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Newsletter

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Editorial

Dear ESTIV members here is the latest edition of the ESTIV newsletter. It includes an update on *in vitro* toxicology, information on what was achieved in the last six months and an account of future plans. It also contains reports on interesting events, such as our *ESTIV Congress 2012* in Lisbon, the *InLiveTox course* in Rome, the Eye Irritation International Work-shop *on the HET-CAM Assay,* in Berlin and the *Symposium on Alternative in vitro methods* held in Italy in December 2012. The last one aimed at characterizing the role of Endocrine Active Substances (EAS) in hormone targeted tissues.

There is interesting news from Australia and Brazil regarding a 3Rs center in Camberra and the creation of SBMAlt, the Brazilian Society of Alternative Methods. Information on upcoming courses, meetings and workshops are included in the Newsletter. I hope you find this information to be interesting.

Best wishes,

Francesca Caloni

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Message from the President

The year 2012 was marked by a number of highlights for our society, including the 17th ESTIV Congress on 16-19 October in Lisbon, Portugal, the formal registration of our society and the election of a new Executive Board. With a very warm welcome by the local organizer, the Portuguese Toxicology Association (APTox), the ESTIV 2012 Congress numbered over 200 participants from Europe but also from countries such as Australia, Brazil, Japan, Saudi Arabia and USA. A special thanks has to be given to all of those who contributed organizationally, financially and for the high quality presentations given during the four-day Congress. We were delighted that one fourth of the attendants were young scientists, bringing fresh air and high standard presentations to the congress. Three of these young participants were granted young scientist awards. One of the novelties included the organization of a practical training course as a satellite to the congress, much appreciated by the fully booked attendance. We hope to renew the successful experience in the upcoming ESTIV Congress which is due to take place with an all-inclusive formula in Egmond aan Zee, The Netherlands on 11-14 June 2014. We are of course counting on you to come !

Last year ESTIV became a registered society, which gives us a legal status facilitating future activities and collaborations. The new statutes of ESTIV were adopted in the spring of 2012 and new bye-laws will soon be sent to all members for electronic voting. Consequently, the Executive Board now has new duties, which include informing our members on the finances and activities of the society at least once a year, so do expect to receive further information on that matter in the first half of 2013.

Finally, during the General Assembly in Lisbon, our members voted on the new composition of the ESTIV Executive Board, to which I'm very enthusiastic to take the lead. Also, I would like to take the opportunity to give a special acknowledgement to Greet Schoeters who has been a bright and open

President, as well as to Sjeng Horbach and Horst Spielmann who had to leave the Executive Board due to their expiration of term. Without them ESTIV would not be where it is today. We're happy to welcome two new Executive Board members: Elsa Casimiro, president of APTox, and Jan van der Valk, president of the upcoming ESTIV 2014. The new Executive Board has set as objectives for the upcoming years, to: *i)* promote further collaboration with corporate members and similar societies across the world; *ii)* further encourage education and training on *In vitro* Toxicology; *iii)* continue to serve as a network to foster exchange of scientific knowledge through the organization and promotion of meetings, workshops and congresses; and *iv)* encourage the participation of young scientists in all our activities.

Wishing all our members a brilliant 2013 with many professional successes!

Chantra Eskes

President of ESTIV

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ESTIV 2012 Congress

October 2012 was an exciting time for many ESTIV members that attended the ESTIV2012 Congress in Lisbon. It was the first time the ESTIV Congress was hosted in Portugal, being co-organized by ESTIV and the Portuguese Toxicology Association (AP Tox). The congress included a wealth of basic and applied research, shared with more than 200 participants representing 28 countries.

As in previous ESTIV events, the congress provided a forum where scientists and students from academia and industry, involved in the development and use of alternative methods in toxicology could network, learn about the new *in vitro* molecular technologies and computational tools which will open new avenues to future developments.

The Congress was officially opened with welcome addresses from the ESTIV and AP Tox Presidents and the representative from Portuguese General-Directorate of Health, Teresa Borges. The opening lecture by Maurice Whelan (EURL ECVAM; JRC) on "The European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) – Keeping pace with change" was followed by the presentation of the Bjorn Ekwall Memorial Award given to Horst Spielmann (FreieUniversity, Germany). During the following three days of the Congress 50 state of the art lectures and 115 posters were presented. They were distributed between nine congress sessions: Dermal toxicity, Ocular toxicity, Computational toxicology and Toxicokinetics, Crossing the transatlantic barriers, Innate immune responses in toxicology, Dermal sensitization, Carcinogenicity testing, Reproductive and developmental toxicity, and Systemic toxicity. A summary report with highlights from each session is available on the ESTIV website (www.ESTIV.org). In addition to the plenary sessions, a student session was held during the first lunch period. Here, the students had the opportunity to present their research. The best presentation was awarded the CellTox prize. This year's prize was awarded to Eva Ramboer. The congress social activities provided a unique opportunity to meet colleagues from around the world while at the same time discover Lisbon city, as well as the rich Portuguese culture and great food.

ESTIV 2012 participants also had the opportunity to take part in the pre-congress and post-congress workshops. The pre-congress workshop on "The Economics of Alternatives" was co-organized by ESTIV, CAAT & IVTIP, and focused on the costs vs. benefit of *in vitro* testing, as well as on strategies to make the application of *in vitro* tests and testing strategies economically

feasible for industry. For the first time, a full day post-congress workshop was organized where participants could gain hands-on experience with computerized *in vitro – in vivo* extrapolation strategies.

