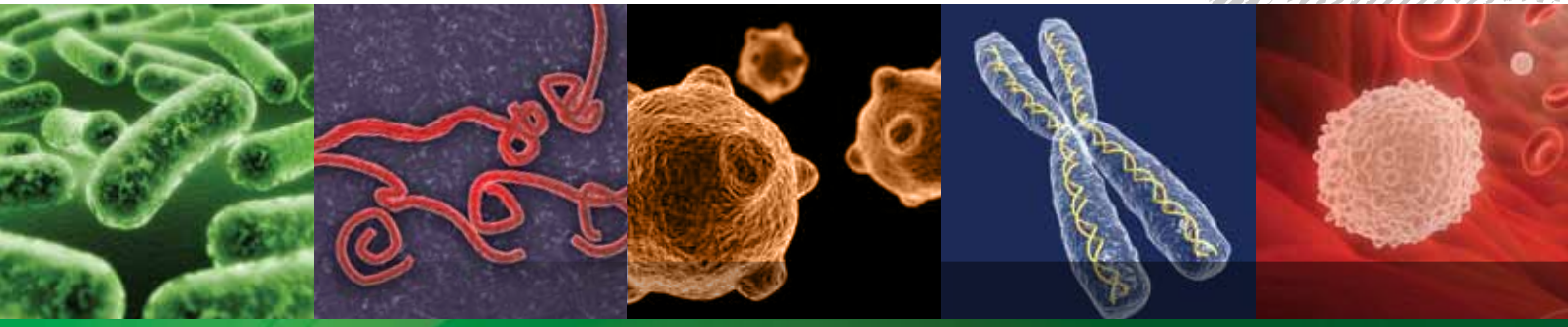
ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS



Annual Report **2010**

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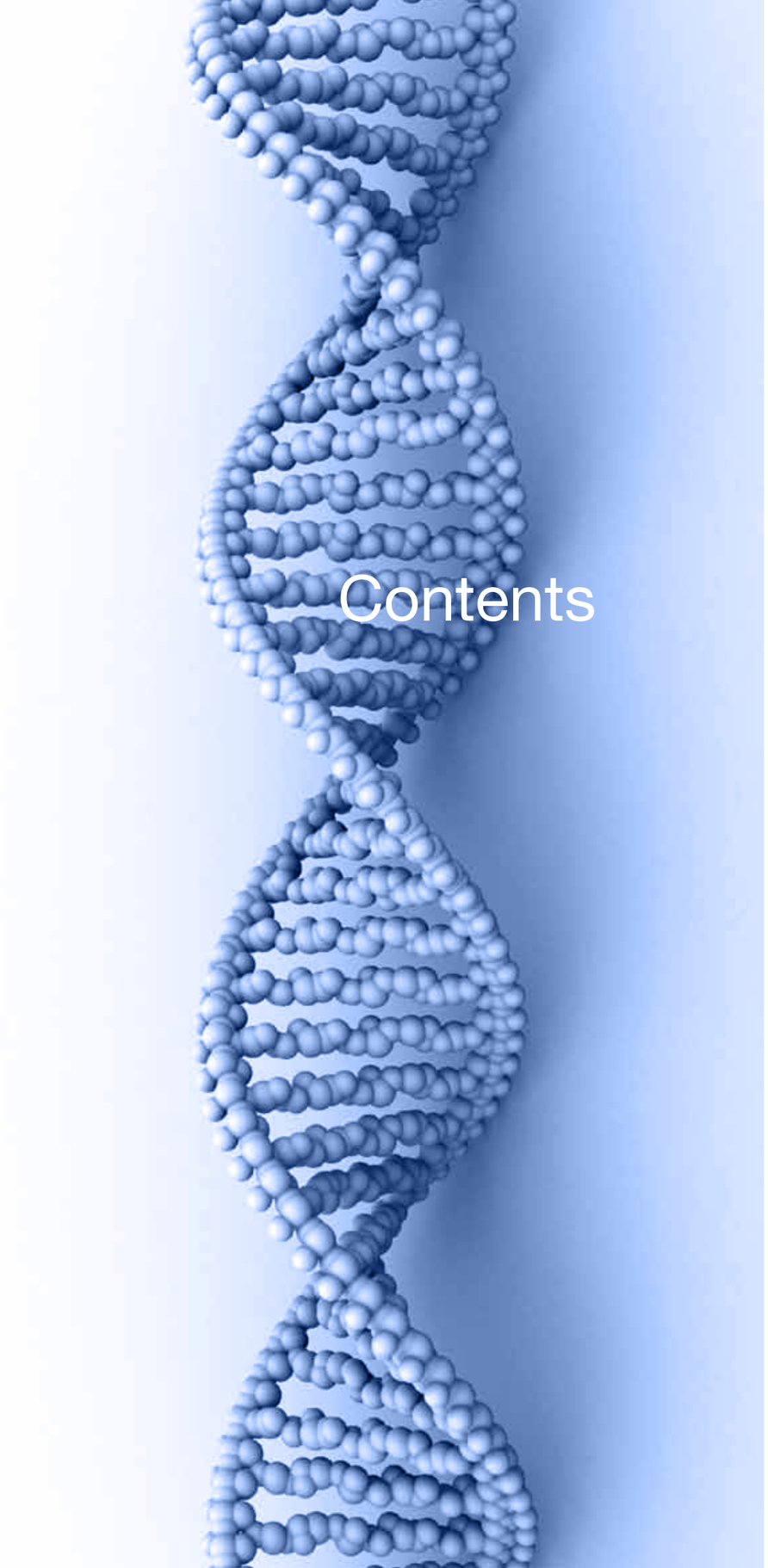

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Introducing **ECETOC**

"The main objective is to identify, evaluate, and through such knowledge help the industry to minimise any potentially adverse effects on human health and the environment ..."

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

ECETOC's main objective is to identify, evaluate, and through such knowledge help the industry to minimise any potentially adverse effects on human health and the environment that may arise from the manufacture and use of chemicals. To achieve this, ECETOC facilitates the networking of suitably qualified scientists from its member companies and co-operates in a scientific context with international agencies, government authorities and professional societies.

ECETOC is governed by a Board of Administration comprising up to 12 senior executives from member companies. The Board is responsible for the overall policy and finance of the organisation and appoints the members of the Scientific Committee which defines, manages and peer reviews the ECETOC work programme.

The outputs of its work programme are manifested as published reports, papers and specialised Workshops. ECETOC also provides scientific representation of manufacturers and users of chemicals via presentations at specialist fora and takes a scientific role in the activities of international organisations and regulatory groups.

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 according to an issues-based science strategy that was launched in 2007. It is broken down into 13 science areas *(see section on the 2010 Science Programme)* that are grouped according to 5 main themes:

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

ECETOC Member **Companies**

At the start of 2011 ECETOC membership comprised the following 44 companies:

AkzoNobel – Tomorrow's Answers Today

ALBEMARLE* — *Associate member company*

AstraZeneca

BASF

Bayer

bp

CEPSA — *Associate member company*

Clariant

Coca-Cola

COLGATE-PALMOLIVE

DOW — Living. Improved daily.

DOW CORNING

DSM

DUPONT

eni

EVONIK INDUSTRIES

ExxonMobil

Roche

Firmenich

Givaudan

Henkel

Honeywell

HUNTSMAN — Enriching lives through innovation

INEOS — *Associate member company*

IFF International Flavors & Fragrances Inc. — *Associate member company*

Johnson & Johnson

L'ORÉAL

Lucite International — Going further — *Associate member company*

MERCK

NOVARTIS

NYCOMED

Pfizer

P&G

Reckitt Benckiser

REPSOL

Rhodia

SC Johnson

Shell Chemicals

SOLVAY

Statoil

syngenta

TOTAL

Unilever

WACKER

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

Membership **benefits**

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 activity.

In so doing, member company employees benefit from access to a high quality network of scientific expertise. 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 incorporated into the work programme and can have a representative on its Scientific Committee.

Any member company employee can freely 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

At ECETOC, science comes first

Recent legislation impacting the chemical industry has some paradoxical requirements. The cosmetics directive will exclude all animal testing by 2013 and requires that the safety assessments be carried out using *in vitro* models. In a similar way the REACH legislation mandates a large increase in testing requirements but requires that *in vivo* testing be used as a last resort. The question arising from this is: what is the science base which allows these good intentions to be satisfied?

When ECETOC was founded in 1978 the sciences of Toxicology and its sister discipline Ecotoxicology were well established. The main reliance for risk assessment was put on *in vivo* studies in rodents and fish respectively. The methodology was based on human clinical medicine in the former case and restricted to observations of mortality in the latter. In the years that followed it became clear that results from rodent studies could give misleading results for human safety. Much effort in the succeeding years went into defining the cause of the misleading results, in the hope that understanding would lead to more relevant risk assessments. This search for understanding looked for the 'mode of action' in types of toxicity. At the end of 2009, ECETOC held a Workshop on this subject, the results of which were published in the open literature quite recently. From this it can be concluded that good ideas, which lead to a change in approach, come slowly in toxicology!

Likewise in the environment: predictions from single species in clean water aquaria may not be the best predictors of impact in the environment. Nevertheless, progress to a holistic model of environmental fate and ecosystem impact is only recently picking up speed. Several ECETOC Task Forces are addressing aspects of this problem.

