ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS

www.ecetoc.org

Annual Report '16

Contents

ECETOC Annual Report 2016

European Centre for Ecotoxicology and Toxicology of Chemicals
2 Avenue E. Van Nieuwenhuyse (Bte 8), B-1160 Brussels, Belgium

About ECETOC

Since 1978 ECETOC, an Industry-funded, scientific, not-for-profit think tank, strives to enhance the quality and reliability of science-based chemical risk assessment

ECETOC at a glance:

- FORUM FOR EXPERT COLLABORATION from world-wide industry, academia and regulatory bodies who work together to develop an agreed understanding on how the State of the Science can be used to improve Risk Assessment by developing novel Tools, Guidance and Frameworks. This is achieved through Task Forces, Expert Meetings and Workshops
- HARNESSES CROSS-SECTORIAL CHEMICAL INDUSTRY EXPERTISE from the leading companies representing industrial chemicals, agrochemicals, consumer products, biomaterials and pharmaceuticals
- IDENTIFIES RESEARCH NEEDS, selects proposals and monitors progress of research projects for the Cefic Long-range Research Initiative (LRI)
- SHARES KNOWLEDGE through freely available Scientific Publications: reviews, articles and workshop reports
- SCIENTIFIC REPRESENTATION for its member companies through presentations at specialist meetings and scientific activities with international agencies, government authorities and professional societies

Purpose
Enhancing the quality of chemicals risk assessment so that chemicals management decisions are reliable and science-based

Values
Providing the best science to help ensure risk management decisions are grounded in science

Vision
ECETOC is recognised as the reference source for industry expertise in regulatory decision making

Mission
Developing and communicating best science practices for risk assessment

Financing
ECETOC is financed by its membership, which is comprised of companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals

Structure
ECETOC is governed by a Board of Administration comprising senior executives from member companies. The Board is responsible for the overall policy and finance of the organisation. The Board appoints the Secretary General and the members of the Scientific Committee which defines, manages and peer reviews the ECETOC work programme. The Board and the Scientific Committee are supported by the ECETOC secretariat which is managed by the Secretary General, who oversees the day to day running of the organisation

Membership

Benefits of Membership

- **EXPERTISE:** Join and make the most of the collective expertise of the entire chemical industry
- **SAVINGS:** Reduce costs to individual companies by coordinated effort
- **INFLUENCE:** Shape industry's science agenda
- **LEARNING:** Through participation in ECETOC scientific activities
- **VOICE:** Amplify the voice of science in decision making

Like a health insurance policy, ECETOC covers:

- **Screening and Prevention** – identifying and reacting to upcoming issues through focused research efforts
- **Diagnosis** – work with experts from industry, regulatory authorities and academia to understand the problem
- **Intervention** – translate science data into rational discussion providing solutions to regulatory questions regarding chemical risk assessment
- **Treatment** – providing practical scientific structures and tools to meet regulatory needs to aid chemical risk assessment
- **Support** – capacity building and networking

As part of a company's overall insurance costs 'science insurance' is affordable and cost effective

Membership is open to companies who manufacture or use chemicals

To learn more and to apply for membership, please contact the ECETOC Secretariat:
Telephone: +32 2 675 3600
Email: info@ecetoc.org

Or write to: ECETOC, Avenue E. Van Nieuwenhuyse 2, bte.8, B-1160, Brussels, Belgium

ECETOC Member Companies

During 2016, the ECETOC Membership comprised the following 31 full Member Companies and 7 Associate Member Companies:

Associate member company

Associate member company

Associate member company

Associate member company

Associate member company

Associate member company

Associate member company

MESSAGE FROM THE

Chairman of the Board

"...ECETOC is becoming more comfortable with change which is essential for ECETOC to continue to be a successful organisation."

It has been another busy and successful year for ECETOC with advances in operating procedures within ECETOC and the scientific programme, as described in the messages in this report from the Secretary General and the Chair of the Scientific Committee. It has also been a year of change in the ECETOC staff with Malyka Galay Burgos and Madeleine Laffont leaving to pursue new opportunities. Change is of course a feature of our contemporary society and all organisations must change and adapt in response to the evolving business environment, globalisation, innovations in technology and the developing regulatory landscape. It is therefore important to be flexible and ensure change is implemented smoothly and successfully to achieve continuity of service. I am pleased to report that we have two new scientists at ECETOC, Alice Brousse and Lucy Wilmot, who have taken leadership in organising ECETOC activities in the areas of human health and environmental science respectively. In accordance with the flexible staffing model that the Board agreed in 2015, both Alice and Lucy have been contracted through PFA Brussels on 1 year contracts with possibility of renewal based on performance.

These changes in staffing model, work practices and the visible transformational programmes described by the Chair of the Scientific Committee, demonstrate that ECETOC is becoming more comfortable with change which is essential for ECETOC to continue to be a successful organisation.

Social media is also being used more widely by ECETOC to show-case our science and boost our professional profile in acting as the scientific voice of the chemical industry.

We continue to build and develop ECETOC presence through:

- Web & social media
- YouTube-type video & webinars
- Meetings and workshops
- Printed papers

In addition to changes in the way ECETOC communicates messages, there is also a change in science generation. While the quality of ECETOC work is still ensured by the expertise of its members, with the reduction of companies investing in toxicological expertise it will become necessary to rely more on broad networks of academics and advisors with specific expertise who can collaborate with ECETOC on specific projects. As described by the Chair of the Scientific Committee and Secretary General, this science model is already in practice particularly in developing frameworks to use 'omics data in decision making.

Ever-evolving expectations and demands shape change and to effectively meet these changing expectations and demands ECETOC is required to continuously change in how it does things, including how we structure the organisation, how we use channels of communication and how we tap into scientific expertise.

However, amongst these changes the strong scientific brand of ECETOC must remain a constant. People do business with those they trust, so the scientific reputation of ECETOC is paramount – this is who we are and will remain a constant.

Similarly, being a science-solutions provider is a constant, as is the consistency in our focus on keeping regulations scientifically honest and robust.

Thus, while the organisation will change and evolve, the foundation of what ECETOC stands for will remain on a bedrock of 3 constants:

1 - Scientific trust & reputation
2 - Problem definition and solution
3 - Impact provider

Our vision is to focus and build the ECETOC presence in scientific regulation to ensure that ECETOC is recognised as being scientifically authoritative and becomes the go-to expert organisation. There has perhaps been a desire to go beyond our focus on product safety regulation and this has resulted in ECETOC addressing too many topics. Even today there is concern about quality engagement versus quantity of engagement. Perhaps this is inevitable considering the broad membership of ECETOC with the different sectors having different priorities. The challenge is to behave in a scientifically trustworthy way to provide solutions that are impactful and resonate with our broad company membership and authorities. Thus, there is a sound argument, as mentioned earlier, for the ECETOC brand to stay confined to keeping chemical regulation scientifically honest and robust. This is the area we are good at, where we have scientific trust and reputation and which we understand and can manage. Perhaps a big fish in a small pond, but with the evolution of chemical regulation the pond is continuously expanding.

"Ever-evolving expectations and demands shape change and to effectively meet these changing expectations and demands ECETOC is required to continuously change in how it does things, including how we structure the organisation, how we use channels of communication and how we tap into scientific expertise."

A principle of ECETOC, and one continuously voiced by the Secretary General, is that if you are not solving problems then you are often simply creating noise and there is a lot of scientific noise about. To rise above this scientific noise, ECETOC remains focused on clear, solvable problems. The Secretary General in his report commented how ECETOC really provides a clear and comprehensive description of problems through robust problem definition to understand underlying causes in order to identify the real problem and how to tackle it.

In summary, the ECETOC brand is built on:

- Who we are - maintaining science presence and keeping scientific trust and reputation
- Solution provider - keeping regulations scientifically robust and honest
- Making a difference - impact

As technology and regulations evolve, how we do things, how we structure the organisation and how we use channels of communication will also change and evolve. However, the strong scientific brand of ECETOC will remain a constant.

Martin Kayser
Chairman of the Board of Administration

ECETOC BOARD OF

Administration

ECETOC Board of Administration

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

The Board is composed of at least six member company representatives. Two Board members are entitled to represent the Associate members. Board members have a two-year mandate and are responsible for the overall policy and finance of the association. The Board is also responsible for appointing the members of the Scientific Committee.

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

Election of Board Members at the 2016 Annual General Meeting:
Dr Julia Fentem (Unilever) and Dr Petra Hanke-Baier (Procter & Gamble) were unanimously re-elected to the ECETOC Board. Dr Robert Rickard (DuPont SHE & Sustainable Growth Center) was due for re-election but he informed the Board a few weeks before the AGM that he was retiring from DuPont and resigning as ECETOC Board member. The Board decided not to find a successor for the time being.

2016 ECETOC Board Members

Martin Kayser *(Chairman)*	BASF
Lorraine Francourt *(Treasurer)*	Dow Europe
Julia Fentem	Unilever
Petra Hanke-Baier	Procter & Gamble
Peter Hertl	Syngenta
Thomas Jostmann	Evonik Industries
Carole Langrand-Lerche	Bayer CropScience
Craig Nessel	ExxonMobil
Karen Niven	Shell
Robert Rickard	DuPont

Members of the Board with the Scientific Secretary and Secretary General

Left to right: Lorraine Francourt (Dow Europe), Carole Langrand-Lerche (Bayer CropScience), Ben van Ravenzwaay (BASF and Chair of the Scientific Committee), Petra Hanke-Baier (Procter & Gamble), Alan Poole (ECETOC Secretary General), Martin Kayser (BASF), Thomas Jostmann (Evonik Industries), Peter Hertl (Syngenta), Craig Nessel (ExxonMobil), Julia Fentem (Unilever) and Karen Niven (Shell)

REPORT FROM THE

Secretary General

"...science cannot resolve all problems, but in many instances understanding the science is the artery through which solutions can be provided."

During the four years since I joined ECETOC, many topics have influenced my thinking on how ECETOC operates, three of which I would like to share in this report.

The first topic is correct Problem Definition.
ECETOC is in the business of providing creative, constructive, practical and applicable solutions to scientific questions and problems enhancing understanding of chemical safety and risk. Clearly, in order to achieve this, it is necessary to understand what the problem is. Problem definition is a deceptively simple task but also simple to get wrong. Defining a problem verbally can often be vague and in many cases the solution will become clear by setting it out in writing and including ideas on how to resolve it. For this reason, the ECETOC Scientific Committee now requires a written and structured description of a problem to ensure it is framed correctly and that there is a good chance of reaching an outcome that is worth investing in. Sometimes following simple steps and processes helps to reframe problems and identify solutions not immediately obvious with often the problem definition ending up at the end of the process rather than at the beginning.

Such management practices and processes help ECETOC see problems within a scientific context that further enhances our reputation for being creative in solving problems. Whilst science cannot resolve all problems, but in many instances understanding the science is the artery through which solutions can be provided.

ECETOC is a major scientific body, if not **the** major scientific body, in Europe providing this artery through which industry, academic and regulatory scientists can channel creative scientific solutions to answer practical questions and problems surrounding chemical safety. As such, the industry must continue to support ECETOC as the scientific platform providing the scientific leadership and creative thinking from which problem definition and solutions flow.

The second topic is Striking a Balance
There are always too many problems for ECETOC to address, with a "tension" between addressing immediate scientific issues such as input to revising technical guidance documents, enhancing the value of existing OECD toxicity testing methods etc. and long term transformational activities to shape how the science will evolve and be used in coming years. Many of these activities have been addressed in this report by Professor Ben van Razenwaay, Chair of the ECETOC Scientific Committee, so will not be discussed here.

As a general rule, the majority of major successes for ECETOC lie in identifying where there is a "pull" or demand for a solution. These include refinement to the ECETOC Targeted Risk Assessment Tool (TRA), providing solutions to grouping nanomaterials to avoid unnecessary testing and the need to have confidence in the use and application of 'omics data in decision making.

To ensure a pull demand requires discussions and participation in meetings and discussions with regulators; this "science market research" helps define the problem and provides interest in the new service to create better networking and acceptability of the solution.

ECETOC is always seeking effective "pull" activities whether this is for immediate action or more long term opportunities. By using a mix of communication skills and tools, including as described above the need to really understand the problem in order to create of the solution, ECETOC provides the scientific organisation and platform where stakeholders can come to looking for solutions to problems. We strive to strike a balance in providing specific scientific products to address immediate expressed needs with those longer-term activities that motivate stakeholders to actively seek out ECETOC knowledge and scientific products.

Whether ECETOC is addressing immediate or longer-term challenges, brand quality, goodwill, quality reliability and reputation are at the centre of everything we do.

The third topic is Rising Above the Noise

In recent years, there has been an expansion of scientific meetings and journals. It seems as if every day I receive invitations to provide articles to new scientific journals or invitations to participate in scientific conferences. ECETOC is part of a scientific mix and, as discussed, we use workshops and scientific publications to make our stakeholders aware of our existence and activities, and to motivate them to actively seek out our scientific products.

One of the major ways we rise above the noise is by providing specific scientific products addressing expressed needs. The challenge is to make our customers aware of the existence of the scientific product.

We do this in various ways including:

- ensuring all products are freely available whether this is a scientific publication or tool;
- distributing all information using the extensive scientific network ECETOC has developed over the years;
- using social media and YouTube like videos where experts in their field provide short descriptions of the application and value of ECETOC activities in a way everyone can understand.

In order to maintain a leadership role in toxicology and continue to be the industry scientific voice in chemical safety and risk assessment, ECETOC must continue to foster the application of science in chemical safety and be efficient and professional in sending knowledge across Europe and beyond.As you can see, there are lots of activities taking place behind the scenes to produce products with tangible benefits to the industry and society and in the coming years I invite all our Members to become more active in ECETOC activities.

Alan Poole
Secretary General

Science Programme

Foreword from the **Scientific Committee Chairman**

Two years ago, we started the ECETOC transformational programme in which the ECETOC Scientific Committee initiated work in our strategic areas; human health, environment and exposure science, requiring input and commitment for a period of 3 to 5 years. The opportunity with these activities is to participate in shaping the future, rather than responding to challenges.

I am glad and proud to be able to say that one of our transformational programmes 'using data from developing technologies wisely' is bearing its first fruits, within a period of 24 months. The programme consists of several work streams; (1) a concept for quality assurance of new technology data considering GLP requirements, (2) Best Practices for establishing pathways to connect results of 'omics data to phenotype and (3) Best Practices for Weight of Evidence approaches for integrating 'omics data.

In the last 12 months, documents were prepared for each work stream by dedicated scientists from academia, regulators and industry under the ECETOC umbrella. In October 2016, these documents were presented and discussed in a three-day workshop. Approximately 45 scientists participated in the event, working in 4 individual groups, covering all three work streams and producing results in 12 break-out sessions. Remarkably, participation involved a great number of representatives of regulatory bodies, including FDA, JRC, RIVM, BfR, OECD and Health Canada.

The documents prepared for the workshop were amended and expanded and are now in preparation for publication as a special issue in a peer-reviewed journal. Moreover, the results of this work will be presented in 2017 at the Society of Toxicology and Eurotox, the two largest platforms for communication of results in the area of human health. With these results and communication strategy in place, we are underway to leaving a science-based footprint in the area of 'omics technologies. I have no doubt that our work will also serve as a blue print for the evolvement of even newer technologies such as the study of epigenetics.

