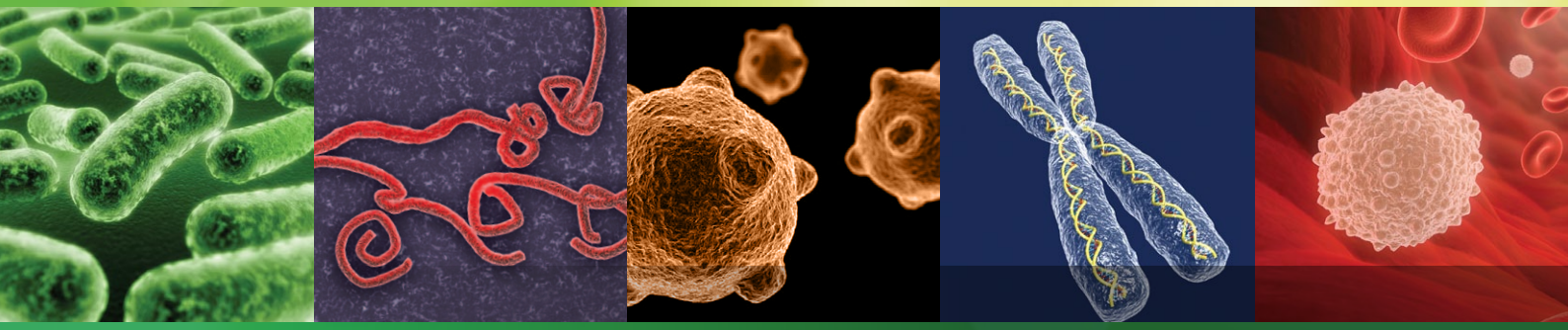
ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS



Annual Report **2011**

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ECETOC at a glance

Established in 1978, ECETOC is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

ECETOC also provides scientific representation for its member companies through presentations at specialist meetings and by participation in the scientific activities of international agencies, government authorities and professional societies. A non-profit, non-commercial and non-governmental organisation, ECETOC prides itself on the objectivity and integrity of its work programme, the output of which is published in the form of peer-reviewed reports and articles in peer-reviewed journals, or as specialised workshops.

Purpose

ECETOC's purpose is to develop concepts, data and positions which underpin the use of scientific principles in the translation of policy into regulation in Europe: to enable the benefits of chemicals to be realised while protecting human health and the environment.

Values

ECETOC has strong values of science and integrity; it works by establishing objective positions and then moving forward, not backwards from a predetermined view.

Vision

ECETOC will be the partner of choice focusing and engaging industry expertise for the European Commission, ECHA, and EFSA in the development of practices and concepts based on science as policy becomes embodied in regulations.

Mission

To promote the use of good science in human and environmental risk assessment of chemicals, biomaterials and pharmaceuticals.

Approach

ECETOC pursues its vision and mission through an issue-based science strategy comprising 10 science areas* grouped under 5 main themes (see chapter entitled 'Science Programme'):

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

*As of 1 January 2011

ECETOC Member Companies

At the start of 2012, ECETOC membership comprised the following 43 companies:

Afton Chemical
Associate member company

AkzoNobel
ALBEMARLE
Associate member company
AstraZeneca
BASF
Bayer
bp
CEPSA
Associate member company

Clariant
COLGATE-PALMOLIVE
DOW
Living. Improved daily.
DOW CORNING
DSM
DUPONT
eni

EVONIK
ExxonMobil
Roche
Firmenich
Associate member company
Givaudan
GSK GlaxoSmithKline
Henkel

Honeywell
HUNTSMAN
Enriching lives through innovation
INEOS ChlorVinyls
IFF International Flavors & Fragrances Inc.
Associate member company
Johnson & Johnson
L'ORÉAL
Lucite International
Going further
Associate member company

MERCK
NIPERA
Associate member company
Pfizer
P&G
Reckitt Benckiser
Rhodia
Chemistry is our world. Responsibility is our way
SC Johnson

Shell Chemicals
SOLVAY
Statoil
syngenta
TOTAL
Unilever
WACKER

Membership **benefits**

"...represent and promote the European chemical industry's science in its relationships with European and international institutions."

Manufacturers and users of chemicals (and biomaterials and pharmaceuticals) can become either a Full or Associate Member of ECETOC according to the proportion of their turnover derived from chemicals, (see www.ecetoc.org/membership). Membership of ECETOC demonstrates the practical commitment of a company to the principles of Responsible Care® via their active scientific and technical contribution to initiatives supporting the safe manufacture and use of chemicals, pharmaceuticals, and biomaterials through good science.

The diversity and range of its members' expertise are key ingredients for ECETOC's achievements in the pursuit of this objective. ECETOC's success depends on member company employees being able to dedicate their time to furthering projects within the framework of an ECETOC task force.

In so doing, member company employees benefit from access to a high quality network of scientific expertise and ECETOC is able to leverage this pool of knowledge in order to represent and promote the European chemical industry's science in its relationships with European and international institutions.

ECETOC member companies benefit from being in a position to influence its scientific agenda. They can propose subjects to be tackled by its work programme and can have a representative on its Scientific Committee.

Any member company employee can request a login to the ECETOC members' site: http://members.ecetoc.org where they can download any ECETOC report, keep track of discussions at Scientific Committee level and check the progress of the work programme.

All ECETOC member companies receive complimentary printed copies of each new ECETOC report and are entitled to request additional printed versions as and when needed.

Message from the Chairman

In 2010, at the Annual Technical Meeting, ECETOC revised its strategy including the mission and vision statements. In this year's report, I would like to comment on how this translated into practice during 2011.

Prior to this strategy review, the vision was: "To be the leading European health and environmental science organisation addressing the safe manufacture, supply and use of chemicals, biomaterials and pharmaceuticals". This vision remains valid, but may be considered to be inward looking and not clearly identifying the audience for our work. Our new vision is much more specific than formerly and now reads: "ECETOC will be the partner of choice focusing and engaging industry expertise for the European Commission, ECHA, and EFSA in the development of practices and concepts based on science as policy becomes embodied in regulations".

"In 2010, at the Annual Technical Meeting, ECETOC revised its strategy including the mission and vision statements. In this year's report, I would like to comment on how this translated into practice during 2011."

The theme of this statement of the association's vision is partnership and co-operation. Since 1996, ECETOC has been recognised as an "NGO in Official Relations with WHO". This relationship has just been reconfirmed by WHO during 2011. Likewise, we have always been ready to co-operate with official organisations and industry associations, as exemplified by our long running partnership with the CEFIC "Long Range Research Initiative" (LRI).

ECETOC has always been involved in practical science which would be relevant to regulation. This is exemplified by our participation in the consortia for REACH technical guidance (PEGs - 'Partner Expert Groups'). Likewise, the development of the targeted risk assessment (TRA) tool was specifically intended to provide a science based approach to first tier risk assessment for the REACH regulations. Similarly, the ECETOC technical report on derivation of DNEL's was specific to this regulation.

There is more to ECETOC than REACH of course. Our pharmaceutical, personal care and agrochemical member companies have their own regulations to address and ECETOC aims to help them with the same science-driven approach.

It is in recognition of the increasingly regulated environment of our industry that we have chosen to emphasise co-operation with official bodies in Europe. This list is, of course, not intended to be prescriptive. Indeed, we also co-operate directly with member states and other scientific bodies. We have long term, if unofficial, relationships with EUROTOX, SETAC, the European Environmental Mutagen Society, to name a few.

However, we recognise that if our science product is without impact at the level of European regulation, ECETOC's relevance could be questioned by its member companies. Consequently ECETOC has signed up to ECHA's transparency register and been accepted as an accredited stakeholder. We consequently have a Board member serving as ECETOC's observer at the "Member State Committee" and a member of our Scientific Committee is an observer to the "Risk Assessment Committee".

Similarly, we are recognised at the Commission and we are consulted for our views on scientific issues. This status resulted in us being invited to attend an ad hoc meeting to discuss the "State of the Science" report on endocrine disruptors and to propose a member for an expert group which will advise DG Environment on this subject.

When we reviewed the strategy in 2010, we had in mind to produce guidance for the prioritisation of our issues. This is at least partly in recognition of the fact that industry's scientific resources are severely stretched to meet the demands of an increasingly regulated environment. Hopefully the new vision will help ECETOC to remain a key resource for its members by ensuring the relevance of the association's activities.

Martin Kayser
Chairman of the Board of Administration

ECETOC Board of Administration

The Board of Administration is empowered by the Annual General Meeting with the management and administration of ECETOC and delegates these tasks on a daily basis to its Secretary General.

The Board is composed of at least six member company representatives. Two Board members are entitled to represent the Associate members. Board members have a two-year mandate and are responsible for the overall policy and finance of the association. The Board is also responsible for appointing the members of the Scientific Committee. Member companies may propose candidates for the Board; these candidates must have managerial duties within their company and possess scientific and technical experience.

ECETOC Board Members (December 2011)

Martin Kayser
BASF
Chairman

Steve Rumford
AstraZeneca
Vice-Chairman and Treasurer

Julia Fentem
Unilever

Petra Hanke-Baier
Procter & Gamble

Peter Hertl
Syngenta

Thomas Jostmann
Evonik Industries

Tamara Nameroff
Shell

Richard Phillips
ExxonMobil

Anne Wallin
Dow

At the 2011 AGM:

Resignations

The Chairman informed participants that Mrs. M. Quirina (DuPont) had retired from the ECETOC Board effective 8 June 2011 having served since 2006.

Election of Board Members

Dr. Thomas Jostmann (Evonik Industries), Dr. Martin Kayser (BASF) and Dr. Richard Phillips (ExxonMobil) were unanimously re-elected to the ECETOC Board, effective 8 June 2011.

Dr. Peter Hertl (Syngenta), Dr. Tamara Nameroff (Shell) and Dr. Anne Wallin (Dow) were unanimously elected as new members to the ECETOC Board.

Report from the Secretary General

Looking back at 2011 gives rise to some quiet satisfaction, not least because I will be leaving ECETOC in 2012. I am happy to be able to report on a successful year. The alarming trend of declining membership has been reversed, with three new companies joining our ranks. First was Afton Chemical, a company specialising in additives for fuels and lubricants. Next came Nipera, a specialist association, whose goal is to promote the health and safety of those exposed to nickel or nickel-containing products in the workplace and general environment. Finally, we were delighted to have the pharmaceuticals giant GlaxoSmithKline join as the year ended.

The year was also productive, with four full reports published along with two workshop reports. The workshop format is becoming more and more popular and the Scientific Committee is being asked to strictly prioritise to ensure that we do not commit to more than our resources can support. We ran three full workshops (which will result in reports), two internal review workshops and symposia at EUROTOX and the European Environmental Mutagen Society.

An indicator of the reputation of ECETOC is the quality of guest speakers and external participants we attract to our workshops. These include notable researchers from the most reputable institutions and senior officials from the European and North American regulatory communities. The workshop reports are produced within a few months of the event and so remain topical and are widely cited in the scientific journals and regulatory publications.

One of our internal review workshops looked at science issues and gaps whose definition results from member companies' experience with REACH. This produced an extensive wish-list which again has had to be prioritised by the Scientific Committee. As I write this several activities identified at that meeting have already started.

I am in a position to hand over an organisation in good health to my successor and this is cause for optimism for the future. Provided ECETOC works on the critical scientific issues which its members need and continues to produce high quality products which are respected by the scientific community at large, its future should be assured.