Progress in other fields of biology has been much more rapid. The human genome was mapped in 2003 and since then a huge blossoming of knowledge regarding the functioning of genetic regulatory processes has taken place. Epigenetics and the study of non-chromosomal DNA have burst on the stage and cell to cell signalling is becoming better understood. In addition, publications concerning the functioning of receptors on the surface and in the nuclei are proliferating. These discoveries are not simply academic in nature, but are leading to a fundamentally better understanding of disease, and therapies using this knowledge are already in use.

So where is the equivalent progress in the safety assessment of chemicals? Much research has been performed in developing alternative methods which would substitute for the standard regulatory tests. It is becoming clear that the rate of progress with this approach is too slow to allow any early replacement of the big studies which use many animals. However, the new technologies which exploit the knowledge from research in receptor, signalling and gene expression promise a radical new approach. The concept relies also on bioinformatics and modelling to create a 'virtual biology'.

This concept was embodied in the 2007 publication of the US Academy of Sciences report 'Toxicology in the 21st Century'. The US EPA launched a huge effort to validate this methodology in a programme called 'Toxcast'. The project involves a large suite of *in vitro* methods, supported by a battery of computational techniques, to extract meaning from the huge quantities of data being produced.

ECETOC members may well be confused regarding the future of these approaches. They have been asking whether this is a 'false dawn" and whether the methods are fit for use in the regulatory context.

In order to answer these questions ECETOC has taken a lead by organising a series of Workshops evaluating the use of 'omics technologies in human and environmental risk assessment. The first of these took place in December 2007, the second in February 2010 and we plan another in 2011. In addition, in 2010, ECETOC published an overview of 'High information content technologies in support of read-across in chemical risk assessment'.

The need to find a new testing paradigm is clear, but will these approaches deliver a system which can replace the conventional (*in vivo*) studies to the satisfaction of the regulators? The science is promising and the technologies are developing fast. While large scale proof of concept is not available, much progress is being made. The dialogue with academic scientists and regulators allows us to offer a balanced view of the science. In this way ECETOC gives its member companies the opportunity to keep in touch with the science, but with the focus on practical application in the regulatory context.

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 representatives. Two Members are entitled to represent the Associate members A category and the Associate members B category respectively.

Members may propose candidates for the Board; these candidates must have managerial duties within their company and possess scientific and technical experience.

ECETOC **Board Members as of December 2010**

Martin **Kayser**
BASF
Chairman

Steve **Rumford**
AstraZeneca
Treasurer

Julia **Fentem**
Unilever

Petra **Hanke-Baier**
Procter & Gamble

Thomas **Jostmann**
Evonik Industries

Richard **Phillips**
ExxonMobil

Mireille **Quirina**
DuPont de Nemours

On the occasion of the 2010 Annual General Meeting, having served two years since their last election, Dr. **Julia Fentem** of Unilever and Mr. **Steve Rumford** of AstraZeneca were unanimously re-elected to the ECETOC Board.

Proposed new Board member Dr. **Petra Hanke-Baier** of Procter & Gamble was endorsed.

Dr. **Hans-Jürgen Bender** of Procter & Gamble resigned his seat on the ECETOC Board having served since 2009.

Report from the Secretary General

The year 2010 in retrospect

In the UK there is an expression made famous by a football commentator (but no-one is sure who said it): 'Football is a game of two halves'. Apart from the banality of the original expression, there is a simple wisdom in the notion that when you are halfway through something, you should be wary about predicting the outcome. So it was with 2010 at ECETOC. The year started with an unprecedented level of activity with the first few months seeing Workshops on nanomaterials, 'omics technologies in chemical risk assessment and the derivation of DNELs (derived no effect levels). This was followed up by an excellent Annual Technical Meeting in June with the revision of ECETOC's strategy as its centrepiece (see the Scientific Committee Chairman's foreword for details).

During the same period we launched several new Task Forces, especially in the environmental fate area. From the secretariat's point of view the workload threatened to overwhelm our capacity. Then came the summer!

It will not be a secret to readers of this report that REACH has consumed a considerable amount of company resource. From our perspective, the diversion of expertise to meet the Phase 1 REACH registration deadline was quite conspicuous. Our regular contributors fell silent and proposals for new activities ceased. After the ATM we held no major event until the start of 2011. This should not be taken to imply that nothing was done during this period at ECETOC. The secretariat was frantically employed in turning the first half of the year's input into output, in particular Technical Report No. 110 and Workshop Report No. 20 concerning DNELs. Likewise twelve on-going Task Forces continued to meet and progress their documents.

These observations, of course, were turned to good use. As the year was coming to a close, the planning started for a Workshop in early 2011 to analyse the experience of the first round of REACH and to identify areas where ECETOC could address the science needs identified in the course of 2010. This Workshop has now taken place (March 2011) and the list of prioritised topics will be used to develop the 2011 science programme.

While the companies which were most affected by REACH registration were giving all their efforts to achieving the deadline, one group of companies was increasing their efforts within ECETOC. Since early 2009 we have been working to accommodate the needs of our pharmaceutical member companies to host Task Forces dealing with environmental risk assessment of their substances. These Task Forces have benefited from the expertise of other companies in the ECETOC membership who have experience and expertise in similar scenarios with other product types.

During the year ECETOC published 2 Technical Reports, 3 Workshop Reports and 6 articles in the open literature. This shows a tendency which is consistent with the intended developments in our way of working, namely: an increase in Workshops and peer reviewed articles and a proportionate decrease in the more traditional Technical Reports. As each of these vehicles has its own merits, our portfolio of outputs is now more balanced than in the past with the publications representing an optimum between the needs of speed, thoroughness and external visibility.

In the meantime, 2011 has got off to a flying start with several new activities; but that is for next year's report.

Neil Carmichael
Secretary General

ECETOC European Centre for Ecotoxicology and Toxicology of Chemicals

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Foreword from the Scientific Committee Chairman

As the new Chairman of ECETOC's Scientific Committee, this is my first opportunity to contribute to the annual report and as you will see from this report it has been a very busy and productive year. A key activity during this time has been a review of the ECETOC strategy that took place at the ATM in June and which produced a list of suggestions for further development. In July 2010, a small group of Scientific Committee members, including the Secretary General and the outgoing and incoming Chairmen of the Scientific Committee, met to develop these ideas into a strategy to take to the Board in September 2010. A series of themes and insights emerged from this process which together started to form the elements of a revised strategy.

It had become clear that ECETOC now serves a wider range of industry segments than previously. General Chemicals were the major force at the time of ECETOC's creation while now the membership is composed of a well equilibrated mix of many sectors of the industry. Many ECETOC activities represent topics which have greater significance for some sectors of our membership than for others. This suggests the need for a statement of unifying values shared by all members. ECETOC has a strong value of science and integrity; it works by establishing a clearly formed series of questions and using a transparent process to establish the pertinent science.

Purpose & Values

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.

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

Although, in society, chemical safety policy is formulated to address a real or perceived risk, the initial considerations often do not include a detailed examination of the science behind the problem or the potential solution. The way that society turns its policy wishes into regulation frequently creates gaps in the science base which need to be filled to make the guidance practical. The primary value of ECETOC to its members lies in addressing these gaps through science and influencing the turning of policy into regulation, and other safety related practice, in a way which allows the benefits of their products to be realised without damaging health or the environment. This forms the basis of ECETOC's purpose and its ambition to be the partner of choice for governments to engage industry in this process.

Although the new strategy has taken some significant focus during the year, the day to day work has of course not stopped. Our science strategy continues to guide the work of ECETOC, and this Annual Report reflects both the volume and range of our recent work. We have also made considerable progress on some key areas of our science strategy and I would like to single out a couple of areas where ECETOC has taken a leading role and is making a considerable impact.

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Activities in Europe continue to highlight the concerns over presence and potential impact of chemical combinations in the environment and the perception that current risk assessment procedures are inadequate. Given this level of concern, the Scientific Committee accepted a proposal for a new Task Force on this topic with the aim of reviewing approaches for assessing impacts on the aquatic environment and developing guidance on suitable methods, identifying research needs and diagnostic tools. Given the current importance of this topic, the Task Force was specifically asked to develop an effective communication strategy to engage key stakeholders. In parallel, another Task Force is looking at the significance of low-dose interactions of chemicals to human safety which is another topic of concern in the current debate. A joint Workshop, based on the output from both these taskforces, is planned to engage the wider scientific community and to address all key scientific areas on co-exposure to chemicals.

Vision & Mission

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.

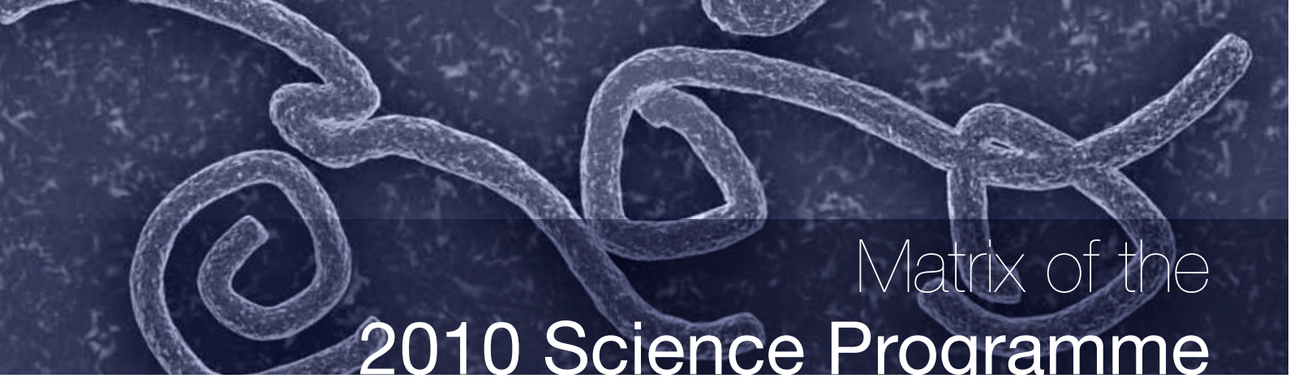
To promote the use of good science in human and environmental risk assessment of chemicals, biomaterials and pharmaceuticals.