ESTIV2012 closed with the award presentation ceremony of the Elsevier/ESTIV Prizes for the overall best young scientist oral and poster presentations. These prizes were received by Marcus Maher and Melinda Bartok. The organisers thanked all the participants and speakers that made ESTIV2012 a success as well as the local organizing committee members, the session moderators and co-moderators, our sponsors and exhibitors.

Elsa Casimiro
APTox

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Preconference workshop: The economics of alternatives

This event was co-organised by ESTIV, CAAT and IVTIP. For the first time in the field of *in vitro* toxicology, a workshop was dedicated to the cost benefits aspects of the use of alternatives. The speakers with different backgrounds from academia, consulting, small-medium enterprises and big companies presented different views to make this analysis.
When looking at this problem from different angles, made it clear that the cost aspect can and will not be a major driver for changing toxicology towards a non-animal approach for the acute and topical endpoints addressed so far.

Cost calculations based upon the predicted requirements for testing of the REACH program, with skin sensitisation and reproductive toxicology as examples, showed that use of alternative tests is complex in the case of developmental toxicity. Skin sensitisation, *in vitro* tests are not necessarily cheaper than in vivo tests or human volunteer tests. Costs largely depend on the suppliers and their location.
Industry seeks a balance between better science and profits. *In vitro* tests need to provide better scientific information and increased confidence, but also costs need to be considered. As shown for skin sensitisation, *in vitro* tests can mimic different steps of the biology of skin sensitisation. However, biological processes are complex and as such it is essential not to mimic complexity by *in vitro* tests, but to focus on the most important endpoints, throughput, technical simplicity and robustness.

Ensuring unlimited availability and wide implementation of *in vitro* models and computational models are needed to guarantee economical benefits. The risk to depend on test systems that are validated but later no longer commercially available should be reduced. One way of achieving this is to provide open source tissue models, such as reconstructed skin or eye models, or to provide free software for computational modelling. Wide availability, right to use and distribute as well as technical transparency are major steps towards sustainable alternative testing. *In vitro* data and information on kinetics can waive testing by supporting categorisation of chemicals and read-across approaches. Costs can be reduced by *in vitro* tests searching for similarities and dissimilarities of compounds making *in vivo* testing more efficient and targeted. This was also illustrated by the approach taken by BASF for the identification of compounds with endocrine disrupting properties and by OncoBioTek, which uses *in vitro* tests as a cost-effective approach to increase drug target selection for cancer treatment in dogs and humans.

The speakers at the round table discussion came to the conclusion that the advantages of the use of alternatives are clearly animal welfare, the ability to test with low amounts of test substance, to address adverse outcome

pathways and to assess human relevance. One of the most important economic benefits of the use of alternative tests is to reduce the time needed for development of a compound. The long periods that are currently needed to bring a new compound onto the market is one of the major concerns of pharmaceutical companies for which alternative testing strategies may be of great value.

Greet Schoeters
ESTIV Leaving-President

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ESTIV 2012: Young Scientist Awards

ESTIV, in collaboration with Elsevier and Celltox, provided three awards at the Lisbon Congress in order to reward and further motivate the participation of students and young scientists at ESTIV Congresses. The task was particularly difficult due to the high quality of students and young scientist presentations at the ESTIV Congress. A total of 13 young scientists ran for the best oral presentation, 30 for the best poster presentation and 5 for the best student's session oral presentation. Three committees, one for each category, were established and decided on the following young scientist winners.

Marcus A. Maher from the Dublin Institute of Technology, Ireland, was granted the Elsevier-ESTIV Best Young Scientist Oral Presentation Award for his lecture on "*Structure activity relationships governing the interaction of nanoparticles with human cells – Predictive models for toxicology and medical applications*".

Melinda Bartok from the University of Bremen, Germany, was granted the Elsevier-ESTIV Best Young Scientist Poster Presentation Award for her poster on "*A 3D Reconstructed Hemi-Cornea Models for Predicting the Eye-Irritating Potential of Chemicals: Results of an Inter-Laboratory Evaluation Study*".

Eva Ramboer from the Vrije Universiteit of Brussels, was granted with the Celltox Award for Student's Session Best Oral Presentation for her lecture on "*The Effect of Epigenetic Modification on Drug Transporters in Primary Rat Hepatocyte Cultures*".

ESTIV, Elsevier and Celltox are pleased to congratulate all of them for their awards and to provide them with a 500 (ESTIV, Elsevier) and 250 Euros (Celltox) prize.

ChantraEskes
ESTIV President

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ESTIV2012 post-conference workshop "*In vivo* extrapolation of *in vitro* data in toxicology: state-of-the-art and challenges"

Following the previous ESTIV2010 conference (Linz, Austria), a questionnaire was sent to young ESTIV members, inquiring about their expectations regarding their involvement in the ESTIV society. From this survey, it became clear that there is great interest in workshops that cover specific topics related to *in vitro* and *in silico* toxicology. Based on this request, the ESTIV Executive Board decided to set up a post conference workshop in Lisbon-Portugal on Saturday 20 October 2012, following the ESTIV2012 conference, dealing with *in vivo* extrapolation of *in vitro* toxicological data. As such, the workshop consisted of a theoretical part (*i.e.* lectures in the morning) and a practical part (*i.e.* a computer exercise in the afternoon).

In the first lecture, Prof. Bas Blaauboer from the University of Utrecht-The Netherlands, addressed opportunities, pitfalls and challenges regarding quantitative *in vitro-in vivo* extrapolations (QIVIVE). He first discussed the actual relevance, advantages and disadvantages as well as a historical perspective of *in vitro* toxicology and methodologies were discussed. Prof

Blaauboer then continued to talk about strategies and difficulties in quantitatively extrapolating *in vitro* cytotoxicity data to the *in vivo* reality were outlined. Integrated QIVIVE testing schemes and physiologically-based pharmacokinetic (PBPK) models were presented. The lecture was ended with some practical case studies, including those of acrylamide and glycolether.

