

# European Society of Toxicology In Vitro

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# Newsletter

Issue No 34 July 2013

### **Editorial**

Dear ESTIV members,

Here is the new ESTIV newsletter including an update on in vitro toxicology and information on what was done in the last six months and what is in preparation for the near future.

Many events on very interesting and current topics are reported in it such as the IVTS meetings and symposium in the UK, Cell Control in a Petri Dish meeting in London, The International Conference of Alternatives to Animal Experimentation in Portugal and the CELLTOX Course 2013 organized in Italy.

Heartiest congratulations to Professor Per Artursson for the Björn Ekwall Memorial Award and to Professor Marcel Leist who received the Felix Wankel Animal Welfare award.

I would like to take this opportunity to remind you about ESTIV 2014 to be held in Egmond aan Zee in the Netherlands, on which the Board is working actively. In fact, ESTIV now has concrete plans to organize its next conference as a joint event together with the summer school of the FP7/Cosmetics Europe SEURAT-1 consortium as well as a meeting of the NOTOX project would also like to thank all members for their contribution and all of those who have collaborated on this issue. Hope you find this information to be interesting.

Have a nice summer and best wishes to all.

Francesca Caloni

### **Message from the President**

Dear colleagues,

As noted in our annual report sent earlier on June, ESTIV is and will continue to be engaged in fostering scientific exchanges through the support of scientific meetings, collaboration with similar societies, and representation at key stakeholders meetings. Furthermore, as a follow-up to the big success encountered with the first practical training course organized by ESTIV during its 2012 Congress in Lisbon, we now aim at organizing training courses dedicated to those interested in having an overview of the in vitro toxicology field from the more basic aspects to the final application. We hope to be able to provide you with further information in short time.

present newsletters provides inspiring insights on a number of activities that took place during the last months. In particular, key milestones have achieved regarding the regulatory acceptance of alternative methods. addition, growing interest from the in vitro toxicology community focuses on more complex endpoints and test systems. Recent developments allow obtaining more relevant models, such as induced pluripotent stem cells based on human cells and new cell lines more representative of normal cells. More complex and organ-like 3D models are also key elements to obtain more relevant models and better predict the effects of a toxicant and/or a drug may have on humans. I hope the information shared here with you can inspire you before a well deserved summer break!

**Chantra Eskes** 

President of ESTIV

## Björn Ekwall Memorial Award 2013



Professor Per Artursson

Professor Per Artursson (Sweden) is the recipient of the Björn Ekwall Memorial Award for the year 2013 in recognition of his scientific achievements in the field of drug design and delivery and for the innovative design and successful implementation of *in vitro* methods in pharmacy and toxicology.

The Björn Ekwall Memorial Award will be given to Professor Per Artursson at the occasion of the 29<sup>th</sup> Workshop of SSCT, 25-27 September 2013, Vilvorde Course Center, Charlottenlund, Denmark. At the workshop, Professor Artursson will deliver the Björn Ekwall Memorial Lecture.

- P. Artursson studied pharmacy at Uppsala University, where he also presented his PhD thesis in 1985. He spent one year as a post doc. fellow at the Medical Products Agency, Uppsala (1986) and one year as a visiting scientist at the Advanced Drug Delivery Ciba-Geigy, **England** (1987) Research. before taking up a position as Assistant Professor in Pharmaceutics. Uppsala University. In 1992 he was appointed to his present post as Professor in Dosage Form Design at the Department of Pharmaceutics, Uppsala University, Sweden. He is also holding a Honorary Doctorate in pharmacy at Kuopio University, Finland.
- P. Artursson has made a significant career in the research of pharmacy, especially in drug absorption, disposition and delivery. He has made globally pioneer research contribution in development of *in vitro* models for the prediction of drug absorption through small intestine. Current research interests are directed towards predictive pharmacokinetics (ADMET) and biopharmaceutics in drug discovery and development. In particular, the

role of drug transporting proteins in the cellular uptake, accumulation, metabolism and elimination of drugs and drug-like molecules is studied.

During the course of his research P. Artursson has developed a number of new, scientifically sound and animal saving, *in vitro* models based on advanced cell and molecular biology. These models have been adopted by the drug industry for the prediction of drug absorption in the drug discovery process. They have also been important for the development of *in vitro* and *in silico* methods in large international studies like MEIC and ACuteTox projects, in which P. Artursson has participated.