A key issue for the chemical industry in 2010 was human health Assessment Factors needed for preparing chemical safety dossiers that were due for the first registration deadline of REACH end November. An ECETOC Task Force had the remit to evaluate recent scientific literature on assessment factors in light of the recommended values published in the Technical Guidance Document of the regulation and those published by a previous Task Force. The recommendations were presented to a Workshop early in the year, where regulators were present and gave many comments. The ECETOC guidance was then published on time for companies to take the recommendations into account for the submitted dossiers.

Both of these issues highlight how ECETOC's approach is evolving to include an increasing use of Workshops to more effectively communicate with and engage the academic and regulatory community. This is consistent with our aim to collaborate with the Commission and key agencies to ensure that good science is the foundation of safety assessment and risk assessment is at the heart of chemical regulation.

Fraser Lewis,
Syngenta

Chairman of the Scientific Committee



Matrix of the 2010 Science Programme

ECETOC pursues its vision and mission according to an issues-based science strategy that was launched in 2007. It is broken down into 13 science areas* that are grouped according to 5 main themes:

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

The reader may wish to note that some activities are relevant to and mentioned in more than one science area.

(*) At the end of December 2010

PRESENCE OF CHEMICALS IN HUMANS

Chemicals in human tissue

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

2010 activity:

- LRI projects concerning biological guidance values (4 projects)
- LRI project on development of a computer programme with a multi-level modelling tool related to health based exposure rates for inhalation, oral intake and/or skin exposure
- Representation at EU Commission Consultative Forum Environment and Health Action Plan

Chemicals in indoor air

Address approaches to assess the impact of chemicals found in indoor air on human health.

2010 activity:

- Childhood asthma and contributing factors (commissioned review)
- LRI project on integrated exposure for RA in indoor environments

Mixtures

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

2010 activity:

- Establishment of a Task Force on low dose interactions
- Progression of a Task Force to develop guidance for assessing the impact of mixtures of chemicals in the aquatic environment
- LRI project on integrated exposure for RA in indoor environments
- LRI project on substances from multiple sources (aggregate exposure)
- LRI project on substances additivity from household products
- LRI project on the capacity of the endocrine system to cope with combined exposure to exogenous endocrine active substances at environmentally relevant concentrations

PRESENCE OF CHEMICALS IN THE ENVIRONMENT

Exposures issues

Achieve recognition by regulators and non-governmental organisations that decisions on the acceptability of the presence of chemicals in the environment require a risk assessment involving both their hazardous concentrations and exposure concentrations.

2010 activity:

- Establishment of a Task Force on understanding the relationship between extraction technique and bioavailability
- Establishment of a Task Force on development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals
- Publication of Workshop Report No. 17 on the significance of bound residues in environmental risk assessment
- Progression of a Task Force to develop guidance for assessing the impact of mixtures of chemicals in the aquatic environment
- Progression of a Task Force on risk assessment approaches for PBT/vPvB or POPs
- Progression of a Task Force on the application of critical body burden (CBB) in risk assessment of substances of very high concern (SVHC)
- Progression of a Task Force on the ERA of ionisable compounds
- ECETOC involvement in the EU 6th Framework Programme: NORMAN Project Advisory Committee
- LRI project concerning cross taxonomic biotransformation potential
- LRI project on relationships of biotransformation across organisms (2 projects)
- LRI project on the environmental relevance of laboratory bioconcentration test
- LRI project on the influence of microbial biomass and diversity on biotransformation
- LRI project on applying and verifying PBT/POP models through comprehensive screening of chemicals
- LRI project on the rapid estimation of Trophic Magnification Factor (TMF) using laboratory, field and computer modelling methods in aquatic organisms
- LRI project on the generation of a validated CBB database and to validate a CBB chronic toxicity range for narcotics

EFFECTS IN HUMANS AND ECOSYSTEMS

Sensitive sub-populations

Provide a focussed scientific opinion for regulatory decision making that is targeted at or affects sensitive sub-populations. Currently, this area comprises mainly children's health outcomes. In the future, it may also address the sub-population of the elderly.

2010 activity:

- Childhood asthma and contributing factors (commissioned review)
- ECETOC involvement in the EU Consultative Forum on the Health and Environmental Action Plan
- LRI project on reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors

Reproductive health

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

2010 activity:

- Establishment of a Task Force on guidance for classification of reproductive toxicants under GHS
- Acceptance of an article submitted for publication in *Regul.Toxicol.Pharmacol* on the Science based guidance for the assessment of endocrine disrupting properties of chemicals
- LRI project on critical evaluation of individual and combined natural and synthetic endocrine active compounds in fish: an *in vitro* & *in vivo* approach
- LRI project on signal transduction pathways and development of alternative approaches to reproductive toxicity testing
- LRI project on characterisation of testicular toxicity using traditional and omic tools
- LRI project on reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors

Biodiversity and ecosystems

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.

2010 activity:

- Progression of a Task Force on exploring novel ways of using SSD to establish PNECs for industrial chemicals
- Progression of a Task Force to develop guidance for assessing the impact of mixtures of chemicals in the aquatic environment

METHODS

Intelligent / integrated testing strategies (ITS)

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 use of animals while providing best quality data for the risk assessment proces.

2010 activity:

- Progression of a Task Force on risk assessment approaches for PBT/vPvB or POPs
- Progression of a Task Force on the application of critical body burden (CBB) in risk assessment of substances of very high concern (SVHC)
- Progression of an RfP Development Task Force on approaches for read-across in chemical risk assessment and publication of its findings as Technical Report No.109
- Progression of a Task Force on the assessment and management of dermal risks from industrial chemicals
- ECETOC involvement in the EU 6th Framework Programme: OSIRIS Project Advisory Committee
- ECETOC involvement in the ECHA Stakeholder Partners Expert Group
- ECETOC involvement in the ECVAM Scientific Advisory Committee
- LRI project on cross-taxonomic biotransformation potential

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- LRI project on the relationship of biotransformation across organisms
- LRI project on signal transduction pathways and the development of alternative approaches to reproductive toxicity testing
- LRI project on mechanism-based characterisation of systemic toxicity for RepDose database substances employing *in vitro* toxicogenomics
- LRI project on overcoming current limitations in metabolism prediction of industrial chemicals
- LRI project on a toxicogenomic approach to enhance the specificity and predictive value of the murine local lymph node assay
- LRI project on TTC for inhalation exposure
- LRI project concerning the reference/validation chemical set for persistence benchmarking
- LRI project on fish cell line & embryo assays
- LRI project on the development and validation of abbreviated *in vivo* fish concentration test
- LRI project on evaluation of test methods for measuring toxicity to sediment organisms
- LRI project concerning a BCF database
- LRI project about the environmental relevance of laboratory bioconcentration test

'Omics' and related technologies

The emerging technologies of genomics, proteomics and metabonomics are already available for hazard if not risk evaluation. This area requires industry involvement to ensure that these technologies are used in an appropriate manner and exploited to their full potential.

2010 activity:

- Organisation of a Workshop on 'Omics in (Eco) toxicology: case studies and risk assessment
- Organisation of a Symposium at EEMS, Oslo, on the use of 'omics in systems biology
- LRI project on the characterisation of testicular toxicity using traditional and omic tools

Risk assessment of innovation

Evaluate and develop approaches for addressing the health and environmental risk assessment for innovative products. At present, activities are focussed on potential health impacts and environmental effects of nanomaterials.

2010 activity:

- Organisation of a Symposium as a post-satellite to the 46th EUROTOX meeting on: Innovation through nanotechnology and nanomaterials
- Publication of a special issue of *Nanotoxicology* on Genotoxicity of Engineered Nanomaterials
- Participation in stakeholder consultation of the Nanogenotox EU-funded Joint Action
- LRI projects looking at the tiered approach to testing and assessment of nanomaterial safety to human health (2 projects)
- LRI project on the assessment of nanoparticle specific effects in environmental toxicity testing

SCIENCE OF RISK ASSESSMENT

Role of chemicals in the causality of disease

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.

2010 activity:

- Childhood asthma and contributing factors (commissioned review)
- LRI project on the reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors
- LRI project on the assessment of risk factors influencing trends in incidence of female breast carcinoma

Risk, hazard and precaution

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 consideration.