Neil Carmichael
Secretary General

Foreword from the Scientific Committee Chairman

2011 has been a busy year with some significant changes for the Scientific Committee. We have said goodbye to two long standing members of the committee. David Owen, who has been a member for seven years and served as Deputy Chair of the committee for the last four, retired from Shell and ECETOC during last year. Also one of our academic members, Peter Calow, has departed for pastures new in the USA where he has joined the University of Nebraska. However, we have also welcomed five new members to the committee in 2011: two industry scientists, Jason Snape from Astra Zeneca and Marie-Louise Meisters from Dupont, and three academic members. They are Leslie Rushton, an epidemiologist from Imperial College London, Lorraine Maltby, an environmental biologist from Sheffield University and Kees van Leeuwen, an ecologist from KWR Watercycle Research Institute. This brings the total to five academic members on the Scientific Committee.

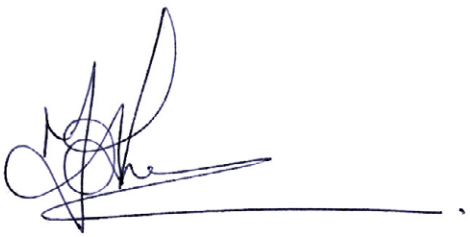
During the last year, we have continued to work through our strategy aimed at using good science to influence policy in Europe. The Scientific Committee has focussed on three key themes which are currently high-profile issues in Europe: Endocrine disruptors, Mixtures/Chemical co-exposures and a review of outstanding science needs for REACH.

Endocrine disruptors:
Over the last year, communication of the ECETOC-developed framework towards risk assessment of endocrine disrupting chemicals continued via a dedicated workshop in May and a symposium at EEMS in July. ECETOC's scheme also played a key role in subsequent meetings on the topic organised by the EU Commission. The ECETOC position being advanced is that specific scientific criteria should be applied to determine endocrine disrupting properties. They integrate, in the form of flow charts, information from both regulatory (eco)toxicity studies and mechanistic/screening studies relying on the nature of the adverse effects detected in regulatory (eco)toxicity studies, that give concern for endocrine toxicity as well as a description and understanding of the mode of action and potency of toxicity.

Mixtures/Chemical co-exposures
As we reported in last year's annual report, chemical regulation has mainly been based on the assessment of single substances, but frequently exposure is to complex mixtures of chemicals, often at very low doses, which has raised the question of whether the current regulatory framework is adequate and protective. Two related task forces have continued their studies and both have now completed or are about to complete their work. Continuing our specific strategy to better communicate the science in this area, there was a successful and timely workshop covering combined low-dose interactions in the environment and upon human health exposure. Participation included key players from both sides of the Atlantic. The outcome from these task forces and workshop will provide a significant science contribution from industry to regulatory motions in the EU.

REACH:
As the dust had settled after the first peak of REACH submissions, it was time to reflect on the experiences and learning gained following the production of the chemical dossiers. We held a workshop open to all member company experts to identify those areas where the science needs further development and where industry can bring in its expertise to bear in addressing gaps. A key area which was identified was read-across and chemical categories, which has led to the formation of a new task force to look into the current knowledge and how it can be applied within a REACH context. A number of other key high priorities were identified for both human health and environment and are now being addressed in ECETOC's work programme.

The ECETOC TRA tool has found its way firmly into REACH IT tools, under Chesar, and has recently been updated. It continues to be a flagship activity of ECETOC to support the implementation of REACH.

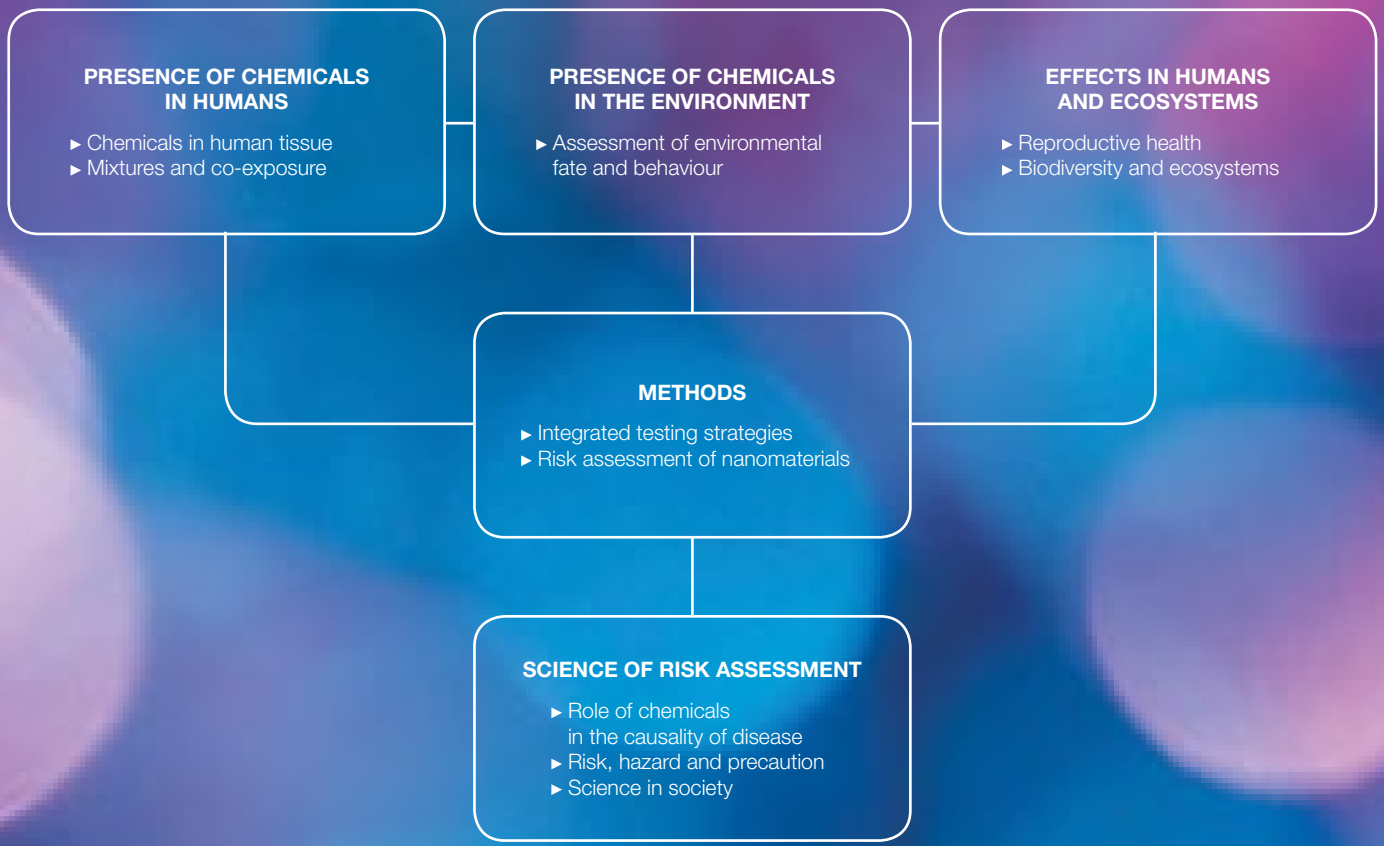


Fraser Lewis,
Syngenta

Chairman of the Scientific Committee

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 the 2010 ATM, ECETOC member companies gave their input on current and future priorities, and this was subsequently evaluated by the Scientific Committee. 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 has been active. More detailed descriptions of the revised science areas with background, objective and desired outcome or impact can be found on the members' website and a printed brochure is available upon request.



Summary of the 2011 Science Programme

Please note that some activities are relevant to and mentioned in more than one science area. LRI projects and external representation within the following science areas are mentioned later in this report.

PRESENCE OF CHEMICALS IN HUMANS

CHEMICALS IN HUMAN TISSUE

Objective: Ensure that the results of biomonitoring studies are placed into appropriate context within risk assessment to human health.

2011 activity

- No current activity except LRI projects and external representation

MIXTURES AND CO-EXPOSURE

Objective: Contribute to the development of a pragmatic, realistic, and science-based framework for the risk assessment of chemical mixtures.

2011 activity

- Progression of a task force on low dose interactions
- Completion of a task force to develop guidance for assessing the impact of mixtures of chemicals in the aquatic environment: its findings published as Technical Report No. 111
- Organisation of a workshop on combined exposure to chemicals; its findings published as Workshop Report No. 22, and also as an article in Regulatory Toxicology and Pharmacology

PRESENCE OF CHEMICALS IN THE ENVIRONMENT

ASSESSMENT OF ENVIRONMENTAL FATE AND BEHAVIOUR

Objective: Develop the understanding of environmental processes that drive the fate and behaviour of chemicals and the role of these processes in risk assessment.

2011 activity

- Progression of a task force on the environmental risk assessment of ionisable compounds
- Progression of a task force on understanding the relationship between extraction technique and bioavailability
- Progression of a task force on development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals

EFFECTS IN HUMANS AND ECOSYSTEMS

REPRODUCTIVE HEALTH

Objective: Ensure that the methods and the testing strategy to identify and characterise developmental and reproductive toxicants are appropriate and optimised.

2011 activity

- Progression of a task force on guidance for classification of reproductive toxicants under GHS
- Organisation of a workshop on risk assessment of endocrine disrupting chemicals; its findings published as Workshop Report No. 21
- Organisation of a symposium on risk assessment of endocrine disrupting chemicals. Publications are in preparation
- Organisation of a workshop on epigenetics and chemical safety. Workshop Report is in preparation

BIODIVERSITY AND ECOSYSTEMS

Objective: Identify the key science issues relevant to risk assessment of chemicals in the environment in a way that is relevant to the potential impact on biodiversity of aquatic and terrestrial ecosystems.

2011 activity

- Progression of a task force on exploring novel ways of using SSD to establish PNECs for industrial chemicals
- Progression of a task force on the application of critical body burden (CBB) in risk assessment
- Completion of a task force to develop guidance for assessing the impact of mixtures of chemicals in the aquatic environment; its findings published as Technical Report No. 111

METHODS

INTEGRATED TESTING STRATEGIES

Objective: Contribute to a more effective approach to hazard and risk assessment. This should also support the further development and application of alternative approaches to hazard assessment and thereby improve the workability of REACH. Good ITS approaches can reduce cost and the use of animals while providing best quality data for the risk assessment process.

2011 activity

- Establishment of a task force on category approaches, read-across, (Q)SAR
- Progression of a task force on the assessment and management of dermal risks from industrial chemicals
- Completion of a task force on refined approaches for risk assessment of PBT/vPvB chemicals; its findings published as Technical Report No. 112
- Submission and acceptance of an article in Toxicology Letters on an overview of values for the threshold of toxicological concern
- Development of targeted risk assessment tool version 3 by task force of the same name
- EUROECOTOX: Consortium Partner in this project and network sponsored under FP7

RISK ASSESSMENT OF NANOMATERIALS

Objective: Develop a series of approaches for addressing health and environmental effects of nanomaterials.

2011 activity

- Establishment of a task force on poorly soluble particles / lung overload

SCIENCE OF RISK ASSESSMENT

ROLE OF CHEMICALS IN THE CAUSALITY OF DISEASE

Objective: Put the presumed associations between chemicals in the environment and disease into their proper scientific perspective. The focus is particularly directed towards rigorous methodology in observational epidemiology.

2011 activity

- No current activity except LRI projects and external representation

RISK, HAZARD AND PRECAUTION

Objective: Take into account all available scientific tools to adequately characterise risk not only based on hazard characteristics but also on exposure data and dose-response considerations.