You may question the relevance of 'omics technologies in the daily work of the classical chemical industry. Let me try to give you some answers; the cost of some of these technologies, such as transcriptomics have gone down to such an extent that virtually every laboratory is able to perform these studies. 'Omics data are high content data and there is a risk that researchers studying the effects of chemicals may come up with results that are open to (wide) interpretation, creating an atmosphere of insecurity and nervousness at the level of industry, regulators and eventually also the population. Therefore, rules and best practises on the development, storage and interpretation of such data are needed.

There are opportunities as well, and I believe that they outweigh the risks. Data from new technologies help to better understand the underlying mechanisms of toxicity. With this knowledge, these technologies can be applied to *in vitro* systems using animal and human cell lines to address the question of human relevance of findings in animal studies. They can also be used to increase the general relevance of *in vitro* studies and have the potential to reveal biomarkers of effect. ECETOC aims to achieve regulatory acceptance of data from new technologies, if these are developed, stored and assessed according to best practises. Many of our member companies already use these data to study the toxicological mode of action of chemicals. Such knowledge is, for example, essential if a compound is expected or known to have a carcinogenic effect in animals, to ensure registration. Moreover, a workshop organised by ECHA in April 2016, acknowledged the use of data from 'omics technologies to improve read-across.

In exposure sciences, the Targeted Risk Assessment steering group has worked on expansion of the TRA tool and has organised meetings at EUROTOX 2016 and shared a training session with ECHA on the use of the TRA at ISES 2016 meeting. The steering team has responded to comments on the TRA in the ETEAM report and have met with delegates from Japan and Korea about use of the TRA in 'Japanese and Korean REACH'. ECETOC continues to refine the TRA and has been involved in a Cefic LRI

project looking at worker dermal exposures and the conservatism of the TRA tool. The ECETOC TRA tool remains one of the major flagships of ECETOC success and will be maintained and continuously improved. An output from the Task Force on 'Advances in consumer exposure science: data, modelling and aggregate exposure assessment' was a landscaping exercise whereby available sources of exposure data and tools for exposure assessment were gathered and structured in a harmonised system. While this database was initially developed in the form of an Excel spreadsheet, it has proven so popular that ECETOC is exploring with a commercial organisation to transform it into online database available to the broad scientific community via the web.

The third transformational programme is called 'Ecological relevance of toxicity assessment schemes', which targets to achieve a more realistic scenario of the environment in our risk assessment procedures. In 2016, ECETOC focused mainly on the role of ecosystem services in environmental risk assessment resulting in the Technical Report no.125 on 'Chemical risk assessment – ecosystem services' and support of 2 LRI-sponsored Workshops on this topic.

Focussing on a limited number of issues where ECETOC can make the difference is the right strategy. What is needed to increase our visibility beyond those directly involved in our work is communication. We have moved from ECETOC reports to peer-reviewed publications, which is a good step in the right direction. Our reports are now summarised and sent to all delegates with a short 'elevator speech' message. What else can we do? Most scientists working in ECETOC task forces or participating in workshops are connected with their peers through social media. In particular, LinkedIn and ResearchGate are used by many of us to inform ourselves about each other's scientific publications. Since 2010, ECETOC has been developing such social media connections and we also encourage our colleagues to make reports and papers, prepared under the ECETOC umbrella, available to those who are connected to us. ECETOC has also decided to work more closely with two professional societies; SETAC for environmental science and Eurotox for human health. We will continue to provide topics for sessions relevant to ECETOC at these organisations, and we will also try to make use of the presence of the great number of participants that are attracted to these meetings to organise sessions and back-to-back workshops / meetings to reduce the amount of travel.

Communication and follow-up on ECETOC activities with regulatory authorities is essential to make a difference. Through such actions, which include publication and presentation of results as well as discussion with regulatory authorities, our concept 'Grouping of Nanomaterials' was largely taken up by ECHA as well as Health Canada and is highly likely to help in reduction of animal testing.

Improvement of communication may also be necessary within our member companies. To attract attention for participation in task forces and workshops, ECETOC relies entirely on the delegates system. The delegates are expected to ensure communication within the member companies. In the age of modern communication, is this still the best way to communicate opportunities to participate? Likewise, are desires which arise in our member companies for ECETOC to engage in a certain science issues effectively addressed via a single delegate? Sometimes, actually frequently, a fast response is necessary and relying on a single person to oversee all activities of ECETOC in the areas of human and environmental health as well as exposure science is a significant task. The delegates, as voting members at the Annual General Meetings will remain an important factor, but I feel that we should also start to explore other ways of improving a two-way communication process between ECETOC and its member companies.

Staying at the forefront of new developments in exposure, toxicology and ecotoxicology will remain a key factor to contribute to science-based risk assessment for ECETOC. At the same time, we should remain alert to the immediate necessities of our membership. It is with this in mind that we have embarked on a new road for our organisation and with the help of all of you, I am convinced that we will remain a unique and successful organisation.

Bennard van Ravenzwaay
Chairman of the Scientific Committee

Staying at the forefront of new developments in exposure, toxicology and ecotoxicology will remain a key factor to contribute to science-based risk assessment for ECETOC.

Highlights of 2016

Completed Task Forces

Guidance for effective use of human exposure data in risk assessment of chemicals

To understand and predict health risks posed by exposure to substances it is necessary to interpret both the toxic properties and the potential exposure to that substance: To understand and predict health risks posed by exposure to substances it is necessary to interpret both the toxic properties and the potential exposure to that substance: **Risk = Fn(Hazard, Exposure)**

While standardised, internationally accepted methods are available to understand hazard and toxicity, standardised methods and tools to measure, describe or make accurate and robust exposure predictions are not so common. In addition, there is sometimes confusion and misunderstanding about what tools and data should be applied to predict exposures for specific circumstances, what the level of precision of these methods is, and in particular how to predict aggregate consumer exposure to a substance that might be contained in a number of consumer products.

This task force activity had two principle aims:

1 - Review the landscape of the various tools and methods available currently to estimate consumer exposures.

2 - By using case studies, the strengths and weaknesses of the various tools and methods for assessing consumer exposures to different classes of substances were examined. In particular, a focus on aggregate exposure was considered and various methodologies and data inputs were reviewed.

Based on these analyses the task force produced:

1 - A set of best practices guiding the use of existing tools that are best suited for specific applications.

2 - A set of recommendations to reduce variability and improve quality of exposure predictions, and to broaden cooperation between industry, academics and the regulatory community to drive activities improving exposure quality.

A workshop was also organised involving experts from industry, academia and the regulatory community to review and discuss the task force output. A synopsis of the meeting together with recommendations for improving quality and reducing variability in consumer predictions are found in ECETOC Workshop Report no.31: *Advances in consumer exposure science: Data, modelling and aggregate exposure assessment. 26th January 2016, Brussels*. (available at **http://bit.ly/ecetoc-wr31**).

It is hoped that the task force report will be of use to both regulatory bodies and industry in providing guidance on the appropriate use of different exposure tools and data for different purposes. Additionally, the task force output should provide a path forward with regards to further research and data that can be gathered by the broader risk assessment community in order to facilitate better exposure assessments in the future.

The task force report has been published as ECETOC Technical Report no.126: *Guidance for effective use of human exposure data in risk assessment of chemicals*. The Executive Summary and free PDF of the report are available at **http://bit.ly/ecetoc-tr126**.

An online database / application is currently under development.

Freshwater ecotoxicity as an impact category in life cycle assessment

Freshwater is a vital component in the global ecosystem. Freshwater is a unique environmental habitat and also essential for human life. Freshwater pollution not only poses a risk to the environment, but it can also impact human health as well. Therefore, it is important to maintain anthropogenic pollution below a threshold that would characterise a risk.

Life cycle assessment (LCA) is a methodology that strives for the assessment of environmental burdens along an entire (product) value chain. This means, for example, a consumer product assessment starts at the extraction of raw materials and it ends with the disposal of the product. All environmentally relevant intermediate stages such as transport, manufacturing steps and product use are accounted for,

considering even secondary resources such as energy consumptions and their associated values chains in full.

One general idea behind LCA is to make ´hotspots´ visible. These are impacts along the life cycle which stand out from the rest. Beyond 'hotspots', life cycle assessment in principle also enables the comparison of products regarding their environmental performance. This use of LCA is integral to the 'Product Environmental Footprint' (PEF) project in the European Union, but it poses greater demands on methodological reliability and data quality. In a series of pilot projects, the methods prescribed in this PEF project were tested for various product types. 'Freshwater Ecotoxicity' is an environmental impact category which is part of such assessment. Several fundamental and practical questions were raised regarding the PEF methodology used to determine and compare the life cycle impact assessment of a product for the 'Freshwater Ecotoxicity' impact.

Thus, ECETOC established a task force to investigate the method employed in the LCA context of PEF. The aim of the task force was to: i) conduct a scientific investigation of the 'USEtox' method for assessment of aquatic ecotoxicity in LCA, based on a simple case study with a virtual down-the-drain product, ii) compare LCA and environmental risk assessment methodology, which both characterise human intervention on the environment and provide a basis for decision-making; and (iii) to provide guidance on the interpretation and scientific relevance of USEtox results in the context of chemical impact assessment and selection of chemical-based (manufactured) products. The report includes an extended discussion of the options that could move forward the discussion of the relevance and practical aspects of assessment of ecotoxicological effects in the framework of LCA.

The document has been published as ECETOC Technical Report no.127: *Freshwater ecotoxicity as an impact category in life cycle assessment*. The Executive Summary and free PDF of the report are available at **http://bit.ly/ecetoc-tr127**.

Guidance on assessment and application of Adverse Outcome Pathways (AOPs) relevant to the Endocrine System

Various European chemical regulations do not allow the marketing or use of substances known to have endocrine disrupting properties – chemicals that induce adverse effects in humans and/or wildlife as a result of interaction with the endocrine system.

Adverse outcome pathways (AOPs) have the potential to be important tools for the assessment of endocrine disrupting properties as they can help identify if an adverse effect observed in an *in vivo* (animal based) study can be plausibly linked to a change in the endocrine system. AOPs could potentially be used to help predict the potential for an adverse effect in humans and/or wildlife from the results of *in vitro* (non-animal based) assays, potentially reducing the requirement for animal testing.

However, if AOPs are to be used to identify and/or predict endocrine disrupting properties, it must be ensured that they are sufficiently robust and fit for purpose. To this end, this Technical Report provides guidance on identifying the basic requirements and how to establish the minimum scientific standards that allow the use of AOPs. The guidance is centred on the different contexts of AOP use such as hazard identification, read-across (predicting potential effects for a chemical based on data for other, similar, chemicals) and risk assessment. These requirements are described as '*Key Elements in Assessment of AOP Utility*' and cover factors such as ensuring that AOPs are consistent with the current scientific knowledge (*Biological Plausibility*) and ensuring that any potential differences amongst species are considered (*Taxonomic Applicability/Species Concordance*).

This guidance will be a useful tool for 1) those looking to develop new AOPs helping to identify the key elements that need to be considered during construction, and 2) those considering applying existing AOPs by providing a list of key elements to be considered to facilitate a critical review and ensure it is fit for the intended purpose.

The document has been published as ECETOC Technical Report no.128: *Guidance on assessment and application of Adverse Outcome Pathways (AOPs) relevant to the Endocrine System*. The Executive Summary and free PDF of the report are available at **http://bit.ly/ecetoc-tr128**.

Task Forces Established

Aquatic toxicity and bioaccumulation of sparingly soluble manufactured particulate substances

In 1996, ECETOC published Monograph No. 26 which reviewed the difficulties of sparingly soluble substances in aquatic toxicity assays. This work helped establish the current paradigm in aquatic environmental assessment, accepted by authorities globally, that the dissolved molecule represents the most relevant exposure condition for aquatic toxicity testing and that testing above the solubility limit does not help to inform environmental risk. The increasing focus on nanomaterials and microplastics in the environment over the last decade is challenging this paradigm and has inspired debate regarding the adequacy of existing aquatic testing frameworks for substances, which are now realised to have potential for emission and transmission in the aquatic environment in varied undissolved / particulate states. The majority of published research that has investigated the potential ecotoxicity of nanomaterials has employed procedures involving exposure to substances above the solubility limit and in the presence of undissolved substance. Relatively little attention is given to defining the physical states associated with known or expected exposure pathways, and the distinction between intrinsic toxicity and physical effects associated with those relevant physical states. The latter is a fundamental requirement in regulatory aquatic toxicology studies.

The need for guidance on when and how to test particulates in aquatic toxicity tests has re-emerged because of the apparent bioavailability of some nanomaterials. Several current activities at the OECD are focused on developing guidance for aquatic hazard and bioaccumulation testing of nanomaterials. Industry is sparsely represented in these fora and there is a risk that this guidance will be inconsistent with currently accepted procedures for 'conventional' substances. This inconsistency can have major consequences for the

chemical industry because there is no single regulatory definition of a nanomaterial, distinguishing it from a conventional particulate substance, which is globally accepted. In Europe, the EC has issued a risk-neutral definition of nanomaterial of such a wide scope that it could encompass most solid particulate substances, regardless of manufacturing intent. If the OECD adopts new test strategies and recommendations for aquatic tests with nanomaterials, there is a risk that existing studies for poorly soluble substances, deemed nanomaterials by some subsequently applied definition, may be considered insufficient for characterising exposure and risk; and new studies following nanomaterial testing recommendations would be requested.

The objectives of this task force are:

- To build upon and update the guidance provided in ECETOC Monograph No. 26 (1996) by critically re-examining the relevance of undissolved particulate substance, from the nano to the macro scale, in aquatic toxicity tests with emphasis on uptake and bioaccumulation.

- To identify circumstances where current aquatic hazard testing approaches are acceptable and make recommendations where a different approach may be warranted for sparingly soluble particulate substances including nanomaterials.

- To develop guidance which assists distinguishing intrinsic toxicity from physical effects, characterising physical effects, and identifying circumstances where physical effects may contribute to population relevant risk.

Geospatial approaches to increasing the ecological relevance of chemical risk assessments

For several decades, the prospective risk assessment of chemicals across all regulatory jurisdictions has followed a generic approach of comparing estimated exposures to toxic thresholds designed to be protective of all species. This approach does not recognise geographic patterns of species distributions or acknowledge that particularly sensitive species may not occupy potentially exposed habitats. Therefore, risk assessments could be overly conservative and restrictive for some uses of chemicals.

Geo-referenced ecological data are becoming increasingly available at spatial resolutions applicable to chemical risk assessment, potentially facilitating enhanced environmental relevance of such risk assessments. Environmental management practices can result in heavily modified ecosystems in terms of both physical characteristics and ecological assemblages. For example, intensively farmed land is managed for crop production and will therefore not support the diversity of species that could be sustained under certain other land uses. Consideration of the spatial patterns inherent to multi-use, multi-stressor landscapes raises important questions about how to assess cumulative effects of chemical stressors in the environment. Given that much of the environment is managed in various ways, greater realism in assessing potential additional stress due to chemical exposure could be achieved if this range of managed and unmanaged environmental typologies and their constituent biological communities were mapped and described. Making representative or even spatially explicit scenarios would enable similarly localised chemical exposures to be assessed with high environmental relevance.

A potential approach would be to describe a range of environmental scenarios representative of ecosystems contained within managed and unmanaged environments, accounting for the various ecosystem services provided by these different portions of the landscape. These scenarios might include occurrence of particular species or traits based on structural and functional diversity, management practices, as well as other biotic and abiotic descriptors. One ongoing initiative that could be included in scenario development is the EC mapping of ecosystem services in Europe (MAES project). This makes it possible to overlay geospatial maps of ecosystem services and biological assemblages with spatially explicit chemical exposures in order to assess potential impacts.

