ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

Annual Report 2007

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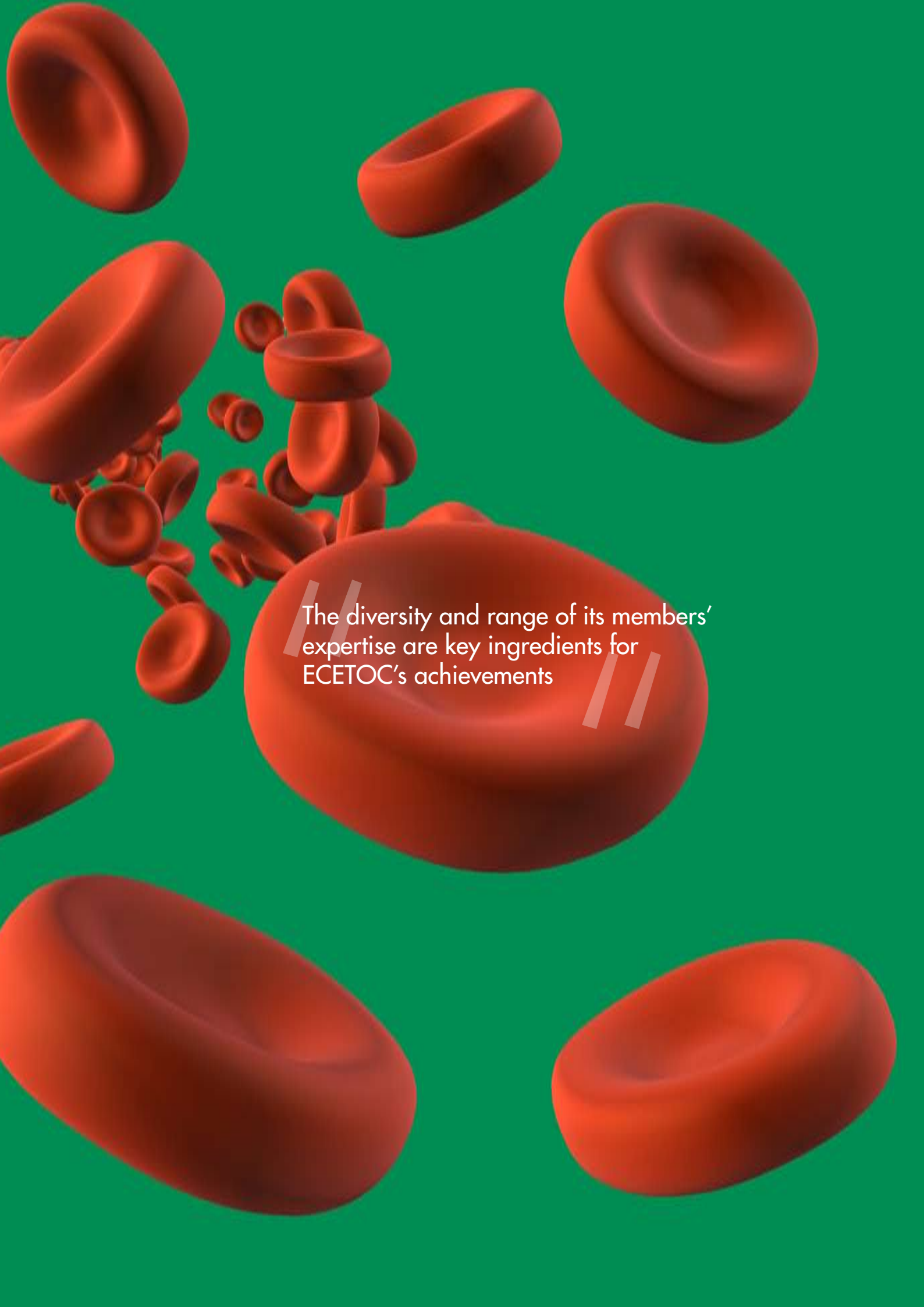


"The diversity and range of its members' expertise are key ingredients for ECETOC's achievements"

INTRODUCING ECETOC

ECETOC was established in 1978 as a scientific, non-profit making, non-commercial association and counts 51* of the leading companies with interests in the manufacture and use of chemicals as its members. An independent organisation, it was established to provide a scientific forum through which the extensive specialist expertise of manufacturers and users could be harnessed to research, review, assess and publish studies on the ecotoxicology and toxicology of chemicals.

The Association's main objective is to identify, evaluate and through such knowledge help industry to minimise any potentially adverse effects on 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 intergovernmental agencies, health authorities and professional institutions.

ECETOC is governed by a Board of Administration comprising up to twelve 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 output 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.

VISION

To be the leading European health and environmental science organisation addressing the safe manufacture, supply and use of chemicals, biomaterials and pharmaceuticals.

MISSION

To use scientific evidence and expert judgement to ensure robust human and environmental risk assessment of chemicals, biomaterials and pharmaceuticals.

APPROACH

ECETOC pursues its vision and mission according to 5-10 year issues-based strategy that was launched in 2007. It has been be broken down into thirteen strategic science areas (see chapter entitled Scientific Programme), grouped according to five themes: chemicals in humans; chemicals in the environment; the adverse effects of chemicals, methods by which we can make assessments and the science of risk assessment.

* as of 1 January 2008

ECETOC MEMBER COMPANIES

At the start of 2008, ECETOC membership comprised the following 51 companies:

3M
AKZO NOBEL
ALBEMARLE CORPORATION *
ALTANA
ARKEMA The world is our inspiration
AstraZeneca
BASF
Bayer *
BORAX
BOREALIS
bp
Ciba
Clariant
Coca-Cola
COLGATE-PALMOLIVE
degussa. Flavors & Fruit Systems
DOW CORNING
Dow
DSM
DUPONT The miracles of science
ExxonMobil
Roche
Givaudan
Henkel
Honeywell
HUNTSMAN Enriching lives through innovation
ICI
INEOS Chlor
IFF International Flavors & Fragrances Inc.
L'ORÉAL
Lucite International * Going further
MERCK
nanogate *
Nestlé
NOVARTIS
PETRESA *
POLIMERI EUROPA AN ENICHEM|UNION CARBIDE VENTURE
P&G
RECKITT BENCKISER
REPSOL
Rhodia
ROHM AND HAAS
SASOL
SC Johnson
SOLVAY
STATOIL
syngenta
TOTAL
Unilever
WACKER

* = Associate member companies

Manufacturers and users of chemicals 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 sound 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: **www.ecetoc.org/members** where they can keep track of discussions at Scientific Committee level and of 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.

REACH: THE EYE OF THE STORM?

The year in retrospect

As we started out in 2007, the industry and other stakeholders were frantically engaged in drafting documents for REACH RIPs 3.2 and 3.3. ECETOC in particular was involved in 3.3 (information requirements), finalising the work of the EWG's (endpoint working groups), which we had set up and in some cases led. The document writing on that level is now over and it seems like everyone is holding their breath.

Many concepts proposed and promoted by ECETOC have found their way into the final approach. The ITS (Integrated testing strategies) approaches we advocated are a core part of the requirements. Key components of the TRA (targeted risk assessment) online tool will be integrated into the final REACH IT tools for assessment of risk in the first tier evaluation.

Throughout 2007, groups of scientists have been examining where science can make a contribution to those areas which are unresolved in the current technical guidance. Workshops were held in 2007 to make progress on biodegradation methodology; key to assigning the "P" of persistent bioaccumulating and toxic (PBT) chemicals. Likewise, a workshop organised by ECETOC and TNO made great progress in defining the use of human data in the evaluation of chemical safety.

One of the most onerous data requirements in REACH is the area of reproductive toxicology. ECETOC is working in partnership with ECVAM, and inputting to OECD, for the development of methodology which has the potential to significantly reduce animal use and expenditure.

ECETOC in the process

These activities illustrate the value of ECETOC in this process. The implementation of REACH is complex and the outcome is the result of contributions from many sources. On the one hand, political expectations will drive the main approaches, while on the other hand the detail has to be practical. The issue at hand is to make the regulation work and for that, it needs to strike a sound balance between science, policy and practicality. ECETOC's role is to interact with the other stakeholders interested in the detail and to contribute the development of workable methodology.

"The implementation of REACH is complex and the outcome is the result of contributions from many sources."

ECETOC has been able to make considerable progress in 2007 and take advantage of what may be quite a short moment of calm. Companies know that REACH is around the corner and are preparing themselves to deal with its challenges. Many companies expect resources to be stretched in the coming years as the legislation is translated from theory into practice. Those companies which are members of ECETOC will be better prepared than others. They have been involved in the process and they know the content. Through debates with the other stakeholders, they have understood their concerns and refined their own approaches.