2011 activity

- Establishment of a task force on potency in carcinogenicity and reproductive toxicity classification
- Establishment of a task force on practical guidance for the risk assessment of genotoxic carcinogens
- Progression of a task force on guidance for classification of reproductive toxicants under GHS
- Progression of a task force on the environmental risk assessment of ionisable compounds
- Progression of a task force to review the available human and clinically relevant data on the use of cyanide antidotes
- Completion of a task force on refined approaches for risk assessment of PBT/vPvB chemicals; its findings published as Technical Report No. 112
- Completion of a task force to critically review all data on linear polydimethylsiloxanes (PDMS) and update JACC Report No. 26: findings published as JACC Report No. 55
- Development of targeted risk assessment tool version 3 by task force of the same name

SCIENCE IN SOCIETY

Objective: Improve public confidence in the science of risk assessment and promote its use in public policy actions. This includes the need to counter the perceptions of bias, vested interest and lack of quality assurance of industry generated data.

2011 activity

- Completion of a task force on the environmental impact assessment for socio-economic analysis of chemicals; findings published as Technical Report No. 113
- Symposium at EUROTOX 2011: Science in Society: Improving the credibility of research in health and environmental science

Highlights of 2011

Exposure to chemical mixtures

A particular focus area for ECETOC in 2011 was the topic of mixtures. Human and environmental chemical risk assessment is predominantly carried out on individual substances, and this is also reflected in most chemical-related legislation. In reality though, humans, fauna and flora are exposed to a variety of substances concurrently. The toxicology of chemical mixtures has usually been addressed through the concepts of concentration or dose addition and independent action, with synergism being acknowledged as only a rare occurrence. Today there is widespread interest in examining the question of whether current risk assessment procedures are adequate for dealing with combined exposure to multiple chemicals. Development of data and methodology for approaching this issue in a scientific fashion is recognised as very important.

Two task forces have been working on much debated aspects of the issue, i.e. 'low-dose interactions' and 'mixtures in the aquatic environment'. Both have been, or are in the process of, finalising and publishing their work. They presented key findings at the ECETOC workshop on 'combined exposure to chemicals' in July, which gave the opportunity to bring this work into context with on-going research and developing scientific frameworks on the issue. At the regulatory level, mixture toxicity has become an issue for endocrine disruptors. There is debate about possible low-dose effects or even enhanced effects upon adventitious co-exposure to more than one substance at doses below the classical NOAEL. This is a continual debate but through its work, ECETOC has made a timely contribution to improving the scientific base.

The participants of the ECETOC workshop summarised their deliberations in the following lines balancing the various views presented. More contextual detail on the arguments made is given in the greenback report (WR 22) available from the ECETOC website.

In the last 10 years, there has been a significant amount of research into the toxicology of mixtures and co-exposure, which has genuinely increased our understanding. Participants at the workshop generally agreed that the WHO/IPCS framework provides a useful tool for risk assessment of combined exposure to multiple chemicals from multiple sources. A suitable problem formulation at the outset of any risk assessment of combined exposures to multiple chemicals was thought to be a fundamental first step.

There was overall recognition that, according to available evidence, in practice the toxicity of mixtures in the environment is often dominated by a few of their components, and that these can be identified by available approaches. In this regard, where relevant data are available, the Maximum Cumulative Ratio approach is a useful tool for both human health and environmental risk assessments.

The current state of knowledge shows that synergy (exceeding additive effects) is rare and appears to be toxicologically significant only at doses at which there is significant toxicity of one or more of the individual components in the combination. The available data indicate that synergy does not normally occur at environmental concentrations of man-made chemicals. For chemicals that have different modes of action, there is currently very little data to support the occurrence of combination effects below their individual predicted no-effect levels. However, in the absence of information on mode of action, dose / concentration addition can be used as the conservative default.

The discussion at the workshop identified a number of areas that require further research, such as better understanding of mode of action, improved methodologies of exposure assessment including assimilation of better databases and data processing methods. The threshold of toxicological concern approach and non-testing methods were suggested as potentially useful tools that also need further development for use in this context.

In recent years, there has been growing public perception and concern about the possibility of 'cocktail effects' of chemicals at very low doses of the single substances (i.e. below levels deemed to be safe for humans and the environment) which are generally not taken into account in regulatory risk assessment. The current evidence offers little support for this; although some of the workshop participants were of the opinion that the current knowledge on combined exposure and effects was too limited to allow such a conclusion. It is important that combined exposures is considered in risk assessment practice – through the use of science-based, targeted and pragmatic tiered approaches. Such approaches should allow identification of any combinations which may require priority attention.

Whilst recognising the importance of addressing the potential risk of combined exposures to chemicals, this should perhaps be seen in light of the various other scientific areas that are important for protecting and improving human health and the environment. However, some workshop participants felt that this view is a general one, which does not only concern the issue of combined exposure and effects of chemicals. Overall though, the use of a tiered approach is strongly recommended to ensure optimum use of resources.

ECETOC Targeted Risk Assessment Tool: TRA version 3 and associated workshop

REACH is the regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals. It entered into force on 1st June 2007. It streamlines and improves the former legislative framework on chemicals of the European Union. One of the key challenges of REACH is that it envisages the registration and evaluation of approximately 30,000 chemicals by producers and importers. Many of these chemicals will be classified and will require Chemical Safety Assessments to support their registration. Faced with such a challenge, both practically and scientifically, suitable tools that are accessible to non-experts are a key need of the REACH process.

To achieve these aims, ECETOC has developed a tiered (step by step) approach for calculating the exposure to and risks from chemicals that might reasonably be expected in defined circumstances of use. The approach addresses exposure to consumers, workers and the environment. The general concept of ECETOC's targeted risk assessment (TRA) is based on the premise that, by making suitably conservative assumptions, broad exposure/risk models can be applied to determine where any further detailed assessment of risks may be required.

Since its launch in 2004, the ECETOC targeted risk assessment tool has proved to be an overwhelming success. Since the release of the TRA version 2 in July 2009, over 11,000 downloads of the tools have been made and many of the major consortia placed the TRA at the heart of their 2010 REACH Registrations.

Following the 2010 registrations, the core group of the ECETOC targeted risk assessment task force has been seeking feedback from users of the tool in order to identify areas where the tools' functionality and accuracy might be further improved. At the same time, ECHA signalled its intent to update its Chesar CSA/ES tool. In this respect, updates to the worker and consumer tools have been developed in close co-operation with ECHA, who intend to incorporate the two human health components of the TRA into the new Chesar version 2. In addition to these two components, a spreadsheet implementation of EUSES is included in the integrated part of the TRA to facilitate environmental assessments. The integrated part of the TRA is also being updated. These new versions have been tested against the TRAv2 and other exposure models.

The new TRA version 3 has been launched together with updated user guides to reflect the changes. In order to explain TRAv3 and update users on the difference between TRAv2 and TRAv3, ECETOC organised a workshop held in Brussels 3rd May 2012. The supplemental Technical Report No. 114 will shortly be published.

Task forces established

Risk, hazard & precaution

Potency in carcinogenicity and reproductive toxicity classification

The classification of chemicals in Europe has reached a tipping point with the real possibility of exclusion and non-listing of chemicals automatically following classification as a Category 1 CMR. Moreover the criteria which are now used to classify a chemical are changing so that many effects which would not have led to classification a few years ago now do so. These changes have followed the introduction of the GHS criteria into the new Classification, Labelling and Packaging Directive which has replaced the Dangerous Substances Directive and the Dangerous Preparations Directive. The drivers for these changes appear to be a desire to simplify the process and codify certain elements of professional judgement which were within the previous systems.

The scientific basis for the changes in the system is not sound. It is based on the premise that certain types of toxic effect, namely carcinogenicity and reproductive toxicity, have dose-response curves which do not have a threshold. If a hazard is identified at high doses the assumption is made that the effect will be seen at a reduced incidence even at dose levels where no biological changes can be discerned in toxicological studies. While there is a theoretical possibility of this happening with some modes of action, such as genotoxicity, research over the last 20 years has shown that this is not the case in the majority of cases.

ECETOC has identified an approach to address this situation through the application of the criteria for classification for Specific Target Organ Toxicity (STOT) to effects which have a theoretical threshold. The argument is that the primary effect is in essence specific target organ toxicity and should be classified as such. Therefore, a task force has been formed with the following remit:

- Building on the work of the task force on classification of carcinogenicity, evaluate the applicability of the specific target organ toxicity (STOT) criteria to the classification of carcinogenicity, reproductive and developmental toxicity. Provide clear guidance on when STOT would be applicable and when it would not by reference to mode of action, dose response relationships and likely exposure of humans.
- Use the concepts obtained and agreed upon by the participants of the endocrine disruption workshop (May 2011) to bring elements of potency into classification guidance.

The plan is to share the guidance with academic and regulatory scientists for their feedback, and then submitted it for publication in a peer-reviewed journal.

Risk, hazard & precaution

Practical guidance for the risk assessment of genotoxic carcinogens

A successful symposium and workshop held in Cavtat (Croatia) in September 2008 reviewed the then current basis for establishing thresholds for some genotoxic carcinogens. The ECETOC-EEMS symposium (co-sponsored by CEFIC-LRI) was entitled "Thresholds for genotoxins and their application to risk assessment". It was followed by a two-day ECETOC-HESI workshop on the "Biological significance of DNA adducts: Summary of follow-up from an expert panel". The latter workshop was supported by the Joint industry group (JIG), an industry organisation which had sponsored a significant program of research in this area. The papers from both events have been published as a special issue of Mutation Research (vol. 678, issue 2, August 2009).

Both the symposium and workshop demonstrated that DNA adducts cannot be considered as genotoxic endpoints, only as markers of exposure to a substance capable of interacting with DNA. In particular, one of the recommendations agreed at the workshop was that "It would be useful to develop guidance on the evidence needed to demonstrate a threshold for mutations from *in vivo* and *in vitro* experiments". Consequently, the Scientific Committee agreed to establish a task force and provide pragmatic guidance, including a scheme, for the risk assessment of genotoxic compounds with and without evidence of a threshold.

Integrated testing strategies

Category approaches, read-across, (Q)SAR

An accepted practice for the assessment of human health and environmental safety of chemicals is the use of models and analogues to fill data gaps for specific endpoints either for single or multiple chemicals that share structural similarities, and/or comparable reactivity or similarities in metabolism in mammals, fish and other organisms. For example, this approach is acceptable, with limitations, in preparing dossiers for REACH, and it supports efforts for reducing animal testing.

With the plethora of models and guidance growing for both human health and the environment, it would be prudent to identify recommended practices. Additionally, the 2013 and 2018 REACH deadlines are pending; these deadlines require lower volume producers and importers to submit chemical safety assessments. A report describing recommended practices in this area would be useful in supporting industry's risk characterisation and prioritisation activities across all sectors.

A task force has been formed to prepare a brief ECETOC 'special report' available by summer 2012. Its remit is to:

- Collate published literature and regulatory guidance describing/cataloguing the development of chemical categories and use of read-across and (Q)SAR in human health and environmental risk assessment.
- Develop recommended practices for identifying chemical categories and analogues to meet scientific rigour, including hazard identification and risk characterisation, and classification and labelling. Develop a proposal how to use SAR in higher tier testing strategies.
- Determine endpoint-specific methods (e.g. (Q) SAR, rule-based models) and their limitations in terms of their predictive value (e.g. with respect to applicability domain). If possible clarify minimum requirements to apply a category approach.