In a subsequent presentation, Dr. Nynke Kramer, also affiliated to the University of Utrecht-The Netherlands, focused on dose metrics in *in vitro* assays. Following a general introduction into dose metrics and *in vitro* assays in toxicology, physico-chemical (*e.g.* pKa) and assay (*e.g.* plastic well plate material) properties that determine free concentrations *in vitro* were discussed. Thereafter, a number of prominent approaches to measure as well as to model free concentrations *in vitro* were presented.
The morning session was ended by Prof. Mark Cronin from Liverpool John Moores University-United Kingdom, who discussed quantitative structure-activity relationships (QSAR), and more specifically what can be learnt from the structure and physico-chemical properties of a chemical with respect to its toxicity. At the start of the lecture, an overview of *in silico* and computational toxicology was provided. Subsequently, the applicability domain of QSAR was discussed and its power was illustrated using QSAR-based prediction of LogP as an example, *in casu* in the context of skin permeability. Another case study related to the role of QSAR in metabolism prediction. Finally, some directions for future QSAR purposes were provided.

During the afternoon session, the participants were given the opportunity to gain hands-on experience with a physiologically-based biokineticmodelling *in silico* tool. During this exercise, they were assisted by Prof. Bas Blaauboer and Dr. Nynke Kramer.
The workshop, which became fully booked soon after its advertisement on the ESTIV2012 website, was attended by 25 participants, mainly youngsters, from 12 different countries in and outside Europe. There was an active interaction between the lecturers and the participants throughout the workshop. An evaluation form was sent around to the participants and from this answers received, it is clear that the workshop was considered of high quality and of great practical value. This once more emphasizes the interest for similar workshops in the future. Similar initiatives will therefore be prioritized by the renewed ESTIV Executive Board. In this respect, the ESTIV Executive Board kindly requests its members to send proposals for topics to be covered in future workshops or similar events to Mathieu Vinken (mvinken@vub.ac.be).

Mathieu Vinken
ESTIV Vice President

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EUROECOTOX

The 1st European Conference on the Replacement, Reduction and Refinement of animal experiments in Ecotoxicology, organized by the European Network for Alternative Testing Strategies in Ecotoxicology – EUROECOTOX (www.euroecotox.eu), a coordinating action funded by the European Community's Seventh Framework Programme, was organized last summer. The conference was hosted by Eawag, the Swiss Federal Institute of Aquatic Science and Technology in Dübendorf, Switzerland, from 28 to 29 June 2012. About 69 participants from academia (62%), industry (22%) and regulators/ stakeholders (16%) did attend.

Participants to the 1st European Conference on the Replacement, Reduction and Refinement of animal experiments in Ecotoxicology (EAWAG Picture Copyright)

The conference provided a good platform for young scientists, experts from academia, industry and regulation in the field of 3Rs of animal tests used in environmental risk assessment. It focused on the current state and future directions of the development, implementation and application of the 3Rs,

from bench to acceptance. The program was based on 8 invited keynote speakers, 26 oral presentations and up to 20 posters, organized in 5 main sessions:
(I) Experimental Approaches, (II) Towards Integration and Implementation, (III) Perspectives and Initiatives towards the 3Rs,(IV) Computational Approaches and (V) a final plenary discussion.

The conference was financially supported by ESTIV, through free access for ESTIV members and two prizes for young scientists' presentations. Julita Stadnicka from EAWAG & ETH (Switzerland) was awarded the best oral presentation entitled '*Predicting chemical concentrations in a fish cell line based on measurements and models*'. An award for the best poster presentation was given to Melanie Knobel (UFZ, Germany & EAWAG, Switzerland) who presented work on the correlation of zebrafish embryo to fathead minnow acute toxicity, considering the relevance of physico-chemical properties, mode of toxic action, test duration and exposure concentration analysis.

The ESTIV student awards for best oral presentation was granted to Julita Stadnicka (left) and poster presentation to Melanie Knobel (right).

The full report from the conference including abstracts of oral and poster presentations is available via the EUROECOTOX web site (final conference proceedings at www.euroecotox.eu).

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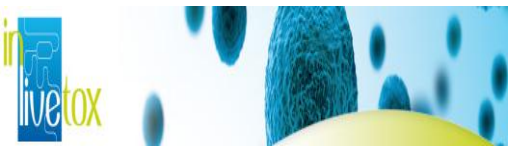
InLiveTox Course 17-18 September 2012, Rome



The establishment of new *in vitro* models requires an evolution of technology in order to allow scientists to implement new and physiologically relevant situations. The word "relevant" refers to the correspondence between *in vitro* models and human physiology. To this end, a modular fluidics system was developed in **FP7 InLiveTox project** (http://www.inlivetox.eu/) to model the response of cells and tissues to ingested nanomaterials (NM). The system is more convenient and ethically less questionable than animal testing as well as more relevant than the *in vitro* single cell culture /co-culture models currently being used.

The model developed by the InLiveTox consortium is based on a modular fluidics-based multi compartmental cell culture system (ILT) aimed at recapitulating NM absorption in the intestinal wall, distribution through the vascular network and metabolism in the liver.

