome profiles) can also be developed this way for screening chemical properties of novel compounds.
- Within the context of risk assessment 'omics data can already add value to risk assessment by improving mechanistic understanding and the identification of modes of action.
- To enhance the acceptance of 'omics data, for such risk assessment purposes, high quality data and a careful design of the biological experiment are essential.
- Mode of action recognition by fingerprints or biomarkers can be enhanced if the changes observed can be causally linked to the toxicological pathway.
- These technologies can potentially serve as a tool for the prioritisation of chemical testing and could help to provide a better (biology based) rationale for chemical grouping under the REACH legislation.
- To better assess the quantitative aspects of 'omics data, more information concerning the sensitivity of 'omics relative to classical toxicology testing is needed. It would seem that transcriptomic information may be more sensitive than classical toxicology, whereas metabolomics appears to be equally sensitive.

In addition, there is a need for better standardisation of methods within the various activities in this dynamic field, particularly in the area of transcriptomics. The participants also agreed that in the near future, 'omics technologies could help to bridge *in vitro* testing to *in vivo* relevance. Guidance (communication of best practices), rather than guidelines will encourage improvements and adaptation to new technical developments.

The workshop concluded that better standardisation, data interpretation and evaluation will build confidence in the value of 'omics technologies – this being essential to increase their (regulatory) use. The workshop therefore called for an international effort to bring together scientists from academia, industry, agencies as well as the risk assessors themselves, to discuss and evaluate the necessary modifications that may be needed to enhance the use of 'omics data in risk assessment.

The Workshop Report is available at the ECETOC website (Workshop Report No. 19).

Science Area: Risk assessment of innovation

Post Satellite to the 46th EUROTOX Meeting

Innovation through Nanotechnology and Nanomaterials
Current Aspects of Safety Assessment and Regulation
22 – 24 April 2010, Dresden, Germany

This symposium was organised as a post-satellite to the 46th EUROTOX meeting in Dresden, Germany, and was attended by 88 experts from academia, governmental and contract research organisations, industry and regulators. Presentations covered characteristics of nanomaterials (NM) in products already on the market and those under development, human and environmental safety, as well as regulatory aspects.

The general consensus was that nanotechnology is a broad field that cannot be defined and regulated uniformly. Available legal instruments are options but no specific one is favoured or may be the right one for all types of NM. Some NM are already covered under existing regulatory frameworks with stronger risk management options, i.e. pharmaceuticals, pesticides and cosmetics; others will probably fall under REACH but this will need prioritisation and cut-off criteria.

Exposure to manufactured NM in relation to naturally occurring NM of similar chemical nature should be understood better, as well as effects upon chronic exposure to NM. Demonstrating the absence of dermal absorption seems to be an acceptable risk assessment method for NM used in cosmetics. Pulmonary exposure to NM is mostly to their agglomerates or aggregates. The primary biological effects may be due to surface reactivity, ion release, inflammation or physical interaction with biological matter. Sub-chronic studies presented for MWCNT showed no extra-pulmonary translocation or toxicity but inflammation in the lung which may be due to pulmonary overload. Some new techniques on *in vitro* testing with cell cultures were shown, but need right positioning within testing strategies.

On-going research is addressing the open questions, but should be complemented with studies on mode of action of different types of NM, the development of analytical techniques and of *in vitro* methods to complement long-term *in vivo* testing. There are numerous studies on exposure to nano-silver, also in environmental matrices. While nano-silver is used in a variety of products, it is however by far not the NM of highest production volume.

A number of publications are foreseen as follow-up to this very successful meeting, along with an educational course at the annual meeting of the German Toxicology Society (March 2011) and a special symposium with the MAK Commission (March 2011).

Following the symposium, a half-day discussion took place about '*in vitro - in vivo* extrapolations for inhalation studies', attended by 16 of the symposium's participants. The topics discussed can roughly be clustered as:

- regulatory aspects / definitions / material characterisation
- standardised models / species extrapolation / dose descriptors for NM / kinetics / modes of action
- correlation of *in vitro* and *in vivo* test methods
- exposure to naturally occurring NM (in comparison to manufactured NM and tobacco smoke)
- co-ordination of testing programmes (industry-/government-sponsored in order to avoid double work), i.e. both laboratory work and bio-monitoring.

The steering committee will evaluate the outcome of this discussion and their proposals will first be shared with the participants of the special workshop for commenting after which attendees of the two-day symposium will be invited to join in those activities.

Science Area: Risk, hazard & precaution

Workshop discusses guidance on assessment factors to derive DNELs

The REACH TGD 'Guidance on information requirements and chemical safety assessment' Chapter R.8 proposes a tiered and systematic approach for the delineation of DNELs (and DMELs) including the application of assessment factors (AF) for extrapolation from animal data to man. Recently, guidance for AF based on human data was added. Building on this guidance, an ECETOC Task Force is preparing additional scientific arguments and pragmatic recommendations for substances on which relevant information was available.