The overall aim of this task force is to review and inform on the use of geo-referenced data to increase the environmental relevance of chemical risk assessment. A key aspect of their work should be to investigate the availability of geo-spatial data needed to derive scenarios based on combinations of data for describing European ecosystems and the services they provide in a range of environmental scenarios.

These aims are complementary to a Cefic LRI project (ECO28) on the development of aquatic scenarios for use in risk assessment. The project aims include an assessment of how lotic assemblages (invertebrates and fish) can be represented by a range of ecological scenarios developed from highly resolved GIS data.

ECHA PBT Guidance Update

This task force represents ECETOC and its members as part of the ECHA consultation for the updating of REACH guidance on PBT substances (substances that are persistent, bioaccumulative and toxic).

Workshops and Symposia

Advances in consumer exposure science: Data, modelling and aggregate exposure assessment

26 January 2016, Park Inn Brussels Midi, Brussels, Belgium

This ECETOC Workshop was originally scheduled to take place 01 December 2015 but due to the security alert in Brussels was moved to 26 January 2016.

To understand and predict health risks posed by exposure to substances it is necessary to understand both the toxic properties and potential exposure to that substance:
Toxic properties x Exposure = Risk

While standardised, internationally accepted methods are available to understand toxic properties, adequate methods and tools to make accurate and robust exposure predictions are not so common. In addition, there is sometimes confusion and misunderstanding about what tools and methods should be applied to predict exposures for specific circumstances, in particular, predicting aggregate consumer exposure to a substance that might be contained in a number of household products.

The Workshop provided the opportunity for experts from industry, academia and the regulatory community to review and discuss the landscape of the various tools and methods available currently to estimate consumer exposures. Also, by using case studies examined the strengths and weaknesses of the various tools and methods for assessing consumer exposures to different classes of substances.

Based on these analyses the Work Shop participants:

- identified best practices guiding the use of existing tools that are best suited for specific applications,
- produced a set of recommendations to reduce variability and improve quality of exposure predictions, and to broaden cooperation between industry, academics and the regulatory community to drive activities improving exposure quality.

A synopsis of the meeting together with recommendations for improving quality and reducing variability in consumer predictions are found in ECETOC Workshop Report no.31: *Advances in consumer exposure science: Data, modelling and aggregate exposure assessment. 26th January 2016, Brussels*.

The Executive Summary and free PDF of the report are available at **http://bit.ly/ecetoc-wr31**.

2016 Human Health and Exposure Science Review Meeting

01-02 February 2016, Pullman Brussels Centre Midi, Brussels, Belgium

In February 2014, the first Human Health Science Scoping Meeting identified 12 priority themes for ECETOC and Cefic LRI consideration. During this 2016 Review Meeting, participants heard about progress and achievements since 2014. They also developed new recommendations for future work through brainstorm sessions. The regulatory community and key chemical sectors gave their views during the meeting to ensure that recommendations are both relevant and impactful.

2016 ECETOC Environment and LRI progress review

2016 ECETOC Environment and LRI progress review

24-25 February 2016, Brussels, Belgium

An update on current ECETOC and LRI environmental projects was presented on the first day to an audience of ECETOC Member Company environmental experts, along with representatives from academia and regulatory bodies. On the second day, ECETOC Member Company scientists participated in a brainstorming session to generate new ideas for the 2016 ECETOC activities and for RfPs within the LRI programme. This annual review is an opportunity for Member Companies to propose ideas and to provide input directly into ECETOC and Cefic LRI scientific programmes. Recommendations from this meeting and the Human Health Science Scoping Meeting are taken into account by the ECETOC Scientific Committee and Cefic LRI when deciding their respective future scientific work programmes.

Noncoding RNAs and Risk Assessment Science

03-04 March 2016, Malaga, Spain

It is well understood that DNA is the basic instruction manual that explains how to make a living organism, such as a human body. RNA is a messenger sent from the coding DNA-sequences called genes to make proteins, the essential building bricks for cells. However, studies of cells also identified RNA that is not directly involved in protein synthesis. Initially these were thought to be 'evolutionary junk' collected over the eon of time in evolution. It is now understood that these noncoding RNAs (ncRNAs) play an important role in gene regulation and disease and that exposure to man-made chemicals can affect how these small molecules work.

In March 2016, ECETOC organised a workshop in collaboration with the Cefic Long-range Research Initiative (LRI) to discuss the state-of-the-art research on ncRNAs as potential biomarkers in regulatory toxicology for the assessment of product safety. A promising avenue is using measurements of ncRNAs as markers of toxicity, particularly tumour induction, which is usually examined in high-tiered studies requiring the use of many experimental animals. Thus, such measurements hold the potential to significantly reduce animal testing for the carcinogenic potential of chemicals. It was however agreed that while significant progress has been achieved careful evaluation is still required to determine the utility of such biomarkers in assessing product safety.

The Workshop identified 3 focus areas for ECETOC to progress the application of ncRNAs for regulatory toxicology:

1 - Comprehensive literature reviews to identify candidate ncRNAs for further assessment as potential biomarkers of toxicity;

2 - Develop consensus on how to conduct and report ncRNA expression profiling in a toxicological context to support applicability for regulatory decision-making;

3 - Conduct experimental projects to evaluate the toxicological relevance of the expression profiles of selected ncRNAs.

It was agreed technical advances in measuring biomarkers such as ncRNAs have the potential to enhance understanding of toxicological effects thereby improving chemical safety assessment and developing new products. ECETOC is encouraged to progress the understanding of how ncRNAs might be involved in toxicological pathogenicity and how measurements of such biomarkers can be used in a regulatory context.

The findings of the Workshop have been published as ECETOC Workshop Report no.32: *Noncoding RNAs and Risk Assessment Science. 3 – 4 March 2016, Málaga*. The Executive Summary and free PDF of the report are available at **http://bit.ly/ecetoc-wr32**.

A paper has also been published:

Aigner A, Buesen R, Gant T, Gooderham N, Greim H, Hackermüller J, Hubesch B, Laffont M, Marczylo E, Meister G, Petrick JS, Rasoulpour RJ, Sauer UG, Schmidt K, Seitz H, Slack F, Sukata T, van der Vies SM, Verhaert J, Witwer KW, Poole A. 2016.

Advancing the use of noncoding RNA in regulatory toxicology: Report of an ECETOC workshop.

Regul Toxicol Pharmacol (In Press, Accepted manuscript available online 20 September 2016)
Doi: 10.1016/j.yrtph.2016.09.018

2016 Annual Technical Meeting: Leveraging ECETOC achievements to support membership needs in global legislation and business development

08 March 2016, Brussels, Belgium

ECETOC brought together 45 scientists, regulatory experts and member company business development managers to explore how ECETOC can help bring best scientific practices into the global regulatory community by developing options for consideration by the ECETOC Board to make ECETOC even more relevant on a global basis.

Improving chemicals risk assessment with refined exposure characterisation

Workshop at EUROTOX 2016
05 September 2016, Seville, Spain

In order that chemicals risk assessments can be seen to be reliable, they must be able to effectively undertake both hazard and exposure assessment. However, the fact that the use of many chemicals is widespread is associated with a high degree of uncertainty in the ability to accurately predict exposure. This uncertainty can undermine steps taken to improve hazard assessment. New approaches to exposure assessment are now being implemented that seek to deliver more reliable risk assessments through the tiered and targeted acquisition and application of exposure information.

At Eurotox in Seville, ECETOC organised a workshop on 'Improving chemicals risk assessment with refined exposure characterisation' at which over 200 people participated. The workshop was chaired by Helmut Greim (Technical University Munich) and included speakers from ECHA, RIVM, academia and industry. The aim of the workshop was to examine how the process of risk assessment can be improved through the implementation of tiered approaches to exposure assessment,

together with the tools and databases being developed to support such methodologies and the roles that different stakeholders can play in supporting the process and its governance.

Theo Vermeire (RIVM) examined the activities in the field now underway at OECD. Chris Money (Cynara Consulting) reviewed the experiences accumulated during the development and support of the ECETOC TRA model. Natalie von Goetz (ETH Zurich) addressed how the acquisition of exposure data might be refined and applied for higher tier consumer assessments. Sarah Tozer (Procter & Gamble) explained with the findings of the recent ECETOC Task Force on modelling aggregate exposure to chemicals from multiple sources. Finally, Andrea Ahrens (ECHA) looked at some of the quality assurance considerations that should accompany exposure models for regulatory risk assessment

The resulting discussions were very active, with many participants positively referring to the role that the TRA now occupies in the process of chemicals risk assessment, both in the EU and beyond. There was a broad consensus that more needs to be done in the risk assessment process to ensure equivalent attention is paid to both hazard and exposure assessments, and the work that ECETOC has accomplished in the field is recognised and valued.

Targeted activities for improving workplace exposure assessments

Session at International Society of Exposure Science (ISES) Annual Meeting, 09-13 October 2016, Utrecht, The Netherlands

In October, ECETOC organised a well-attended symposium at the 26th annual International Society of Exposure Science (ISES) Conference in Utrecht on the theme of 'Targeted activities for improving workplace exposure assessments'. The background results from the challenges that the EU REACH Regulation brings for workplace exposure assessments. Specifically, it examined the expectations placed on industry that relate to how REACH worker exposure estimation should be undertaken in terms of the need to justify and explain positions and assumptions concerning the nature of exposure estimations. This has led to reviews of the adequacy of existing worker exposure assessments and approaches to exposure estimation, in addition to catalysing the need for new research. The wider relevance of these initiatives and the multi-disciplinary approaches employed to address them, together with the changes to occupational hygiene/business etc. practice that appear advisable, were explored during the Symposium.

Dook Noij (Dow) and Andreas Ahrens (ECHA) reviewed the experiences that have arisen from the use of the ECETOC TRA under REACH, which has been used for over 90% of REACH worker CSAs. Susan Hesse (Fraunhofer) described recent activities undertaken to characterise the effectiveness of 'non-standard' exposure control techniques (RMMs) available for the control of solvent exposures and which serve to underpin assumptions contained in the TRA. Jody Schinkel (TNO) shared the findings of a recently completed CEFIC LRI project that explored the reliability of the TRA's dermal exposure estimates. Urs Schlüter (BAuA) examined the constraints presented by available exposure data and models that are intended to be broadly applicable across a range of substance types and use situations. Finally, Chris Money (Cynara Consulting) explored the activities that can be seen to be part of an overall strategy for improving user confidence in worker exposure assessments by the targeted data acquisition and application of information. The Symposium was chaired by Jan Urbanus (Shell).

The resulting discussions were very active, with participants confirming the critical role now played by the TRA under REACH and the techniques available for improved data transparency and robustness, and stakeholder engagement and confidence.

ECHA Chesar and ECETOC TRA

Workshop at International Society of Exposure Science (ISES) Annual Meeting organised by ECETOC and the European Chemicals Agency, 09-13 October 2016, Utrecht, The Netherlands

This workshop provided an introduction to and hands-on experience with the Targeted Risk Assessment (TRA) tool developed by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) and its use in the Chemical Safety Assessment and Reporting Tool (Chesar) of the European Chemicals Agency (ECHA). Chesar is a tool developed by ECHA to carry out chemical safety assessment under REACH, to document it for the authorities (Chemical Safety Report) and to communicate the safe conditions of use into the supply chain (Exposure Scenarios to be attached to the Safety Data Sheet).

Background on the development and use of the ECETOC Targeted Risk Assessment tool and Chesar was presented together with processes and tools known to help improve the efficiency and consistency of TRA and Chesar-based assessments in the context of requirements for reporting under REACH.

Applying 'Omics Technologies in Chemicals Risk Assessment

10-12 October 2016, NH Eurobuilding Hotel, Madrid, Spain

'Omics technologies hold the promise of generating detailed information faster, more accurately and easier than ever before. These emerging technologies could help reduce animal testing, with the ultimate goal of replacing animal testing altogether. They could further increase the number of substances that can be accurately and efficiently tested in a given time. Finally, and importantly, they could identify new and emerging risks through toxicological screening and the provision of reliable biomarkers. Yet current methodological and analytical uncertainties limit the application of 'omics technologies

in regulatory toxicology. Best practice for generating and storing, processing, and interpreting 'omics data is needed so that the outcomes of 'omics-based studies can be reliably verified and confidently integrated into regulatory hazard and risk assessment.

Against this background, ECETOC convened a workshop *Applying 'omics technologies in chemicals risk assessment* that took place from 10-12 October 2016 in Madrid, Spain. Ahead of the workshop, ECETOC multi-expert teams drafted frameworks towards establishing best practices (i) for a Good-Laboratory Practice (GLP)-like context for collecting, storing and curating 'omics data; (ii) for processing 'omics data, and (iii) for weight-of-evidence (WoE) approaches for integrating 'omics data. Additionally, the key objective (iv) to establish pathways to connect 'omics data to phenotypic alterations was addressed, albeit without in advance drafting of a framework. At the workshop, presentations served to further elucidate these four key objectives and the contents of the drafted frameworks, also by providing background information, e.g. on relevant case studies or related ongoing activities. Importantly, four breakout sessions and extensive plenary sessions provided ample opportunity for in-depth discussions on the four key objectives of the workshop.

Altogether 37 experts attended the workshop representing the European Commission; the Organisation for Economic Cooperation and Development (OECD); national authorities from EU Member States, EU associated countries and the United States; academia; industry and independent consultants. An additional three experts contributed to the workshop in the form of video or dial-in presentations.

A paper, reporting on the workshop, will be published in due course.

Human Evidence for Chemical Respiratory Sensitisation – How to Use it and How to Improve it

27-28 October 2016, Madrid, Spain

In 2015 an ECETOC taskforce published the results of a review of the available data to consider the relevant endpoints that can be used to describe Chemical Respiratory Allergy (CRA) and to inform our understanding of threshold effects[1]. The aim of the review was to determine whether chemical respiratory allergy should be regarded as a threshold, or as a non-threshold, toxicity, and to recommend appropriate methods for deriving safe concentrations of chemical respiratory allergens.

As discussed in the taskforce publication[1], although there is evidence that the acquisition of sensitisation to chemical respiratory allergens is a dose-related phenomenon, and that thresholds exist, currently the mechanisms involved in CRA are not fully elucidated, there is uncertainty regarding routes of exposure and no validated models exist for identification of respiratory sensitising substances. Neither are there any methods suitable for the routine assessment of threshold values for sensitisation of the respiratory tract by chemicals. As a result, human thresholds of induction and elicitation are poorly characterised which creates uncertainty surrounding the safe use of H334 (previously assigned the risk phrase R42) classified substances.

More robust human threshold data would help refine the current risk assessment approaches for the use of such materials, both from occupational and consumer exposure standpoints. Additionally, members of the taskforce identified that clearer guidance was required on how to use existing human data for the evaluation of respiratory sensitisers in weight of evidence assessments.

Therefore, a workshop was held with a view to:

- Develop best practice guidance on how to assess and use available human data for the identification of respiratory sensitisers, including the creation of a framework for the interpretation of quality of evidence and weighting to be applied.

- Drive discussions on identifying human biomarkers for respiratory sensitisation to chemical allergens and the use of such tests in prospective monitoring of workforces to identify more accurate threshold data.

Two key publications were highlighted as pre-read material for workshop participants. These were Kimber et al 2013 and North et al 2016[2,3].

Sixteen international scientific experts from industry and academia participated in the workshop where on day 1, after a series of expert presentations, participants were split into two break-out groups to discuss the following:

A - What are the criteria for data admissibility and weighting for classification?

B - The identification of biomarkers for chemical respiratory allergens and for sensitisation of the respiratory tract?

On day 2 the conclusions from day 1 were reviewed and all participants considered a third discussion point:

C - Assessment of sensitising potential: relevance for classification and SVHC.