ECETOC's value can easily be underestimated in the development of such legislation. If ECETOC did not exist, who would the European Commission turn to for the chemical industry's scientific input? Who would assume the role of finding a consensus in industry's approach?

The immediate and longer term future

In the near future, ECETOC will continue to contribute scientific evidence to the European regulatory process e.g. in areas such as the risk assessment of PBT chemicals. Also on the agenda are some scientific questions, such as what will be the acceptability of QSAR methods, *in vitro* toxicology studies, read across and other approaches? Answers to these questions are urgently needed to avoid unnecessary animal use and contain cost.

It is our intention that the science strategy launched last year will allow us to anticipate and address such issues before they become critical. Sharing the load of winning a generic argument should be repaid in reduced effort on specific issues.

Our ability to share the load depends on our member companies. As 2007 progressed, more mergers and takeovers in our industry were announced and this had an impact on ECETOC membership. We will be losing two member companies in 2008 and with that their scientific and material contributions. As I remarked in my message last year, the resources available to the industry are becoming dangerously stretched. I encourage member companies to continue to support the strategic efforts of ECETOC because it will help them in their struggle with the day to day demands of compliance with the new legislation.

Another reason is to assist their efforts in managing succession. Many of their more senior experts are getting ready for well-earned retirement. Indeed several key individuals took that step last year, including Geoff Randall the former chairman of the scientific committee. Much of the experience gained by those senior scientists was honed in ECETOC task forces at an earlier stage in their careers. Younger scientists benefit enormously from participation in ECETOC task forces. They learn by example from the more experienced members and also contribute energy and new ideas. We encourage member companies to view employee participation in ECETOC activities as a fast track way for them to become more knowledgeable and effective members of their company.

Jochen Rudolph, Evonik Degussa
Chairman of the ECETOC Board of Administration


Younger scientists benefit enormously from participation in ECETOC task forces.

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. Since the start of 2006, two further 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 end December 2007

Jochen Rudolph, Evonik Degussa, *Chairman*

Martin Kayser, BASF, *Treasurer*

David Gartside, AstraZeneca

Charles Murray, Procter & Gamble

Mireille Quirina, DuPont de Nemours

On the occasion of the 2007 Annual General Meeting, and in connection with his retirement from Unilever, ECETOC delegates accepted the resignation of Bart Sangster from the Board.

Having served two years since their last election, the following members' re-election to the Board was unanimously approved at the 2007 annual general meeting: David Gartside (AstraZeneca), Martin Kayser (BASF), Charles Murray (Procter & Gamble Eurocor) and Jochen Rudolph (Degussa).

REPORT FROM THE SECRETARY GENERAL

Implementation of the science strategy

When I arrived at the end of 2006, we were still digesting the output of that year's Annual Technical Meeting, the 'Futures workshop'. By the time we wrote the Annual Report, we had assembled all these great ideas into themes and within those themes, the 'Strategic Science Areas' (SSA). We were still not sure at that point how to give life to this concept. Since then we have developed a working method and we are now using this approach to structure all of the activities of ECETOC, from the Scientific Committee's agenda to the choice of subjects for the 2008 Annual Technical Meeting. The latter being generated around our newest SSA 'Science in Society'.

Science in society

ECETOC's science strategy has given us a new perspective on what we are trying to do here at the association. This came from a realisation that communication of scientific analysis was also part of our 'raison d'être.' Endeavours in developing good science go in vain if the results are ignored. As a result we are starting to probe into the area where natural science and social science overlap. One outcome is the organisation of a symposium to be held at EUROTOX in October of this year entitled: *The role of science in society and industry sponsorship of environmental and health research*. In this symposium, we will attempt to confront the issues in a sensitive but important area. As industry spends a significant amount in the area of health and environmental research, it is essential that this research is trusted and considered on an equal basis with research funded by any other source.

Likewise, the 2008 Annual Technical Meeting will tackle a delicate, but important topic: the cost and benefit of risk reduction. ECETOC's traditional frame of reference is in the tools of risk assessment. The new frontier however, is the quantification of 'acceptable risk' and the transformation of the debate from a subjective to an objective discussion. As always, the emphasis will be on the science.

New technology

Under the theme 'Methods,' one of the SSAs of considerable interest to our member companies is 'Risk Assessment of Innovation.' ECETOC has launched several new activities into this area in 2007. A new task force has been set up to look at the suitability of OECD testing guidelines for testing nanomaterials. Also, and with the support of Cefic-LRI, we held a very successful symposium on the (geno)toxicology of nano-particles.

Another area covered by 'Methods' is the SSA 'Omics and Related Technologies.' Many scientists are sceptical, others are fearful, about the use of this technology in risk assessment. To address this issue and assess the possible role for these techniques, a workshop was organised in Malaga in December.

REACH related activities

As our involvement in the Endpoint Working Groups (EWG's) came to an end, the spin-off activities gathered pace. Many scientific dilemmas were identified during the development of guidance documents. As these appeared, we tried to find ways to resolve them. The regulators and industry have been trying to find a way to use their accumulated knowledge for chemicals which have been in use for many years. In many cases there is experience from exposure to these chemicals in the work-place. This 'human data,' needs to be taken into account in the overall evaluation. A task force is working on a framework for the use of data and they were invited by the European Commission to run a workshop on this topic in cooperation with TNO. The direct result of this workshop is that ECETOC and TNO have now been asked to draft guidance on this subject for the REACH Technical Guidance Document.

A persistent question since the start of discussions on REACH implementation has been the thorny issue of 'PBT' chemicals. ECETOC has already published a technical report on the risk assessment of PBT chemicals at the end of 2005. This report identified experimental uncertainties resulting from the standard laboratory tests for biodegradability. In June of 2007, ECETOC held a workshop near Manchester to discuss the issues with these methodologies and identify research needs to resolve them. This event was co-sponsored by the Environment Agency for England and Wales and attracted participants from academia and regulatory authorities in North America and Europe as well as many ECETOC member companies.

Member company developments

As mergers and takeovers continue apace, it is hard to keep track with member companies disappearing inside others or changing their names. An unfortunate consequence is the loss of ICI due to acquisition by another member company: Akzo Nobel. Borax were acquired by Rio-Tinto several years ago and have now also offered their resignation from ECETOC. In both cases they will remain members until the end of 2008. On the positive side, we were happy to welcome a new member company. Givaudan is one of the world's leading flavour and fragrance companies and has already been active in several ECETOC initiatives.

Strategic networks

ECETOC's ability to influence the scientific world depends not only on the quality of its work, but also on the network of contacts it develops. This year saw continued development of relationships with key actors in the field of health and environmental safety, which can be illustrated with a few examples:

We visited the WHO (IPCS) in Geneva and they reciprocated with a presentation to the scientific committee. We deepened our relationship with organisations with similar vocations, notably ILSI-HESI, which has lead to several joint activities

We developed contacts in the area of animal replacement, refinement and reduction, particularly with NC3Rs in the UK and ECVAM. Our OutReach activity in France has lead to a visit to INERIS, a major French public research institute and an agreement to cooperate when the opportunity arises. Our invitations to experts from many prestigious research and government institutions to participate in our workshops continues to extend our recognition and develop our credibility.

Secretariat developments

When Martin Holt left ECETOC in February 2007 to return to the UK, there was the risk of the environment programme grinding to a halt. Luckily, Martin agreed to help keep key activities going and saw through several to successful conclusion. Others have been handed over to Malyka Galay-Burgos who joined us in September to assume responsibility for the environment programme. Malyka comes from the University of Cardiff and brings extensive expertise in environmental science combined with 'hands on' experience with genomics. The team also welcomed Anita Jennings in April 2007, our new multilingual secretary, bringing our staff back to previous levels.

Neil Carmichael
ECETOC Secretary General

COMMENTARY FROM THE NEW SCIENTIFIC COMMITTEE CHAIRMAN

It was a great honour to take on the role of Chairman of the Scientific Committee in June 2007. I first worked on an ECETOC task force in the early 1980s, and I learned a lot from the experience. I am still learning from my involvement with ECETOC, working both with colleagues I have known for many years and with those I have met recently. They all share a passion for using science wisely and this is the key to the continued success of ECETOC.