To present the InLiveTox concept and fluidic systems to researchers involved in *in vitro* toxicity testing and barrier models, a practical training course on integrated fluidic models for *in vitro* testing was organized by Prof. Arti Ahluwalia from the Interdepartmental Research Center "E. Piaggio" (University of Pisa, Italy) and Dr. Isabella De Angelis from the Istituto Superiore di Sanità (ISS, Rome, Italy) at ISS on 17 – 18 September 2012. The event was also in part supported by CELLTOX (Italian Association of *In vitro* Toxicology, www.celltox.it).

The course, mainly addressed at young scientists, consisted of a theoretical introduction and several practical demonstrations of bioreactors set up and functioning.

In the first part of the program, several lectures showed the main aspects of: 3R philosophy (I. De Angelis), *in vitro* alternatives to animal testing (C. Nastrucci), nanotoxicology principles (F. Barone), theoretical description of fluidics and scaling (A. Ahluwalia) and InLiveTox system (ILT0

and ILT2) description & Logistics for laboratory (S. Ahmed – T. Sbrana).

In laboratory activities, participants were able to: *a)* set up a one and two chamber flow experiment using different bioreactors (ILT0, ILT2, MCmB) systems; *b)* assemble the ILT2 and perform a TEER measurement under double flow conditions; *c)* assemble and set up the MCmB; *d)* used the InLiveTox system to build a fluidic circuit for simulating NM absorption across the intestinal barrier through to the vascular circulation and liver.
A detailed protocol of the experimental part was provided to all participants.

Given the success of the course it is planned to organize a new edition in 2013.

Isabella de Angelis
ISS, Rome

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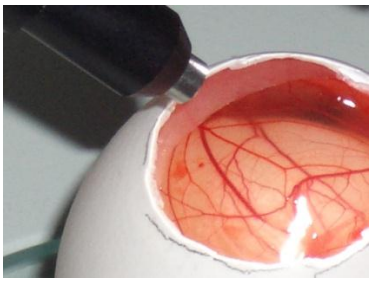
Eye Irritation International Workshop on the HET-CAM Assay BfR, 29-30 October 2012, Berlin Germany



A two-day International Workshop took place concerning the use of the HET-CAM assay for eye hazard regulatory assessment on the 29th and30th October 2012 in Berlin, Germany. This was organized by the Federal Institute for Risk Assessment (BfR) together with Services & Consultation on Alternative Methods (SeCAM) and co-sponsored by the BfR and the European Partnership for Alternative Approaches to Animal Testing (EPAA). The aim of the workshop was to make recommendations on the most relevant HET-CAM protocol(s) and prediction model(s) for the different uses and purposes of the test method for regulatory eye hazard assessment. The workshop was attended by 30 participants from regulatory agencies, validation centres (ECVAM, ICCVAM, JACVAM and BraCVAM), OECD, various industrial sectors, contract test laboratories, European associations and academic scientists with expertise on the HET-CAM assay.

In general good agreements and conclusions were achieved on the following points addressed by the workshop participants:

- The most suitable HET-CAM protocol(s) and prediction model(s) for the identification of chemicals inducing serious eye damage and recommendations for advancing validation of the HET-CAM assay for that purpose;
- The most suitable HET-CAM protocol(s) and prediction model(s) for the identification of chemicals not requiring classification for eye irritation and recommendations for advancing validation of the HET-CAM assay for that purpose;
- Recommendations for HET-CAM protocol optimization.

The scientific manuscript is now prepared so that the issues addressed during the workshop, as well as the main recommend-dations and conclusions achieved, can be shared with the larger scientific community.

ChantraEskes
SeCAM, Switzerland

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International Workshop on Current and future prospects of alternative methods for cosmetics safety testing, 29 & 30 November 2012, Brasilia DF, Brazil

A two-day International Workshop took place on the use of alternative test methods for cosmetics safety testing on the 29th and 30th of November 2012 in Brasilia DF, Brazil. The workshop addressed the current scientific, regulatory and industrial aspects regarding the use of alternative methods and strategies to replace and/or reduce animal testing for cosmetic products testing. The location of Brazil was chosen due to the fact that Brazil is one of the world's largest markets for cosmetic products. Recent developments in the country have led to an interest to implement alternative methods for scientific purposes. Brazilian testing requirements also still differ from those of other world regions, especially for cosmetic products, as it continues to rely on animal testing, including the requirement for finished product animal

testing of cosmetics, a practice no longer used in Europe, North America, and most other regions.

The event was sponsored by the Humane Society International (HSI) and organized by Services & Consultation on Alternative Methods (SeCAM) in collaboration with Brazilian authorities and major stakeholders from the cosmetics sector. (THIS IS DUPLICATED Presentations were distributed in four sessions addressing:

- The cosmetic regulations and testing requirements in Brazil and Europe;
- Latest scientific developments taking place in the US and Europe on the use of alternative methods for safety assessment of chemicals and cosmetics including the US EPA ToxCast program, the European program for systemic toxicity testing Seurat-1, the AXLR-8 international cooperation, and the proposal for an automated tissue engineering platform (skin factory);
- The Brazilian regulatory requirements linked to alternative test methods; and
- The current industrial practices in using alternatives and non-animal testing for the safety assessment of cosmetics.

The event ended with a round-table discussion between Brazilian, US and European representatives from regulatory bodies, validation centres, cosmetics associations, CROs and NGOs. The applicability of alternative and non-animal methods for the safety assessment of cosmetics and other products was discussed from different angles. In particular that the European safety assessment is generally undertaken based on the ingredients of a formulation and that the Brazilian safety assessment relies on the outcomes obtained with the entire formulation itself. This may be one of the reasons why Brazil still relies on animal testing for finished cosmetic products. Furthermore, it was noted that the implementation of alternative methods for scientific purposes in Brazil is still new, with the first legislation on the protection of animals used for scientific purposes being adopted only in 2008. As such, Brazilian regulatory agencies are still in a process of organization, but there is a tendency and willingness to go towards international harmonization and an implementation of internationally agreed test methods such as those proposed by the OECD.