Finally, all key discussion points and conclusions were recapitulated in a final plenary session where several key activities were identified to begin to address the workshop objectives, which were to:

- Define and promote a consistent, best practice, strategy for the evaluation of available human data for respiratory sensitizers, for use by regulators in formal decision-making processes.

- Publish a consensus opinion on the research required for the identification of human biomarkers of chemical respiratory sensitisation, and application in prospective monitoring of workforces with the ultimate aim of refining current human threshold data to reduce uncertainty in current risk assessment approaches.

A workshop report will be published in due course.

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Toxicology 318:32-9.

[3] **North CM, Ezendam J, Hotchkiss JA, Maier C, Aoyama K, Enoch S, Goetz A, Graham C, Kimber I, Karjalainen A, Pauluhn J, Roggen EL, Selgrade M, Tarlo SM, Chen CL. 2016.**

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Developing a strategy to improve the hazard and risk assessment of difficult to test multi-component substances

Joint ECETOC - RIFM Workshop
02-04 November 2016, Gaylord Palms, Kissimmee, Florida, USA, preceding the SETAC World Congress

This international workshop was held to address risk assessment challenges for complex mixtures of substances (e.g., multi-constituent substances (MCSs), substances of unknown or variable composition, complex reaction products or biological materials (UVCBs)). International regulatory frameworks (specifically REACH, Canada's DSL Categorization and Chemicals Management Plan assessments, and USEPA's Premanufacturing Notification (PMN) process) have highlighted the complexities of registering, characterizing fate, exposure, hazard and ultimately assessing the risk of complex chemical mixtures, whether from manufacturing environments or plant-derived materials. Several industrial sectors (e.g., petrochemicals, personal care products, resins/rosins) have developed frameworks and methodologies for characterization and analysis of these complex substances. This workshop was designed to identify best practices and key research needs to support environmental risk assessment.

The workshop participants agreed that there is a need for a succinct, peer-reviewed publication that will highlight the current status and needs related to risk assessment for difficult-to-test multi component substances. This will include some basic discussions of the definitions and scope of substances classified as UVCBs and MCSs. In addition, emphasis will be given to evaluation of tiered strategies / approaches as well as characterization of uncertainty and variability within the various methodologies. Follow-up work, potentially comprised of peer-reviewed manuscripts, will focus on highlighting key principles from selected case examples, where various approaches were employed and evaluated for specific, real-world UVCB and MCS examples. This distillation of principles will help identify challenges and needs, and highlight specific research needs, including method development, effects-driven approaches, models, and other tools.

Group photo of the participants at the RIFM/ECETOC Workshop on difficult to test multi-component substances

The RIFM/ECETOC Workshop provided a platform for key sectors and regulators to identify best practices and key research needs to support environmental risk assessment of these complex substances. Initial outcomes from this workshop were presented at SETAC's World Congress in Orlando, and will be presented at the SETAC EU meeting in Brussels in May 2017 as part of a jointly organised session: *Improving the environmental assessment of complex composition substances and mixtures for Chemicals Management*.

Expert Working Groups

AOP/MoA of Reproductive Health Ontology

This ontology provides a way for data and information on developmental toxicology from different sources to be structured and shared in an understandable way. By using a common vocabulary and a user-friendly structure, it is envisioned that this particular ontology will allow scientists to make connections and understand relationships between common pathways resulting in adverse reproductive health outcomes.

Such a tool will help scientists and toxicologists predict the possibility of a substance producing developmental toxicity without the need for comprehensive animal testing. It is intended that this ontology can support work currently ongoing at the OECD to reduce reliance on animal testing by moving to a better understanding of the modes of action and biological pathways causing toxic effects.

This ECETOC Special Report no.19: *Building a Prenatal Developmental Toxicity Ontology*, can be freely downloaded at **http://bit.ly/ecetoc-sr19**.

A paper is also in preparation to be published in the Open Scientific Literature.

ECETOC Transformational Programmes

As part of the ECETOC Board decision to spend part of its resources on Thought Leadership, a set of Transformational Programmes addressing topics of longer term scientific relevance have been established aimed at producing transformational change in chemicals management. These are in general horizontal themes to be completed over 3-5 years. 3 programmes were initiated during 2015:

Using Molecular Data Wisely

The Programme: *Using Molecular Data Wisely* responds to a growing need to understand how to get the best value out of the increasing generation of large volumes of 'omics' data. Currently, there is no guidance on how to produce, store or interpret omics data in the regulatory context. Principles for a common path forward should be established so regulators can have confidence in using omics data for better decision-making and standard operating procedures based on best practice for each technology will ensure consistent application in laboratories. With this in mind, ECETOC has developed a tripartite Transformational Programme:

1 / Establish a set of principles for data production and storage in a standardized and GLP-like way in order to ensure similar paths and principles are adhered to across multiple laboratories.
2 / Establish a framework on how to analyse omics data, starting with transcriptomics. Expert Meetings during 2015 resulted in a draft framework.
3 / Develop a weight of evidence approach that assesses transparency, consistency and vulnerability to bias to aid risk assessors make scientific judgements on how to apply 'omics data to risk assessment. Achieving our goals would set quality criteria to ensure data quality, reproducibility and confidence in decision making. It could help facilitate regulatory acceptance of data from new technologies whilst protecting against interpretation of poor data, developed lacking the quality standards.

A workshop was held in Madrid in October 2016 (see details under 'Workshops and Symposia' earlier in this report) and the results will be presented at the (US) Society of Toxicology (SOT) Annual Meeting, Baltimore MD, USA in March 2017 and at EUROTOX 2017 in Bratislava, Slovakia in September 2017.

ECETOC Activity: Ecological Relevance of Risk Assessment
This activity will address the complexity and variability in Risk Assessment (RA) by improving ecological relevance to enable better risk mitigation and risk management.

The programme comprises 3 key elements:

1 / Assessing the effects of chemicals in ecological communities
Strategic objectives:
- Drive development of spatially explicit effect assessment approaches for higher tier risk assessment
- Develop effect assessment approaches accounting for temporal variation in population dynamics and community composition
- Develop proposals on how the effects of chemical mixtures on ecological communities could be assessed

2 / Exposure science for higher tier risk assessment
Strategic objectives:
- Assess the state of the science in exposure science and developments needed to refine higher tier risk assessment
- Develop models to generate exposure profiles accounting for spatial and temporal variation

3 / Ecosystem service-based approaches for landscape scale risk assessment and risk management
Strategic objectives:
- Evaluate the use of an ecosystem services approach to setting protection goals to inform chemical risk assessment
- Facilitate engagement of the chemical industry, academia and regulators to advance the practical implementation of the ecosystem service approach in chemical risk assessment and risk management
- Task Force to be established on *Geospatial approaches to increasing the ecological relevance of chemical risk assessments*

Globalisation of ECETOC Targeted Risk Assessment (TRA) Tool
TRA exposure model was made available in 2004. Since then the TRA tool has continued to evolve and attract attention both inside and outside Europe for chemicals regulation.

The TRA Tool has had a major beneficial impact on REACH (Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals) since there was no other way chemical safety assessments (CSAs) could be compiled. More than 80% of the CSAs submitted in the first two rounds of REACH registrations have been based on the TRA and, according to the most recent communications from ECHA, the worker part of the TRA has been applied in >90% of instances where CSAs are required as part of REACH registrations.

With this continued interest, ECETOC has established a TRA Steering Group to define, manage and lead how the TRA will be developed into the medium to long term. The purpose of this group is to scope options (which may entail targeted consultation with key interest groups); consult with stakeholders (including potentially those outside Europe); and finally, to develop and execute a plan to expand the use and applicability of the TRA Tool beyond Europe and REACH. Hence, ECETOC welcomed visits to the ECETOC offices during 2016 by Japanese and South Korean delegations to learn more about the TRA Tool and to present their national equivalents. ECETOC and its TRA Steering Group look forward to developing this collaboration as part of the ECETOC transformational programme and also the translation into Japanese by the Japanese Chemical Industry Ecology Toxicology & Information Center (JETOC) of the ECETOC Technical Reports supporting the current version of the TRA Tool.

ECETOC is also continuing to work with ECHA to address questions raised about the conservatism of the TRA model and to explore opportunities to protect workers' health in the workplace.

Communicating the Science

2016 was another productive year for ECETOC with the publication of 8 ECETOC reports and 7 Papers in the Open Scientific Literature on subjects as diverse as: building a prenatal developmental toxicity ontology, human exposure data in risk assessment of chemicals, noncoding RNA in regulatory toxicology, freshwater ecotoxicity as an impact category in life cycle assessment, toxicity thresholds for aquatic ecological communities and assessing impacts of chemical exposures, assessment and application of adverse outcome Pathways (AOPs) relevant to the endocrine system, to name but a few.

Another major accomplishment was the launch in May of the new ECETOC website, which introduces 'Topics' pages grouping information, publications and a series of YouTube video interviews with experts on some of the most important topics in the ECETOC Science Programme. For easy access, most ECETOC Reports can now also be read online and PDF downloads no longer require registration. An added bonus is that search engine spiders can now catalogue the entire content of ECETOC reports which increases their visibility in search results. Development of the website continues and a series of language options were added in December to spread the visibility of ECETOC even further afield. Currently, the 'static' parts of the website are available in: Arabic, Chinese, English French, German, Italian, Japanese, Korean, Polish, Portuguese, Russian and Spanish.

The Tools section of the website is best known for the Targeted Risk Assessment (TRA) Tool, but a nano-grouping risk assessment tool has been developed and is currently being adapted to coincide with discussions at ECHA on nano-grouping and read-across of chemicals. Work has also started on a human exposure data tool following the 2016 task force report on effective use of human exposure data in risk assessment of chemicals and associated workshop on advances in consumer exposure science: data, modelling and aggregate exposure assessment (see Technical Report no.126 and Workshop Report no.31).

Visit the new website at **http://www.ecetoc.org**

Publications

ECETOC's primary outputs are 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 published reports and articles published in in the open scientific literature.

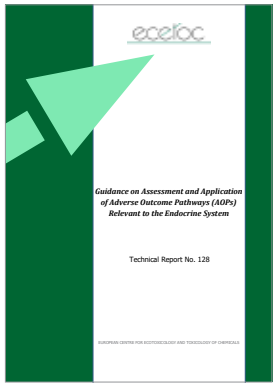
Technical Reports address specific aspects of the science used in evaluating the hazards and risks of chemicals to human health and the environment. (Note: Since 2009, 'Monographs', which were comprehensive reviews of generic topics or issues fundamental to the application of good science in evaluating the hazards and risks of chemicals, and 'Documents', which were scientific briefing papers addressing emerging issues, are also published as Technical Reports.

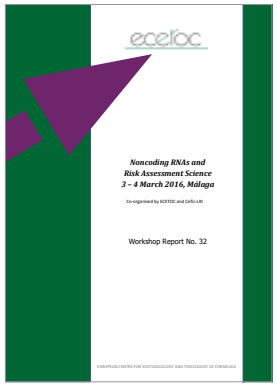
Workshop Reports are summaries of the discussions and conclusions derived from ECETOC sponsored scientific workshops.

Scientific Articles are publications in peer-reviewed journals.

JACC Reports (Joint Assessment of Commodity Chemicals) are comprehensive reviews of all available toxicological and ecotoxicological data on specific chemical substances, predominantly those having widespread and multiple uses. Each report presents a hazard assessment and identifies gaps in knowledge. The standard format may be extended in support of EU or other international risk assessment, or setting of an occupational exposure limit value. Special Reports are compilations of data targeted to specific regulatory issues/demands.

Please note that, as part of our continuing drive for efficiency and environmental care, all ECETOC publications are now distributed exclusively in electronic format. All reports can be freely downloaded from **http://www.ecetoc.org/publications**





Reports Published by ECETOC during 2016

Special Report no.19: Building a Prenatal Developmental Toxicity Ontology [Published August 2016]

Technical Report no.126: Guidance for Effective Use of Human Exposure Data in Risk Assessment of Chemicals [Published November 2016]

Technical Report no.127: Freshwater ecotoxicity as an impact category in life cycle assessment [Published November 2016]

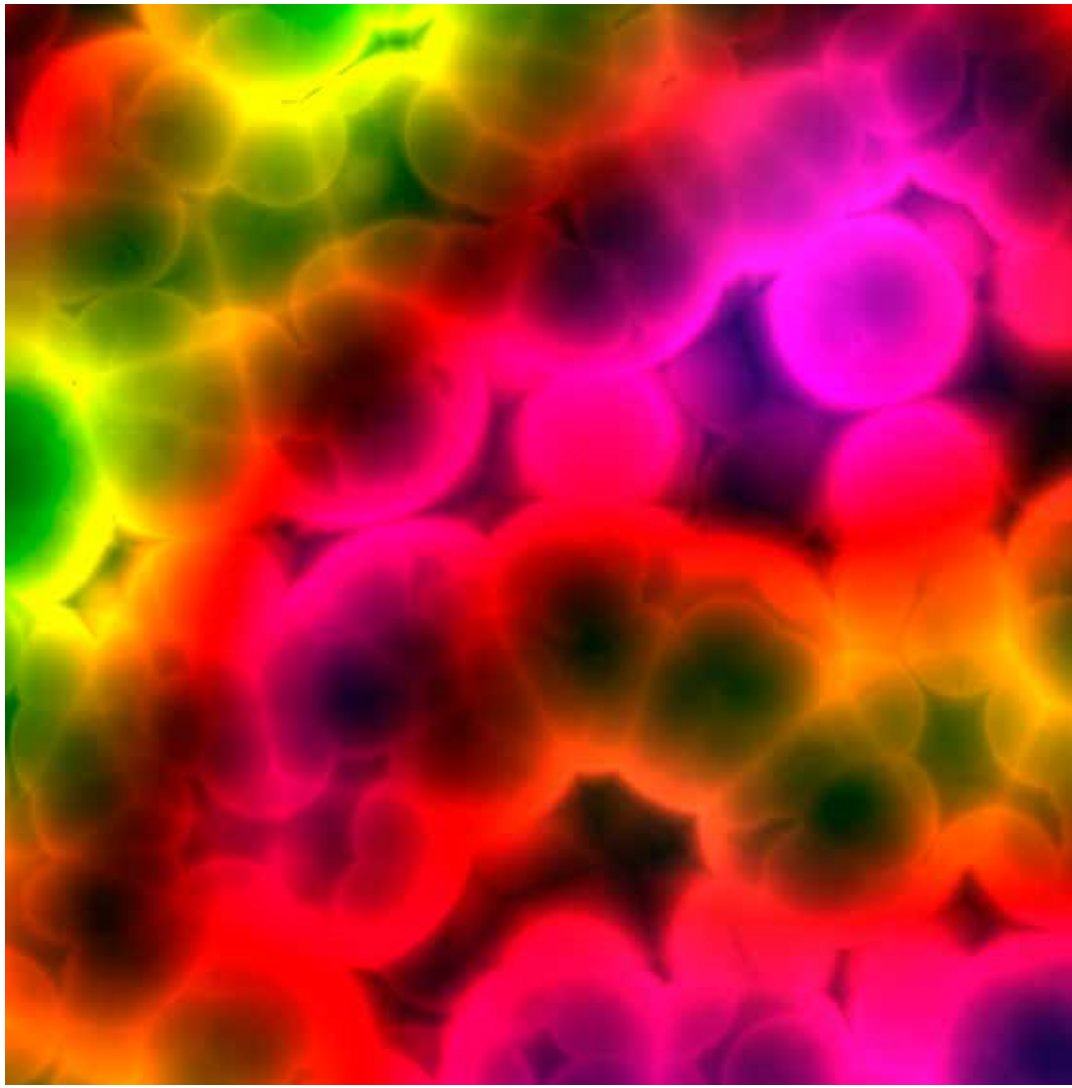
Technical Report no.128: Guidance on assessment and application of Adverse Outcome Pathways (AOPs) relevant to the Endocrine System [Published December 2016]