2010 activity:

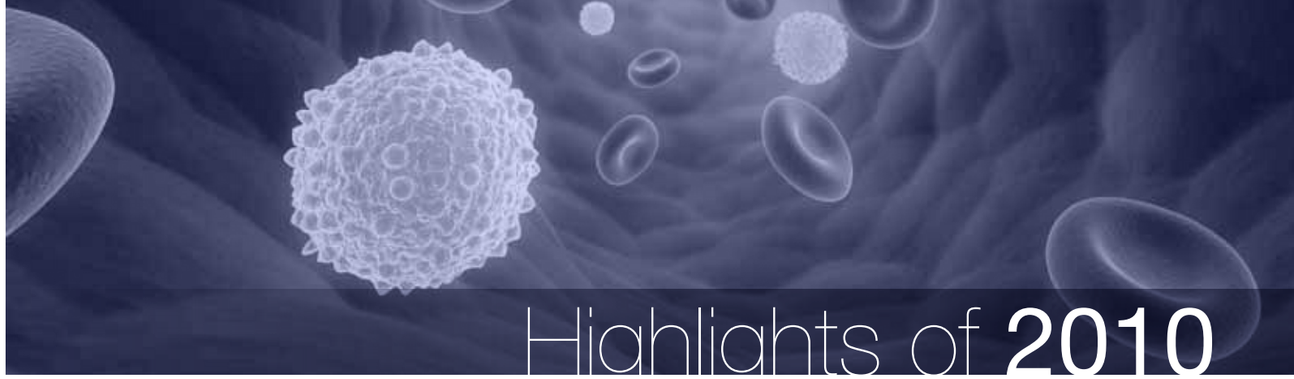
- Establishment of a Task Force on guidance for classification of reproductive toxicants under GHS
- Progression of a Task Force on guidance for assessment factors to derive DNEL and publication of its findings as Technical Report No.110
- Organisation of a Workshop on assessment factors to derive DNEL and publication of its Workshop Report No. 20
- Progression of a Task Force on risk assessment approaches for PBT/vPvB or POPs
- Progression of a Task Force on the application of critical body burden (CBB) in risk assessment of substances of very high concern (SVHC)
- Progression of a Task Force Task Force on the ERA of ionisable compounds
- Progression of a Task Force on exploring novel ways of using SSD to establish PNECs for industrial chemicals
- Progression of a Task Force to review the available human and clinically relevant data on the use of cyanides antidotes
- Progression of a Task Force to critically review all data on linear polydimethylsiloxanes (PDMS) and update JACC report No. 26
- Acceptance of an article submitted for publication in *Regul.Toxicol.Pharmacol* on the Science based guidance for the assessment of endocrine disrupting properties of chemicals
- Acceptance of an article submitted for publication in *Critical Reviews in Toxicology* on Using mode of action information to improve regulatory decision-making: An ECETOC/ILSI RF/HESI workshop overview

Science in society

Promote the use of science in EU decision making, to improve the image of industry science with EU policymakers and other scientists, and to enhance the acceptance of science by the general public.

2010 activity:

- Progression of a Task Force on the environmental impact assessment within the socio-economic analysis of chemicals



Highlights of 2010

Task Forces established

Low-dose Interactions

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

ECETOC has formed a Task Force to review relevant literature and known examples, and to evaluate whether the evidence on low-dose interactions demonstrates any effects that are 'unexpected' in light of current toxicology theory. In case of the latter, they should determine if specific modes of action are frequently associated with this. The Task Force also evaluates the adequacy of current risk assessment practice in light of the conclusions drawn.

Guidance for Classification of Reproductive Toxicants under GHS

The Globally Harmonised System of Classification and Labelling of Chemicals (GHS) has been introduced into the EU legislative framework under CLP Regulation No. 1272/2008. It is replacing the current guidelines under the Directives 67/548/EEC and 1999/45/EC. Regulatory authorities worldwide are beginning to use the GHS criteria and it is already being noticed that their interpretation varies in different parts of the world. In 2009, ECETOC published guidance for the classification of chemicals with regard to the endpoint of carcinogenicity, which incorporated the concept of potency. This guidance has been well received, and building on this approach the Scientific Committee recommended developing similar guidance for the application of the GHS criteria to reproductive toxicity. Many chemicals which have not yet been assessed for their potential in this area will be tested under REACH, and cut-off criteria currently applied to agrochemicals may be applied to other categories of chemicals. It is deemed important that industry has a clear position to contribute to the way chemicals are classified for reproductive toxicity.

This Task Force is asked to prepare guidance on the application of the UN GHS criteria for the classification of chemicals for reproductive (developmental, fertility, lactation) toxicity, including consideration of mode of action, potency and exposure. They would also monitor and provide input to the ECHA PEG 3.6 (revision of the guidance on CLP).

Science Needs in Support of REACH Network

For most member companies of ECETOC, a special focus in 2010 was to finalise the first registration dossiers for REACH. To support an effective implementation of the legislation, the Scientific Committee has started to look for areas where scientific opinions need to be further developed. These should then be proposed for the on-going ECETOC science programme. A network of Scientific Committee members, i.e. those actively involved in REACH processes, was convened to share the learning from the review of communication on REACH (e.g. RAC and MSC documents, TGD updates) and discuss upcoming issues. A focussed event in early 2011 is being planned to gain input from the wider ECETOC membership.

Understanding the relationship between extraction technique and bioavailability

An ECETOC Workshop 'Significance of Bound Residues in Environmental Risk Assessment' was held on 14-15 October 2009 in Brussels. The conclusions (see ECETOC Workshop Report No. 17) state that 'non-extractable residues are currently characterised by a pragmatic extraction approach by determining whether they are extractable or not. This extraction approach has been historically implemented with various solvents under varying conditions and not necessarily linked to the properties of the chemical, nor the matrix. There is a need to develop a standard framework for extraction methods and to associate the extractable fractions (leachable and NER [non-extractable residues]) with both a level of bioavailability (accessibility) and appropriate test organism(s) for the appropriate environmental compartment. It is recognised that the development of new methods to screen bioavailability of such fractions may be needed to validate this association. This exercise would support a consistent interpretation of the data and provide a transparent basis for assessing the potential risk of NER.

Consequently, an ECETOC Task Force has been commissioned to develop a framework for intelligent extraction strategies with the following terms of reference:

- Review current literature describing extraction methods for various chemical groups in different environments and how these different methods correlate with the bioavailability of chemicals in different media.
- Understand the current state of knowledge regarding the mechanisms of binding which may contribute to the rationale for defining the appropriate extraction methods.
- Understand the threshold where extractive techniques transition to 'destructive' methods, resulting in the loss of sample matrix integrity and subsequent ability to characterise the intact chemical.
- Propose a framework for an intelligent extraction strategy and make recommendations for future research topics, if necessary.

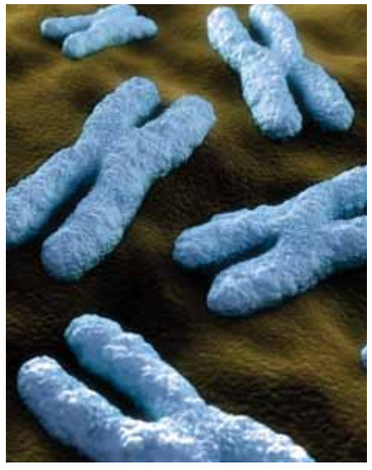
Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals

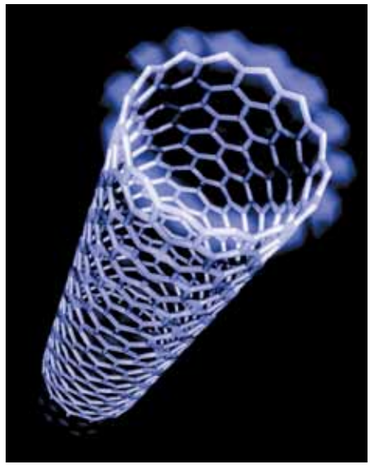
Background Bound residues (BR), including non-extractable residues (NER), are an important factor in PBT (Persistence, bioaccumulation and toxicity) assessment and risk assessment of chemicals. Precautionary risk assessments usually assume 100% bioavailability, i.e. all of the chemical present, is available for degradation or to have potential toxic effects on the biota. This precautionary approach generally overestimates the exposure concentration by the amount that is not available and therefore overestimates the level of risk to biota in the environment. It is also well documented that chemicals that are irreversibly bound to solids are less degradable and less toxic than the total residue would predict. Even though it is a position that has been recognised by ECPA (2000), and referenced by REACH (2008) and OECD test guidance (2002), there is no agreed guidance on how to determine what is available or not, and how it should be considered in the risk assessment.

An ECETOC Workshop 'Significance of Bound Residues in Environmental Risk Assessment' was held on 14-15 October 2009 in Brussels, where thirty-eight leading experts in environmental fate, ecotoxicity and environmental risk assessment participated. The Workshop aimed at reviewing what is known about 'bound residues', to identify what issues may exist in respect to their use and interpretation in environmental risk assessments, and to identify areas of science that require further research. The main output of this Workshop (ECETOC Workshop Report No. 17) was a framework outlining a possible decision tree for improving the risk assessment of NER, together with the identification of key research needs to address gaps in the current knowledge base.

Many of these research projects will take a number of years to deliver and hence there is a clear need to agree an interim approach to address the impact of NER on current risk assessments for aquatic and terrestrial organisms. To this end the Scientific Committee of ECETOC decided to establish a Task Force to:

1. Critically evaluate the proposed risk assessment framework developed following the ECETOC Workshop and assess its utility as an interim approach for regulatory assessment of chemicals.
2. Develop suitable guidance and trigger values to enable the decision tree to be used and test the utility of the scheme using suitable case studies.
3. Provide guidance on study design to provide the appropriate quality of data needed for the risk assessment framework to function within a regulatory decision making system.