ChantraEskes
SeCAM, Switzerland

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Symposium on "Alternative *in vitro* methods to characterize the role of Endocrine Active Substances (EAS) in hormone targeted tissues" 17th December 2012, Rome

The Symposium on "Alternative in vitro methods to characterize the role of Endocrine Active Substances (EAS) in hormone targeted tissues" was held in Rome (Italy) December 17th, at the Istituto Superiore di Sanità (ISS). The event was organized jointly by the ISS, i.e. the Italian Governmental Health Institute, IPAM (Italian Platform for Alternative Methods), affiliated with the European Consensus-Platform for Alternatives (ECOPA) and CAAT-Europe (Center for Alternative to Animal Testing). About 60 participants attended the Symposium.

The aim of the Symposium was to emphasize the role of alternative methods in the evaluation of potential EASs through a lively discussion between invited speakers and participants. EASs identification is currently a high priority for regulatory authorities in most EU and OECD countries/regions and, presently, no accepted *in vitro* methods are available for risk evaluation.

Moreover, EASs are challenging classical concepts in toxicology, due to their suggested "low dose effects" and "non-monotonic dose responses", and for these reasons, they may lead to innovative approaches in risk assessment.

The Symposium program was divided into four sessions, to give an overview of the state-of-art in EAS investigation by alternative methods, highlighting the academic, regulatory and industrial points of view as well presenting critical issues in human targets of endocrine disrupters and their metabolic fate.

In the introductive session an overview of the different aspects of the problem was presented by five different speakers: T. Hartung (Endocrine disruption as the pilot of mapping the human toxome), C. Rovida (Implementation of regulatory issues), A. Mantovani (Endocrine Active Substances / EASs: understanding modes of action for risk assessment), J. Steinkellner (Exploration of alternative methods for toxicity assessment of pesticide metabolites) and S. Cinelli (Improving test methods in the spirit of the 3Rs; the point of view of a contract research organization).

Session 1 focused on the consequences that EAS may have on the reproductive system. The invited speakers were: S. Lorenzetti (A prostate perspective on male fertility and EASs: from toxicogenomics to phenotypic anchoring); M. Spanò (Human sperm (epi)genetic biomarkers to assess the impact of EASs on male reproductive function) and L. Paulesu (*In vitro* effects of EASs in human placenta).

Session 2 recognized that the effect of EASs should not be limited to the reproductive apparatus with the contributions of: I. Bendik-Falconnier (Endocrine active nutrients explored in human-bone cell cultures), R.A. Smith (The use of cell models in determining neuronal responses to EASs) and A. Ahluwalia (Dynamic *in vitro* organ models of metabolism).

Finally in the last session, the relevance of kinetics in the definition of EASs was highlighted by: E. Testai (The role of biokinetics in *in vitro* tests and in the interpretation of results), F. Yves Bois (Physiologically-based modeling of ovarian steroid hormones synthesis for EASs' health risk assessment) and D.R. Dietrich (EASs contra human & environmental health: Relevant or playground for merchants of doom).

More information about symposium scientific program and speakers presentations will be available soon on IPAM website (http://www.ipamitalia.it/). Some copies of the abstract book are also available at the scientific secretariat (laura.narciso@iss.it.).

Isabella de Angelis
ISS, Rome

Highlights

The OECD has recently published four proposals for Test Guidelines based on *In vitro* test methods for the safety assessment of chemicals. These include the following draft Test Guidelines (TG):

- Draft revised TG 431 on *In vitro* Skin Corrosion: Reconstructed Human Epidermis (RhE);
- Draft revised TG 437 on the Bovine Corneal Opacity and Permeability (BCOP) Test Method for Identifying Chemicals Inducing Serious Eye Damage and Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage;
- Draft revised TG 438 on the Isolated Chicken Eye (ICE) Test Method for Identifying Chemicals Inducing Serious Eye Damage and Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage; and
- Draft Test Guideline on the Cytosensor Microphysiometer (CM) Test Method: An *in vitro* Method for Identifying Ocular Corrosive and Severe Irritant Chemicals as well as Chemicals not Classified as Ocular Irritants

The proposed TG are available for consultation on the following website: http://www.oecd.org/env/chemicalsafetyandbiosafety/testingofchemicals/section4healtheffects.htm .

Transnational Access at VITO through FP7 QNano Research Infrastructure – 3rd call for proposals

QNano aims to establish a pan-European analytical research infrastructure whose purpose is to drive high quality research and testing practices for assessment of the potential risks posed by nanomaterials. The Transnational Access (TA) component of the FP7 QNano Research Infrastructure is dedicated to providing Users from the

European nanosafety community access to nanomaterials processing, characterisation and exposure assessment facilities. Access to 15 major European research sites is via a single application and evaluation process. The central principle of access provision is to offer the Users a full range of services from standard nanomaterials, tuition in best practice, laboratory support and training, and a suite of protocols for all aspects of nano-materials processing and characterisation in a biological context.