I was fortunate to take over from Geoff Randall, who had guided the Scientific Committee to shape the current science strategy which was conceived in 2006. Geoff has a unique ability to engage people and he used that strength in gaining major input from the 2006 Annual Technical Meeting.

The strategy has helped us to decide our scientific programme for the next few years. Our main recent focus has been on providing the European Commission with scientific input for the implementation of REACH. That phase is nearing its end and in 2006/7, we needed to look into the future again to identify the areas where our expertise will be needed. The strategy provides our point of reference for us as we shape our programme of activities.

At the end of 2007 the Scientific Committee reviewed our strategic science areas and we discovered that we had some areas where there were lots of activities, such as in our traditional areas of testing methodology, but also several areas, where we need to invest more efforts. Although we identified "Indoor Air" as a strategic science area, we currently have no activity in this area, so we have started to evaluate what contribution we could make.

"We have to pay attention to how our science is viewed by a wide range of stakeholders, including members of the public."

Our strategy review also revealed that we have to pay attention to how our science is viewed by a wide range of stakeholders, including members of the public. We have also started to develop our thinking in the strategic area of science in society. One area of special concern for us is to examine just how successful the present hazard assessment/risk assessment/risk management paradigm really is in preventing adverse effects. We are looking at a major initiative into the causality of disease, and to the contribution of chemicals to the overall burden.

We are still grappling with how to bring in new technology and understanding into risk assessment. ECETOC held a workshop on the role of genomics in December 2007, which highlighted the need to look at overall pathways rather than individual data points when trying to interpret the results of studies. We must pay equal attention to the development of new safety assessment paradigms, rather than focusing on new methods. The structure that was developed in the 1970s needs a major overhaul, and it will not be possible to implement it for REACH because of the numbers of chemicals involved. This presents us with a massive opportunity to increase the accuracy of our testing strategies and reduce the cost in terms of finance and the use of animals. It also poses a huge threat if new systems are developed which are unnecessarily conservative. Our strategy will help us to deliver a thorough understanding of the science underpinning risk assessment which will be needed to find the right balance.

John Doe, Syngenta
Chairman of the Scientific Committee

Strategic Science Area	2007 Activities
PRESENCE OF CHEMICALS IN HUMANS	
Chemicals in human tissue ECETOC will seek to ensure that the results of biomonitoring studies are placed into appropriate context in the human health risk assessment process.	• Progression of an ECETOC task force to develop an interpretation framework for human data • Monitoring of 4 LRI projects concerning biological guidance values • Monitoring of 3 LRI projects concerning key biomarkers
Chemicals in indoor air The overall aim of this SSA is to address approaches to assess the impact of chemicals found in indoor air on human health.	• *Under review in 2008*
Mixtures The objective is to contribute to the development of a pragmatic, realistic, and science based framework for the risk assessment of chemical mixtures.	• Progression of the assessing mixtures in human health risk assessment ECETOC task force • Progression of the TTC values for industrial chemicals ECETOC task force (monitoring of a project with Fraunhofer Institute ITEM) • ECETOC involvement in the WHO/ IPCS international workshop on aggregate/cumulative risk assessment in March 2007 • Publication of ECETOC Technical Report No. 102 in December 2007 by the task force on using mode of action information to support efficient ecotoxicity testing of specifically acting chemicals
PRESENCE OF CHEMICALS IN THE ENVIRONMENT	
 **Exposure pathways** The presence of chemicals in the environment can be construed to represent a danger to the environment itself and accordingly to human health. This area requires the promotion of an approach which uses sound dose response principles in the evaluation of risk.	•Progression of a task force on biodegradation kinetics •Organisation of workshop... • ECETOC involvement in the EU 6th Framework Programme: NORMAN Project Advisory Committee • ECETOC involvement in the EU 6th Framework Programme: RISKBASE Project Advisory Committee • Monitoring of an LRI project on the integrated environmental fate and human food chain bioaccumulation model for polar and non-polar organic substances • Monitoring and review of 2 LRI projects concerning cross taxonomic biotransformation potential • Monitoring of an LRI project on relationships of biotransformation across organisms

EFFECTS IN HUMANS AND ECOSYSTEMS

Sensitive sub-populations

Certain sub-populations, notably children, may be assumed to be more sensitive than healthy adults. This strategic area is intended to test and explore this hypothesis.

- ECETOC involvement in the EU Consultative Forum on the Health and Environmental Action Plan
- Maintenance of a children's health network, based on members of a former task force

Reproductive health

The overall aim of this SSA is to ensure that the methods and the testing strategy to identify and characterise developmental and reproductive toxicants are appropriate and optimised.

- Launch of an ECETOC task force to develop triggering/waiving criteria for the extended one-generation reproduction toxicity study in July 2007 (see page 20)
- ECETOC involvement in the working group on reprotoxicity potency of the ECB C&L Health Effects Group
- Monitoring of an LRI project entitled: signal transduction pathways and development of alternative approaches to reproductive toxicity testing
- Selection of an LRI project entitled: male reproductive health and endocrine toxicity: application of toxicogenomics

Biodiversity and ecosystems

ECETOC will seek to identify and react to key science issues relevant to global regulatory assessments of chemical impacts on biodiversity of aquatic and terrestrial ecosystems.

- Progression of an ECETOC task force to develop PBT case studies
- Organisation of an ECETOC workshop on the application of 'omic' technologies in toxicology and ecotoxicology in December 2007
- Publication of ECETOC Technical Report No. 102 in December 2007 by the task force on using mode of action information to support efficient ecotoxicity testing of specifically acting chemicals
- Selection of an LRI project about population dynamics modelling for ecotoxicology

Strategic Science Area	2007 Activities
METHODS	
 **Integrated Testing Strategies (ITS)** The overall aim of this SSA is to 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 costs and the use of animals while providing best quality data for the risk assessment process.	• Progression an ECETOC task force to develop an interpretation framework for human data. • Launch of an ECETOC task force on cardiac sensitisation test methods in January 2007 (see page 19) • Launch of an ECETOC task force to development triggering/waiving criteria for the extended one-generation reproduction toxicity study in July 2007 (see page 20) • Launch of an ECETOC task force to review cyanide antidotes in January 2007 (see page 20) • Launch of an ECETOC task force to review the OECD test guidelines for nanomaterials in November 2007 (see page 21) • Launch of an ECETOC task force to enhance the ECETOC online targeted risk assessment tool at the start of 2007 (see page 22) • Progression of the TTC values for industrial chemicals ECETOC task force. • Progression of an ECETOC task force to develop PBT case studies • Progression of the assessment and management of dermal risks from industrial chemicals • Launch of an ECETOC task force in August 2007 concerning potency values from the local lymph node assay and their application to classification, labelling and risk assessment (see page 21)
 **Omics' & 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.	• Publication of ECETOC Technical Report No. 102 in December 2007 by the task force on using mode of action information to support efficient ecotoxicity testing of specifically acting chemicals • Organisation of an ECETOC workshop on the application of 'omic' technologies in toxicology and ecotoxicology in December 2007 (see page 25)
 **Risk assessment of innovation** The purpose of this activity is to develop a series of approaches for addressing the health and environmental risk assessment for innovative products.	• Launch of an ECETOC task force to review the OECD test guidelines for nanomaterials in November 2007 (see page 21) • Organisation of a symposium at EEMS 2007 on the toxicology/genotoxicity of manufactured nanoparticles in September 2007 (see page 24)

SCIENCE OF RISK ASSESSMENT

Role of chemicals in the causality of disease

This strategic area aims to put the presumed associations between chemicals in the environment and disease into its proper scientific perspective

- Launch of an ECETOC task force to critically review the data on the carcinogenicity of formaldehyde (see page 19)