Task Forces **completed**

Approaches for read-across in chemical risk assessment

Read-across exploits information on structurally related (similar) analogues to derive hypotheses about the activity of the new chemical and hence predict its toxicity without experimental testing. Large existing databases on traditional toxicological endpoints and mechanisms of action are available that can be searched by data mining and cheminformatics tools (a selection is presented in the report). In addition, high-information-content techniques such as 'omics (toxicogenomics and metabolomics in particular) can be utilised to generate and test these hypotheses, notably about the mechanism of action. Examples are given in the report for phthalates, oestrogens and skin sensitisers.

There is scope for improvement of the heuristics of analogue identification and hypothesis generation. Furthermore, real examples of using high-information-content data are needed to support read-across, e.g. to provide a biology based rationale for chemical grouping.

The report, 'High information content technologies in support of read-across in chemical risk assessment', published as Technical Report No. 109, presents a synopsis and recommends new research. It includes a request for proposals for the Cefic LRI.

Guidance on assessment factors to derive DNEL

In the REACH Technical Guidance Document, chapter R.8 'Characterisation of dose [concentration]-response for human health' proposes a tiered and systematic approach for the delineation of DNEL (and DMEL). This approach is supported by ECETOC in principle, but it appeared advisable to provide additional scientific arguments and recommendations for the derivation of DNEL (to note: DMEL were not addressed). This Task Force, starting its work in mid-2009, critically assessed the approaches laid out in the REACH TGD, re-visited the previously published guidance on assessment factors (TR 86) and supplemented this with an updated review of the literature published on this topic during the intervening years. For most chemicals a DNEL will solely be based upon animal data. But for some health effects data derived in humans will be an additional and important source of information. Hence, the conclusions from TR 104, providing a guide for an integrative framework for human and animal data, have also been referred to in the report. The overall guidance by the Task Force has been published as Technical Report No. 110.

ECETOC, in line with the R.8 guidance, recognise that the use of 'informed' assessment factors is preferred over 'default' assessment factors wherever possible, whether supported by substance-specific data or, for example, by read-across to other chemicals or mechanisms of action. The use of informed assessment factors for hazard and risk assessment is well-established and has been used for many years by organisations such as the Scientific Committee on Occupational Exposure Limits (SCOEL) and national competent authorities to set occupational exposure limits. The guidance in TR 110 is illustrated by a number of case studies drawn from, for example, SCOEL documentation, for which the outcome of assessments based on default (REACH TGD, chapter R.8) versus ECETOC recommended assessment factors has been compared.

Workshops **held**

Omics in (Eco)toxicology: Case Studies and Risk Assessment 22-23 February 2010

In 2007, ECETOC organised a Workshop on the application of 'omics technologies in toxicology and ecotoxicology. In 2010 a Workshop was held in Malaga on 22 and 23 February to review the progress made since then on the application of 'omics technologies to chemical safety, and assess the potential impact of these new technologies on the risk assessment of chemical substances.

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

The following conclusions were drawn in a final plenary session:

- 'Omics data are particularly valuable for understanding modes of action (MoA) via underlying molecular patterns and by exploring

responses to model compounds in highly standardised systems.

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

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

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

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

Guidance on Assessment Factors to Derive DNEL, 25 March 2010

As part of the Task Force activity with the same title (see under Task Forces completed), a Workshop was organised on 25 March 2010 in Barza d'Ispra/Italy. The draft guidance was presented and demonstrated by a number of case studies. A parallel project carried out by the Fraunhofer Institute for Toxicology and Experimental Medicine for the detergent's industry initiative ERASM (Environmental Risk Assessment and Management) was also presented in the Workshop. The participants, amongst them representatives from regulatory authorities, discussed the proposals and assessed where the science could be further developed in support of the implementation of REACH. Feedback received was taken into account in the final TR 110. The outcome of the Workshop has been published as Workshop Report No.20.

Symposium: Innovation through Nanotechnology and Nanomaterials, 22-24 April 2010

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

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

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

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

Following the Symposium, a half-day discussion took place about '*in vitro* - *in vivo* extrapolations for inhalation studies', attended by about a quarter of the Symposium's participants.

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The topics discussed can roughly be clustered as:

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

Publication of the presentations and overall outcome in a learned journal is in progress.

Symposium: Use of 'omics to elucidate mechanism of action and integration of 'omics in a systems biology concept 16 September 2010

ECETOC and EEMS (European Environmental Mutagen Society) have jointly organised a Symposium entitled 'Use of 'omics to elucidate mechanism of action and integration of 'omics in a systems biology concept'. The Symposium was co-funded by CEFIC-LRI and held on 16 September 2010 as part of the annual meeting of EEMS in Oslo. The organisation of regular symposia has allowed ECETOC and EEMS to continue a successful relationship for more than 10 years. The papers of these symposia form critical state-of-the-science reviews; they have been published in the open literature.

This year's Symposium in Oslo consisted of the following topics and speakers:

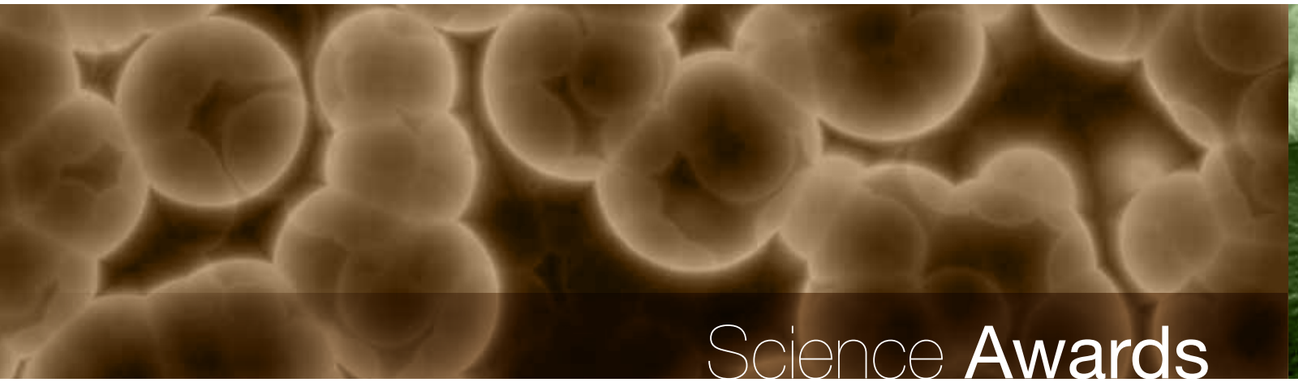
- Welcome – Neil Carmichael, ECETOC.
- Liver toxicogenomics within the pharmaceutical industry: From *in vivo*, to slice, to permanent cell line – Willem Schoonen, MSD.
- Sources of variation in baseline gene expression levels from toxicogenomics study control animals – Chris Corton, US EPA.
- Metabolomics, a tool for early identification of toxicological effects and an opportunity for biologically based chemical grouping under REACH – Bennard van Ravenzwaay, BASF.
- Toxicogenomics for genotoxicity and carcinogenicity prediction: The role of microRNA – Joost van Delft, University of Maastricht.
- Prediction in the face of uncertainty: A Monte Carlo strategy for systems biology of cancer treatment – Christoph Wierling, Max Planck Institute for Molecular Genetics.
- Closing remarks – Bennard van Ravenzwaay, BASF.

The whole session including debate after each presentation was attended by up to 200 persons. It was chaired by Jos Kleinjans, University of Maastricht and Gunnar Brunborg, Norwegian Institute of Public Health.

The above-mentioned speakers are a selected group of scientists who had made similar presentations at the ECETOC Workshop on the 'Use of 'omics in (eco) toxicology: Case studies and risk assessment' held in Málaga in February 2010 (Workshop Report No.19). The conclusions of the Symposium in Oslo are fully in line with those made at the Málaga ECETOC Workshop. Both events built on an earlier ECETOC Workshop in 2007; 'Application of 'omic technologies in toxicology and ecotoxicology' (Workshop Report No. 11).

The conclusions of the recent Oslo Symposium (based on the previous ECETOC Workshops) can be summarised as follows:

- 'Omics sciences are taking their place among other hazard and risk assessment tools and are particularly valuable for understanding modes of action.
- 'Omics sciences add value to risk assessment by improving mechanistic understanding and identifying modes of action. However, 'Omics sciences at this time cannot be used for quantitative risk assessments – transcriptomics may be more sensitive than classical toxicology, whereas metabolomics appears to be equally sensitive. Alterations in individual parameters in 'omics studies are unsuitable to derive NOAELs. 'Omics NOAELs should be based only on specific patterns of change for potentially relevant biological effects, causally related to an adverse effect.
- Specific patterns of change obtained in 'omics studies are being developed and used for the early identification of toxicological modes of action in the screening for novel compounds.
- These technologies can potentially serve as a tool for prioritisation of chemical testing and could provide a better (biology-based) rationale for chemical grouping under the REACH legislation.
- Good quality study design and data are essential to improve the confidence level and increase the likelihood of regulatory acceptance.