VITO will enable Users to access equipment and facilities for nanoparticle exposure assessment, including *in vitro* biological assays, proteomics and transcriptomics platforms, and occupational exposure measurements, and for *in-situ* and *ex-situ* nanoparticle characterisation (material characterisation and imaging, mass spectrometry, and chemical analysis).
An overview of equipment per category is available at http://www.qnano-ri.eu/uploads/QNano_TA/Posters/VITO-TAF-Poster.pdf.
The deadline for the third call is March 15, 2013. Dates of the next calls will be published at the website.
Contact VITO-TAF: Inge Nelissen, vito-ta@qnano-ri.eu

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LUSH 2012 Award

The Lush Prize is a new initiative from 2012, aimed to reward effective projects and individuals who have been working towards the goal to replace animal use in product safety testing. This is a collaboration between Lush and Ethical Consumer. Lush is a campaigning manufacturer and retailer of fresh handmade cosmetics with shops in 49 countries. The Prize is one element of its recently-launched 'Fighting Animal Testing' campaign..Ethical Consumer Research Association is a UK-based research and consultancy co-operative focused on working with companies and consumers around effective ethical choices.

By combining an invitation for open public nominations with a series of Research Papers the Lush Prize seeks to identify genuine excellence in the sector each year. A panel of ten independent judges including research scientists, campaigners, politicians, members of the public and academics, select winners from a short-list. The 2012 Prize Winners were as follows:

Science Prize: Institute for Health and Consumer Protection, Italy, for their work on toxicity pathways in hepatoxicology and developmental toxicology (£50,000).

Lobbying Prize: (1) Humane Society International, USA, for their work on removing animal tests from the EU's non-food pesticide regulations (£40,000); (2) Federation of Indian Animal Protection Organisations (FIAPO), India, for their research and lobbying on animal testing in India (£5,000); (3) People for the Ethical Treatment of Animals (PETA) India, for their work with Indian regulators on a cosmetics testing ban (£5,000).

Training Prize: (1) Institute for *In vitro* Sciences, USA, for their vital work on training researchers in non-animal methods from Brazil to Japan (£25,000); (2) InterNICHE, for their work in training in former Soviet states, South America and Africa (£25,000).

Young Researcher Prize: (1) Elizabeth Woehrling, UK, for her work on the development of a new *in vitro* test for neurotoxicity (£12,500); (2) Felix Rivera-Mariani, USA for work on expanding an existing non animal test into new areas (£12,500); (3) Chiara Scanarotti, Italy, for her work on skin sensitisation and chemical mixtures (£12,500); (4) Line Mathiesen, Denmark, for her work on studying the impact of toxics on placental tissue (£12,500).

Public Awareness Prize: (1) Japan Anti-Vivisection Association, Japan, for their successful campaign to persuade Shiseido to abandon animal testing (£30,000); (2) Decipher Films, Canada for their feature film 'Maximum Tolerated Dose' on animal testing (£10,000); (3) VITA Animal Rights Centre, Russia for their work on awareness raising with the Russian media (£10,000).

www.lushprize.org/lush-prize-winners-2012/

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Creation of The Brazilian Society of Alternative Methods (SBMAlt)

During the last years, Brazil has taken several steps forward regarding the use and application of alternative methods to animal testing. September 2011 marked the establishment of the Brazilian Centre for the Validation of Alternative Methods (BraCVAM), followed in 2012 by the creation of the National Network on Alternative Methods RENAMA (Rede Nacional de Métodos Alternativos ao uso de animais). Its most recent creation dated from November 2012 is the Brazilian Society on Alternative Methods, i.e., SBMAlt or Sociedade Brasileira de Métodos Alternativos. Its creation took place during the 1st Latin American Congress on Alternatives to Animal Use in Education, Research and Industry, held in Niteroi, Brazil. The SBMAlt aims to promote the exchange of scientific knowledge on alternative methods to the use of animals for scientific experimentation, including toxicology, education and training purposes.

ChantraEskes
ESTIV President

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In memory: Joan Albert Vericat

Our friend Joan Albert Vericat was a Spanish toxicologist who occupied several teaching positions at the Autonomic University of Barcelona until 1987, when he chose to continue his scientific career in the industry. He has worked for the pharmaceutical industry in Italy, where he was Head of the Department of Genetic and Cellular Toxicology of the Research Toxicology Centre, S.p.A, France as Manager of the Department of Genetic and Exploratory Toxicology of Sanofi-Synthelabo and Spain, being Head of the Department of Toxicology of J. Uriach & Company and Director of Preclinical Development of Noscira S.A. He has been involved in the board of different international entities related to alternatives, such as the Industrial *In vitro* Toxicology Platform and the European Society of Toxicology *in vitro*. He has also been a very active member of the Board of REMA, the Spanish Platform on Alternatives. Few days before his unexpected death the 4th July 2012, he gave a very provocative presentation on the need for adequate training of toxicologists to meet the needs of the industry. He was also very active in the design of the programme of the next congress of the Spanish Association of Toxicology.

REMA has organized *in memoriam* of Joan Albert the VI Workshop of REMA entitled "Progress in the implementation of Alternative Toxicological Methods", the 18th January 2013. We covered topics such as the assessment of nanomaterials, the entry into force of Directive 2010/63/EU on the protection of animals used for scientific purposes, the project Tox21 and the new models required by the industry, one of his favourite topics. He was a friend who will always remember.

Guillermo Repetto
President of REMA- Spanish Network for the Development of Alternative Methods
http://www.remanet.net/

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Meetings calendar

26-27 January 2013

International Conference of Alternatives to Animal Experimentation

Almada, Portugal

www.icaae.com/index.html

4-6 march 2013

2nd Annual Cell Line Development and Engineering Asia

Shanghai, China

14-16 May 2013

IVTIP 2013 Annual Meeting

2013: State of the art on alternatives from an industrial point of view: ready for regulation?