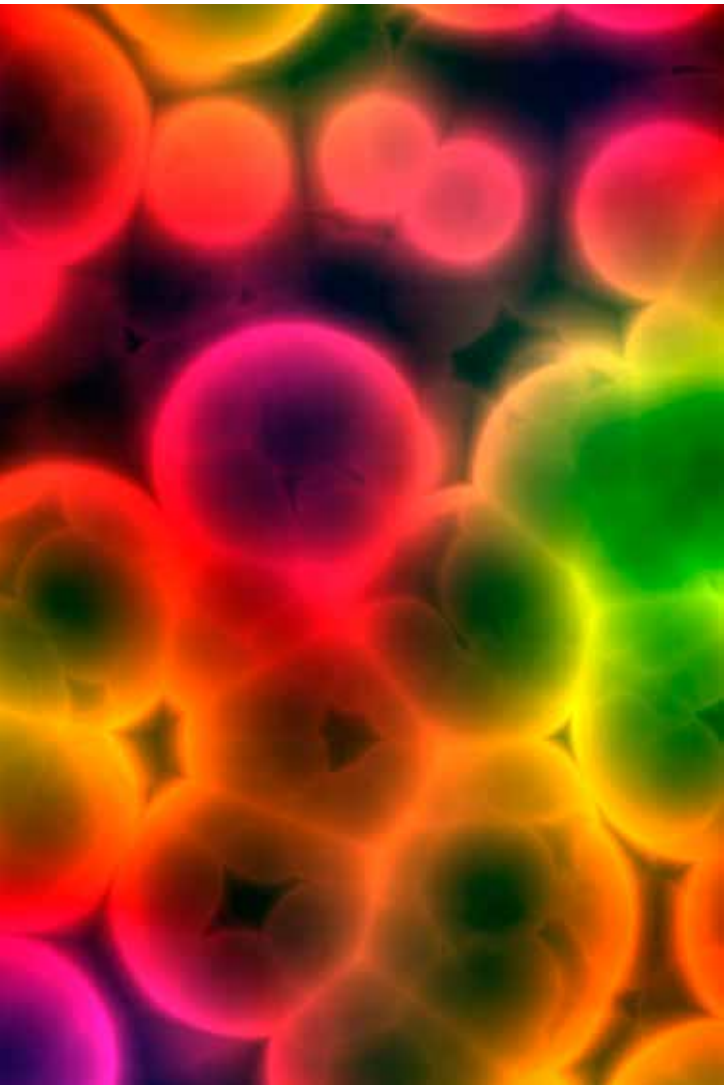
Workshop Report no.29: Defining the role of chemical activity in environmental risk assessment within the context of mode of action: Practical guidance and advice. 29-30 October 2015 Snowbird, Utah, USA [Published August 2016]

Workshop Report no.30: The Role of Epigenetics in Reproductive Toxicity. 12-13 November 2015, Brussels [Published August 2016]

Workshop Report no.31: Advances in Consumer Exposure Science: Data, Modelling and Aggregate Exposure Assessment. 26 January 2016, Brussels [Published August 2016]

Workshop Report no.32: Noncoding RNAs and Risk Assessment Science. 3-4 March 2016, Málaga [Published August 2016]





Articles Published in the Open Scientific Literature during 2016

Aigner A, Buesen R, Gant T, Gooderham N, Greim H, Hackermüller J, Hubesch B, Laffont M, Marczylo E, Meister G, Petrick JS, Rasoulpour RJ, Sauer UG, Schmidt K, Seitz H, Slack F, Sukata T, van der Vies SM, Verhaert J, Witwer KW, Poole A. 2016.

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Belanger S, Barron M, Craig P, Dyer S, Galay-Burgos M, Hamer M, Marshall S, Posthuma L, Raimondo S, Whitehouse P. 2016.

Future needs and recommendations in the development of species sensitivity distributions: Estimating toxicity thresholds for aquatic ecological communities and assessing impacts of chemical exposures.

Integr Environ Assess Manag (Open Access in preparation) [Epub 29 September 2016 ahead of print]
Doi: 10.1002/ieam.1841

Struijs J, van de Meent D, Schowanek D, Buchholz H, Patoux R, Wolf T, Austin T, Tolls J, van Leeuwen K, Galay-Burgos M. 2016.

Adapting SimpleTreat for simulating behaviour of chemical substances during industrial sewage treatment.

Chemosphere 159:619-27
Doi 10.1016/j.chemosphere.2016.06.063. Epub 2016 Jun 24

Maltby L, Jackson M, Whale G, Ross Brown A, Hamer M, Solga A, Kabouw P, Woods R, Marshall S. 2016.

Is an ecosystem services-based approach developed for setting specific protection goals for plant protection products applicable to other chemicals?

Sci Total Environ Available online 24 December 2016, ISSN 0048-9697 (Open Access)
Doi: 10.1016/j.scitotenv.2016.12.083

Moore NP, Beekhuijzen M, Boogaard PJ, Foreman JE, North CM, Palermo C, Schneider S, Strauss V, van Ravenzwaay B, Poole A. 2016.

Guidance on the selection of cohorts for the extended one-generation reproduction toxicity study (OECD test guideline 443).

Regul Toxicol Pharmacol 80:32-40 (Open Access)
Doi: 10.1016/j.yrtph.2016.05.036

Brown AR, Whale G, Jackson M, Marshall S, Hamer M, Solga A, Kabouw P, Galay-Burgos M, Woods R, Nadzialek S, Maltby L. 2016.

Towards the definition of specific protection goals for the environmental risk assessment of chemicals: A perspective on environmental regulation in Europe.

IIntegr Environ Assess Manag 2016 Aug 10
Doi: 10.1002/ieam.1797 (Open Access)

Thomas P, Mackay D, Mayer P, Arnot J, Galay Burgos M. 2016.

Response to comment on 'Application of the activity framework for assessing aquatic ecotoxicology data for organic chemicals'.

Environ Sci Technol 50(7):4141-4142
Doi: 10.1021/acs.est.6b00864

Contributing to International Initiatives

Representation, Presentations and Posters at Specific Meetings

9th Implementation of Global Chemical Safety Regulations in Russian and CIS Corporations
20-22 April 2016, Amsterdam, Netherlands
Participation by Alan Poole (ECETOC)

SETAC Europe 26th Annual Meeting: Environmental contaminants from land to sea: continuities and interface in environmental toxicology and chemistry
22-26 May 2016, Nantes, France
Member of the Organising Committee: Malyka Galay Burgos (ECETOC)

ICCA-LRI & NIHS Workshop – Meeting the Global Challenge of Applying New Scientific Methods to Improve Environmental and Human Health Risk Assessments
15-16 June 2106, Awaji Island, Japan
Participation by Alan Poole (ECETOC)

52nd Congress of the European Societies of Toxicology (Eurotox)
04-07 September 2016, Seville, Spain
Participation by Alan Poole (ECETOC)
Workshop W02: Improving chemicals risk assessment with refined exposure characterisation

SETAC / iEOS - Joint Focused Topic Meeting on Environmental and (eco)toxicological Omics and Epigenetics: Science, Technology and Regulatory Applications
12-15 September 2016, Ghent, Belgium

- Session 3: (Eco)toxicological omics
  Presentation by Tim Gant (Public Health England, UK): Towards developing a Framework for transcriptomics and other Big Data analysis for regulatory application
- Session 6: Epigenetics in risk assessment: academia, industry and regulator perspective

Keynote speaker Alan Poole (ECETOC): Industry perspective

International Society of Exposure Science (ISES)
09-13 October 2016, Utrecht, The Netherlands
Poster presentation: Re-analysis of the ETEAM Database for the ECETOC TRAv3 Model
Barone N[1], Bachler G[2], Keller D[3], Money C[4], Noij D[5], Tibaldi R[1]

[1]ExxonMobil, [2]Shell Health, [3]Henkel, [4]Cynara Consulting, [5]Dow

7th Euro-Global Summit on Toxicology and Applied Pharmacology
24-26 October 2016, Rome, Italy
Presentation by Alan Poole (ECETOC): 'Guidance on the selection of cohorts for extended one-generation reproduction toxicity study (OECD 443)'

7th World Congress / SETAC North America 37th Annual Meeting (Orlando, FL)
10 November 2016, Orlando, Florida, USA
Two posters presented:

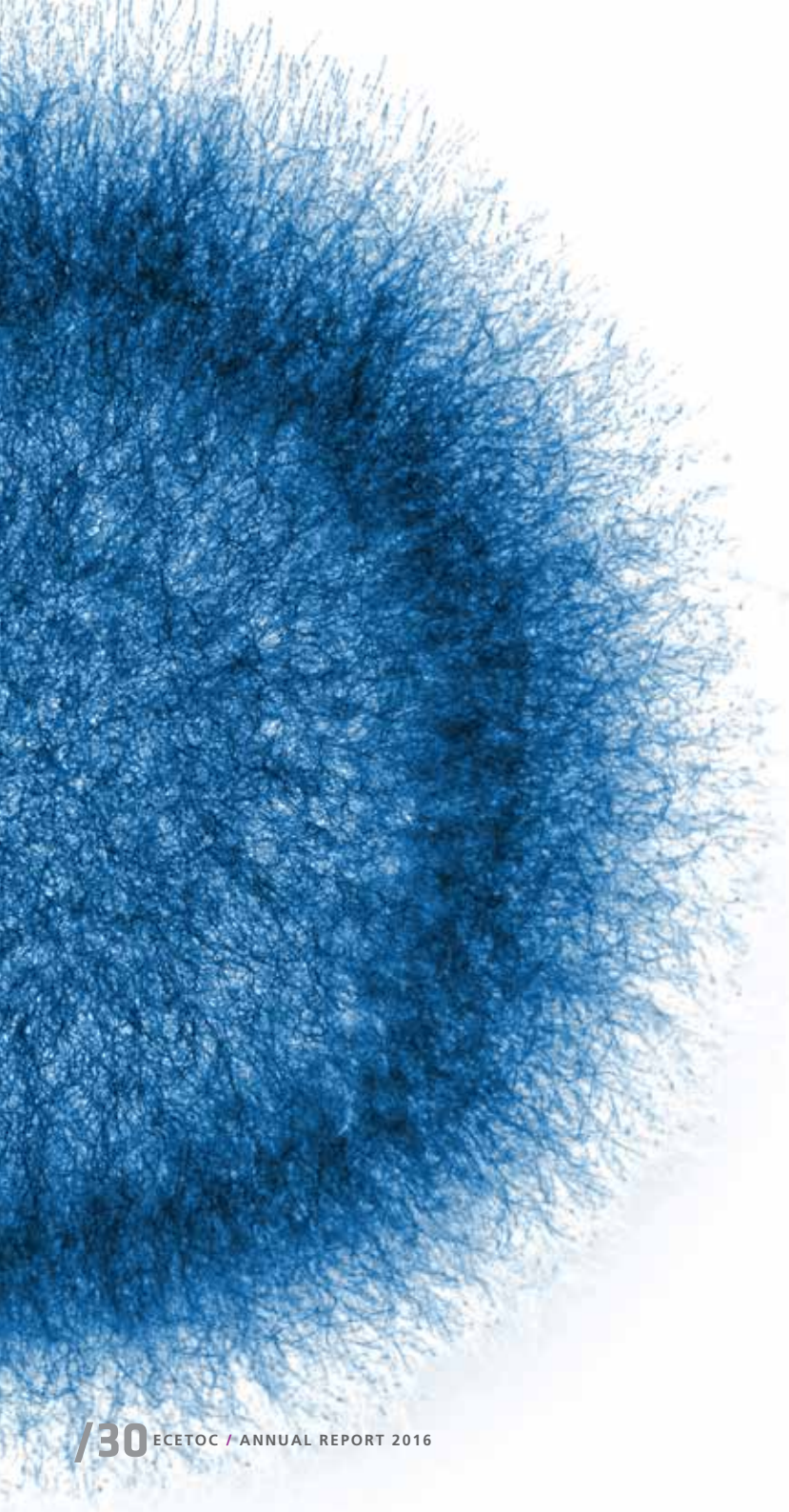
- RIFM/ECETOC WS: Developing a strategy to improve the environmental risk assessment of difficult to test multi-component substances Part 1: Background
  Romanas Cesnaitis[1], Joop de Knecht[2], Karen Eisenreich[3], Marc Fernandez[4], Malyka Galay-Burgos[5], Miriam León-Paumen[6], Karen Jenner[7], Delina Lyon[8], Dan Salvito9, Diederik Schowanek[10], Joy Worden[8]

[1]ECHA, [2]RIVM, [3]USEPA, [4]Environment and Climate Change Canada, [5]ECETOC, [6]ExxonMobil, [7]Givaudan, [8]Shell, [9]RIFM, [10]Procter&Gamble

- RIFM / ECETOC WS Developing a strategy to improve the environmental risk assessment of difficult to test multi-component substances Part 2: Workshop Output
  Romanas Cesnaitis[1], Joop de Knecht[2], Karen Eisenreich[3], Michelle Embry[4], Marc Fernandez[5], Miriam León-Paumen[6], Karen Jenner[7], Delina Lyon[8], Dan Salvito[9]

[1]ECHA, [2]RIVM, [3]USEPA, [4]HESI, [5]Environment and Climate Change Canada, [6]ExxonMobil, [7]Givaudan, [8]Shell, [9]RIFM

18th Annual Cefic LRI Workshop 'AOPs and Genomics: how useful, how to address risk, and where next?'
16-17 November 2016, Brussels, Belgium
Participation by Alan Poole and Madeleine Laffont (ECETOC)



Input to Specific Projects and Reports

6th Framework Programme Co-ordination Action Project 'Norman'
Participation in Advisory Board on behalf of ECETOC
by Stuart Marshall (Unilever)

7th Framework Programme Co-ordination Action Project 'EUROECOTOX'
The EUROECOTOX, EU-FP7 funded project and network promotes cooperation between research centres, industry and other stakeholders in Europe devoted to the R&D and application of Alternative Testing Strategies in Ecotoxicology. Since December 2012 the network has been coordinated by Dr Malyka Galay Burgos of ECETOC, one of the EUROECOTOX partners.