Science Awards

With the objective to recognise 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 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 2010 ECETOC SPONSORED THE FOLLOWING AWARDS FOR YOUNG SCIENTISTS AND IS PROUD TO ANNOUNCE THIS YEAR'S WINNERS:

Environmental science related award

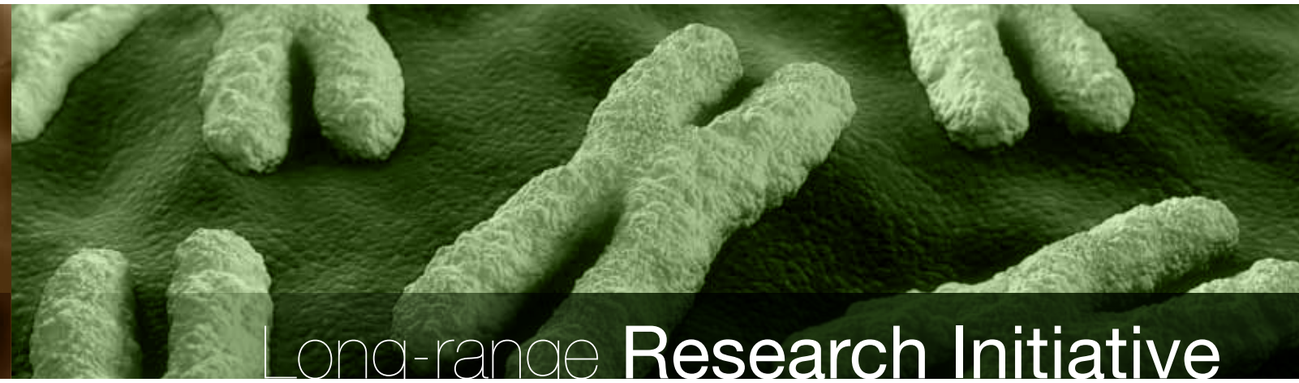
This year's Young Scientist Award on environmental research was won by **Anne-Marie Boulay** from the École Polytéchnique, Montréal, Canada.

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

Human health science related award

This year's Young Scientist Award on human health related research has been awarded to **Céline Brochot**, INERIS, France, and to **Taku Tanaka**, University Piacenza, Italy, for their work on combining multimedia models with physiologically based pharmacokinetic (PBPK) modelling as part of the European project 2-FUN.

Their work was presented in a poster at this year's meeting of the IUTOX (International Union of Toxicology) / EUROTOX congress on 19-23 July 2010 in Barcelona.



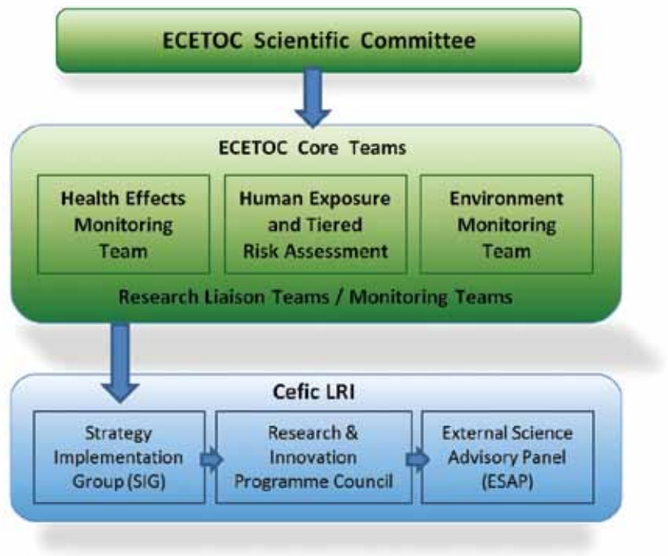
Long-range Research Initiative

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 co-ordinating 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 2010 with the support of specially recruited selection teams (below marked with *). One project was successfully finalised: 'Evaluation of signal transduction pathways in model organisms as critical mediators of developmental toxicity' and publication in the open literature is in preparation. The current research portfolio under the health effects programme looks as follows.:

Theme: Presence of chemicals in humans

Mixtures
- The capacity of the endocrine system to cope with combined exposure to exogenous endocrine active substances at environmentally relevant concentrations (*)

Theme: Methods

Intelligent / integrated testing strategies (ITS)
- Overcoming current limitations in metabolism prediction of industrial chemicals
- A toxicogenomic approach to enhance the specificity and predictive value of the murine local lymph node assay
- Mechanism-based characterisation of systemic toxicity for RepDose database substances employing *in vitro* toxicogenomics *

'Omics and related technologies
- Characterisation of testicular toxicity using traditional and omic tools **

Risk assessment of innovation
- Tiered approach to testing and assessment of nanomaterial safety to human health

Theme: Science of risk assessment

Role of Chemicals in Causality of Disease
- Reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors ** / ***
- Assessment of risk factors influencing trends in incidence of female breast carcinoma

** Also addresses the Strategic Science Area: Reproductive health

*** Also addresses the Strategic Science Area: Sensitive sub-populations

Human Exposure and Tiered Risk Assessment **Monitoring Team**

Indoor air contaminants represent a widespread and sometimes significant source of exposure, particularly when seen within the context of the extended time periods in which individuals spend their work and leisure time. In addition, there is no standard methodology by which the potential health risks might be characterised and compared.

Theme: Presence of chemicals in humans

Chemicals in indoor air
- A new project was started on '**Integrated exposure for RA in indoor environments**' project builds on existing databases and integrating existing models, covers different routes and various agents of consumer exposure. The research includes human biomonitoring and other approaches like fuzzy logic and neural networks. GIS visualisation is envisaged.

Mixtures
- Many substances are present in several different types of products or articles (sources) that may be used or come in contact with one same person in the course of time. There is an increasing realisation of the need to consider the potential exposure to a substance as a consequence of its presence in multiple sources. Consequently, a new project was begun on '**Realistic estimation of exposure to substances from multiple sources**'. Using a tiered approach, from mechanistic to probabilistic, the project aims to estimate multiple/aggregate exposure. The proposal covers consumer and other indoor environmental chemicals. Several models will be linked into one 'expert system'. Similarly, another new project was started to enable realistic estimations of '**Aggregate exposures to household chemicals**', i.e. exposure to one chemical from different household consumer products, this time using a modelling approach. Current models have not yet been systematically evaluated against experimental measurements (e.g. biomonitoring). PBPK modelling will be used to compare biomonitoring to multi-source exposure calculations. In this process, the suitability of biomonitoring for aggregate exposure model validation will be assessed.

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Chemicals in human tissue

By the year end, the project on '**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**' was completed. It concerns a generic, cross-chemical predictive PBTK-model with multiple entry routes running as application in MS Excel. The model enables simulation of the level of chemicals in body tissue/fluid levels under various exposure scenarios. A related project was continued on the '**Development of a tiered set of modelling tools for derivation of biomonitoring guidance values**'. Both computational tools were developed to assist in the derivation of biomonitoring guidance values.

Theme: Methods

Intelligent / integrated testing strategies

On '**TTC for inhalation exposure'** (tiered risk assessment), the HETRA group assisted by external experts could recommend one proposal for research. The selected project is expected to aid in the evaluation of existing toxicity studies regarding toxic potency (NOAEL versus benchmark dose, kinetics/metabolism, and route specific differences), MoA and structural alerts (including descriptors of irritant potency). This is should improve the criteria for structural alerts and lead to better definition or replacement of the existing Cramer classes used to derive different TTC values. The emphasis will be to develop a new TTC approach for inhalation exposure and compare this with existing concepts for oral exposure. A decision tree approach could be developed for this exposure route.

Environment **Monitoring Team**

Two new projects secured funding and were initiated in 2010 with the support of the Liaison Research Teams. These were: 'Evaluation of test methods for measuring toxicity to sediment organisms', and 'Critical evaluation of individual and combined natural and synthetic endocrine active compounds in fish: an *in vitro* & *in vivo* approach'. The current research projects under the Environment Monitoring Team look as follows:

Theme: Presence of chemicals in the environment

Exposure issues
- Cross taxonomic biotransformation potential
- Relationships of biotransformation across organisms (2 projects)
- Environmental relevance of laboratory bioconcentration test
- Influence of microbial biomass and diversity on biotransformation
- Applying and verifying PBT/POP models through comprehensive screening of chemicals
- 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: Effects in humans and ecosystems

Reproductive health
- Critical evaluation of individual and combined natural and synthetic endocrine active compounds in fish: an *in vitro & in vivo* approach

Theme: Methods

Intelligent / integrated testing strategies
- Fish cell line & embryo assays
- Development and validation of abbreviated *in vivo* fish concentration test
- Evaluation of test methods for measuring toxicity to sediment organisms

Risk assessment of innovation
- Assessment of nanoparticles specific effects in environmental toxicity testing

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.

Technical Reports address specific applications of the science of chemical risk assessment.

Workshop Reports are summaries of the discussions and conclusions derived from ECETOC's Workshops.

JACC Reports (Joint Assessment of Commodity Chemicals) are comprehensive reviews of toxicological and ecotoxicological data on individual chemical substances.

Special Reports are prepared following requests from external organisations as a basis for their own definite publication.

Finally, ECETOC publishes articles in the open scientific literature.

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Reports published by ECETOC

Technical Reports

No. 109 High information content technologies in support of read-across in chemical risk assessment. (December 2010)

No. 110 Guidance on assessment factors to derive a DNEL. (October 2010)

Workshop Reports

No. 17 Significance of Bound Residues in Environmental Risk Assessment (February 2010)

No. 19 'Omics in (eco)toxicology: case studies and risk assessment (June 2010)

No. 20 Workshop on Guidance on Assessment Factors to Derive a DNEL (December 2010)

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 freely downloaded from www.ecetoc.org.