Southampton, UK

Deadline for abstracts: 01.02.2013

www.ivtip.org

17-20 April 2013

Meeting of the European Society for Clinical Investigation

Albufeira, Portugal

www.esci2013.eu

28-31 May 2013

XXXIII Interntional Congress of the European Association of Poisons Centres and Clinical Toxicologists

Copenhagen, Denmark

www.eapcct.org/index.php?page=congress1

1-4 September 2013

Eurotox 2013 - Interlaken, Switzerland

Deadline for abstracts: 28.02.2013

www.eurotox2013.com

25-27 September 2013

SSCT 29th Scientific meeting

Charlottenlund, Denmark

Deadline for abstracts: 01.06.2013

www.ssct.se

20-23 November 2013

CIFARP – 9th International Congress of Pharmaceutical Sciences

Ribeirão Preto, Brazil

www.cifarp.com.br/site/

11-14 June 2014

18th Congress of the European Society of Toxicology *In vitro*

Egmond aan Zee, The Netherlands

www.estiv2014.org

24-28 August 2014

9th World Congress on Alternatives and Animal Use in Life Sciences: "Humane Science in the 21st Century"

Prague, Czech Republic

www.wc9prague.org

EXTENDED SCOPE

The R&D and testing facility for alternative toxicological applications and ecotoxicity testing at VITO, known as CARDAM, has extended its scope in line with ongoing strategic activities at the VITO department of Applied Biological & Molecular Systems (ABS): next to toxicological methods and strategies, applications in human health diagnostics and effect-based monitoring are now part of the core business.

From January 2013 onward, CARDAM activities will therefore be fully incorporated by VITO. We remain dedicated to excellence in research collaborations, to testing services and to continuous improvement of our quality standards.

We offer:

- Research & Development: application and development of biological and molecular methods for human health diagnostics and effect-based monitoring
- Validation of alternative biological test methods (RRR principles)
- GLP/non-GLP contract testing: alternative methods, biodegradation and ecotoxicity

For more information:
Alternative methods: hilda.witters@vito.be
Ecotoxicity: reinhilde.weltens@vito.be

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US workshop: "Scientific roadmap for the future of animal-free systemic toxicity testing"

The scientific challenges of developing *in vitro* approaches to systemic toxicity testing are formidable. These challenges have taken on greater urgency in the context of the 2013 deadline for marketing cosmetics in Europe that are free of animal-testing, including for systemic and chronic endpoints. We believe the time is ripe to advance a forward-looking strategy to develop the science for the systemic, chronic toxicities for cosmetics and others products. We strongly believe that such a focused effort applies to regions outside of Europe and products and industries outside of cosmetics.

In the context of our transatlantic think tank for toxicology (t^4), we held a workshop about a year ago to develop 5 white papers on systemic toxicity, taking a larger perspective on how to make further progress. The outcome has been published as "A roadmap for the development of alternative (non-animal) methods for systemic toxicity testing," by Basketter et al. in *ALTEX* (see www.altex.ch/en/index.html?id=50&iid=129&aid=1). The roadmap was favorably reviewed and discussed at a follow-up meeting in Brussels in March, 2012, co-organized by numerous organizations including ESTIV and attended by some 150 expert. We would like to hold a similar public discussion of the roadmap in the US. We foresee a two-day event, divided into three slots each. The first five slots would cover the five white papers, the last one a general way-forward discussion. We expect that the event be held in the Washington, DC area in Spring 2013. We currently are identifying a date and venue, possibly at an FDA facility in nearby Maryland.

We would like to stress that this workshop is meant to be a scientific process. We do not aim to make political recommendations. We are focusing on a roadmap for scientific progress.

CAAT US

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3Rs Center at Australia National University (ANU) Canberra

Brett Lidbury, Associate Professor in Alternatives to animal research and Medical Advances Without Animals Trust (MAWA) Fellow, Australia National University (ANU) recently visited CAAT and met with various faculty and staff members to share ideas and information about starting an alternatives center in Canberra, Australia. Dr. Lidbury reported back that, since arriving back in Canberra, he was granted approval to start an alternatives “Unit” within the John Curtin School of Medical Research (JCSMR – http://jcsmr.anu.edu.au). He plans to launch the unit early in the New Year. Dr. Lidbury plans to include links from the Altweb and CAAT sites in his website, and CAAT hopes to post news and updates from Canberra on Altweb. A collaboration agreement is in preparation.

Recent publications of ESTIV members

Abass K and Pelkonen O The inhibition of major human hepatic cytochrome P450 enzymes by 18 pesticides: Comparison of the N-in-one and single substrate approaches. Toxicol *In vitro*, in press

Abass K, Lämsä V, Reponen P, Küblbeck J, Honkakoski P, Mattila S, Pelkonen O and Hakkola J (2012) Characterization of human cytochrome P450 induction by pesticides. Toxicology (294), 17-26

Abass K, Turpeinen M, Rautio A, Hakkola J and Pelkonen O (2012) Metabolism of pesticides by human cytochrome P450 enzymes *in vitro* – survey. In: Insecticides - Advances in Integrated Pest Management– FarzanaPerveen (Ed.) ISBN 979-953-307-667-5, pp. 165-194

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IIVS Wins First Annual Training Prize by Lush Cosmetics

IIVS received the first annual Lush Training Prize during an award ceremony in London on 15 November. The prize, a joint project between Lush and Ethical Consumer magazine, recognizes individuals or organizations who have excelled in establishing training programs to make scientists aware of the range of available non-animal testing methods.