Risk assessment of nanomaterials
Poorly soluble particles/lung overload

The majority of the data on respiratory effects of inhaled poorly soluble particles (PSP) stems from rat inhalation studies. This relates to the rat-specific effect pattern of 'lung overload' for the inhalation toxicity of PSP. The relevance of the rat as a model for the assessment of repeated exposures to PSP for humans has been questioned by a number of analyses since the rat was shown to be particular sensitive towards these effects compared to other rodents, non-human primates and humans. The last comprehensive review was developed in the year 2000 (ILSI 2000). Although above mentioned phenomena are known for a long time, it has recently become a more prominent issue for the derivation of DNEL under REACH registrations, setting of exposure limits and for classification and labelling at the United Nations SCEGHS in 2009 and further input has been requested from industry. With this in mind, the Scientific Committee established a task force to prepare a review and organise a workshop on the relevance of lung overload effects seen in rats for human health in terms of classification and DNEL derivation. In particular, the task force has been asked to focus their discussions on:

- Mechanistic interpretation of lung overload effects in humans and animals
- Parameters that characterise lung overload
- Compare effect levels from animal studies to realistic worker exposure, on a quantitative basis
- Relevance of existing/new epidemiology studies in humans
- Lung overload effects from nanomaterial inhalation studies.

Task forces completed

Mixtures and co-exposure

Biodiversity and ecosystems

Guidance for assessing the impact of mixtures of chemicals in the aquatic environment

The potential risk from combinations of chemicals in the environment has recently moved up the scientific, regulatory and political agenda as a result of the increasing concern about the potential impact on the environment from a 'cocktail effect' and the perception that current risk assessment procedures are inadequate.

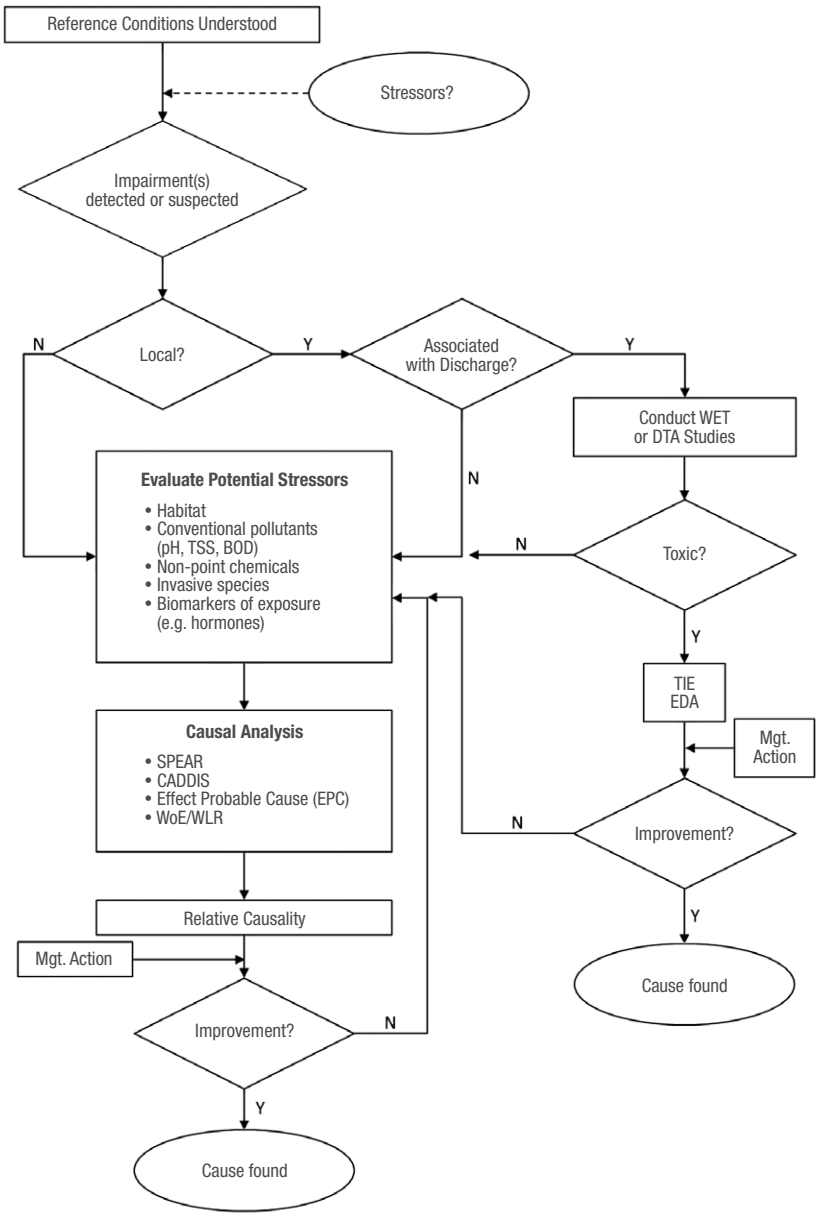
In this report, field based approaches for assessing impacts on the aquatic environment and develop guidance on suitable methods are reviewed; case studies are used to identify research needs, including how methods can be implemented and what diagnostic tools are required; and the value of retrospective assessment in assessing environmental capacity for future industrial development is considered. Finally, a framework is presented which will retrospectively allow the evaluation of the potential impact of chemicals or chemical mixtures in the environment (see figure 1).

The toxicity of chemical mixtures is relatively well understood through the concepts of concentration addition and independent action, with synergism being acknowledged as only a rare occurrence. It is generally accepted that concentration addition should be used as a default first tier in environmental risk assessment of mixtures. Prospective risk assessments are generally done at the level of single substances, some of which are in fact mixtures themselves, or known mixtures of substances in chemical products. The assessment factors employed in the different conservative risk assessment processes under which these are regulated may cover the potential for any combined effects from exposure to multiple substances.

Retrospective causal analysis and in particular eco-epidemiological studies allow the contribution of chemical mixtures to be determined. These studies can show that mixture impacts may be spatially quantified in aquatic ecosystems, and there is a need to understand site-specific stressor combinations in order to define effective measures to improve ecological status. The limited datasets available show that whilst chemicals may be responsible for some environmental impacts, they are by no means the only or even the most important factor.

Two recommendations are made here. The first is to improve biological traits associated with non-perturbed sites. There is still a relative paucity of data regarding the life histories of most taxa (plant, invertebrate and vertebrate) associated with exceptional water

Suggested approach to assessment of ecologic risk of mixtures of chemicals in the aquatic environment



quality. For example, the relative frequency of intersex of most fish species in the relative absence of chemical exposure is not known at present. Further, the relationships of intersex and population structure for most species are not known. In essence, basic ecological research is needed to understand reference-condition structure and function. Such research will provide the basis for refined predictions (both pro- and retrospective) for biological expectations per site and hence, a more accurate measure of biological impairment.

The second recommendation is to improve diagnostics that distinguish chemical factors from physical / chemical factors responsible for biological impairments. While many statistical and the best professional judgment approaches have been utilised to distinguish chemical effects versus other stressors with regard to diagnosing biological impairments – there still exists relatively few examples and well utilised approaches that could eventually become standard guidelines for stressor diagnostics. Issues regarding site, river reaches, catchments and regional scale assessments can require highly different methodologies, and therefore highly different diagnostics. Sufficient experience exists to begin the road toward guideline development. With appropriate diagnostic guidelines, appropriate interpretations of the importance of chemical mixtures compared to other factors can be made, therefore leading to better water quality management decisions.

Framework for environmental assessment

- Reference condition and ecological status evaluation
- Need to establish cause before management
- WET/DTA
- TIE/EDA
- Causal Analysis – US EPA
- Eco-epidemiology

The findings of the task force have been published as Technical Report No. 111 available from the ECETOC website: direct link http://bit.ly/ecetoc-tr111.

Integrated Testing Strategies

Risk, hazard & precaution

Risk assessment approaches for PBT/vPvB chemicals

Many national, or regional, regulations and regional or global conventions exist that identify and prioritise substances of concern based on their hazardous properties. The criteria for identifying such substances under these various instruments are not the same but have many similarities through cut-off values associated with a chemical's persistence (P), bioaccumulation (B) and toxicity (T). Criteria for PBT first came on the agenda within the EU in the revision of the Technical Guidance Document (TGD) on risk assessment (EC, 2003). This document assigned criteria to identify substances of concern as PBT or very persistent and very bioaccumulative (vPvB) based on their half-lives in selected environmental media, their bioaccumulation in biota and their long-term ecotoxicity. This hazard based approach to chemical management was argued on the basis that 'safe' environmental concentrations for such substances cannot be established with sufficient reliability due to the unacceptably high level of uncertainty associated with quantitative risk assessment, the concerns that accumulation of such substances would be practically difficult to reverse, and the need to protect pristine (marine) environments. These concerns were then reflected in the EU REACH legislation which effectively removed risk assessment as the regulatory decision making tool for substances classified as PBT or vPvB.

Building upon a previous ECETOC report to develop a framework for the risk assessment of PBT chemicals (ECETOC, 2005a), this report reviews the scientific developments that have been made and details the on-going research that is being carried with the specific aim of reducing the uncertainty of risk assessments of PBT/vPvB chemicals.

Several case studies have been analysed and the literature on newly developed methodologies has been reviewed and the task force has concluded that the use of refined methodologies, which include the use of appropriate and/or improved test procedures, is strongly dependent on the nature of the respective chemical and its exposure characteristics. Therefore the choice of methodologies needs to be made on a case by case basis.

The findings of the task force have been published as Technical Report No. 112 available from the ECETOC website: direct link http://bit.ly/ecetoc-tr112.

Science in society

Environmental impact assessment for socio-economic analysis of chemicals: principles and practice

Under REACH, there are provisions to use Socio-Economic Analysis (SEA) to grant an authorisation to substances of very high concern (Article 60); and in decisions about restrictions (Article 68). Similar provisions are used as derogations in the EU water and environmental liability legislation. This requires that the benefits from environmental protection should be greater than the costs for the action to be worthwhile. For industry, SEA may be the only route for countering proposals for no authorisation and for moderating proposals for restrictions. Therefore, it depends crucially on having the risks expressed in ways that can be valued, i.e. in terms of units of life or ecology saved by the banning or the restrictions.

The topic was already discussed at an ECETOC workshop in June 2008 (WS Report 13), and this evolved then into forming a task force with a broad representation of risk assessors and (environmental) economists, and with ECHA as observer and adviser. The task force was charged with reviewing relevant existing principles and practices on Environmental Impact Assessment and establishing a user-friendly framework for use in a SEA focusing on REACH.

The focus of the report is on the ecological impacts of chemicals rather than on their human health impacts. It is the former where many of the most profound challenges are, and the ECHA guidance for socio-economic analysis associated with both restrictions and authorisation in the REACH process identifies the need for more work in this area. The report argues for as much quantification as possible, with the ideal of monetisation so that a cost-benefit analysis can be carried out. However, there are enormous challenges in ascribing monetary values, especially to non-marketed ecological goods or services. This report draws attention to a number of possible scenarios whereby the outputs of risk characterisations might be linked to quantified ecological impacts through such methods as species-sensitivity analysis, smart modelling, making connections to ecological quality status and using an ecosystem services approach. To date, however, none of these methods is developed to the extent that they could be easily applied. Thus, there will be a need for pioneering efforts in these areas.

The report has been published as Technical Report No. 113 available from the ECETOC website: direct link http://bit.ly/ecetoc-tr113.

Risk, hazard & precaution

Linear polydimethylsiloxanes (PDMS) and update of JACC Report No. 26

Findings published as JACC Report No. 55

The above TF could successfully conclude its deliberations in 2011 when the Scientific Committee adopted the final report for publication (as JACC No. 55). The report has been produced as part of the ECETOC Joint Assessment of Commodity Chemicals (JACC) programme and updates an earlier ECETOC review. The new report presents a critical evaluation of the toxicity, physico-chemical properties, and environmental fate and effects of linear polydimethylsiloxanes (PDMSs), a type of non-volatile (odourless), fluid (viscous) "silicones" that are virtually insoluble in water. PDMSs are widely used in industrial, consumer, food and medicinal or pharmaceutical applications.