ECHA Guidance on registration [Published November 2016]
ECETOC representative: Marie-Amélie Pail, (Dupont)

ECHA Nanomaterials-related Appendix to the Guidance on Registration [Draft published May 2016]
ECETOC representative: Karin Wiench, (BASF)

ECHA Update of the Guidance for identification and naming of substances under REACH and CLP, limited to a proposed new appendix addressing the Substance Identity Profile (SIP) concept. [Published December 2016]
ECETOC representative: Sylvia Jacobi, (Albemarle)

ECHA Guidance update related to the 8th ATP to CLP: one single PEG to update:

- Guidance on the application of the CLP Criteria
- ECHA Guidance on labelling and packaging in accordance with Regulation (EC) No 1272/2008 [Published September 2016]

ECETOC representative: Jackie Wennington, (ExxonMobil)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), nanomaterials-related Appendix to Chapter R.6: on QSARs and grouping of chemicals
ECETOC representative: Karin Wiench, (BASF)

ECHA Update of the Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.7a, Section R.7.5 (related to repeated dose toxicity only) [Draft published May 2016]
ECETOC representative: Wera Teubner (BASF)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.7a, Section R.7.6 (reproductive toxicity) [Published December 2016]
Participation on behalf of ECETOC by Christine Palermo (ExxonMobil)

ECHA Updates to existing Appendices to Chapters R.7a, R7.b and R7.c of the Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA (Endpoint specific guidance) on 'recommendations for nanomaterials' covering environmental endpoints
ECETOC representative: Karin Wiench, (BASF)

ECHA Updates to existing Appendices to Chapters R.7a and R7.c of the Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA) (Endpoint specific guidance) on 'recommendations for nanomaterials' regarding human health endpoints
ECETOC representative: Karin Wiench, (BASF)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.7b, (Sediment Compartment) Published February 2016)
Participation on behalf of ECETOC by Gordon Sanders (Givaudan)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.7.2, (Irritation / Corrosion) [Published December 2016]
Participation on behalf of ECETOC by Pauline McNamee (P&G)

ECHA Update of the Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.11, Part C and specific sections of Chapters R.7b and R.7c (related PBT/vPvB assessment) [Drafts published June 2016]
ECETOC representative: Sylvia Jacobi, (Albemarle)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.14: Occupational exposure estimation and Part D: Exposure scenario building [Published August 2016]
PEG R14: Michael Haack, (Wacker Chemie)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.15: Consumer exposure estimation [Published July 2016]
PEG R15: Carlos Rodriguez, (P&G)

ECHA Guidance on Information Requirements and Chemical Safety Assessment (IR&CSA), Chapter R.16: Environmental exposure estimation [Published February 2016]
PRG R16: Johannes Tolls, (Henkel)

ECHA Update of the 'Guidance on Labelling and Packaging in accordance with regulation (EC) No. 1272/2008' [Published September 2016]
Participation on behalf of ECETOC by Gerd-Uwe Spiegel (Dupont)

ECHA Endocrine Disruptor Expert Group
Participation on behalf of ECETOC by Remi Bars (Bayer)

ECHA Nanomaterials Working Group
Participation on behalf of ECETOC by Karin Wiench (BASF)

ECHA Partner Expert Group: 'Introductory Guidance on the CLP Regulation'
Participation on behalf of ECETOC by Ingolf Kühn (BASF)

ECHA PBT Partner Expert Group
Participation on behalf of ECETOC by Michiel Claessens (DuPont)

ECHA PBT Expert Group
The Expert Group advising ECHA on PBT issues has regularly met since May 2013. Participation on behalf of ECETOC by Sylvia Jacobi (Albemarle)

ECHA Risk Assessment Committee (RAC)
Participation as an observer on behalf of ECETOC by Alan Poole (ECETOC)

ECVAM Stakeholder Forum (ESTAF)
Participation on behalf of ECETOC by Remi Bars (Bayer)

Endocrine Disrupter Expert Advisory Group to the EU Commission (ED EAG)
Participation on behalf of ECETOC by Remi Bars (Bayer) and James Wheeler (Syngenta, now at Dow)

OECD Extended Advisory Group on Molecular Screening and Toxicogenomics (EAG MST)
Participation on behalf of ECETOC by Remi Bars (Bayer)

OECD Endocrine Disrupters Testing and Assessment (EDTA) Advisory Group
Participation on behalf of ECETOC by Remi Bars (Bayer)

SETAC Europe 2016 Scientific Committee and 26th Annual Meeting
Member: Malyka Galay Burgos (ECETOC)

STFC / NERC Bioinformatics and Environmental 'Omics Network
The overarching objective of the network is to build bridges between scientific communities in bioinformatics and environmental 'omics. The network will be co-aligned with the establishment of the new UK National Environmental Research Council (NERC) Environmental 'Omics Synthesis Centre (EOS), which has the remit of exploring emerging areas of bioinformatics and environmental 'omics and their application to environmental problems. ECETOC was represented by Malyka Galay Burgos until her departure from ECETOC in July 2016.

WHO/IPCS Chemical Risk Assessment Network
Participation on behalf of ECETOC by Alan Poole (ECETOC)

Science Awards

Since 2003, ECETOC has been recognising talented young scientists by sponsoring annual Science Awards to outstanding works of science. ECETOC sponsored the following awards during 2016:

Environmental science related award

SETAC Europe 26th Annual Meeting: Young Scientist Awards (YSA)

22-26 May 2016, Nantes, France

The ECETOC Best Platform Award honours the early career scientist with the best platform presentation at the SETAC Europe Annual Meeting. The award at SETAC Europe, Nantes 2016, went to Yuan Pan, of the University of Sheffield, United Kingdom, for her presentation on 'Using the ecosystem services framework to link scientific research and policy-making: a case study of Lake Tai, China.' More information on the SETAC Nantes meeting can be found at http://nantes.setac.eu

Yuan Pan receiving her award at SETAC Nantes

Human health science related award

Eurotox 2016: ECETOC Christa Hennes Young Scientist Award

04-07 September 2016, Seville, Spain

This is a Best Poster Award for toxicological research into mechanisms and risk assessment, selected by a panel in which ECETOC participates at the EUROTOX Annual Meeting. In 2014, the award was re-named in memory of the late Dr Christa Hennes, former ECETOC Human Health Sciences Manager, who was instrumental in its organisation.
At EUROTOX, Seville 2016, this award was won by Marlon Jetten of Maastricht University for her abstract: 'Development of short- term assay(s) to predict dermal cancer potential of petroleum streams'.
The winner receives a monetary prize and a free invitation to the following year's Eurotox meeting. Eurotox 2016 website: http://www.eurotox2015.com/

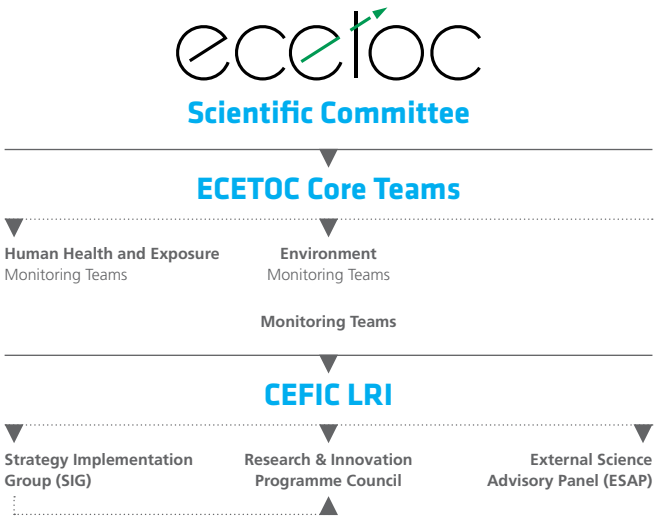
ECETOC Contribution to

Cefic Long-Range Research Initiative

Since 1996, the Long-range Research Initiative (LRI) Programme of Cefic, the European Chemical Industry Council, has been providing proactive scientific data on which the entire industry and regulatory bodies can draw to address societal concerns on a reliable basis.

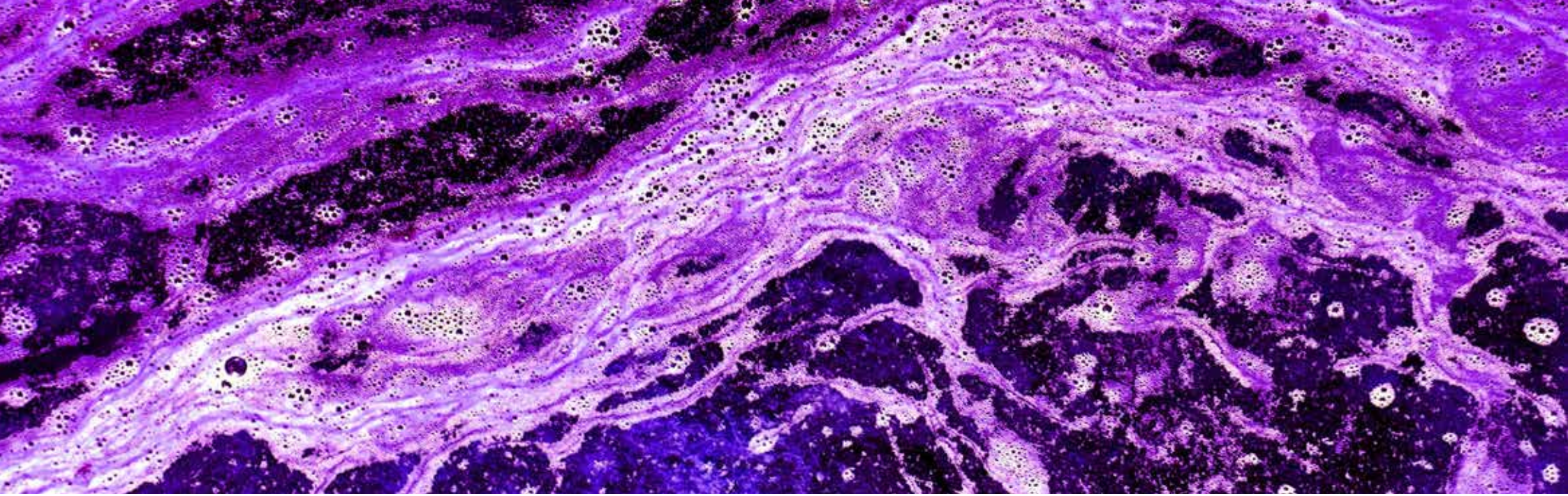
ECETOC Contribution to Cefic Long-range Research Initiative

As a fundamental basis for a sustainable chemical industry and a complement to Responsible Care, LRI presents a research programme that is forward-looking and ambitious, but also realistic and coherent. LRI invests in long-term research and delivers transparent, quality-assured scientific data, open to the broad public.



As the scientific partner to Cefic LRI, ECETOC provides scientific support to the LRI and input into the Research Programme by managing the scientific evaluation of applications for funding, recommending the best research proposals and monitoring the progress of selected LRI projects. In particular ECETOC is 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.



Human Health and Exposure Monitoring Teams

5 projects were completed during 2016 (marked below with#) and 3 new projects secured funding and were initiated with the support of the monitoring teams (marked below with*). The current research projects are:

AIMT4#: Moving from DECO towards OECD
[Completed December 2016]
Principal investigator: Dr. Danyel Jennen, Maastricht University (UM), Maastricht, The Netherlands

AIMT5: Building a Prenatal Developmental Toxicity Ontology, integrating existing biological, chemical, *in silico* models and *in vitro* methods and data, aiming at an alternative integrated AOP/MoA framework for mechanistic hazard and risk assessment in developmental toxicology
Principal investigator: Prof. Dr. Aldert Piersma, RIVM, National Institute for Public Health and the Environment, The Netherlands

AIMT6: CON4EI: CONsortium for *in vitro* Eye Irritation testing strategy
Principal investigator: Dr. An Van Rompay, Flemish Institute for Technological Research (VITO), Belgium

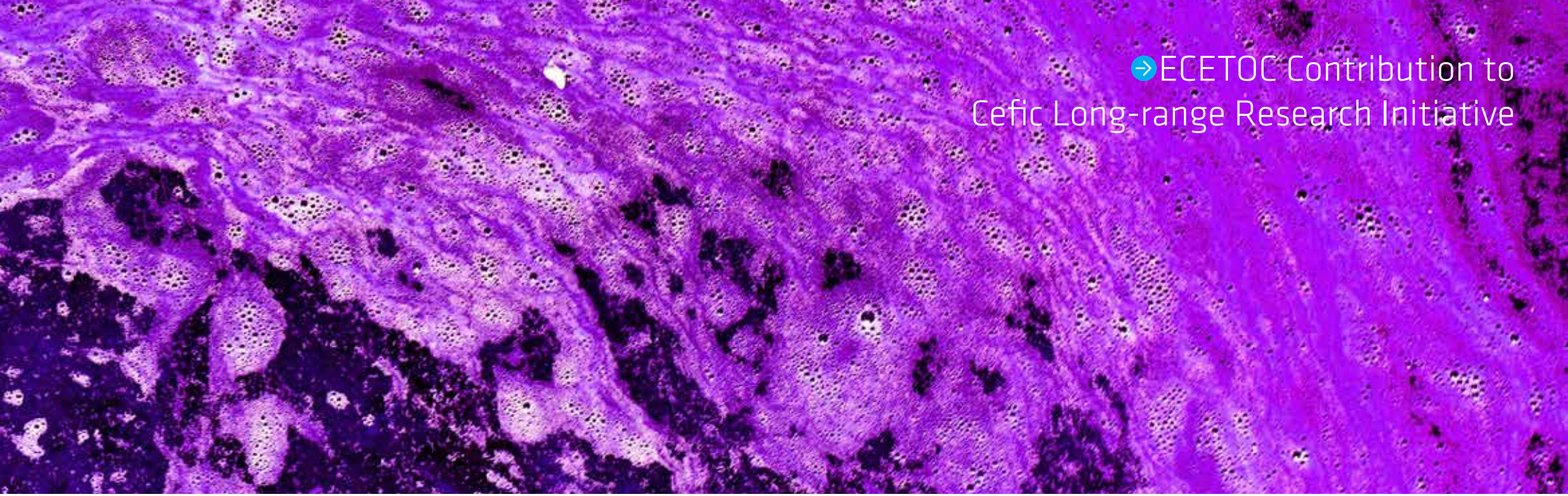
AIMT7*: *RVis: Open Access PBPK Modelling Platform*
Principal investigator: Dr. George Loizou, Health and Safety Laboratory (HSL), United Kingdom

AIMT8*: Assessing New Methodology for Repeat Dose Toxicological Hazard Assessment by "Equivalent Protection" Criteria
Principal investigator: Dr. Sylvia Escher, Fraunhofer ITEM, Germany

B11: Integrated external and internal exposure modelling platform
Principal investigator: Assoc. Prof. Dimosthenis Sarigiannis, Centre for Research and Technology Hellas, Thessaloniki, Greece

B12#: Assessing the relevance of the dust contribution to substances from consumer products and articles
Principal investigator: Dr. Natalie von Götz, ETH, Safety and Environmental Technology Group, Zürich, Switzerland [Completed June 2016]

B13#: Development of a mechanistic *in silico* multi-scale framework to assess dermal absorption of chemicals
Principal investigator: Prof. Gerald Kasting – University of Cincinnati, OH, USA [Completed September 2016]



ECETOC Contribution to Cefic Long-range Research Initiative

B15: Developing a robust method of allocating efficiency measures to regulatory instruments in the chemicals industry
Principal investigator: Prof. Len Levy – Cranfield University, United Kingdom

B16#: External validation of Tier-1 workers dermal exposure estimates in ECETOC TRA.
Principal investigator: Dr. Jodi Schinkel, Netherlands Organisation for Applied Scientific Research (TNO), The Netherlands
[Completed June 2016]

B17: Human exposure to emerging chemicals present in the indoor environment
Dr. Marja Lamoree, VU University Amsterdam, The Netherlands

B18: Database on Carcinogen Dose-response, including Information on DNA reactivity, for TTC and beyond
Prof. Mark Cronin, Liverpool John Moores University, United Kingdom

B19*: Extrapolating the Applicability of Worker Exposure Measurement Data
Rfp advertised in 2016. Selection Team meetings held 27 September and 18 October 2016
Principal investigator: Dr. ir. Wouter Fransman, TNO, The Netherlands

C3: A comprehensive Epigenomic profile of liver tissue from Rat and Mouse
Principal investigator: Prof. Richard Meehan, University of Edinburgh, United Kingdom