The approaches developed were presented at a workshop that took place on 25th March 2010 in Barza d'Ispra/Italy. The ECETOC guidance was demonstrated by a number of case studies. A parallel project carried out by the Fraunhofer Institute for Toxicology and Experimental Medicine for the detergent's industry initiative ERASM (Environmental Risk Assessment and Management) was also presented. 55 participants, 8 of which came from regulatory authorities, discussed the proposals made and assessed where the science could be further developed in support of the implementation of REACH. The outcome of the workshop will be summarised in a Workshop Report and the feedback received will be taken into account in the final ECETOC Technical Report. The reports are targeted for finalisation this summer.

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Science area:
Reproductive health
+
Risk, hazard and precaution

Guidance for Classification of Reproductive Toxicants under GHS

The Globally Harmonised System of Classification and Labelling of Chemicals (GHS) has been introduced into the EU legislative framework under CLP Regulation No. 1272/2008. It is replacing the current guidelines under the Directives 67/548/EEC and 1999/45/EC. Regulatory authorities worldwide are beginning to use the GHS criteria and it is already being noticed that their interpretation varies in different parts of the world. Further to this, many chemicals which have not yet been assessed for reproductive toxicity will be tested under REACH, and cut-off criteria currently applied to agrochemicals may be applied to other categories of chemicals. It is important that industry has a clear position to contribute to the way chemicals are classified for reproductive toxicity.

ECETOC recently published guidance for the classification of chemicals with regard to the endpoint of carcinogenicity, which incorporated the concept of potency. This guidance has been well received. Building on the approach for carcinogenicity, a task force has been formed with the remit to develop guidance for the application of the GHS criteria to reproductive (developmental, fertility) toxicity that will include consideration of mode of action, potency and exposure.

ECETOC Young Scientist Awards
Best Platform Award presentation at SETAC

This year's ECETOC Young Scientist Award on environmental research was won by Ms. A.M. Boulay from the École Polytéchnique, Montréal, Canada.

She was chosen for the award for her excellent research on 'Using GIS to evaluate regional human health impacts from water use' and the platform presentation at the annual conference of SETAC Europe on 23rd-27th May 2010 in Seville.

LATEST Publications

Reports:

Technical Report No. 108	Collation of Existing Marine Biodegradation Data and its Use in Environmental Risk Assessment (Published December 2009)
Workshop Report No. 17	Significance of Bound Residues in Environmental Risk Assessment. 14-15 October 2009, Brussels (February 2010)
Workshop Report No.19	'Omics in (Eco)toxicology: Case Studies and Risk Assessment 22-23 February 2010, Málaga (July 2010)

Scientific Article:

Embry M R, Belanger S E, Braunbeck T A, Galay-Burgos M, Halder M, Hinton D E, Léonard M A, Lillicrap A, Norberg-King T, Whale G. 2010. The fish embryo toxicity test as an animal alternative method in hazard and risk assessment and scientific research. *Aquatic Toxicology* 97, Issue 2, 15 April 2010, Pages 79-87 doi:10.1016/j.aquatox.2009.12.008

Other:

2009 Annual Report (June 2010)

Poster for SETAC 2010 on Environmental Risk Assessment of Bound Residues (May 2010)

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. It is financed by 49 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.

Website

Be sure to visit www.ecetoc.org to view our activities and to download our publications

AGENDA

July

19-23	IUTOX 2010 - XII International Congress of Toxicology Barcelona, Spain
30	Approaches for read-across in chemical risk assessment TF meeting, ECETOC, Brussels

August

02	Risk assessment approaches for PBT/vPvB or POPs TF meeting, ECETOC, Brussels
10	Science needs in support of REACH - Network teleconference
17	ERA of ionisable compounds TF teleconference
18	LRI - EMT - ECO 14B Monitoring team teleconference
26	Linear polydimethylsiloxanes TF teleconference
30	Cyanides antidotes TF meeting Monheim-am-Rhein, Germany

September

8-9	ERA of ionisable compounds TF meeting, ECETOC, Brussels
10	LRI - HEMT teleconference
13	Low-dose interactions TF meeting, ECETOC, Brussels
14	Board of administration meeting, ECETOC, Brussels
16	Symposium at EEMS 2010 Use of 'omics in systems biology Oslo, Norway
20-21	Development of guidance for assessing the impact of mixtures of chemicals in the aquatic environment TF meeting, ECETOC, Brussels
21	Environmental impact assessment for socio-economic analysis of chemicals TF meeting, ECETOC, Brussels
22	187th Scientific Committee meeting, ECETOC, Brussels

October

04	Cyanides antidotes TF meeting, ECETOC, Brussels
05	LRI HETRA project B7-ETH meeting ECETOC, Brussels
19-20	188th Scientific Committee meeting, ECETOC, Brussels
21-22	Linear polydimethylsiloxanes TF meeting, ECETOC, Brussels

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