Articles published in the open scientific literature

☐ Carmichael N, Bausen M, Boobis AR, Cohen SM, Embry M, Fruijtier-Pölloth C, Greim H, Lewis R, Meek ME (Bette), Mellor H, Vickers C, Doe J.

Using mode of action information to improve regulatory decision-making: An ECETOC/ILSI RF/HESI workshop overview.

Critical Reviews in Toxicology, Volume 41, Number 3, March 2011, Pages 175-186 (submitted and accepted in 2010).

* * *

☐ Heinrich J.

Influence of indoor factors in dwellings on the development of childhood asthma.

International Journal of Hygiene and Environmental Health, Volume 214, Issue 1, January 2011, Pages 1-25 (submitted and accepted in 2010) [review commissioned by ECETOC].

* * *

☐ Donner M, Tran L, Muller J, Vrijhof H.

Editorial - Genotoxicity of Engineered Nanomaterials.

Nanotoxicology, Volume 4, Number 4, December 2010, Pages 345-346.

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☐ Donner M, Tran L, eds.

Genotoxicity of Engineered Nanomaterials.

Nanotoxicology, Volume 4, Number 4, December 2010, Pages 345-424.

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

Science based guidance for the assessment of endocrine disrupting properties of chemicals.

Regulatory Toxicology and Pharmacology, Volume 59, Issue 1, February 2011, Pages 37-46 (submitted and accepted in 2010).

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☐ Embry MR, Belanger SE, Braunbeck TA, Galay Burgos M, Halder M, Hinton DE, Léonard MA, Lillicrap A, Norberg-King T, Whale G.

The fish embryo toxicity test as an animal alternative method in hazard and risk assessment and scientific research.

Aquatic Toxicology, Volume 97, Issue 2, April 2010, Pages 79-87.

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Online Communication

During 2010, ECETOC's online presence was further strengthened through revisions to the public website aimed at clearer navigation and easier access to the latest content and newsletters. The emphasis for the members' website was on the continued development of resources for ECETOC Task Forces and Workshops.

External Representation

Representation at specific meetings or input to specific projects:

☐ **CESIO / CES / EFFCI / LRI Workshop: Applicability of skin sensitisation testing methods for regulatory purposes**

Brussels, Belgium
02-03 February 2010

ECETOC was represented by Christa Hennes of ECETOC.

☐ **JRC Workshop: Aquatic ecotoxiology – can we improve its influence on policies and risk management**

Copenhagen, Denmark
06-07 May 2010

ECETOC was represented by Stuart Marshall of Unilever.

Representation in on-going expert groups:

☐ **WHO/IPCS Harmonization Project Core Group**

ECETOC was represented by John Doe of Syngenta and Chairman of the ECETOC Scientific Committee, followed by Ben van Ravenzwaay of BASF, Member of the ECETOC Scientific Committee.

☐ **Consultative Forum on Environment and Health** organized by EU Commission

ECETOC was represented by Peter Boogaard of Shell.

☐ **ECHA Risk Assessment Committee (RAC)**

ECETOC was represented by Marie-Louise Meisters of DuPont and Chris Money of ExxonMobil.

☐ **ECHA Member States Committee (MSC)**

ECETOC was represented by David Owen of Shell and Neil Carmichael of ECETOC.

☐ **ECHA Committee for Socio-Economic Analysis (SEAC)**

ECETOC was represented by Christa Hennes of ECETOC who presented the status of its related Task Force at a SEAC meeting in March 2010 in Helsinki.

☐ **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 of ECETOC.

☐ **6th Framework Programme Integrated Project 'OSIRIS'**

ECETOC was represented in the Advisory Panel by Watze de Wolf of DuPont, followed by David Owen of Shell. Christa Hennes of ECETOC participated in the third OSIRIS stakeholder Workshop in March 2010 in Berlin.

☐ **6th Framework Programme Co-ordination Action Project 'NORMAN'**

ECETOC was represented in the Advisory Panel by Watze de Wolf of DuPont, followed by Stuart Marshall of Unilever.

☐ **OECD Working Party on Manufactured Nanomaterials**

ECETOC was represented (via BIAC) in the project on alternative methods in nanotoxicology by Monika Maier of Evonik, David Warheit and Mike Kaplan, both of DuPont.

☐ **Nanogenotox EU-Funded Joint Action**

ECETOC participated in the stakeholder consultation via Maria Donner of DuPont and Markus Schulz of BASF.

Presentations and Posters

☐ **SETAC Europe Annual Meeting**:

Seville, Spain
23-27 May 2010

- Guidance on identification of endocrine disrupting chemicals *(platform and poster presentation by Arnd Weyers, Bayer CropScience).*
- Risk assessment approaches for PBT/vPvB or POPs *(poster with communication by Ian Malcomber, Unilever).*
- Bound residues (*poster in the LRI booth by Malyka Galay Burgos, ECETOC).*

☐ **ECPA Regulatory Conference**

Seville, Spain
27-28 May 2010

ECETOC was represented by Neil Carmichael of ECETOC; he presented the ECETOC report on 'Guidance on identification of endocrine disrupting chemicals'.

☐ **IUTOX 2010**

Barcelona, Spain
19-23 July 2010

WHO framework (on combined exposure to multiple chemicals in risk assessment) case study: carbamates *(platform presentation by Elizabeth Shipp of Bayer Cropscience).*

☐ **Society for Risk Analysis Annual Meeting**

Salt Lake City, USA
05-08 December 2010

Integration of Human and Animal Data in Chemical Risk Assessment *(poster presentation by Dr Karlene S. Lavelle (ExxonMobil Biomedical Sciences, USA).*

☐ **SETAC North America Annual Meeting**

Portland, Oregon, USA.,
07-11 November 2010

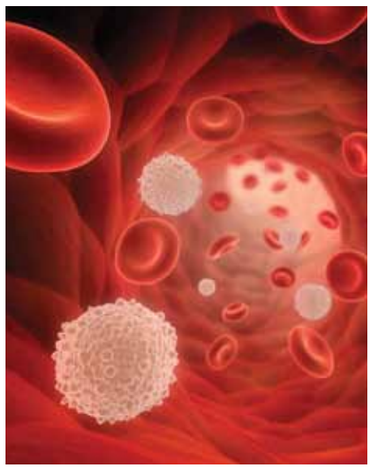
Bridging Science With Communities

ECETOC was represented by Todd Gouin of Unilever.

Members of the Scientific Committee

At the end of 2010, the Scientific Committee comprised the following members:

Fraser Lewis (Chairman)	Syngenta
David Owen (Vice Chairman)	Shell Chemicals
Remi Bars	Bayer CropScience
Peter Calow	Roskilde University
David Farrar	Ineos Chlor
Andreas Flückiger	F. Hoffmann-La Roche
Helmut Greim	Technical University Munich
Guiseppe Malinverno	Solvay
Stuart Marshall	Unilever
Chris Money	ExxonMobil Chemical
Mark Pemberton	Lucite
Carlos Rodriguez	Procter & Gamble
Dan Salvito	RIFM on behalf of IFF
Gerard Swaen	Dow Chemical
Johannes Tolls	Henkel
Saskia van der Vies	Amsterdam Free University
Ben van Ravenzwaay	BASF
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

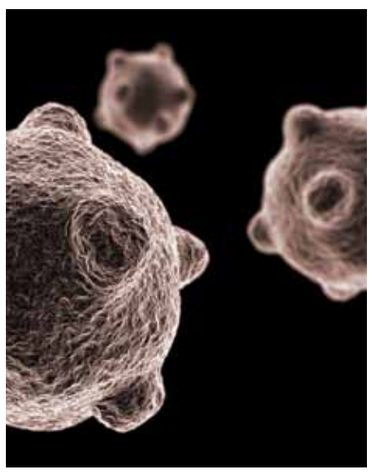
Ian Cummings
Communication, Web & Media Manager

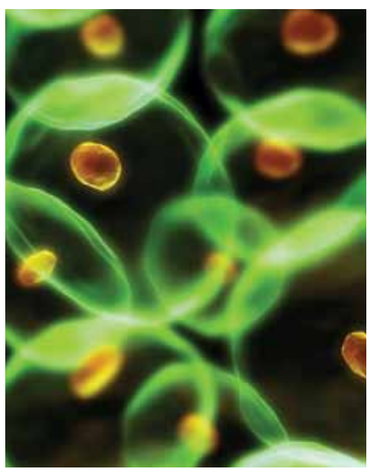
Geneviève Gérits
Office Manager

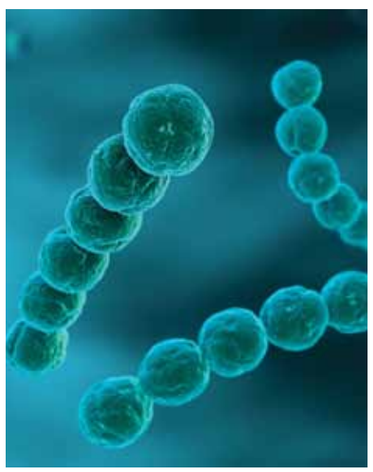
Christine Yannakas
Administrative Assistant