"At IIVS we believe the change to non-animal testing methods will be hastened through education and training. Seeing, touching, using these methods first-hand and understanding the results will change perceptions and practices," said Rodger Curren, President of IIVS, during the awards ceremony. This thought was echoed by IIVS's Vice President of Program Development, Erin Hill, who stated: "Our trainings change the fuzzy image of 'alternatives' into the reality of better science and the removal of animal pain and suffering."

The Lush Training Prize is one of 5 categories the cosmetics company recognized. Others include the Science Prize, Young Researcher Prize, the Public Awareness Prize and the Lobbying Prize. Over 180 nominations were submitted and a panel of 10 independent judges picked the winners from a short-list compiled by the Lush Prize Team.

IIVS shares the award with InterNICHE, an international network focusing on animal use and alternatives within biological sciences, medical and veterinary medical education. To learn more about the Lush Prize or view the award ceremony video, please visit www.lushprize.org

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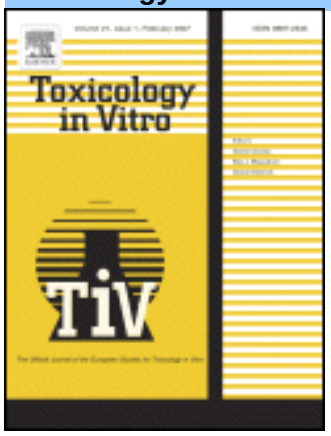
Memorandum of Understanding Signed with EPAA

During its 8th annual conference in Brussels, the co-chairs of the European Partnership for Alternative Approaches to Animal Testing (EPAA) signed a memorandum of understanding with IIVS President, Rodger Curren. The agreement signifies the establishment of a strategic partnership between the two groups dedicated to combining resources and collaborating to promote international awareness and education in non-animal testing methods.

Held on 16 November, the annual conference was attended by 150 delegates from regulatory agencies, the European Commission and representatives from the seven industries that EPAA represents. DG Enterprise and Industry's deputy director general, Antti Peltomaki, stressed that while Europe has pioneered efforts in the 3Rs, further progress could only be secured through international cooperation. "Strong international cooperation is the future of alternatives to animal testing" stated Peltomaki during his keynote speech.

To support this effort the EPAA will provide sponsorship of up to 100,00 euro over the next two years to support IIVS international training activities in key regions of the world where regulatory agencies still require animal testing.

Toxicology *in vitro*



Official Journal of the European Society of Toxicology in vitro

Editors: Daniel Acosta, Frank A. Barile Bas J. Blaauboer

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ESTIV Corporate member

The Centre for Advanced Research & Development on Alternative Methods (CARDAM) devotes itself to replace and reduce the use of animals in safety testing, maintaining a high quality safety assessment.http://www.cardam.eu/CARDAM

Novozymes is a world leader in bio-innovations. Together with customers across a broad array of industries, Novozymes creates industrial bio-solutions, which both improves our customers' business and the use of the planet's resources

http://www.novozymes.com/en

Epithelix proposes innovative *in vitro* solutions for respiratory diseases and chemical testing. It provides reconstituted human *in vitro* tissues with long shelf-life and associated services for research laboratory, personal care, chemical and pharmaceutical industry.

http://www.epithelix.com/index.php?lang=en

We Innovate Healthcare

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80'000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. In the pharmaceutical research field, Roche is committed to support *in vitro* approaches to assess efficacy and toxicity of compounds, as a sign of its strong commitment with the 3R-principle.

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Thor is a multinational manufacturer and distributor of biocides, flame retardants, personal care ingredients and other speciality chemicals.

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ESTIV Affiliated Societies

Associazione Italiana Tossicologia *In vitro* - CellTox

Dutch-Belgium Society for *In vitro* Methods–INVITROM

UK *In vitro* Toxicology Society – IVTS

Scandinavian Society for Cell Toxicology – SCCT

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ESTIV membership fee

Membership fee
The membership for an individual member for 2012 is € 30,00. If you are also a member of one of the affiliated societies (CellTOX, SSCT, INVITROM, IVTS), the membership amount to € 18,00.

Method of Payment
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Due to the high costs of applying for and cashing EuroCheques, please do not use this means of payment.

It is also possible to pay the membership fees by our convenient and secure online credit card payment services (PayPal), To use these services, please visit the ESTIV website at www.estiv.org

Laura Suter-Dick

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ESTIV e-mail list

ESTIV has an e-mail list, which has the potential to be a very valuable resource. There are many types of questions that you could pose to the list, whether you are a junior or a senior scientist. To send a message to all ESTIV members on the list (presently more than 200 colleagues), simply address your e-mail to estiv@freelists.org
Please do not be concerned about security. This is a "closed" list, which means the "list-owner" (Jan van der Valk) is able to select who is allowed to join. Only ESTIV members can receive the message. The ESTIV secretary advises the "list-owner" of eligible members. If you have never received a message from the ESTIV list, it is because you have not informed us of your e-mail address. Please correct this by sending a message to me at j.vandervalk@uu.nl, and your name will be added.

Jan van der Valk

"ESTIV also owns a group on LinkedIn, to communicate and to allow ESTIV members to update each other on career moves, etc.
The group is only open to ESTIV members. Search for the group "ESTIV" and register".

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Monique Adolphem, Michael Balls, Diane Benford, Bas Blaauboer, Bob Combes, Sjeng Horbach, Horst Spielmann, Jan Van der Valk, Flavia Zucco,

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For more information on ESTIV and membership application contact

Alison Gray (ESTIV Secretary)
E-mail: secretariat@estiv.org

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