Risk, hazard and precaution

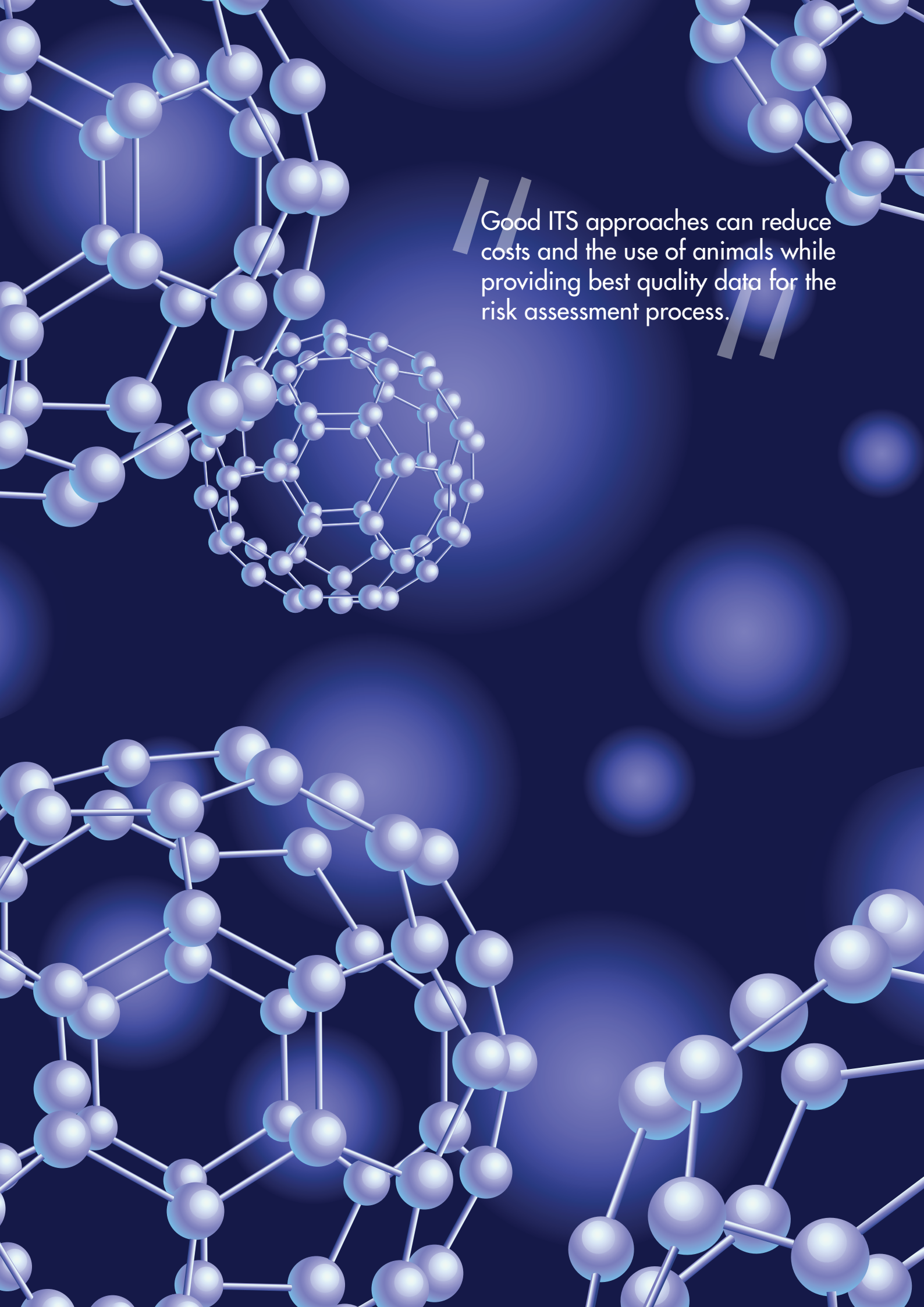
The precautionary principle can lead to unrealistic worst case assumptions based on an evaluation of hazard. It is important to use all available scientific tools to adequately characterise the real risk. This implies increased emphasis on exposure and dose response information

- Progression of an ECETOC task force to develop PBT case studies
- Progression of an ECETOC task force on biodegradation kinetics.
- Progression of the TTC values for industrial chemicals ECETOC task force, which was launched in June 2006
- Launch of an ECETOC task force to prepare guidance for carcinogen classification guidelines under GHS in April 2007 (see page 21)
- Launch of an ECETOC task force in August 2007 concerning potency values from the local lymph node assay and their application to classification, labelling and risk assessment (see page 21)
- Launch of an ECETOC task force on linear polydimethylsiloxanes (see page 21)
- Publication of ECETOC JALL Report No. 53 on cyanides in september 2007
- Co-ordination of REACH RIP 3.3 Endpoint Working Groups
- Member company inputs to RIP 3.2 concerning DNELs, PBTs, Exposure Scenarios
- Organisation of a symposium at EUROTOX 2007 Annual Meeting in October 2007 entitled "from a hazard- to a risk-based classification of carcinogens" (see page 25)

Science in society

ECETOC will seek out activities to promote the use of science in EU decision making to improve the image of industry science with EU policymakers and to enhance the acceptance of science by the general public

- ECETOC will organise two events in 2008.
  A workshop : *'Counting the costs and benefits of chemical control: the role of environmental risk assessment in socio-economic analysis' in June and a symposium 'the role of science in society and industry sponsorship of environmental and health research'* in October. at he Eurotox 2008 annual meeting



"Good ITS approaches can reduce costs and the use of animals while providing best quality data for the risk assessment process."

ECETOC ESTABLISHED THE FOLLOWING NEW TASK FORCES

Carcinogenicity of formaldehyde

The International Agency for Research on Cancer (IARC) announced its intention to review all substances already classified as Human Carcinogens in a future volume of its series of monographs on the evaluation of carcinogenic risks to humans. For each agent that is classified as carcinogenic to humans (Group 1), volume 100 will contain a concise Monograph. This volume will contain fewer details on each agent than are typically found in other monographs, but there will be no reduction of scientific accuracy or quality.

Among compounds to be reviewed will be Formaldehyde which was most recently reviewed in 2004 (with the IARC monograph being published in 2006 (Vol 88)). ECETOC examined the issue of human carcinogenic risk from formaldehyde in 1995 (Technical Report No. 65). But since that time, considerable new data has been generated, in particular via epidemiological and mechanistic studies (which can now be considered by IARC under the principles of the new preamble to monographs).

To contribute on behalf of the chemicals industry, ECETOC established a task force to critically review the following data on formaldehyde: genotoxicity and DNA reactivity, chronic toxicity and carcinogenicity studies in animals, mechanistic studies in animal and human tissue and epidemiological studies in humans. From the above, the task force is requested to provide an appraisal of the nature of the carcinogenic hazard of formaldehyde and the relevance to human risk. This will take the form of a review paper for publication in a suitable peer reviewed journal.

Cardiac sensitisation test methods

It is well known that aliphatic hydrocarbons and their halogenated derivatives can cause sensitisation of the myocardium to the effects of adrenaline, resulting in cardiac arrhythmias. This effect is a key element in the health risk assessment of these substances, in particular, fluorocarbons. The effect can be modelled in dogs, but there is no internationally accepted protocol for the study. Relevant protocols have been developed in the UK and the USA, but they have key differences which might impact on the outcome of the study. Regulatory authorities apply different risk assessment approaches when extrapolating the data to humans. The issue has been the subject of a recent review by Brock *et al*, 2003[a]. In addition, there is a lack of consensus about the mode of action involved. If more fully understood, this could lead to a recommendation for an alternative test or screening protocol.

In response, ECETOC set up a task force to conduct a critical review of the existing protocols for studies in the dog using acknowledged experts in the field (these include experimental practitioners, past and present, supported by the Global Fluorocarbon Producers Forum).

The objectives are to recommend the most appropriate protocol for the conduct of the dog study and provide guidance on interpretation of the

data from the study and its use in risk assessment processes. Furthermore, the task force is asked to comment on the validity of the physiologically-based pharmacokinetic model that has been developed for use with the study. There should also be a discussion of the likely mechanism of the effect with a view to recommending an approach to the development of an alternative method for the assessment of the effect.

[a] *Brock WJ, Rusch GM, Trochimowicz HJ. 2003. Cardiac sensitization: methodology and interpretation in risk assessment. Regul Toxicol Pharmacol 38:78-90.*

Cyanides antidotes

Acute cyanide poisoning, although a rare affliction, is an extremely serious event due to the potentially fatal outcome. Although there is broad agreement on the immediate first aid that should be taken in the event of acute cyanide poisoning, there is no such international agreement on a first line antidote treatment, with different countries favouring different antidote regimes. Current applied antidote therapies include: oxygen and sodium thiosulphate used world-wide, sodium and amyl nitrites mostly in USA, dimethylaminophenol in Germany, dicobalt edetate (Kelocyanor) in UK, and hydroxocobalamine in France. α-ketoglutarate is currently also considered as a potential antidote to cyanide.

The seven above antidotes have been shown to be of some use in the treatment of acute cyanide poisoning. However there has been no attempt made, to date, to rank their efficiency using scientific arguments. Europe's and other world-wide producers of HCN and its common salts have long recognised that the present divergent use of antidote regimes creates confusion and is undesirable. ECETOC with assistance of the WHO International Programme on Chemical Safety (IPCS), therefore, established a task force to review all available data, both company and published, regarding the use and efficacy of cyanide antidotes.