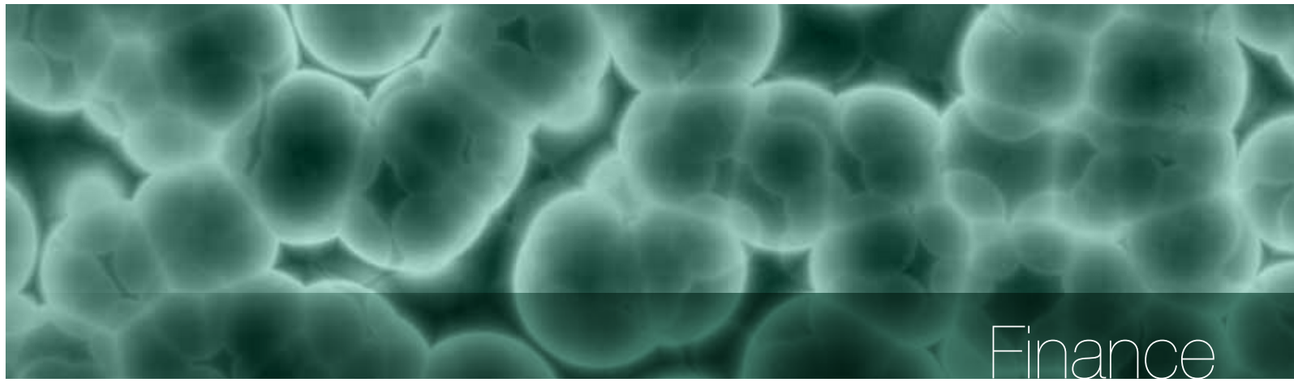
Anita Jennings
Administrative Assistant

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.









Finance

INCOME ACTUAL 2010 IN EURO

Subscription	
43.5 Full Members	1,370,250
5 Associate A Members	45,000
0 Associate B Members	
Total Subscription Income	1,415,250
Bank interest	3,756
Document sales	0
Project-related	244,901
Total	**1,663,907**

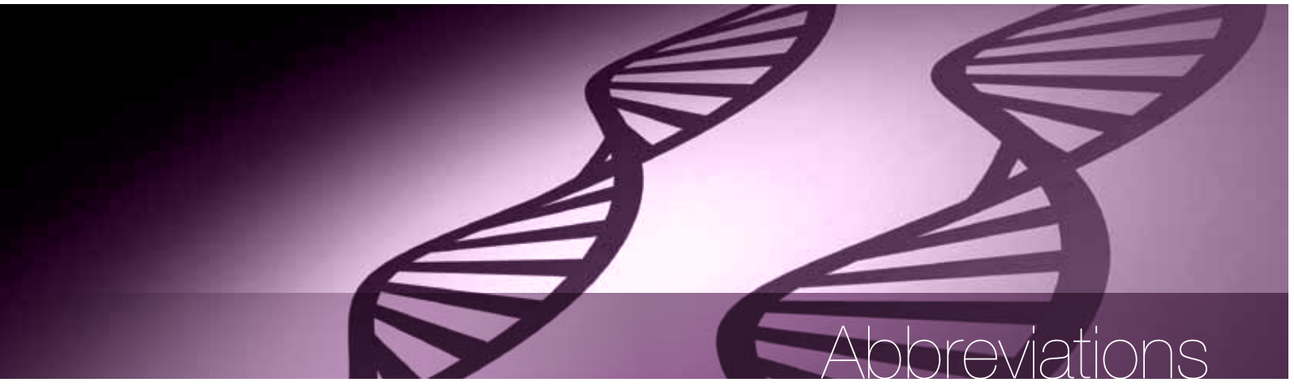
EXPENDITURE ACTUAL 2010 IN EURO

Salaries (and related expenses)	930,188
Office running expenses	201,067
Travel expenses on mission	8,287
Meetings and consultants	315,659
Professional services	13,219
Bank charges	2,237
Capital expenditure	4,943
Publications	25,435
Miscellaneous	10,037
Website	13,070
Total	**1,524,142**

BALANCE SHEET AND RESERVES ACTUAL 2010 IN EURO

Balance Sheet	
Income	1,663,907
Expenditure	1,524,142
Operating margin	139,765
Reserves*	
Opening	1,851,612
Operating margin	139,765
Closing reserves	**1,991,377**

* Estimated Reserve Required: 595.000



Abbreviations

AIMT
CEFIC's Alternative Issues Management Team.

BCF
Bio-concentration factor.

BIAC
Business and Industry Advisory Committee to the OECD.

BR
Bound residue.

CBB
Critical Body Burden.

Cefic
European Chemical Industry Council.

CES
Centre Européen des Silicones.

CESIO
European Committee of Organic Surfactants and their Intermediates.

DMEL
Derived minimum effect level.

DNA
Deoxyribonucleic acid.

DNEL
Derived no effect level.

ECB
European Chemicals Bureau.

ECHA
European Chemicals Agency.

ECPA
European Crop Protection Association.

ECVAM
European Centre for the Validation of Alternative Methods.

EEMS
European Environmental Mutagen Society.

EFFCI
European Federation for Cosmetic Ingredients.

EFSA
European Food Safety Authority.

EMT
Environment Monitoring Team.

EPA
(US) Environmental Protection Agency.

ERA
Environmental risk assessment.

ERASM
Environmental Risk Assessment and Management.

ESAC
ECVAM Scientific Advisory Committee.

EU
European Union.

EUROTOX
Association of European Toxicologists and European Societies of Toxicology.

GHS
Globally Harmonized System of Classification and Labelling of Chemicals.

GIS
Geographic Information System.

HEMT
Health Effects Monitoring Team.

HETRA
Human Exposure and Tiered Risk Assessment Monitoring Team.

IFF
International Flavors & Fragrances.

IPCS
International Programme on Chemical Safety.

ITS
Intelligent / integrated testing strategies.

IUTOX
International Union of Toxicology.

JACC
Joint Assessment of Commodity Chemicals.

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

LRI
Cefic's Long-range Research Initiative.

MoA
Mode of action.

MSC
ECHA Member States Committee.

MWCNT
Multi-walled nanotubes.

NER
Non-extractable residues.

NM
Nanomaterials.

NOAELs
No observed adverse effect level.

OECD
Organisation for Economic Cooperation and Development.

PBPK
Physiologically-based pharmacokinetic (modelling).

PBT
Persistence, bioaccumulation and toxicity.

PBTK
Physiologically-based toxicokinetic (modelling).

PDMS
Polydimethylsiloxanes.

PEG
ECHA Partner Experts Groups.

PNEC
Predicted no effect concentration.

POP
Persistent organic pollutant.

RA
Risk assessment.

RAC
ECHA Risk Assessment Committee.

REACH
EU regulatory framework for the Registration, Evaluation and Authorisation of Chemicals.

REACH TGD
REACH Technical Guidance Document.

RepDose
Fraunhofer ITEM database of NOELs/ LOELs in repeated dose studies.

RfP
Request for proposal.

RIFM
Research Institute for Fragrance Materials.

RNA
Ribonucleic acid.

RSS
Really Simple Syndication (web feed format).

SCOEL
Scientific Committee on Occupational Exposure Limits.

SEAC
ECHA Committee for Socio-Economic Analysis.

SETAC
Society of Environmental Toxicology and Chemistry.

SIG
LRI Strategy Implementation Group.

SSD
Species Sensitivity Distributions.

SVHC
Substances of Very High Concern.

TGD
Technical Guidance Document.

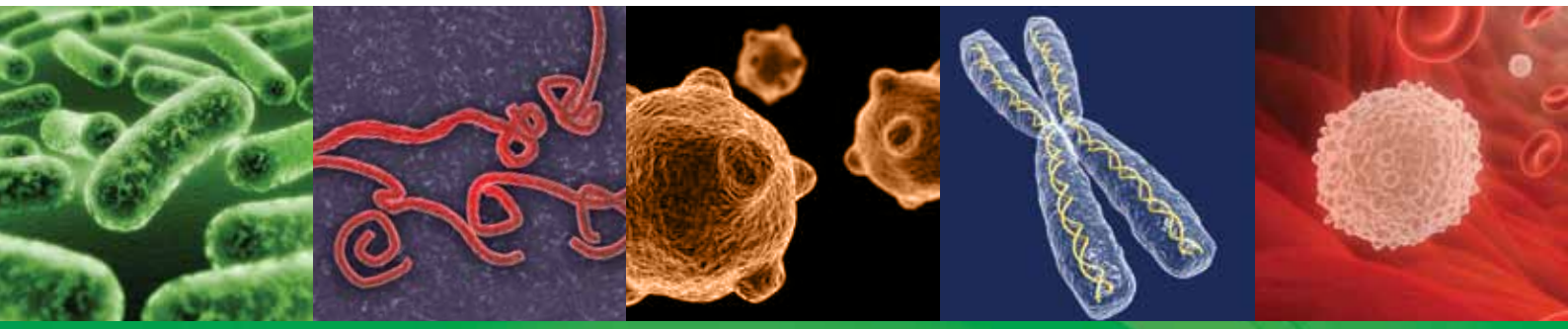
TMF
Trophic Magnification Factor.

TTC
Threshold of Toxicological Concern.

UN
United Nations.

vPvB
Very persistent very bioaccumulative.

WHO
World Health Organization.



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

ECETOC AISBL

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