EMSG57: Endocrine disruptors and obesity, diabetes and heart disease: State of the science and biological plausibility
Principal investigator: Dr. Judy LaKind, LaKind Associates, Catonsville, MD, USA

EMSG58#: Human adverse health effects of endocrine active substances: assessment of the quality of individual epidemiological studies and of the overall mechanistic and epidemiologic evidence
Principal investigator: Prof. Carlo La Vecchia, IRCCS - Istituto di Ricerche Farmacologiche Mario Negri (IRFMN), Milan, Italy
[Completed October 2016]

HBM5: A(ESAP) Human Exposure to chemical mixtures present in indoor environments
Principal investigator: Dr. Greet Schoeters, VITO Flemish Institute for Technological Research, Belgium

N5: Histopathology of rats exposed to Barium sulfate nanoparticles by life-time inhalation exposure – Effects and Biokinetics
Principal investigator: Dr. Dirk Schaudien, Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany

Environmental Monitoring Teams

6 projects were completed during 2016 (marked below with#) and 6 new environmental projects secured funding and were initiated in 2016 with the support of the monitoring teams (marked below with*). The current research projects are:

ECO8.3#: Fish cell line and embryo assays: follow up to the CEllSens ECO8/8.2 project [completed in 2015: In collaboration with the NC3Rs, a Round-Robin test of the RTgill-W1cell line assay was carried out in 2016]
Principal investigator: Prof. Kristin Schirmer, Eawag, Switzerland

ECO19#: Towards more ecologically realistic assessment of chemicals in the environment [Completed in 2016: Final Workshop held 09-10 February 2016, Como, Italy]
Principal investigator: Dr. Frederik De Laender, Ghent University, Belgium

ECO20.2: Development of an alternative testing strategy for the fish early life-stage (FELS) test (OECD 210) [Extension to ECO20]
Principal investigator: Prof. Dr. Dries Knapen, University of Antwerp, Belgium

ECO21.2#: Mechanistic Bioaccumulation Model(s) for Ionogenic Organic Substances in Fish [Extension to ECO21 completed in 2016]
Principal investigator: Dr. Jon Arnot, ARC Arnot Research & Consulting Inc, Canada

ECO22#: Advancing the use of passive sampling in risk assessment and management of contaminated sediments: an inter-laboratory comparison study on measurements of freely dissolved (bioavailable) concentrations using different passive sampling formats [Extended and completed in 2016]:
Principal investigator: Dr. Michiel Jonker, University of Utrecht, The Netherlands

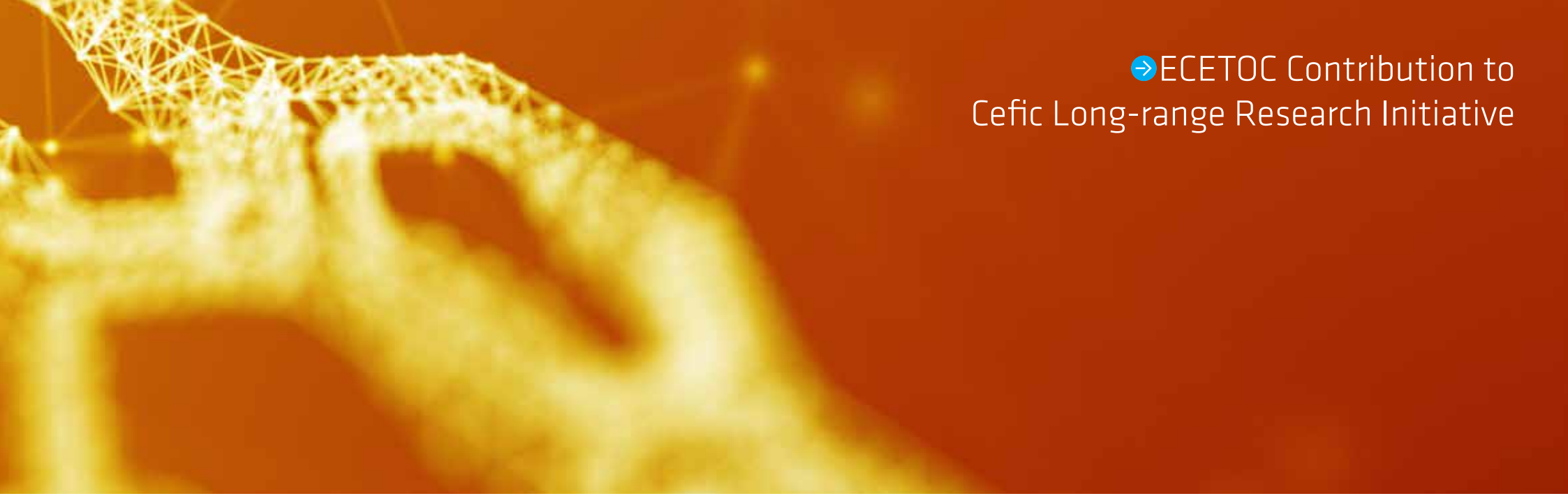
ECO23: Time-Integrative Passive sampling combined with Toxicity Profiling (TIPTOP): an effect-based strategy for cost-effective chemical water quality assessment
Principal investigator: Dr. Timo Hamers Phd, IVM, VU University, Amsterdam, The Netherlands

ECO24#: Computer based prediction of the formation of Non-Extractable Residues (NER) of xenobiotics and their metabolites in soils and sediments with regard to their environmental hazard [Completed 2016]
Principal investigator: Dr. Gerrit Schüürmann, Helmholtz Centre for Environmental Research (UFZ), Leipzig, Germany

ECO25: Development of Soup Tests for the Risk assessment of NER in Soil
Principal investigator: Dr. Joop Harmsen, Alterra Wageningen UR, The Netherlands

ECO26#: Adapt SimpleTreat for simulating behaviour of chemical substances during industrial sewage treatment [Completed 2016]
Principal investigator: Prof. Dik van de Meent, Radboud University, The Netherlands

ECO27: Chemicals: Assessment of Risks to Ecosystem Services (CARES)
Principal investigator: Prof. Lorraine Maltby, University of Sheffield, United Kingdom



ECETOC Contribution to Cefic Long-range Research Initiative

ECO28: Modelling approaches for a scenario based assessment of chemically induced impacts on aquatic macroinvertebrate communities (MACROMOD)
Principal investigator: Dr. Monika Hammers-Wirtz, Research Institute for Ecosystem Analysis and Assessment, (gaiac), Germany

ECO29: Application of chemostat systems to include adaptation of microbial communities in persistency testing
Principal investigator: Dr. John Parsons, University of Amsterdam (UvA), The Netherlands

ECO30: Expanding the applicability domain of the chemical activity approach for hazard and risk assessment
Principal investigator: Dr. Jon Arnot and Dr. James Armitage, ARC Arnot Research & Consulting Inc., Toronto, Canada

ECO31: Identifying strategies that will provide greater confidence in estimating the degradation rates of organic chemicals in water, soil, and sediment
Principal investigator: Dr. Damian Helbling, Cornell University, USA

ECO32: Environmental risk assessment of poorly soluble substances: Improved tools for assessing biodegradation, (de)sorption, and modelling
Principal investigator: Prof. Dr. Andreas Schäffer, Aachen University, Germany

ECO33*: Strengthening the use and interpretation of dietary bioaccumulation tests for hydrophobic chemicals
Rfp advertised in 2016. Selection Team meeting held 07 October 2016
Principal investigator: Dr. Frank Gobas, Frank Gobas Environmental Research, Canada

ECO34: A tiered testing strategy for rapid estimation of bioaccumulation by a combined modelling - in vitro testing approach
Principal investigator: Prof. Kristin Schirmer, Eawag, Switzerland

ECO35: Interference of hepatotoxicity with endocrine activity in fish
Principal investigator: Prof. Dr. Thomas Braunbeck, University of Heidelberg, Germany

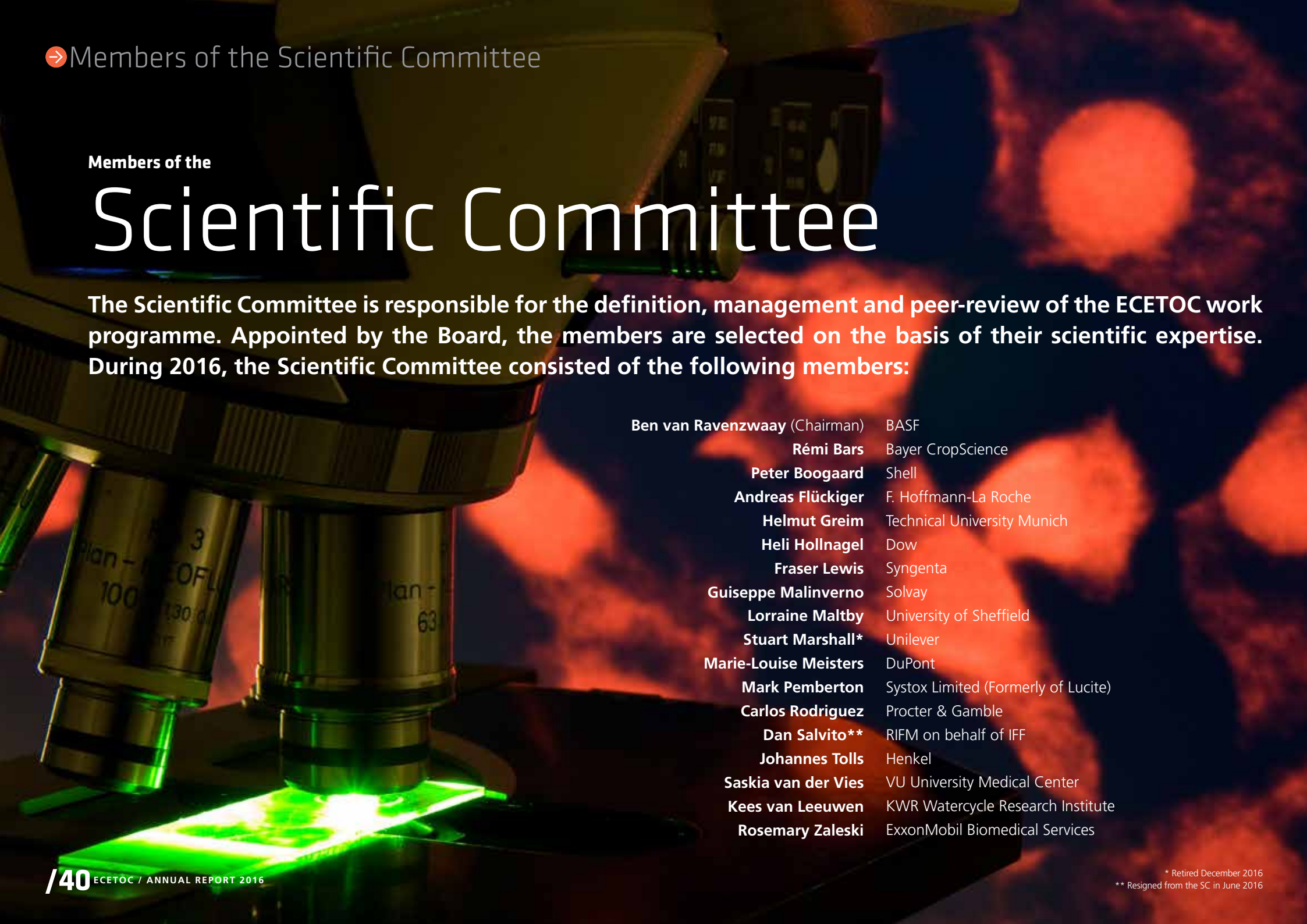
ECO36*: Building improved in-vitro exposure assessment capability Rfp advertised in 2016. Selection Team meeting held 04 October 2016
Principal investigator: Prof. Beate Escher, Helmholtz Centre for Environmental Research, UFZ Leipzig, Germany

ECO37*: Development and validation of alternative methodologies for predicting bioaccumulation of surfactants
Rfp advertised in 2016. Selection Team meeting held 03 October 2016
Principal investigator: Dr. Steven Droge, University of Amsterdam, The Netherlands

ECO38*: Improving determinations of water solubility for 'difficult-to-test' substances
Rfp advertised in 2016. Selection Team meeting held 03 October 2016
Principal investigator: Prof. Philipp Mayer, Technical University of Denmark, Denmark

ECO39*: Review, ring-test and guidance for TKTD modelling
Principal investigator: Dr. Roman Ashauer, York University, United Kingdom

ECO40*: Validation of an alternative, non-vertebrate, BCF test using the freshwater amphipod Hyalella Azteca.
Rfp advertised in 2016. Selection Team meeting held 06 October 2016
Principal investigator: Dr. Christian Schlechtriem, Fraunhofer IME, Germany



Members of the

Scientific Committee

The Scientific Committee is responsible for the definition, management and peer-review of the ECETOC work programme. Appointed by the Board, the members are selected on the basis of their scientific expertise. During 2016, the Scientific Committee consisted of the following members:

Ben van Ravenzwaay (Chairman)	BASF
Rémi Bars	Bayer CropScience
Peter Boogaard	Shell
Andreas Flückiger	F. Hoffmann-La Roche
Helmut Greim	Technical University Munich
Heli Hollnagel	Dow
Fraser Lewis	Syngenta
Guiseppe Malinverno	Solvay
Lorraine Maltby	University of Sheffield
Stuart Marshall*	Unilever
Marie-Louise Meisters	DuPont
Mark Pemberton	Systox Limited (Formerly of Lucite)
Carlos Rodriguez	Procter & Gamble
Dan Salvito**	RIFM on behalf of IFF
Johannes Tolls	Henkel
Saskia van der Vies	VU University Medical Center
Kees van Leeuwen	KWR Watercycle Research Institute
Rosemary Zaleski	ExxonMobil Biomedical Services

* Retired December 2016
** Resigned from the SC in June 2016

Members of the

Secretariat

The ECETOC Secretariat is responsible for the co-ordination and management of the scientific work programme, ensuring that the tasks assigned 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. During 2016, the Secretariat comprised the following members:

Alan Poole	Secretary General
Malyka Galay Burgos*	Environmental Sciences Manager
Madeleine Laffont**	Human Health Scientist
Geneviève Gérits	Office Manager
Ian Cummings	Communications, Media and Web Manager
Christine Yannakas	Administrative Assistant
Agnieszka Harris***	Administrative Assistant
Francesca Uguccioni***	Administrative Assistant