The aim is to identify (an) antidote(s) of choice, taking into account the type of cyanide poisoning:

- HCN and its salts (immediate effect),
- Cyanogenic compounds including cassava, nitriles and nitroprusside (delayed effect)
- Mixed intoxication (e.g. fire smoke CO and cyanide).

Development of triggering/ waiving criteria for the extended one-generation reproduction toxicity study

In the forthcoming EU Chemicals Regulation (REACH), developmental/reproductive toxicity testing will be a key component for the risk assessment of chemicals, and is very resource-intensive in terms of animal numbers, costs and time. However, there are currently no methods in sight that totally replace this kind of safety testing in animals, short- to mid-term. Consequently, new testing strategies leading to a reduction and/or refinement of animal use immediately should be applied as broadly as possible.

In an EPAA (European Partnership for Alternative Approaches to Animal Testing) workshop held on November 14, 2006, which was attended by more than thirty experts from industry, regulators and the EC and hosted by BASF in Ludwigshafen, it was discussed in detail and agreed that the extended one-generation study as developed by the ACSA (ILSI/HESI) project could in principle be applicable to safety testing under REACH as a replacement for the two-generation study (OECD 416). However, it was also agreed that the complex ACSA protocol has to be modified in order to meet the recommendations connected to chemical safety testing. This will deliver animal welfare benefits with regard to both refinement and a reduction in the number of animals used (more than 40 % compared to the two-generation study).

To implement this new test method into safety testing under REACH, however, the methodology has to be formally validated. The validation would consist of setting up a final test protocol (SOP), experimental work (feasibility study) as well as retrospective validation of the endpoints used. US EPA and ECVAM agreed to take the lead on the validation and three companies (BASF, Bayer and Syngenta) volunteered to conduct experimental work.

A major modification of the test protocol for the use under REACH will be to design reliable trigger/waiving criteria for the modules for developmental toxicity testing foreseen in the ACSA protocol. It was agreed that an expert group should be set up to develop these trigger/ waiving criteria. Through cooperation with EPAA, a strong link to the European Commission and to

European regulators will be given.

The work of this task force will be to prepare a discussion paper in which triggering and waiving criteria are proposed (including suggestions, if necessary for validation work) and to prepare a multi-stakeholder workshop in which paper shall be presented and discussed.

Guidance for classification of carcinogens under GHS

The criteria for classification and labelling under the GHS (globally harmonised system) have been finalised. Regulatory authorities worldwide are already beginning to use these GHS criteria and it was noticed that their interpretation varied in different parts of the world. Therefore, it was considered important to develop guidance for the application of the GHS criteria, in particular with respect to the endpoint carcinogenicity. This was also of relevance in the context of REACH as one their implementation projects i.e. RIP 3.6 was to include guidance for the application of GHS under EU regulatory systems.

A task force was commissioned by the Scientific Committee with the aim of developing guidance for the classification of carcinogens under GHS.

Linear polydimethylsiloxanes

In 2007, the European Silicone Industry Association (CES, a sector group under CEFIC) requested ECETOC to update its existing JACC Report on linear polydimethylsiloxanes, in the light of considerable new scientific research conducted on these materials. The task force that was established aims to review all existing literature and other information available to date, and identify gaps in knowledge and propose studies to fill those gaps. The report is expected to serve as a basis for risk assessment, classification and/or setting an occupational exposure limit.

Nanomaterials and OECD Test guidelines

The scientific discussion regarding the properties of nanomaterials has raised the question whether current OECD test guidelines are capable of appropriately addressing their toxicological profile and environmental behaviour. Therefore, the OECD 'Working Party on Manufactured Nanomaterials' established a project to review the existing guidelines and identify possible needs for development of new and/or revision of existing ones by the end of 2008.

The ECETOC Scientific Committee decided to contribute to this process by establishing a task force to review existing OECD Test Guidelines; to identify key endpoints, exposure routes and critical effects; to evaluate whether existing guidelines suitably address these; to develop recommendations for possible needs to generate new or revised guidelines; to develop guidance on how to prepare and administer dosing material for studies; and to evaluate other currently used non-OECD methods *(in vitro/in vivo)* that have potential to be used to refine the testing strategy for the hazard and risk assessment of nanomaterials.

Potency values from the local lymph node assay: Application to classification, labelling and risk assessment

Under the forthcoming REACH legislation and the guidelines for its implementation, testing for skin sensitisation will be limited to the local lymph node assay (LLNA). The measure of potency of skin sensitisation in the LLNA is the EC3 value, i.e. the concentration causing a threefold increase in the lymph node stimulation index. Within the current Directive 67/548/EEC, cut-off criteria for classifying and labelling materials as R43 are based on the percentages of guinea pigs with positive responses in either the Buehler (15%) or the Magnusson & Kligman (30%) tests.

Further to this, concepts are emerging for the assessment of the risk to skin sensitizers which challenge the prevailing paradigm that for skin sensitisation specific concentration-response curves and corresponding no effect

concentrations cannot be derived. The task force will also be requested to collate the current approaches in this field and to evaluate their usefulness for risk assessment.

Targeted risk assessment

The ECETOC targeted risk assessment (TRA) task force reported in 2004 (Technical Report 93), together with a supporting web based tool **(https://www.ecetoc-tra.org)**. Since 2004, over 900 users have registered with ECETOC to gain access to the tool and benefit from its abilities. As part of the process for maintaining the integrity and relevance of the TRA approach, ECETOC has also held a number of stakeholder workshops with experts from member companies and the Competent Authorities with the aim of identifying where and what further modifications may be necessary.

The TRA task force was reconvened in 2006 with the aim of reviewing the current basis for the approach and making recommendations for further improvements. The task force's recommendations were delivered to the Scientific Committee in May 2007 and have subsequently been scoped in terms of the work effort (and costs) required to integrate them into an updated version of the TRA tool. At the same time, the TRA activity has been recognised under the REACH RIP 3.2 activities on the development of Chemical Safety Assessments as been the preferred approach for evaluating (at the Tier 1 level) worker health risks. The RIP 3.2 activity has also concluded that the tool presents the potential for being adopted for evaluating consumer health risks, subject to clarification (and agreement) of the basis of several default assumptions.

The TRA task force is now actively working on ensuring that the environmental portion of the tool receives similar recognition to the human health elements. A project is already underway, with strong interest being expressed by the Commission/ EChA, that serves to provide a user-friendly basis for carrying out environmental exposure assessments (using a spreadsheet version of EUSES) that is linked to suitable default parameters that are representative of current industry situations.

ECETOC is therefore now engaged in active discussion with EChA concerning the role that the TRA activities would serve under REACH, the expectations of EChA relating to the tool (and ECETOC), the ongoing stewardship of the tools scientific integrity, together with issues of funding and resourcing to execute the developments. All in all, the activities of the TRA task force can be seen to have had a profound impact. The concept of tiered risk assessment is now embraced under REACH; parts of the tool have been formally adopted as the preferred approach; and an active constructive discussion has been sustained with the Commission and other regulatory agencies. ECETOC's role in identifying and maintaining innovation in scientific excellence in the area of exposure and risk assessment continues to be recognised.

ECETOC CONCLUDED THE FOLLOWING TASK FORCES:

Fluoroalkanes

ECETOC's Scientific Committee adopted another critical evaluation in the ongoing JACC series reviewing the toxicology and ecotoxicology of selected fluoroalkanes. This time it was an update on difluoromethane (HFC-32) including results of recent and unpublished studies conducted by the Programme for Alternative Fluorocarbon Toxicity Testing (PAFT). Furthermore, work was progressed on a report with toxicity profiles of possible impurities and by-products in commercial fluorocarbons.

Cyanides

In 2007, ECETOC published a critical evaluation of the toxicity and ecotoxicity data of cyanides, including hydrogen cyanide (HCN), sodium and potassium cyanides (NaCN and KCN) and acetone cyanohydrin (ACH), in the 2 volume JACC Report No. 53.

The four cyanides were reviewed together because, under physiological and environmental conditions, they will be present as HCN, which is the common toxic species (ACH dissociates into acetone and HCN). During the preparation of the review, draft versions were made available to the European Commission's Scientific Committee on Occupational Exposure Limits and the WHO International Programme on Chemical Safety for use in its Concise International Chemical Assessment Documents. The document is expected to be particularly useful as a resource for forthcoming hazard/risk assessment under current OECD and EU schemes (OECD Existing Chemicals Programme, EU REACH - Registration, Evaluation and Authorisation of Chemicals).