Almost all PDMS discarded 'down-the-drain' is expected to be removed during sewage treatment. Any PDMS released into the environment will strongly sorb to particulate matter in water and soil. PDMSs are immobile in soil and sediment, but will break down slowly (abiotic) to dimethylsilanediol, which is soluble in water and can biodegrade to carbon dioxide, water and inorganic silicate, as demonstrated in the laboratory. Due to its molecular size, bioconcentration of PDMS is very unlikely. PDMSs are not detected in surface waters, except at low concentrations downstream from wastewater treatment plants.

PDMS has no effects when tested on aquatic organisms (fish, daphnia, algae), sediment-dwelling organisms (e.g. midge larva) and little or no effect on soil organisms (e.g. earthworm). PDMS is lethal to insects when applied directly, probably due to a physical rather than toxicological action.

Humans may be exposed to PDMS via oral ingestion and dermal contact. In laboratory animals, PDMS had a low potential for absorption via these routes. Swallowed PDMS is rapidly excreted unchanged in the faeces. Aerosolised PDMS may give rise to inhalation exposure, but there is no indication of any adverse effects. PDMS is not a skin irritant or a skin sensitizer and it is only mildly to non-irritating to the eyes.

Acute and repeated dose toxicity studies conducted in laboratory animals on PDMS of different viscosities do not show any significant adverse effects. Long-term chronic/carcinogenicity and reproductive toxicity studies were also without adverse effects. PDMS is not mutagenic *in vitro*.

In humans, PDMS has no effect on the immune system. PDMS is used in urology, ophthalmology and dermatology (skin correction). Autoimmune disorders (e.g. scleroderma) cannot be linked to PDMS. Several human diseases (connective tissue, atypical connective tissue, rheumatic and autoimmune diseases, and breast cancer) have been reported after injection of PDMS (for cosmetic purposes) or placement of breast implants (made of high viscosity PDMS). These diseases are, however, not associated with PDMS.

Overall, PDMS does not present a risk to the environment or to human health.

The report has been published as JACC Report No. 55, available from the ECETOC website: direct link http://bit.ly/ecetoc-jacc55.

Workshops

Reproductive health

Risk assessment of endocrine disrupting chemicals

9-10 May, 2011, Firenze, Italy

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.

Risk assessment of endocrine disrupting chemicals workshop group photo

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 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.

The findings of the workshop have been published as ECETOC Workshop Report No. 21, available from the ECETOC website: direct link http://bit.ly/ecetoc-wr21. In 2012, an article has been submitted and accepted for publication in *Regulatory Toxicology and Pharmacology*. A corrigendum to the previous article on the same subject has also been published.

Mixtures and co-exposure

Combined exposure to chemicals

11-12 July 2011, Berlin, Germany

Combined exposure to chemicals workshop group photo

ECETOC held this two-day workshop to review a number of key scientific areas which are relevant in the assessment of the health and environmental impact of combined exposures to chemicals. It focussed on the state of the science and on technical aspects of co-exposure, and discussed reliable and pragmatic approaches to risk assessment of combined exposures to chemicals. Sixty-six participants attended, representing academia, industry and regulatory bodies. Following presentations on the state of the science, breakout group sessions took place to address specific questions and to discuss where the science may need further developing.

The article under 'Highlights' in this Annual Report gives more background on the topic. The findings of the workshop have been published as ECETOC Workshop Report No. 22, available from the ECETOC website: direct link http://bit.ly/ecetoc-wr22.

Reproductive health

Epigenetics and chemical safety

5-6 December 2011, Rome, Italy

Epigenetics is a rapidly developing and expanding biological science. In order to increase our understanding of how the science of epigenetics is involved in (eco)toxicology, a solid understanding of the biology and variation of the epigenome is essential to better assess concerns about possible adverse health effects related to epigenetic changes. In particular, very little is known about which epigenetic alterations are part of normal variability and what could be considered adverse and, hence, pose a health risk. To obtain a better insight on the current state of the art of epigenetics and to discuss its potential applications in (eco) toxicology, ECETOC organised a workshop with expert participants in the field of epigenetics as well as (eco)toxicological risk assessment.

Epigenetic regulation of gene activity appears to be a general mechanism to maintain cell function, homeostasis, proliferation and differentiation. This indicates that epigenetic mechanisms are likely to be a key component in biology. Although epigenetics is still a very young science, some mechanisms appear to be well established. DNA methylation and histone modification have been identified as important factors in epigenetic regulation.

Epigenetics and chemical safety workshop group photo

Another fascinating aspect is that, in plant organisms, it has been shown that DNA methylation epialleles can be transmitted over multiple generations and maintained in the population. The situation is believed to be different in mammals where embryonic development is characterised by two waves of global DNA methylation erasure (in pre-implantation embryos and primordial germ cells) that theoretically prevent the transmission of DNA methylation patterns through generations.

Finally, microRNAs (miRNAs), a large family of non-coding RNAs that are evolutionarily conserved, endogenous, and 21-23 nucleotides in length need to be taken into account. miRNAs regulate gene expression by targeting messenger RNAs (mRNAs) by binding to complementary regions of transcripts to repress their translation or mRNA degradation. miRNAs are encoded by the genome, and more than 1000 human miRNAs have been identified so far. How miRNAs function in regulating animal cell responses to environmental chemical stimuli is an unexplored field of compound risk evaluation.

The outcome of the workshop indicates that there are major gaps in knowledge on the extent of background variability in epigenetic processes and their normal dynamic range. Moreover the magnitude of change necessary for a cellular effect (be it adverse or adaptive), windows of susceptibility, the extent of autoregulation and redundancy in the system is not known.

We do have evidence however that toxicants are capable of affecting the epigenome. Several examples were discussed in this workshop and can be found in this report What we do not know is which of the changes are directly associated with chemical exposure and adverse effects and which changes are the result of the cell's attempt to maintain homeostais, i.e. in effect beneficial.

In addition to presenting the state of the art, we have tried to focus in the workshop on a number of basic issues which need to be addressed when new scientific information becomes available that has potential value for enhancing the quality of the risk assessment process. In a nutshell, here are some of the conclusions from our debate. Epigenetic changes are a mode of action, rather than a mechanism of action. It is uncertain which endpoints of (eco)toxicology will be particularly affected by epigenetic changes. Micro-RNAs appear to be a part of the regulatory mechanisms affecting gene expression, it is a matter of debate if these should be included under the term "epigenetic". Epigenetic changes are not adverse *per se*. One of the major challenges will be to examine the nature of an epigenetic change.

What can we expect of epigenetics? Certainly another layer of complexity and most likely another mechanism by which the cell is able to integrate information in cascades of feedback mechanisms in an attempt to provide the best response to changes in its environment. We are witnessing a revolution in biology. The discovery of epigenetic regulations of cell functions is changing our understanding of cell biology in a profound way. We are starting to understand how complex epigenetic regulations are, implying a range of mechanisms which appears to be expanding in short time. The significance of epigenetic changes for classical (eco)toxicological endpoints is not yet clear and some of the methodologies for measuring such changes are also still developing. At this time it is probably too early to use epigenetic information within standard risk assessment paradigms. We can expect that epigenetic information will contribute to understanding of the basic processes of cellular responses to environmental stressors (be it chemical or physical in nature). This understanding should lead to a better assessment of the consequences of exposure to such stressors.

The outcome of the workshop will be published as Workshop Report No. 23.

Symposia and other meetings

Environment progress review meeting

27-28 January 2011, Brussels, Belgium

The aim of the scoping meeting was to inform ECETOC member company scientists of progress in current and recently completed LRI projects and to identify ideas for consideration as new LRI projects or for ECETOC activities. The first day reviewed existing / recent LRI projects. The second day, attended by company experts only, focused on identifying new ideas for ECETOC or LRI activities.

Science in society

Review meeting on REACH-Driven Science Needs

1 March 2011, Brussels, Belgium

When compiling chemical safety dossiers for the first registration phase of REACH, it has become apparent that there are aspects in the Technical Guidance Documents, and hence in the dossiers, which will likely lead to queries by ECHA. Reasons for this are areas where the guidance is deficient or contradictory, or where the underpinning science remains weak. To support an effective implementation of the legislation, the Scientific Committee had already started to look for areas where scientific opinions need to be further developed and which should be proposed for the on-going ECETOC science programme, short-term and longer-term. For a focused input from the wider ECETOC membership, a one-day meeting was held.

The comprehensive output of the meeting was subsequently analysed and presented to the Scientific Committee for further prioritisation and with a view on how they fit into the ECETOC science strategy. In the meantime, new activities deriving from the review have started, some other are in planning. Specific information is available via the ECETOC members' website.

CEllSens-Eco8: Lessons Learnt

15 May 2011, at SETAC Europe, Milan, Italy

The goal of the CEllSens-Eco8 project was to develop a strategy to predict acute fish lethality using fish cell lines and fish embryos. Specifically, this CEFIC-LRI/UK-DEFRA supported project addressed the replacement of the fish acute toxicity test (OECD 203) by improving assay conditions and exploring various toxicological endpoints in fish cells and zebrafish embryos. Furthermore, sub-lethal endpoints were explored as pilot explorations toward alternatives for fish chronic toxicity testing.

The CellSens team, with the support of ECETOC and Cefic-LRI, invited all interested parties from academia, industry and regulation to explore the project results and discuss their implications in the context of a strategy to refine, reduce or replace fish tests.

The workshop took place in the morning prior to the SETAC Europe Meeting on 15 May 2011 in the Milano Convention Centre. The CellSens team laid out the project design based on the original working hypotheses and presented the outcome of the research with particular focus on:

- the construction and utility of the CEllSens chemical list;
- pitfalls in testing chemicals of varying physico-chemical properties and strategies to overcome these pitfalls;
- results of the screening of the CEllSens top 30 chemicals with improved testing design and in light of available fish acute toxicity data;
- the established Quality Management Handbook and Standard Operating Procedures.

Reproductive health

EEMS 2011 Symposium: Risk assessment of endocrine disrupting chemicals

6 July 2011, Barcelona, Spain

Jointly organised by ECETOC and the European Environmental Mutagen Society (EEMS), the symposium was held on the third day of the annual meeting of EEMS in Barcelona with ECETOC being the sole sponsor. The symposium was well received by the more than 80 (out of 240) participants, leaving room for questions after each of the 6 presentations and a lively general discussion at the end.

Ir Vrijhof (ECETOC), co-chair with Dr David Kirkland (EEMS), opened the symposium with a brief introduction of ECETOC and its common history of symposia with EEMS for more than 10 years. The special issues from these symposia form critical state-of-the-science reviews that have been published in the open literature.

Dr Kirkland explained that the connection between genotoxicity / mutagenicity and endocrine disruption (ED) caused by chemicals may not be obvious at first glance. There are, however, two firm links: (i) both represent general modes of action related to carcinogenesis and the induction of reproductive effects, and (ii) in current risk assessment approaches (at least in the EU) hazard identification is immediately followed by regulatory action, without taking exposure into account (basically non-threshold risk assessment approaches). As there is currently no scientific evidence for the absence of a threshold for endocrine mediated effects, ECETOC organised two workshops to review the definition and discuss the risk assessment of ED chemicals. Highlights of these workshops (Barcelona, June 2009; Firenze, May 2011) were presented at the EEMS symposium.