In 2004, he founded a new unit at his department, dedicated to pharmaceutical screening and informatics: the Centre for Pharmaceutical Informatics (CPI) and in 2010, the unit was transformed into the National Platform for Drug Optimization and Pharmaceutical Profiling (UDOPP). This platform provides information and support, as well as collaborative research, to academia and industry almost entirely based on *in vitro* and *in silico* methods.

P. Artursson is listed as one of the world 100 most cited scientists in Pharmacology and Toxicology since 2004 (ISI). He has published about 150 original articles, 18 review articles and 18 book chapters.

Professor Erik Walum Vice-president of the Björn Ekwall Memorial Foundation walum@glucoxbiotech.com www.bemf.eu

### **Felix Wankel Animal Welfare Award**

Marcel Leist, co-director of CAAT-Europe at the University of Konstanz, has been awarded the Felix Wankel Animal Welfare Award for his work on in vitro test systems in the area of reproductive toxicology. The work used differentiating stem cells to model human nervous system development and disturbances. He shares this prestigious award with Stephan Reichl, who was recognized for his work on human cornea models. The Felix-Wankel research prize is

the oldest of its kind. Candidates are chosen approximately biannually through the veterinary faculty of the University of Munich, and international recipients have included Bruce Ames, Peter Singer, Karel Hala and Coenraad Hendriksen, among others.

More information can be found at: http://www.aktuelles.uni-

konstanz.de/presseinformationen/2013/38/.

# Report on IVTS 2012 meeting 20-21 November 2012

The IVTS 2012 two day meeting at the University of London's Senate House in the of Bloomsbury, focused cardiotoxicity, reproductive toxicity, renal toxicity, and epigenetics in toxicology. IVTS meeting received positive feedback on the quality of talks and scientific content, and is grateful to the speakers, exhibitors and attendees who made the meeting a great success. Christine Mummery (from Leiden University Medical Centre. The Netherlands) started the meeting with a plenary overview of the use of human pluripotent stem cells to provide in vitro models for cardiotoxicology. James Sidaway (AstraZeneca) then followed by describing the use of human embryonic stem cell derived cardiomyocytes to develop in vitro models and high content analysis (HCA) to fill a perceived gap in screening of structural cardiotoxicants. The theme of HCA continued with Michael Cross (MRC Centre for Drug Safety Science, University of Liverpool) looking human cardiac at microvascular endothelial cells and their role in cardiovascular drug toxicity. Gary Mirams (University of Oxford) closed the session on an *in silico* theme, describing how previously generated data on many compounds had been used to derive a computational model of QT interval prolongation in a simulated rabbit This type of modelling has the mvocvte. potential to replace animal tissue experiments in the future to derive data for risk assessment of drugs for effects on cardiac ion channels.

The renal toxicity session started with Jamie Davis (University of Edinburgh) providing an excellent overview of the problems and possible solutions for developing functional

kidnev models. Colin Brown (Newcastle University) described using human and rodent proximal tubule models to help understand species differences in pharmacokinetic profiles and drug transport, and Daniela Riccardi (Cardiff University) described the use of human primary renal cells to look at the effects of anti-cancer drugs specifically targeting fibroblast growth factor receptors on mineral ion homeostasis. The lack of good renal cell lines was addressed by Moin Saleem (University of Bristol) and he described the conditional immortalisation of cells using a temperature sensitive SV40T transgene and also hTERT immortalisation methods to produce more representative cell lines.

The second day began with Aldert Piersma (RIVM Centre for Health Protection, The Netherlands) who gave a comprehensive overview of the most promising and popular alternatives for developmental toxicity testing with a focus on rat whole embryo culture, use of zebra fish and the embryonic stem cell Anita Naidoo (GlaxoSmithKline) discussed methods. practicalities problems encountered in the development of an in vitro model of the blood-testis barrier (BTB) using adult rat cells. The theme of the BTB was continued by Philippe Durand (Kallistem) who described relatively long term rat seminiferous tube cultures (up to four weeks), to investigate testicular dysgenesis syndrome (in particular the effects of dibutyl phthalate) and illustrated the difficulties involved in recapitulating in vitro phenotypic effects seen in vivo.