ECETOC ORGANISED THE FOLLOWING WORKSHOPS:

Refinement of mutagenicity/ genotoxicity testing 23-24 April 2007

The use of alternative testing strategies to reduce the use of animals is becoming increasingly important and alternative approaches have been proposed for some toxicological endpoints but others, such as that for mutagenicity or genotoxicity, still need to be developed for more widespread application.

The aim of this workshop was to review the challenges of current *in vitro* testing and developments for future *in vitro* type tests for mutagenicity and genotoxicity.

Some 40 invited scientific experts from industry, academia, and governmental agencies participated in the event which began with detailed presentations that lead into 5 breakout sessions and concluded with a plenary review of the working group's conclusions.

The workshop concluded that current *in vitro* testing methods were effective in detecting genotoxic carcinogens, albeit with some false positive findings. While current methods can detect genotoxic chemicals, they are relatively ineffective at detecting non-genotoxic carcinogens, so safety testing would benefit from introducing new methods. The workshop identified areas where new improved methods are required and made some specific recommendations for future research on method development e.g. by applying genomic technologies which are detailed in Workshop Report No. 9.

Biodegradation and Persistence, 26-27 June 2007

A conclusion of the December 2006 ECETOC Environmental Programme review was the need to maintain the momentum for improvements to be developed in the approach to biodegradation testing, the STEP workshop and the RIP 3.3 endpoint working group (degradation). Consequently a 2-day workshop, co-sponsored by the Environment Agency for England and Wales, was held 26-27 June 2007. There were 38 participants from academia, industry and the regulatory community. The major output (published as ECETOC Workshop Report No.10) agreed a number of research activities (8 RfPs) that, if funding could be found, would improve the current approaches to the evaluation of the persistence of chemicals in the environment.

The areas identified were:

Validation chemical set
Bioavailability and bound residues

I. Effect of temperature on biodegradation

II. Impact of low substrate concentrations on biodegradation

III. F:M and microbial density and diversity

IV. Role of pre-exposure

V. Measuring half-lives and assessing variability

VI. Analytical methods to support biodegradation

These Requests for Proposal (RfPs) were discussed and prioritised further at the ECETOC Environmental Programme Review Meeting that took place in 17-18 January 2008 in Brussels.

Toxicology/genotoxicity of manufactured nanoparticles, 11 September 2007

For the 9th year in a row, ECETOC, with the sponsorship of Cefic-LRI, organised a symposium at the annual meeting of EEMS, the European Environmental Mutagen. This symposium sought to present new data from on-going industry/ academic projects on genotoxicity and draw attention to related relevant aspects such as characterisation, exposure, transportation, mode of action and immuno-translocation. The programme included presentations on these aspects plus the results of genotoxicity testing of typical nanoparticles (TiO2 and ZnO) and newly engineered nanofibres (nanotubes). The symposium was attended by over 200 (out of a total of 350) conference participants and the audience, including many key scientists, showed a high interest in this new topic. In his conclusions, ECETOC Secretary General, Neil Carmichael highlighted the stability of the test system and specific dosimetry as major challenges for nanoparticle investigations. Earlier, studies often lacked sufficient characterisation of the test material or lacked appropriate control groups, i.e. in the absence of microparticle treated groups, it is impossible to decide whether nanoparticle-mediated adverse effects are intrinsic to the test material or specific for particle size. Even in present studies, a change of conditions might

alter the results and influence the conclusions, especially in *in vitro* models. Material reaching the tissue might have different characteristics, e.g. in case of intratracheal instillation. So far, there were few reports of direct genotoxic effects of nanoparticles. Indirect genotoxicity mediated by toxicity might allow for the derivation of thresholds. In all, to be useful for risk assessment, the model system had to be well characterised and representative of the conditions of exposure.

From a hazard- to a risk-based classification of carcinogens, 9 October 2007

ECETOC organised a session on the aforementioned subject as part of the EUROTOX conference in 2007. It began with an overview on the current situation of carcinogen classification, including the GHS criteria, and the subsequent presentations provided information on developments of new thinking on the topic within different regulatory bodies and organisations.

Comments confirmed that this had been a timely event because it built on on-going discussions about, for example, exposure considerations for the classification and labelling of carcinogens. The session was very well attended and received much positive feedback for the excellent presentations and the engaged audience discussion.

The application of omic technologies in toxicology and ecotoxicology: case studies and risk assessment, 6-7 December 2007

This workshop, held in Malaga on 6-7 December aimed to review progress made 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. It was deemed a success, with the majority of the attendees welcoming the workshop's outcome.

In terms of format, there were a number of short speeches (15 speakers) and 3 syndicates addressed specific questions on conditions to generate omic data, dose-response and predictivity. These were followed by lively discussions in plenary. In all, the 29 participants (both toxicologists and ecotoxicologists) concluded that omics are beginning to find their place among other regular tools for hazard/risk assessment.

Following the event, it is planned that an ECETOC Workshop Report will be written by the organisers (with input from all participants) and a paper, on which some of the speakers will be asked to collaborate, will be published in the open literature.

The workshop proposed developing quality standards and guidance for regulatory purposes (e.g. biomonitoring) and developing a (mechanistic) NOTEL indicative of early patterns of change. In case of ecological change, the NOTEL should allow to extrapolate from individual to population. The workshop recommendations have the potential to stimulate scientific research and will contribute to the development of future activities within ECETOC's science programme.

"ECETOC's role in identifying and maintaining innovation in scientific excellence in the area of exposure and risk assessment continues to be recognised."

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 sound science.

Since then the format of the Award may have varied, however the objectives have remained the same.

In 2007, ECETOC was pleased to be able to issue three types of Science Award:

- for health sciences
- for environmental sciences
- for epidemiology related research.

Health sciences related research

On the occasion of the 2007 EUROTOX (Federation of European Toxicologists and Societies of Toxicology) Annual Congress 7-10 October in Amsterdam, The Netherlands, ECETOC was pleased to present its Young Scientist Awards to two researchers who had worked together on their posters entitled *'Aging influences segment-specific toxicity of the proximal tubule caused by chemicals.I. Histopathological and biochemical findings'* by **Rossella Defazio** et al., and *'II. Gene expression in kidney tissue'* by **Arianna Chiusolo** et al., both from GlaxoSmithKline, Verona, and the Department of Environmental Medicine and Public Health, University of Padova, Italy.

Environmental science related research

Within the framework of its commitment to encourage promising scientists, ECETOC supported the Young Scientist Best Platform Award at the 2007 SETAC (Society of Environmental Toxicology and Chemistry) Europe Annual Meeting, last 20-24 May in Porto, Portugal.

ECETOC was pleased to present this award to **Mr. Thijs van Boxtel** of the Vrije Universiteit Amsterdam for his platform presentation: *'Mechanisms of toxicity of polybrominated phenoxyphenols and anisols of natural and anthropogenic origin in the zebra fish.'*

Epidemiology related research

For the first time in 2007, ECETOC sponsored a young scientist award for epidemiology related science in association with the International Commission on Occupational Health's Scientific Committee on Epidemiology in Occupational Health (EPICOH).

On the occasion of their Annual Congress (Banf, Canada, 9-12 October 2007) this was awarded to **Jennifer Cavallari**, Department of Environmental Health, Harvard School for Public Health, for her poster titled *'Circadian variation of heart rate variability following metal-rich fine particle exposures in boiler maker construction workers.'*

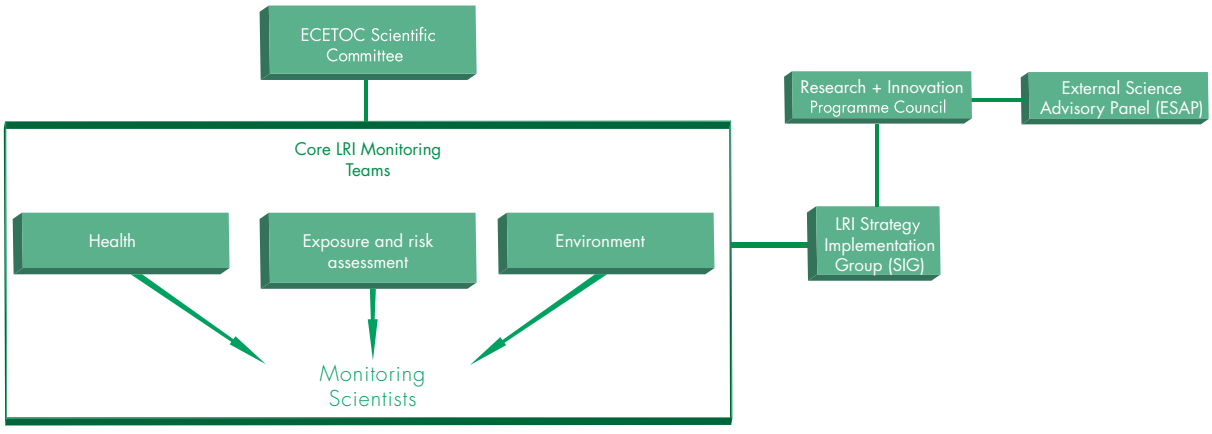
The winners of all three awards have been encouraged to use the awarded prizes for the advancement of their careers.