Dr. van Ravenzwaay (BASF) started the symposium with a historical perspective on ED based on the effects noted in the late 1980's with Vinclozoline. This was followed by an introduction into novel technologies to efficiently identify EDs. Prof. Dekant (University of Würzburg) then continued with an overview of the toxicodynamics and the importance of kinetics for EDs and he proposed to apply normal risk assessment procedures to ED chemicals. Dr. Lewis (Syngenta) provided an overview of the results of the first ECETOC workshop which addressed the question how to identify an ED using the Weybridge definition of ED. What is basically required is that adverse effects noted in an apical animal study are clearly linked with an endocrine mode of action.

Dr. Dewhurst (UK Pesticide Safety Directorate) then proceeded to present the joint CRD-BfR (UK-German health authorities) view on how to perform a risk assessment of EDs within the current EU legislation. The key element in discriminating between EDs of concern and those of high concern (those requiring risk reduction measures) is the potency of the effect. The UK and Germany propose to use the well-known and accepted specific target organ toxicity (STOT) criteria for systemic toxicity to define potency.

Prof. Benahmed (Centre Hospitalier Universitaire de Nice) presented important and new scientific aspects of the effects of EDs on reproduction. These included specific windows of sensitivity as well as findings from transcriptomics

studies. Finally Dr. Fegert (BASF) presented the ECETOC concept of risk assessment of EDs, lastly reviewed at the Firenze workshop. The ECETOC concept includes the same elements as proposed by CRD & BfR, but, in addition also takes into account the specificity of the effect (i.e. the dose levels at which ED effects are noted relative to general toxicity).

In his closing remarks, Dr. van Ravenzwaay reminded EEMS participants that the general agreement at both workshops was that a proper risk assessment of chemicals causing adverse effects mediated through an endocrine mode of action is the best way to assess their safety. The concepts proposed are attempts to introduce elements of risk assessment into a law which has neglected this key element in toxicology.

This was followed by a general debate among the audience. The agreement at the end was that there is no scientific reason why ED should be treated differently from any other mode of action that has a threshold. Thus, there is no reason not to apply a risk assessment approach, i.e. the initial proposal made by Kirkland and Dekant was not challenged.

Science in society

Symposium at EUROTOX 2011: Science in Society: improving the credibility of research in health and environmental science

29 August 2011

When ECETOC revised its Science Strategy last year, it retained the area 'Science in Society', however, it was not one of the areas which received the strongest support. The most probable reason for this is that the concept is less self-evident than some of the other science areas. However, 'Science in Society' is critical to the effectiveness of ECETOC. Simply put, it is about the societal relevance of what we do and our ability to put our arguments across. Factors which influence our ability to do this include the credibility of industry science and our ability to communicate in ways which make our science meaningful. The main activities in this area, so far, have been in the areas of 'Socio-economic analysis' and in 'bias and credibility'. The first of these deals with cost and benefit in environmental risk. The second requires addressing sources of bias and identifying the means to detect and neutralise such bias.

ECETOC's main activities in this area go back to June 2008 when we held a workshop at the Annual Technical Meeting entitled: 'Counting the costs and benefits of chemical controls: role of environmental risk assessment in socio-economic analysis'. This workshop led to a taskforce which has recently reported (TR113). Also in 2008 (October) at the EUROTOX meeting in Rhodes, we hosted a session entitled: 'The role of science in society and industry sponsorship of environmental and health research' with eminent speakers from Academia and industry. This session elicited such interest that EUROTOX invited us to consider a follow up session.

Accordingly, ECETOC organised a workshop in August at EUROTOX 2011 in Paris entitled: 'Science in Society: improving the credibility of research in health and environmental science'. Despite being one of four parallel sessions, there was 'standing room only' in our meeting room.

The four speakers selected different aspects of this subject leading to a very lively discussion. Dr Gerard Swaen (Dow and ECETOC Scientific Committee) presented the ECETOC initiative to have observational epidemiology studies registered to reduce publication and reporting bias and increase transparency regarding study design. Professor Peter Calow (University of Nebraska and latterly of the ECETOC Scientific Committee) emphasised that all scientists are subject to bias and this should be systematically taken into account. The most important tools for this were transparency of study design and rigorous peer review.

Dr José Tarazona (European Chemicals Agency, Risk Assessment Committee), described mechanisms put in place in the new regulatory frameworks of REACH and CLP. He described the ways of working in these committees to avoid conflict of interest and emphasised the assurance of transparency which came from publication of committee decisions. Finally Professor Helen Håkansson (Karolinska Institute, Sweden) presented a concept of unified standards for the training of risk assessors with a view to raising scientific standards in this area.

Judging by the interest shown by the attendees, this area is considered to be important by many professionals in the field of risk assessment. Hopefully with initiatives like these, the discussion can move from finger pointing to a more constructive debate on mechanisms to reduce the impact of bias on decisions. For ECETOC, Science in Society will remain a key area, even if sometimes difficult to grasp. The emphasis will need to be on clarity, consistency and objectivity. We should not just require it of ourselves, but of our fellow scientists also.

EUROECOTOX group photo at the October 2011 workshop

EUROECOTOX

EUROECOTOX (the European network for alternative ecotoxicology testing strategies in Ecotoxicology) is a two year project which was officially launched in 2011. It is a coordination action funded by the FP7 Environmental programme and has, as its main objectives, the integration of European activities on the replacement, refinement and reduction of animal experiments in ecotoxicology and to promote the validation of new alternative testing methods.

The network is managed by consortium of eight European organisations with scientific backgrounds in environmental toxicology. ECETOC is a partner in this project. Their role is to provide technical advice, scientific input and independent comments and assessments on the various aspects of the project. To meet their goal, EUROECOTOX has conducted a review of activities addressing alternative toxicity methods which are either under development or close to validation. The review focused on:

- *Mapping of European research capacity by preparing an index of European R&D groups working in alternatives for ecotoxicity tests and methods.*
- *Identifying alternative ecotoxicological test methods under R&D and validation. Analysing the scientific, ethical, regulatory, and industrial relevance and development status.*
- *Classifying main European Stakeholders promoting alternative ecotoxicity and the use of the 3Rs. These include organisations, platforms and groups, representatives from industry, environmental agencies, validating agencies and regulatory bodies.*
- *Identifying relevant international R&D and institutional activities in alternative ecotoxicological test methods and strategies development.*
- *Documenting current EU legislation requiring ecotoxicity testing with vertebrates.*

The network is also involved in the:

- *Identification of the rate-limiting steps to reduce or replace the use of vertebrate animals in eco-toxicological testing in Europe*
- *Identification and promotion of new alternative test methods under R&D*

A dedicated Website (http://www.euroecotox.eu) has been set up as part of the networking promoting activities and to aid in the dissemination of the Coordinating Action results.

The network held a closed workshop in October 2011, when 45 international experts with backgrounds in research, industry and regulation met at the Helmholtz Centre for Environmental Research, Leipzig, Germany to discuss European perspectives on alternatives to animal experiments in environmental risk assessment. The discussions were focused on the aspects of limitations of alternative methods and regulatory acceptance, future research needs and overall recommendations and addressed: acute and chronic toxicity in fish and birds; endocrine disruption in fish and amphibians; bioaccumulation in fish; non-testing approaches; alternative testing approaches and sublethal/alternative endpoints.

The network is planning to hold the "First European Conference on the future of alternative testing for eco-toxicity safety assessment" on 28-29th June 2012. Further information and a link to register can be found at https://sites.google.com/a/euroecotox.eu/networkeuroecotox/euroecotox-conference

Science Awards

With the objective of recognising young scientists, ECETOC has been active in the provision of an annual Science Award to outstanding works of science since 2003.

The 1st Science Award was accorded on the occasion of its ECETOC's 25th Anniversary to recognise the achievements of three promising European investigators in the fields of science relevant to its mission of supporting the safe manufacturing and use of chemicals, pharmaceuticals and biomaterials through good science. Since then the format of the Award may have varied, however the objectives have remained the same.

In 2011 ECETOC sponsored the following awards for young scientists and is proud to announce this year's winners:

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 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.

Human health science related award

This year's Young Scientist Award on human health sciences research, presented at the EUROTOX annual meeting, has been awarded to Amy Zmarowski of NOTOX, Netherlands, for her poster presentation: "Differential effects of methylazoxymethanol and MK-801 administration on learning and memory impairment in Sprague Dawley and Wistar Han rats".

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 price and a free invitation to the following year's EUROTOX meeting.

Long-range Research Initiative

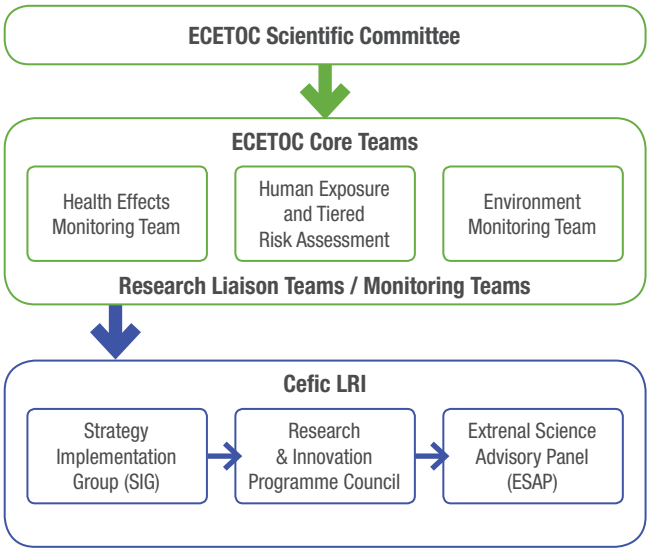
The idea for LRI began in the USA in 1996, with the goal of responding to public and stakeholder concerns through scientific investigation. The focus is on gaps in industry's knowledge and understanding that are critical for risk assessment. The broad aim is a validated infrastructure of scientific advice on which the entire industry and regulatory bodies will draw to respond more quickly and accurately to the public's questions. Today's LRI is jointly managed by the American Chemical Council, Japanese Chemical Industry Association, and European Chemical Council (CEFIC).

The LRI sponsors research to help address some of the priorities of the European public health strategy: improving risk assessment of chemicals; and more specifically monitoring effects of chemicals on health; understanding the environmental factors in human health; establishing endocrine disruption references; and coordinating research, data and activities at a European level. LRI also addresses many of the environmental objectives of the European Union, including: linking environmental factors to health effects; understanding and reducing chemical risks to environment; and improving animal testing in risk assessment.

ECETOC has been a key partner to CEFIC from the earliest stage of the LRI process. It provides scientific support into the LRI, and input into the Research Programme.

Within the LRI, ECETOC has the responsibility of maintaining three 'core teams' consisting of industry scientists, who manage the scientific evaluation of applications for funding, recommend the best research proposals and monitor of the progress of selected LRI projects. In particular they are responsible for the:

- Development of topics for research to be considered by the LRI Strategy Implementation Group (SIG). (A core team may organise a workshop with academic, government and industry scientists for this purpose.)
- Drafting of 'requests for proposals' (RfPs) based on ideas submitted by CEFIC and ECETOC stakeholders in the LRI process.
- Setting up selection teams of industry and external experts to choose the best research proposals in response to published RfPs and making recommendations to LRI SIG concerning the funding of the proposals.
- Establishment of scientific liaison with the selected institutions and 'monitoring' the scientific quality and progress of the projects.