The free communications included a variety of talks: Obinna Ubah (University of Aberdeen), the IVTS poster prize winner at the March 2012 British Toxicology Society meeting, described his anti-cancer studies with novel mitochondrial targeted flavonoidbased molecules. Lucinda Cowling (University of York) discussed histone acetylation of normal human urothelial cells exposed to cadmium as a measure of epigenetic effects of this human carcinogen, Gary Hutchison (Edinburgh Napier University) showed effects of nanoparticles on Sertoli cells which is part of the EUFP7 'Managing Risk of engineered Nanoparticles (MARINA)' project, and finally Robin Williams (Royal Holloway, University of London) ended

the session with a presentation on the use of the social amoeba *Dictyostelium* as a new model for early identification of emetic liability of drugs.

The final session of the meeting focussed on epigenetics in toxicology and linked IVTS 2012 with the Industrial Genotoxicity Group (IGG) of the UK Environmental Mutagenesis (UKEMS). Lorraine (University of Nottingham) gave us a fantastic introduction to epigenetics and how understanding epigenetic modifications during embryonic development may provide insights into our understanding of functional relevance. Nessa Carey (Pfizer) followed with some interesting human-relevant examples of where epigenetics may be involved such as foetal alcohol syndrome and development of anticancer drugs which target the epigenome of cancer cells. She also highlighted how such drugs are used and the importance of intergenerational transmission of epigenetic changes.



Stephanie Ravenscroft receiving her award from Pratibha Mistry (IVTS Chair, I) and Karl Herbert

Early career scientists at the meeting were eligible for either their poster or oral presentation to be included in the meeting The IVTS 2012 winner was, competition. Stephanie Ravenscroft (University Liverpool), for her poster "The role of endothelial cells in drug-induced cardiotoxicity". Stephanie was awarded a £200 prize, free Society membership for a year and will be invited to present her work at the IVTS 2013 meeting.

# International Conference of Alternatives to Animal Experimentation

26-27 January, Almada, Portugal

As the first event of this kind to be held in Portugal, the conference specifically aimed at promoting the debate and sharing of information regarding the 3R's policies on animal use and highlighting the replacement of animal models for suitable and ethical alternatives, such as *in vitro* and *in silico* models, as well as alternative experimental designs.

The event was organized by the Portuguese Society for Humane Education (SPEdH) and co-sponsored by the Almada City Council, the European Partnership for Alternative Approaches to Animal Testing (EPAA), Hotel Melia Capuchos, Fundação Luso-Americana para o Desenvolvimento (FLAD), Liga Portuguesa para os Direitos do Animal (LPDA) and Mercado do Site.

The conference had approximately 100 participants coming from universities, animal facilities, research laboratories, regulatory agencies, cosmetic industry, animal welfare NGO's as well as general public willing to learn more on this subject.

The vast majority of Portuguese students and researchers attending the congress were positively impressed by the alternatives presented at the conference and became interested on the subject. The general public gained valuable tools to be more participative as decision makers and people from different backgrounds and different perspectives on the animal experimentation issue gained more knowledge and respect towards each other, allowing for constructive dialogues. All Portuguese participants agreed that Portugal needs to have more investment in the field of Alternatives to Animal Experimentation and after this conference this is one step closer to happening.

# **CELLTOX Course – March to June 2013:** "Alternative methods – replacement"



The Italian Association for in Vitro Toxicology (Celltox, www.celltox.it) organized the first training course on "Alternative methods – replacement". The objectives of this course were within the aims of the Association: "...to promote the use of in vitro systems in pharmacological and toxicological research...and to organize courses to train young researchers...".

The event, for its high scientific and innovative content and also for being organized without external sponsoring, was accredited as ECM (Education Continuous in Medicine) at the Italian Ministry of Health by assigning 5 credits per module.



CELLTOX Board members (from left to right): L.Golzio (Secretary), M. Meloni (President), G. Mazzoleni, C. Urani (Treasurer)

The event was supported by the University of Milano Bicocca (UniMIB, Italy) and by the Ethic Committee of the same University, and hosted by the Department of Earth and Environmental Sciences of UniMIB.

More than 40 participants attended, coming from Academia (teachers, researchers, PhD students), Hospitals, Private and Public Research Institutes and Laboratories, and with many heterogeneous Industry, backgrounds (e.g., Biological and Environmental Sciences, Biotechnology. Pharmacy, Veterinary Medicine, Medicine).

The lessons were divided into 4 modules of one day each from March to June.

Experts both from the legislative and regulatory areas, and from the basic to very innovative applied biological and toxicological research provided their expertise and exchanged their knowledge.