BACKGROUND

The Cefic Long-range Research Initiative (LRI) is a strategic research programme to identify and fill gaps in our understanding of the hazards posed by chemicals and to improve the methods available for assessing the associated risks. Since the establishment of the programme in 1998, ECETOC has been a partner organisation. In the early days, all requests for proposal (RfPs) were written following ECETOC STOTS (state of the science reviews). As LRI has developed, so the role of ECETOC has evolved. It is now slightly different, but remains key to the programme's success.

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 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

The ECETOC support team for the LRI health effects programme, i.e. the HEMT (health effects management team), continued to monitor the on-going projects under phase II. The selection for a new project 'male reproductive health and endocrine toxicity: application of toxicogenomic technologies to develop a mechanistic-based risk assessment' was successfully completed and the project has started at the end of the year. Proposals for new projects that would fit into the 2008 focus areas of LRI were developed, e.g. on nanomaterials.

Human Exposure and Tiered Risk Assessment (HETRA)

Four new HETRA projects were started in 2007. These concerned the development of guidance values for use in the interpretation of human biological monitoring data. Ongoing investigations looked at the background incidence and variations of key biomarkers in the general population, and the nature of the accidental misuse of chemicals and chemical products.

By the year end, the 'RepDose' inventory of repeated dose toxicity data had been enlarged to include nearly 1,500 experimental studies on 500 compounds. The RepDose database was extended to allow for evaluation of reproductive toxicity and refinement of the threshold of toxicological concern.

Finally, in 2007, a study on the potential application of the human 'intake fraction' as a tool for targeting chemical risk assessments was concluded.

Environment

Subjects, which recent LRI funded environment activites have tackled included cross taxonomic biotransformation potential, a BCF database, a strategy to predict acute fish lethality using fish cell lines and fish embryos, QSARs, the bridge between environmental fate & human health effects modelling, biomagnification, PBTs, omics, biodegradation & persistance and mode of action. In 2007, four new environmental projects secured funding. Two were on the establishment of relationships of biotransformation across organisms, another concerned the investigation of the environmental relevance of the laboratory bioconcentration test and another was on population dynamics modelling for ecotoxicology.

"ECETOC's ability to influence the scientific world depends not only on the quality of it's work, but also on the network of contacts it develops."

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.

ECETOC's own publications now comprise the following:

- Monographs are comprehensive reviews of generic topics or issues fundamental to the application of sound science in evaluating the hazards and risks of chemicals to human health and the environment.
- Technical Reports address specific applications of the science in evaluating the hazards and risks of chemicals to human health and the environment.
- Documents are scientific briefing papers, addressing emerging issues.
- JACC Reports (Joint Assessment of Commodity Chemicals) are comprehensive reviews of toxicological and ecotoxicological data on individual chemical substances.
- Special Reports are compilations of data targeted to specific regulatory issues/ demands.
- Workshop Reports are summaries of the discussions and conclusions derived from ECETOC sponsored scientific workshops.

Reports published by ECETOC

Monographs

No. 37 Biomarkers in Children and Adults
(Published as a special section of Toxicology Letters, by Elsevier, July 2007)

Technical Reports

No. 102 Integrated Testing Strategies in Ecotoxicology: Mode of Action Approach for Specifically Acting Chemicals
(Published December 2007)

JACC Reports

No. 53 Cyanides of Hydrogen, Sodium and Potassium, and Acetone Cyanohydrin (CAS No. 74-90-8, 143-33-9,151-50-8 and 75-86-5)
(Published September 2007)

Workshop Reports

No. 9 Workshop on the Refinement of Mutagenicity/Genotoxicity Testing
23-24 April, Malta
(Published September 2007)

No. 10 Workshop on Biodegradation and Persistence
26-27 June, Holmes Chapel
(Published September 2007)

Complementary ECETOC publications are provided on publication and by request to member companies, the academia, national and supra-national organisations, and a wide range of industry observers such as non-governmental organisations. In addition, ECETOC publications are requested by a range of commercial non-member organisations, who value their contents.

Reports published in peer-reviewed open literature

Testing strategies to establish the safety of nanomaterials: conclusions of an ECETOC workshop.

David B. Warheit, DuPont Haskell Laboratory; Paul J. A. Borm; Hogeschool Zuyd, The Netherlands; Christa Hennes, ECETOC; Jürgen Lademann, Universitätsklinikum Charité, Germany

Inhalation Toxicology
19, 8, 631-643, 2007.

The ECETOC approach to targeted risk assessment; lessons and experiences relevant to REACH

Chris D. Money, ExxonMobil; Sylvia Jacobi, Albermarle; Mike G. Penman, ExxonMobil Biomedical Services; Carlos Rodriguez, Procter & Gamble; Chris de Rooij, Consultant; and Gauke Veenstra, Shell International

Journal of Exposure Science and Environmental Epidemiology (2007), 17, S67–S71

ONLINE COMMUNICATION

The Board of Administration agreed on a budget to renovate the ECETOC's online communication in 2007, which will begin in 2008.

EXTERNAL REPRESENTATION

Representation at specific meetings or input to specific projects:

- Deutsche Gesellschaft für Pharmakologie und Toxikologie Workshop on Acute Reference Dose
  48th Frühjahrstagung, Mainz, Germany
  12 March 2007
  Neil Carmichael of ECETOC participated as a member of the workshop panel
- WHO/IPCS Workshop on Aggregate/ Cumulative Risk Assessment
  Washington/DC, USA
  19-21 March 2007
  Carlos Rodriguez of Procter&Gamble participated on behalf of ECETOC
- UK Health and Safety Laboratory Workshop on PBPK Modelling
  Chania/Crete, Greece
  25-28 April 2007
  Richard Phillips of ExxonMobil participated on behalf of ECETOC
- Extended OECD/IPCS Advisory Group Meeting on Toxicogenomics
  US EPA Research Triangle Park, North Carolina, USA
  24 May 2007
  Remi Bars of BayerHealthcare participated on behalf of ECETOC
- European Commission DG SANCO Public Consultation on Nanomaterials:
  ECETOC expert group provided input to the SCENIHR opinion on 'the appropriateness of the risk assessment methodology in accordance with the technical guidance documents for new and existing substances for assessing the risks of nanomaterials'
- OECD Working Party on Manufactured Nanomaterials:
  Karin Wiench of BASF represented ECETOC (through BIAC) in project 2 on human health and environmental safety research strategies
- 6th Framework Programme Co-ordination Action Project 'RiskBase':
  Andrew Riddle of AstraZeneca has been a member of the Advisory Panel on behalf of ECETOC
- 6th Framework Programme Co-ordination Action Project 'NORMAN':
  Mike Comber of ExxonMobil has been a member of the Advisory Panel on behalf of ECETOC
- 6th Framework Programme Integrated Project 'OSIRIS':
  Watze de Wolf of DuPont has been a member of the Advisory Panel on behalf of ECETOC
- REACH RIP 3.2-2 Consortium:
  Chris Money of ExxonMobil represented ECETOC and co-ordinated various input provided via the ECETOC expert network
- REACH RIP 3.3-2 Consortium:
  David Owen of Shell International represented ECETOC and co-ordinated various input provided via the ECETOC expert network
  Many employees of ECETOC member companies were nominated for participation in the various endpoint specific working group

Representation in on-going expert groups:

- WHO/IPCS Harmonisation Project Core Group:
  John Doe of Syngenta represented ECETOC
- EU Commission Consultative Forum on Environment and Health Action Plan:
  Dirk Pallapies of BASF represented ECETOC
- ECB TC C&L - Expert Group on Reproduction Toxicity Potency:

Steffen Schneider of BASF represented ECETOC

- ECVAM Scientific Advisory Committee:
  Tom Hutchinson of AstraZeneca represented ECETOC
- ECB TC C& L - General Issues for Health and Environmental Effects:
  Christa Hennes of ECETOC represented ECETOC
- ILSI Europe, Environment and Health Task Force:
  Martin Holt and Malyka Galay Burgos of ECETOC represented ECETOC

Posters and Presentations

- SETAC European Annual Congress,
  20-24 May, Porto, Portugal
  Members of the ECETOC Mode of Action Task force: T. Hutchinson (AstraZeneca), D. Caldwell (J&J), A. Hartmann (Novartis), M. Holt (ECETOC), D.Huggett (U.North Texas, formally of Pfizer), C. Oberwalder (BASF), F. Mastrocco (Pfizer), S.Maund (Syngenta), D. Versteeg (Procter & Gamble) presented a poster entitled: 'Focussing on protein targets at the core of mode of action ecotoxicology: ECETOC case studies.'
- SETAC European Annual Congress,
  20-24 May, Porto, Portugal
  Members of the ECETOC PBT Task Force: P. Thomas (Akzo Nobel), M. Holt (ECETOC), P. Lemaire (Arkema), I. Malcomber (Unilever), D. Salvito (RIFM), R. Thompson (AstraZeneca) presented a poster entitled: 'A Weight of Evidence (WoE) Approach for determining Mode of Action: An ECETOC Case Study.'
- EUROTOX European Annual Congress,
  7-10 October, Amsterdam, The Netherlands
  Members of the Carcinogen Classification Task Force: D. McGregor (Consultant), M. Binaglia (Solvay), A. Boobis (Imperial College), P. Botham (Syngenta), C. Hennes (ECETOC), L. Hoffstadt (ExxonMobil), S. Hubbard (Borax), T. Petry (ToxMinds, on behalf of SC Johnson), A. Riley (BP), D. Schwartz (Nycomed), presented a poster entitled: 'Classification of carcinogens under GHS: Proposals for guidance.'

OUTREACH MEETINGS

OutREACH meetings were established in 2003 with the primary aim to improve the dialogue between ECETOC as an organisation and employees of its member companies.

During 2007, one such meeting was hosted by an ECETOC member company, DuPont in France. Kindly organised by the office of Mireille Quirina, ECETOC Board Member from DuPont, several presentations by scientific committee members offered participants a taster of the work going into a range of current ECETOC task forces.

MEMBERS OF THE SCIENTIFIC COMMITTEE

ECETOC SCIENTIFIC COMMITTEE MEMBERS AS OF END DECEMBER 2007

John Doe, Syngenta, *Chairman*
David Owen, Shell Chemicals, *Vice Chairman*
Remi Bars, Bayer Cropscience
Peter Calow, Roskilde University*
Watze de Wolf, DuPont de Nemours
David Farrar, Ineos Chlor
Andreas Flükiger, F. Hoffman La Roche
Helmut Greim, Technical University Munich*
Giuseppe Malinverno, Solvay
Stuart Marshall, Unilever Research
Chris Money, ExxonMobil
Mark Pemberton, Lucite International
Carlos Rodriguez, Procter & Gamble
Gerard Swaen, Dow
Johannes Tolls, Henkel
Saskia van der Vies, Vrije Universiteit Amsterdam*
Ben van Ravenzwaay, BASF
Eckhard von Keutz, Bayer HealthCare
Hans-Jürgen Wiegand, Evonik Degussa

(* academic members)

Geoff Randell hands over the chairmanship to John Doe

The Scientific Committee met 6 times in 2007 and benefited from the dedicated contribution of the aforementioned members, including Mike Comber (ExxonMobil) and Tom Hutchinson (AstraZeneca) who resigned from the Committee and from their respective companies during the year.

At the end of May 2007, Geoff Randall retired from the Committee and handed over the chairmanship to John Doe (Syngenta). In addition, the Committee was pleased to welcome Johannes Tolls (Henkel) as a new member.

SECRETARIAT

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.

In 2007, Martin Holt retired from ECETOC and was replaced by Malyka Galay-Burgos, a specialist in environmental sciences and the omics technologies. ECETOC's administrative staff was also reinforced by Anita Jennings, who joined the team in April 2007.

Neil Carmichael, *Secretary General*

Christa Hennes, *Health Sciences Manager*

Henk Vrijhof, *Chemicals Programme Manager*

Malyka Galay-Burgos, *Environmental Sciences Manager*

Charlotte Amiri, *Web & Media Manager*

Geneviève Gérits, *Office Manager*

Christine Yannakas, *Secretary*

Anita Jennings, *Secretary*

FINANCE ACTUALS 2007 IN EUROS

INCOME

Subscription

Full Members	1.480.500
Associate members	39.000
Total Subscription Income	**1.519.500**
Bank Interest	20.682
Document Sales	3.386
Project-related	326.034
Total Income	**1.869.602**

EXPENDITURE

Salaries (and related expenses)	907.049
Office Running Expenses	260.077
Travel Expenses on Missions	18.825
Meetings and Consultants	361.381
Professional Services	26.074
Bank Charges	4.080
Capital Expenditure	2.545
Publications	26.430
Miscellaneous	12.252
Website	10.000
Total Expenses	1.628.713

BALANCE SHEET AND RESERVES

Balance Sheet

Income	1.869.602
Expenditure	1.628.713
Operating Margin	240.888

Reserves[1]

Opening	1.419.858
Operating Margin	240.888
Closing Reserve	1.660.747

[1]Estimated Reserve Required 700.000

GLOSSARY OF ABBREVIATIONS

ACH	Acetylcholine
ACSA	Agricultural Chemical Safety Assessment
CAS	Chemical Abstracts Service
Cefic	European Chemical Council
CES	Centre Européen des Silicones
DG	Directorate General (department of the European Commission)
DG SANCO	Directorate General for Health and Consumer Protection
DNEL	Derived no effect levels
ECB	European Chemicals Bureau
EChA	European Chemicals Agency
ECVAM	European Centre for the Validation of Alternative Methods
EEMS	European Environmental Mutagen Society
EPA	US Environmental Protection Agency
EPAA	European Partnership for Alternative Approaches to Animal Testing
EU	European Union
EUROTOX	Federation of European Toxicologists and Societies of Toxicology
EUSES	European System for the Evaluation of Substances
EWG	Endpoint working group
GHS	Globally Harmonized System of Classification and Labelling of Chemicals (UN)
HCN	Hydrogen Cyanide
HETRA	Human Exposure and Tiered Risk Assessment
HFC	Hydrofluorocarbon
IARC	International Agency for Research on Cancer
ILSI-HESI	International Life Sciences Institute – Health and Environmental Science Institute
INERIS	L'Institut National de l'Environnement Industriel et des Risques), France
IPCS	WHO's International Programme on Chemical Safety

ITS	Intelligent/Integrated Testing Strategies
JACC	Joint Assessment of Commodity Chemicals
KCN	Potassium Cyanide
LLNA	Local Lymph Node Assay
LRI	Long-range Research Initiative
MOA	Mode of action
NC3Rs	UK National Centre for the Replacement, Refinement and Reduction of Animals in Research
NOTEL	No Observable Transcription Effect Level
OECD	Organisation for Economic Co-operation and Development
PAFT	Programme for Alternative Fluorocarbon Toxicity Testing
PBT	Persistent, bioaccumulative and toxic
QSAR	Quantitative Structure Activity Relationship
REACH	EU regulatory framework for the Registration, Evaluation and Authorisation of Chemicals
RfP	Request for proposals
RIP	REACH Implementation Project
SETAC	Society of Environmental Toxicology and Chemistry
SOP	Standard Operating Procedure
SSA	Strategic Science Area
TC C&L	Technical Committee on Classification and Labelling of Dangerous Substances
TGD	Technical guidance document
TNO	Nederlandse Organisatie voor toegepast-natuurwetenschappelijk onderzoek The Netherlands
TRA	Targeted Risk Assessment
TTC	Threshold of toxicological concern
UNEP	United Nations Environment Programme
WHO	World Health Organisation

ECETOC, European Centre for Ecotoxicology and Toxicology of Chemicals, was established in 1978 as a scientific, non-profit making, non-commercial association, financed by 51 of the leading companies with interests in the manufacture and use of chemicals. A stand-alone organisation, it was established to provide a scientific forum through which the extensive specialist expertise in the European chemical industry could be harnessed to research, review, assess and publish studies on the ecotoxicology and toxicology of chemicals.

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