Health Effects Monitoring Team

Two new projects were initiated in 2011 with the support of specially recruited selection teams (below marked with *). Three projects were successfully finalised:

- *Assessment of risk factors influencing trends in incidence of female breast carcinoma*
- *Overcoming current limitations in metabolism prediction of industrial chemicals*
- *Characterisation of testicular toxicity using traditional and omic tools*

The current research portfolio under the health effects programme, monitored by the ECETOC team, looks as follows (arranged by strategic theme of the LRI programme):

Theme 'Intelligent testing strategies':

- A toxicogenomic approach to enhance the specificity and predictive value of the murine local lymph node assay

Theme 'Acceptance of new technologies and products':

- Tiered approach to testing and assessment of nanomaterial safety to human health
- Towards standardized testing guidelines (reproductive toxicity) relevant to nanomaterials
- Mechanism-based characterisation of systemic toxicity for RepDose database substances employing *in vitro* toxicogenomics
- Data-integration for endpoints, cheminformatics and omics(*)

Theme 'Health impact of complex environments':

- Reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors
- Combined low-dose exposures to anti-androgenic substances
- Animal and human NOAELs: cross-species comparison, inference and synthesis(*)

Human Exposure and Tiered Risk Assessment (HETRA) Monitoring Team

A HETRA team assisted by outside scientists selected two proposals for new research. While LRI funding was decided, the actual projects could be started in the reporting year. One project is aimed at developing assessment strategies for dermal exposure from consumer products and articles. The other project will investigate the representativeness of single human biomonitoring (HBM) samples. By the year end, HETRA saw the completion of two computational (modelling) tools for the derivation of biomonitoring guidance values. In all, the HETRA team monitored 9 projects in 2011 as follows.

Theme 'Better characterisation of actual exposures':

- Integrated exposure for RA in indoor environments

Theme 'Tiered approaches to risk assessment':

- Improvement of the TTC concept for inhalation exposure and derivation of thresholds with the database Repdose

Theme 'Nature of determinants of human exposure':

- Realistic estimation of exposure to substances from multiple sources
- Determining the nature of chemical substance additively from household consumer products
- Dermal exposure assessment strategies – Characterising the nature of dermal exposure from consumer products and articles

Theme 'Role of biomarkers':

- Understanding inter- and intra-individual variability in HBM spot samples – Representativeness of single HBM) samples
- Development of a computer program with a multi-level modelling tool related to health based exposure rates for inhalation, oral intake and/or skin exposure
- Development of a tiered set of modelling tools for derivation of biomonitoring guidance values
- Structured data acquisition via *in vitro* metabolism screens to enhance computational tools

Environment Monitoring Team

One new project secured funding and was initiated in 2011 with the support of the Liaison Research teams. This was: 'Identifying limitations of the OCED water-sediment test (OECD 308) and developing suitable alternatives to assess persistence'.

The current research projects under the Environment Monitoring Teams look as follows:

Theme 'Intelligent testing strategies':

- Identifying limitations of the OCED water-sediment test (OECD 308) and developing suitable alternatives to assess persistence
- Evaluation of test methods for measuring toxicity to sediment organisms
- Applying and verifying PBT/POP models through comprehensive screening of chemicals
- Environmental relevance of laboratory bioconcentration test
- Influence of microbial biomass and diversity on biotransformation
- Fish cell line & embryo assays

Theme 'Acceptance of new technologies and products':

- Assessment of nanoparticles specific effects in environmental toxicity testing
- Development and validation of abbreviated *in vivo* fish concentration test (2 projects)
- Rapid estimation of TMF using laboratory, field and computer modelling methods in aquatic organisms
- Generate a validated CBB database and validate a CBB chronic toxicity range for narcotics

Theme 'Health impact of complex environments':

- Critical evaluation of individual and combined natural and synthetic endocrine active compounds in fish: an *in vitro* & *in vivo* approach
- Relationships of biotransformation across organisms (2 projects)

Communication

Publications

ECETOC's primary outputs are its published state of the science reports that are compiled as a result of the scientific partnerships formed in the framework of ad-hoc issues-based task forces. These take the form of both ECETOC's own publications and the publication of its reports in peer-reviewed journals.

In 2009 ECETOC ceased producing reports designated as a 'Monograph' or a 'Document'.

Instead, 'Monographs', which were comprehensive reviews of generic topics or issues fundamental to the application of good science in evaluating the hazards and risks of chemicals, and 'Documents', which were scientific briefing papers, addressing emerging issues, are all to be published as Technical Reports.

- → **JACC Reports** (Joint Assessment of Commodity Chemicals) are comprehensive reviews of all available toxicological and ecotoxicological data on specific chemical substances, predominantly those having widespread and multiple uses. Each report presents a hazard assessment and identifies gaps in knowledge. The standard format may be extended in support of EU or other international risk assessment, or setting of an occupational exposure limit value.
- → **Special Reports** are compilations of data targeted to specific regulatory issues/ demands.
- → **Technical Reports** address specific applications of the science in evaluating the hazards and risks of chemicals to human health and the environment.
- → **Workshop Reports** are summaries of the discussions and conclusions derived from ECETOC sponsored scientific workshops.

Reports published by ECETOC

Technical Reports

No. 111 Development of guidance for assessing the impact of mixtures of chemicals in the aquatic environment (October 2011)

No. 112 Refined Approaches for Risk Assessment of PBT/vPvB Chemicals (October 2011)

No. 113 Environmental Impact Assessment for Socio-Economic Analysis of Chemicals: Principles and Practice (August 2011)

JACC Reports

No. 55 Linear Polydimethylsiloxanes CAS No. 63148-62-9 (Second Edition) (December 2011)

Workshop Reports

No. 21 Risk Assessment of Endocrine Disrupting Chemicals 9-10 May 2011, Florence (Published November 2011)

No. 22 Combined Exposure to Chemicals 11-12 July 2011, Berlin (Published October 2011)

Complementary copies of ECETOC reports are provided to member companies, the academia, government authorities and international agencies, and some non-governmental organisations. All reports can be downloaded without charge from www.ecetoc.org.

Articles published in the open scientific literature

Bars R, Broeckaert F, Fegert I, Gross M, Hallmark N, Kedwards T, Lewis D, O'Hagan S, Panter G H, Weltje L, Weyers A, Wheeeler J and Galay Burgos M. 2011.

Corrigendum to "Science based guidance for the assessment of endocrine disrupting properties of chemicals". Regul Toxicol Pharmacol 59:37-46. Doi: 10.1016/j.yrtph.2011.04.005

Lavelle KS, Schnatter RA, Travis KZ, Swaen GM, Pallapies D, Money C, Priem P, Vrijhof H. 2012.

Framework for integrating human and animal data in chemical risk assessment. Regul Toxicol Pharmacol 62:302-312. doi: 10.1016/j.yrtph.2011.10.009. Available online 17 November 2011

Hennes EC, Galay Burgos M, Hamer M, Pemberton M, Travis K, Rodriguez C. 2012.

Workshop: Combined exposure to chemicals. Regul Toxicol Pharmacol 63:53-54. doi: 10.1016/j.yrtph.2012.02.008

Hennes EC. 2012.

An overview of values for the threshold of toxicological concern. Toxicology Letters. doi: 10.1016/j.toxlet.2012.03.795 (Available online 30 March 2012)

Online Communication

The ECETOC public website continues to evolve and during 2011 a set of language sites were developed. Apart from the default English content, the key parts of the website are now offered in French, German, Spanish, Italian, Chinese and Japanese; as a result there has been a large upswing in visits from countries using these languages, indeed the Japanese homepage is currently the 3rd most visited page of the website after "Targeted Risk Assessment" and the English homepage. There has also been a marked increase in the number of press releases being published in the trade press, and "Chemical Watch" now regularly reports on ECETOC workshops.

In an effort to simplify and streamline the report-creation process for task forces and other workgroups, ECETOC developed an online joint editing platform which was launched in May 2011. This makes it much easier to keep a steady and organised work flow, with task force members promptly contributing when necessary.

External Representation

REPRESENTATION AT SPECIFIC MEETINGS AND INPUT TO SPECIFIC PROJECTS AND REPORTS:

→ 2nd International Risk Assessment Conference: 'Global risk assessment dialogue'

26-28 January 2011
Brussels, Belgium

ECETOC was represented by Neil Carmichael (ECETOC)

→ DNT3 Conference: 'Advancing the science of developmental neurotoxicity testing for better safety evaluation'

10-13 May 2011
Varese, Italy

Neil Carmichael (ECETOC) chaired the session on 'The use of in vitro and non-mammalian species for risk assessment

→ OECD Report on 'Novel endocrine assays and endpoints'

1 September 2011

The (former) task force on 'Endocrine disrupting effects' submitted detailed comments (via BIAC) on the report "Detailed Review Paper on the state of the science on novel in vitro and in vivo screening and testing methods and endpoints for evaluating endocrine disruptors"

→ DG SANCO SCs Preliminary Opinion on 'Toxicity and assessment of chemical mixtures'

9 September 2011

Two ECETOC task forces: 'Low-dose interactions' and 'Development of guidance for assessing the impact of mixtures of chemicals in the aquatic environment' jointly compiled and submitted detailed comments

→ EFSA Draft Scientific Opinion 'Exploring options for providing preliminary advice about possible human health risks based on the concept of Threshold of Toxicological Concern'

15 September 2011

Member company experts on the TTC concept gave input to submitting detailed comments

→ Draft OECD TG 426

28 September 2011

Member company experts gave input to submitting detailed comments on the draft document "Risk assessment of developmental neurotoxicity: evaluation of test guidelines and guidance documents" to Prof. Håkansson (Karolinska Institute)

→ WHO/IPCS Workshop: 'Guidance for immunotoxicity assessment for chemicals'

3-4 October 2011
Bilthoven, Netherlands

Naveed Honarvar (BASF) and Winfried Steiling (Henkel) participated on behalf of ECETOC

→ JRC-EASAC Joint Event: 'Impact of engineered nanomaterials on health: considerations for benefit-risk assessment'

18 October 2011
Brussels, Belgium

ECETOC was represented by Christa Hennes (ECETOC)

→ European Risk Forum Meeting: 'The importance of the quality of scientific evidence for managing risks'

8 November 2011
Brussels, Belgium

Neil Carmichael (ECETOC) participated as a panellist in the roundtable discussion

→ 6th Framework Programme Integrated Project 'OSIRIS'

ECETOC was represented in the Advisory Panel by David Owen (Shell) followed by Christa Hennes (ECETOC). She participated in the stakeholder workshop in March 2011 in Leipzig

→ 6th Framework Programme Co-ordination Action Project 'NORMAN'

ECETOC was represented in the Advisory Panel by Stuart Marshall (Unilever)

→ 7th Framework Programme Co-ordination Action Project 'EUROECOTOX'

ECETOC is a partner in the project and is represented by Malyka Galay Burgos (ECETOC). She participated in the expert meeting in October 2011 in Leipzig

→ ILSI Europe environment and health task force on the impact of crop production on water quality

ECETOC was represented by Malyka Galay Burgos (ECETOC)

→ Nanogenotox EU-Funded Joint Action

ECETOC participated in the stakeholder consultation via Maria Donner (DuPont) and Markus Schulz (BASF)

REPRESENTATION IN STANDING EXPERT GROUPS:

→ WHO/IPCS Harmonization Project Core Group

ECETOC was represented by Ben van Ravenzwaay (BASF) and Vice-Chairman of the ECETOC Scientific Committee

→ ECHA Risk Assessment Committee (RAC)

ECETOC was represented by Marie-Louise Meisters (DuPont) and Chris Money (ExxonMobil)

→ ECHA Member States Committee (MSC)

ECETOC was represented by Tamara Nameroff (Shell) and Neil Carmichael (ECETOC)

→ ECHA Partner Experts Groups (PEGs)

ECETOC was represented by 16 industry experts from the ECETOC network

→ ECVAM Scientific Advisory Committee (ESAC)

ECETOC was represented by Neil Carmichael (ECETOC)

→ ECVAM Stakeholder Forum (ESTAF)