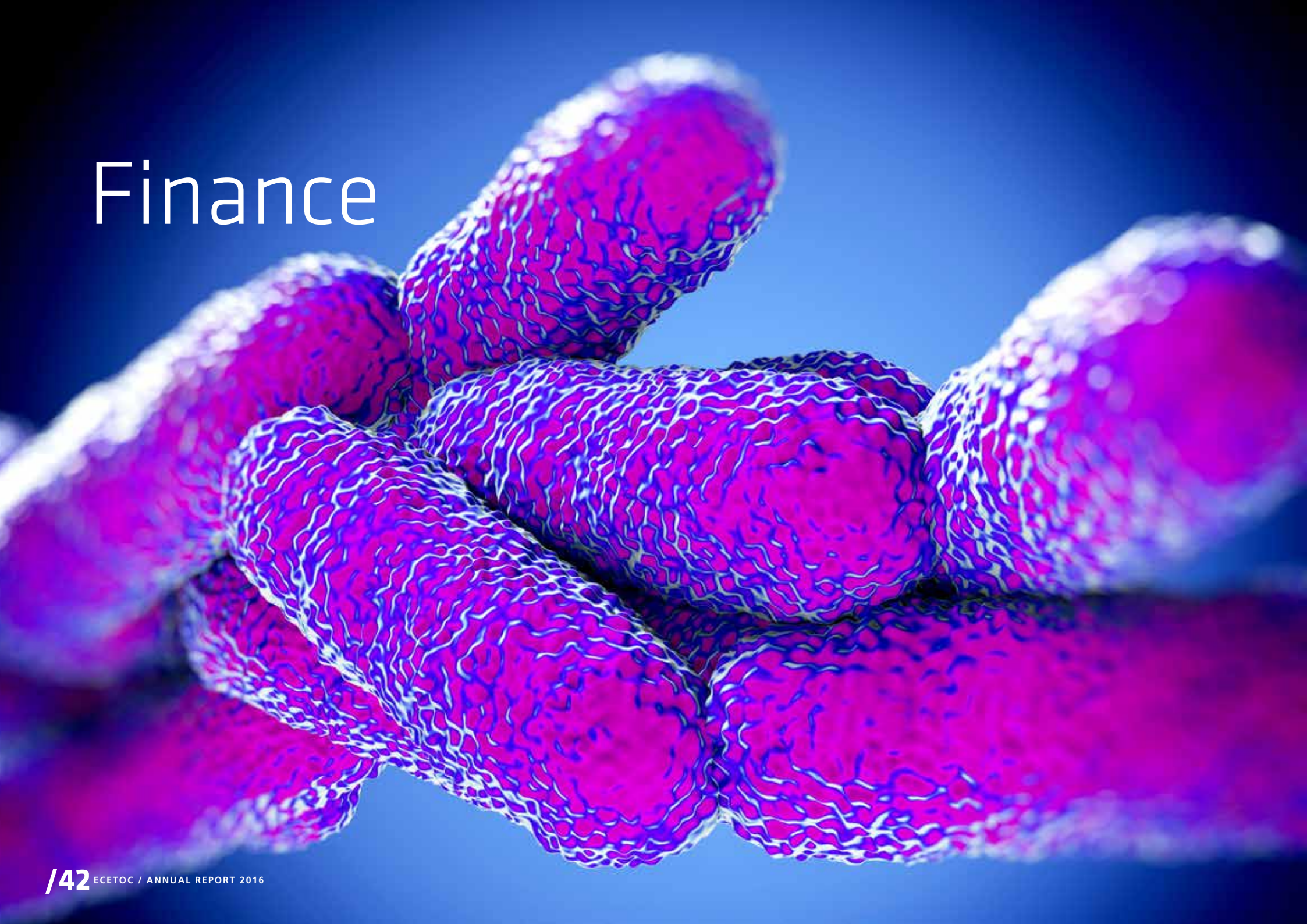
*Dr Malyka Galay Burgos, Environmental Sciences Manager since September 2007, left ECETOC in July to follow a new course in her career. The ECETOC Environmental Sciences Programme benefitted immensely from Malyka's expertise in environmental science combined with 'hands on' experience with genomics. Lucy Wilmot, Consultant with PFA-Brussels, took over this post in January 2017.

**Dr Madeleine Laffont, Human Health Scientist since 2014, left ECETOC at the end of 2016 to begin a new venture. Madeleine became a highly-valued member of the team during her time at ECETOC. Alice Brousse, Consultant with PFA-Brussels, took over this post in January 2017.

***Agnieszka Harris left ECETOC in September 2016 and was replaced by Francesca Uguccioni.

The Secretariat thank Malyka, Madeleine and Agnieszka for their contributions to ECETOC and wish them well in their new careers.

Finance



INCOME ACTUAL 2016 IN EURO

Subscription	
31 Full Members	1.069.500
7 Associate A Members	70.000
Total Subscription Income	**1.139.500**
Bank Interest	3.469
Investment income	0
Project-related	300.000
Exceptional income	63.249
Total	**1.506.218**

EXPENDITURE ACTUAL 2016 IN EURO

Salaries (and related expenses)	776.177
Office Running Expenses	200.791
Travel Expenses on Missions	4.373
Meetings and Consultants	384.891
Professional Services	23.686
Bank Charges	3.091
Capital Expenditure	14.339
Publications	15.421
Miscellaneous	53.195
Website	49.737
Total	**1.525.701**

BALANCE SHEET AND RESERVES ACTUAL 2016 IN EURO

Balance Sheet	
Income	1.506.218
Expenditure	1.525.701
Operating Margin	-19.483
Reserves*	
Opening	2.070.675
Operating Margin	-19.483
Closing Reserve	**2.051.192**

*Estimated Reserve Required: 268.000

Abbreviations

Abbreviations

AGM: Annual general meeting

AOP: Adverse outcome pathways

BfR: The German Federal Institute for Risk Assessment

Cefic: European Chemical Industry Council

Chesar: (ECHA) CHEmical Safety Assessment and Reporting tool.

CLP: Classification, Labelling and Packaging

CRA: Chemical respiratory allergy

CSA: Chemicals Safety Assessment

DNA: Deoxyribonucleic acid

DSL: Domestic substances list

EAG MST: (OECD) Extended Advisory Group on Molecular Screening and Toxicogenomics

EC: European Commission

ECETOC: European Centre for Ecotoxicology and Toxicology of Chemicals

ECHA: European Chemicals Agency

ED EAG: Endocrine Disrupter Expert Advisory Group to the EU Commission

EDTA: (OECD) Endocrine Disrupters Testing and Assessment Advisory Group

EOS: (NERC) Environmental 'Omics Synthesis Centre

ERA: Environmental risk assessment

ESTAF: ECVAM Stakeholder Forum

EU: European Union

EUROECOTOX: European Network for Alternative Testing Strategies in Ecotoxicology

Eurotox: Association of European Toxicologists and European Societies of Toxicology

FDA: (US) Food and Drug Administration

FELS: Fish early life-stage

GIS: Geographic information system

GLP: Good Laboratory Practice

HBM: Human biomonitoring

ICCA: International Council of Chemical Associations

IPCS: International Programme on Chemical Safety

IR&CSA: (ECHA Guidance on) Information Requirements and Chemical Safety Assessment)

ISES: International Society of Exposure Science

JACC: Joint assessment of commodity chemicals

JRC: (EC) Joint Research Centre

LCA: Life cycle assessment

LRI: Cefic's Long-range Research Initiative

MAES: Mapping and assessment of ecosystems and their services

MoA: Mode of action

MCS: Multi-constituent substance

NC3Rs: National Centre for the Replacement, Refinement and Reduction of Animals in Research

ncRNA: Noncoding RNA

NER: Non-extractable residue

NERC: (UK) National Environmental Research Council

NORMAN: Network of reference laboratories, research centres and related organisations for monitoring of emerging environmental substances

OECD: Organisation for Economic Co-operation and Development

PBT: Persistent, bioaccumulative toxic

PEF: Product environmental footprint

PEG: (ECHA) Partner Expert Group

PMN: Premanufacturing notification

RA: Risk Assessment

RAC: (ECHA) Risk Assessment Committee

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

RfP: Request for proposal

RIVM: The Dutch National Institute for Public Health and the Environment

RNA: Ribonucleic acid

SC: (ECETOC) Scientific Committee

SETAC: Society of Environmental Toxicology and Chemistry

SIG: (Cefic Long-range Research Initiative) strategy implementation group

SOT: (US) Society of Toxicology

STFC: Science and Technology Facilities Council, UK

SVHC: Substance of very high concern

TRA: Targeted risk assessment

UNEP: United Nations Environment Programme

US EPA: Environmental Protection Agency

USEtox: USEtox is a scientific consensus model endorsed by the UNEP/SETAC Life Cycle Initiative for characterising human and ecotoxicological impacts of chemicals

UVCB: Substances of unknown or variable composition, complex reaction products or biological materials

WHO: World Health Organisation

WoE: Weight-of-evidence

Notes

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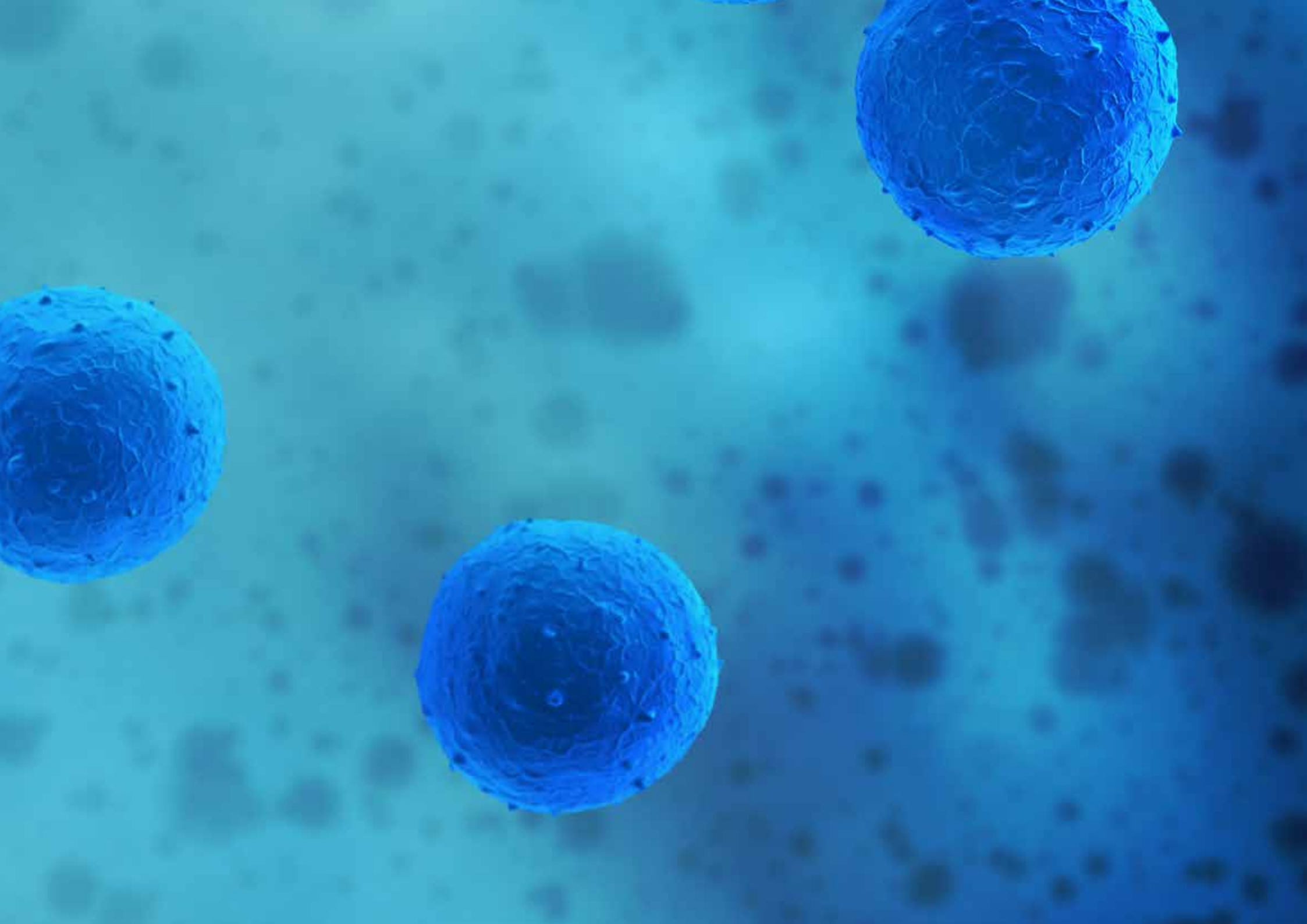

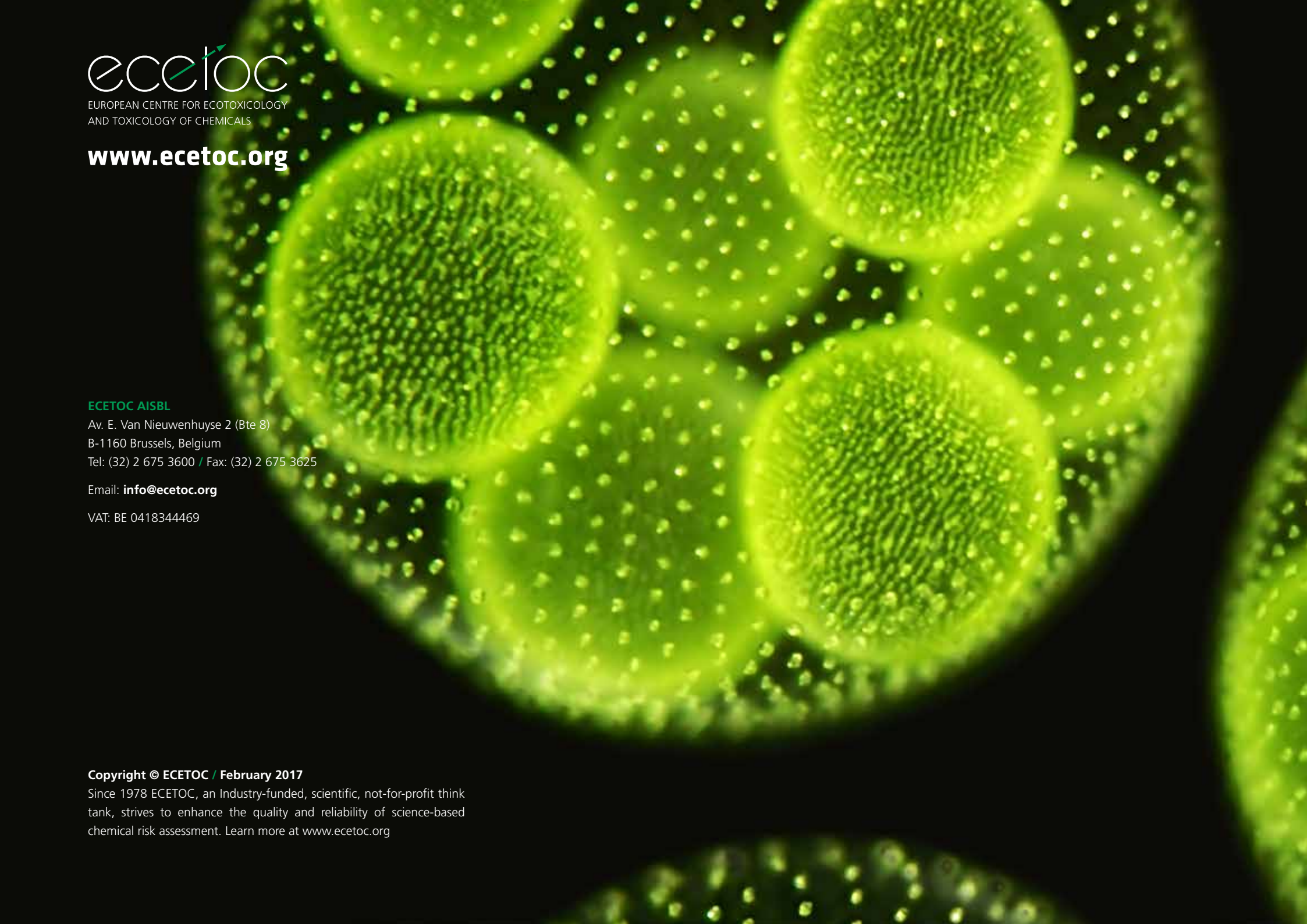

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EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS

www.ecetoc.org

ECETOC AISBL
Av. E. Van Nieuwenhuyse 2 (Bte 8)
B-1160 Brussels, Belgium
Tel: (32) 2 675 3600 / Fax: (32) 2 675 3625

Email: **info@ecetoc.org**

VAT: BE 0418344469

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