ECETOC was represented by Remi Bars (Bayer CropScience)

→ EU Commission Consultative Forum on Environment and Health Action Plan

ECETOC was represented by Peter Boogaard (Shell)

→ OECD Working Party on Manufactured Nanomaterials

ECETOC was represented (via BIAC) by Hans-Jürgen Wiegand (Evonik Industries)

PRESENTATIONS AND POSTERS:

→ 21st Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC Europe) on "Ecosystem protection in a sustainable world: a challenge for science and regulation"

15-19 May 2011
Milan, Italy

- Special Session on precision versus practicality; the derivation, construction and experience of the ECETOC TRA human exposure tools. *Speaker: Chris Money (ExxonMobil)*
- Environmental risk assessment of ionisable organic chemicals. *Poster presentation by Todd Gouin (Unilever) on behalf of the task force on ERA of ionisable compounds*
- Assessing the impact of mixtures in the environment, an ECETOC task force. *Poster presentation by Mick Hamer (Syngenta) on behalf of the task force on the development of guidance for assessing the impact of mixtures of chemicals in the aquatic environment*

→ 21st International Congress of the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT)

24-27 May 2011
Dubrovnik, Croatia

- Epidemiology of cyanide/nitrile poisoning and survey of antidotal treatment used in Europe. *Platform presentation by Herlinde Smet (Poisons Centre Brussels) on behalf of the task force on cyanides antidotes*
- Systematic review of efficacy and adverse effect of methemoglobin forming antidotes in cyanide poisoning. Preliminary results. Efficacy and adverse reaction of methemoglobin forming antidotes in cyanide poisoning. *Platform presentation by Thomas Zilker (Technische Universität München) on behalf of the task force on cyanides antidotes*

→ 8th World Congress on Alternatives and Animal Use in the Life Sciences

21-25 August 2011
Montreal, Canada

- 3Rs alternatives for detection of endocrine disruptors: broadening our possibilities. *Platform presentation by Tzutzuy Ramirez (BASF) by invitation through ECETOC*

→ International Toxicology of Mixtures Conference: Evidence-based approaches for toxicology and risk assessment of chemical mixtures

21-23 October 2011
Arlington, Virginia, USA

- A review of integration between chemicals at low doses. *Poster presentation by Rosemary Zaleski (ExxonMobil) on behalf of the 'Low-dose interactions' task force*

→ 31st Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC North America) on "Bridging science with communities"

7-10 November 2011
Boston, Massachusetts, USA

- Environmental risk assessment of ionisable organic chemicals. *Platform presentation by Todd Gouin (Unilever) on behalf of the task force on ERA of ionisable compounds*

Members of the Scientific Committee

Fraser Lewis (Chairman)	Syngenta
Ben van Ravenzwaay (Vice Chairman)	BASF
Remi Bars	Bayer CropScience
David Farrar	INEOS ChlorVinyls
Andreas Flückiger	F. Hoffmann-La Roche
Helmut Greim	Technical University Munich
Guiseppe Malinverno	Solvay
Lorraine Maltby	University of Sheffield
Stuart Marshall	Unilever
Marie-Louise Meisters	DuPont
Chris Money	ExxonMobil Petroleum & Chemical
Mark Pemberton	Systox Ltd. (formerly of Lucite)
Carlos Rodriguez	Procter & Gamble
Leslie Rushton	Imperial College London
Dan Salvito	RIFM on behalf of IFF
Jason Snape	AstraZeneca
Gerard Swaen	Dow Chemical
Johannes Tolls	Henkel
Saskia van der Vies	Amsterdam Free University
Kees van Leeuwen	KWR Watercycle Research Institute
Hans-Jürgen Wiegand	Evonik Industries

Members of the Secretariat

Neil Carmichael
Secretary General

Christa Hennes
Health Sciences Manager

Henk Vrijhof
Chemicals Programme Manager

Malyka Galay-Burgos
Environmental Sciences Manager

Ian Cummings
Communication, Web & Media Manager

Geneviève Gérits
Office Manager

Christine Yannakas
Administrative Assistant

Sonia Pulinckx
Administrative Assistant

The ECETOC Secretariat is responsible for the co-ordination and management of the scientific work programme, ensuring that the tasks allocated by the Scientific Committee are accomplished in a timely fashion. ECETOC's continued success relies greatly on its Secretariat. This team of dedicated professionals supports the scientists engaged in the work of the ECETOC programme in meeting the objectives set by the Scientific Committee.

Anita Jennings, Administrative Assistant since 2007, left the ECETOC secretariat in June 2011 in order to spend more time with her family. She was replaced by Sonia Pulinckx.

Finance

INCOME ACTUAL 2011 IN EURO

Subscription	
39 Full Members	1,228,500
6 Associate Members	54,000
Total Subscription Income	1,282,500
Bank interest	6,585
Investment income	27,887
Project-related	213,611
Total	**1,530,583**

EXPENDITURE ACTUAL 2011 IN EURO

Salaries (and related expenses)	950,548
Office running expenses	189,155
Travel expenses on missions	11,716
Meetings and consultants	268,224
Professional services	26,287
Bank charges	3,392
Capital expenditure	3,638
Publications	26,833
Miscellaneous	16,499
Website	11,653
Total	**1,507,945**

BALANCE SHEET AND RESERVES ACTUAL 2011 IN EURO

Balance Sheet	
Income	1,530,583
Expenditure	1,507,945
Operating margin	22,638
Reserves*	
Opening	1,991,377
Operating margin	22,638
Closing reserves	**2,014,015**

* Estimated Reserve Required: 550.000

Abbreviations

3Rs
Replacement, refinement and reduction of animals in research

BfR
German Federal Institute for Risk Assessment

BIAC
Business and Industry Advisory Committee to the OECD

CAS
Chemical Abstracts Service

CBB
Critical body burden

Chesar
Chemical safety and report tool

CEFIC
European Chemical Industry Council

CLP
Classification, labelling and packaging

CMR
Carcinogenic, mutagenic or toxic for reproduction

CRD
Chemicals Regulation Directorate

CSA
Chemical Safety Assessments

DEFRA
(UK) Department for Environment, Food and Rural Affairs

DG Environment
European Commission Directorate-General for the Environment

DG SANCO
European Commission Directorate-General for Health and Consumer Affairs

DNA
Deoxyribonucleic acid

DNEL
Derived no effect level

DTA
Direct toxicity assessment

EASAC
European Academies Science Advisory Council

ECHA
European Chemicals Agency

ECVAM
European Centre for the Validation of Alternative Methods

ED
Endocrine disrupter / Endocrine disrupting chemical

EDA
Effect directed analysis

EEMS
European Environmental Mutagen Society

EFSA
European Food Safety Authority

EPA
(US) Environmental Protection Agency

ES
Exposure scenarios

ESAC
ECVAM Scientific Advisory Committee

ESTAF
ECVAM Stakeholder Forum

ET&C
Environmental Toxicology and Chemistry

EU
European Union

EUROECOTOX
European Network for Alternative Testing Strategies in Ecotoxicology

EUROTOX
Association of European Toxicologists and European Societies of Toxicology

EUSES
European unified system for the evaluation of substances

GHS
Globally harmonised system of classification and labelling of chemicals

HBM
Human biomonitoring

HESI
Health and Environmental Sciences Institute

HETRA
Human exposure and tiered risk assessment

ILSI
International Life Sciences Institute

IPCS
International Programme on Chemical Safety

JACC
Joint assessment of commodity chemicals

JIG
Joint industry group

JRC
Joint Research Centre; The European Union's scientific and technical research laboratory and an integral part of the European Commission

LOEL
Lowest observed effect level

LRI
Cefic's Long-range Research Initiative

MSC
(ECHA) Member States Committee

NER
Non-extractible residues

NGO
Non-Governmental Organisation

NOEL
No observed effect level

OECD
Organisation for Economic Co-operation and Development

PBPK
Physiologically-based pharmacokinetic (model)

PBT
Persistent, bioaccumulative toxic

PDMS
Polydimethylsiloxane

PEG
(ECHA) Partner Experts Group

PNEC
Predicted no effect concentration

POP
Persistent organic pollutant

PSP
Poorly soluble particles

QSAR
Quantitative structure activity relationship

R&D
Research and development

RAC
(ECHA) Risk Assessment Committee

RAIDAR
Risk assessment identification and ranking

REACH
EU regulatory framework for the registration, evaluation and authorisation of chemicals

RepDose
The database of NOELs/LOELs in repeated dose studies

RfP
Request for proposal

RIPs
REACH implementation projects

RIVPACS
River Invertebrate Prediction and Classification System

SAR
Structure-activity relationship

SCEGHS
(UN) Sub-Committee of Experts on the GHS

SEA
Socio-economic analysis

SETAC
Society of Environmental Toxicology and Chemistry

SIG
LRI strategy implementation group

SPERC
Specific environmental release categories

SSD
Species sensitivity distributions

STOT
Specific target organ toxicity

TGD
Technical guidance document

TIE
Toxicity identification evaluation

TMF
Trophic magnification factor

TOX21
A collaboration between EPA, National Institutes of Environmental Health Sciences/National Toxicology Program, National Institutes of Health/National Human Genome Research Institute, NIH Chemical Genomics Center (NCGC) and the Food and Drug Administration

TR
ECETOC technical report

TRA
Targeted risk assessment

TTC
Threshold of toxicological concern

UVCB
Substances of unknown or variable composition

vPvB
very persistent very bioaccumulative

WET
Whole effluent toxicity testing

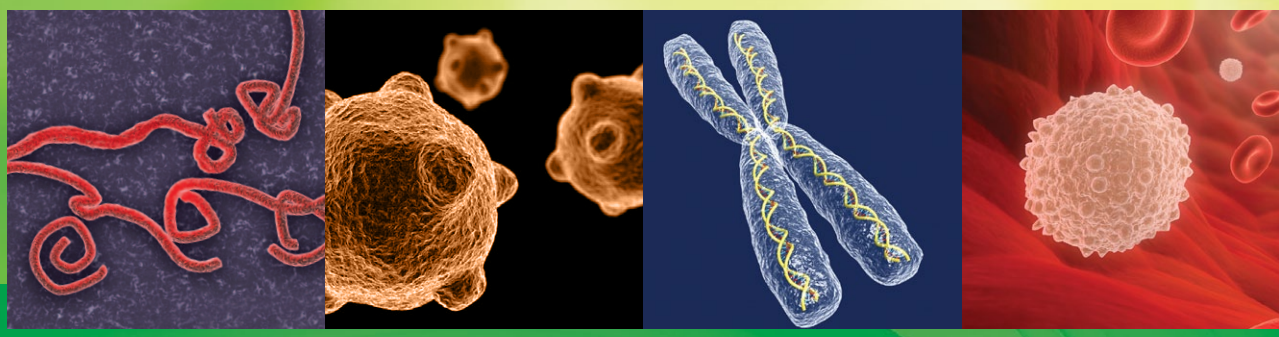
WHO
World Health Organisation

WoE
Weight of evidence

Established in 1978, ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

ECETOC AISBL

Av. E. Van Nieuwenhuyse 4 (Bte 6)
B-1160 Brussels, Belgium
Tel: (32) 2 675 3600
Fax: (32) 2 675 3625
Email: info@ecetoc.org
Website: www.ecetoc.org
VAT: BE 0418344469



Established in 1978, ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

ECETOC AISBL

Av. E. Van Nieuwenhuyse 4 (Bte 6)
B-1160 Brussels, Belgium
Tel: (32) 2 675 3600
Fax: (32) 2 675 3625
Email: info@ecetoc.org
Website: www.ecetoc.org
VAT: BE 0418344469