The topics addressed were divided into:

- Module I: "Actuality on Alternative Methods"
- Module II: "Regulatory and applicative aspects"
- Module III: "The models for the alternative methods 1"
- Module IV: "The models for the alternative methods 2"

All modules were very intense and followed with great interest by the participants at the end of the lectures. Pleasant and fruitful discussions continued during lunch time and at the end of the day. All the participants briefly presented their fields of activity. Interestingly, for many of them it was the first introduction to alternatives and this experience represented abasis to start introducing alternative methods in their respective research programs.

The event produced a "think tank" committed to disseminate the principles of the 3Rs and to give new ideas and stimuli to the Association.

The organizers acknowledge all the speakers for their willingness and enthusiasm in presenting their areas of expertise, and their ability to stimulate the interest and active discussions from participants.



Participants to CELLTOX Course 2013

We, as organizers, aimed at responding the big need for courses on the scientific divulgation of the 3Rs culture. Certain that the "seed" of the 3Rs culture has been planted

into new fields, we continue working into the implementation of strong connections between researchers and other organizations and developing more and more reliable alternative methods.

Chiara Urani Celltox

# Report on IVTS Symposium at the BTS Spring Meeting, 07-10 April 1013, Solihull, UK

This year, the IVTS symposium at the British Toxicology Society (BTS) was entitled "Surrogate species: the bridge between in vitro models and regulatory toxicology Joanne Livermore (University of species". Manchester) described the specific use of Galleria mellonella (wax moth) for screening toxicity of antimicrobials. This was followed by two talks embracing up-to-date 'omics and pathway approaches in two invertebrate Mark Viant (University of Birmingham) discussed the use of Daphnia with the aim of discovering predictive molecular markers of ecologically relevant toxic responses. Matthew Rand (University of Rochester School of Medicine and Dentistry, U.S.A.) followed this with discussion of the discovery and validation of toxicity gene pathways in *Drosophila*. Adrian Harwood (Cardiff University) then went on to describe the utility of the social amoeba, Dictyostelium, as a cell-based system to probe drug mechanisms, cytotoxicity and teratogenicity. Hilda Witters (VITO, Belgium) finished the session with a comprehensive account of the validation of Zebrafish embryo and larval assays to study developmental and neurotoxic potential of chemicals and drugs. In addition, congratulations are due to Philip Probert of Newcastle University who was awarded the IVTS Poster Prize at the Philip's poster "Metabolic and meeting. Toxicity Screening Potential of **B13** Progenitor-Derived Hepatocyte-like Cells" can be viewed at: http://www.ivts.org.uk/site/ early-career-support/.

Report on Cell Control in a Petri Dish meeting, 19 April 2013

On 2013, the IVTS held a joint meeting with the Cell Control in a Petri Dish collaborative network on the 19th April in central London entitled 'In vitro assay development and its application in toxicity testing'. Speakers and delegates were drawn from both industry and academia providing a vibrant atmosphere and networking opportunities. Delegates learned about a variety of in vitro models and assay approaches that could enable improved in vitro detection of toxicities. Robin Williams (Royal Holloway, University of London) described the use of the social amoeba. Dictvostelium to detect emesis of new chemical entities. This was followed by Amy Pointon (AstraZeneca) describing the use of stem cells in toxicity testing, with a specific focus the in vitro detection cardiotoxicity. Kelly BeruBe (Cardiff University) followed with a highly entertaining talk involving the use of 3D glasses to help describe the development and use of a working model of the human lung (Metabo-Rod Benson then went on to lung™). describe the use and challenges of high throughput imaging using 2D and 3D in vitro models. To conclude the morning session, Colin Brown (Newcastle University) described the development of in vitro models of nephrotoxicity, particularly focusing on the role of drug transporters and the biomarker Kim1. The afternoon session started with a Giese (ProBioGen) bv Christoph describing the development and application of an organoid model of the human lymph node. This was followed by Colin Wilde (AvantiCell Science) discussing availability of human primary cells. The final talk of the day was by David Fluri (InSphero) describing the development, characterisation and application of liver and cardiac 3D spheroids. To learn more about this event please visit: http://www.nottingham.ac.uk/ pharmacy/cell-control-in-a-petri-dish.aspx.

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# NOTOX Predicting long term toxic effects using computer models based on systems characterization of organotypic culture

With the enforcement of the complete ban on animal testing for cosmetics (11<sup>th</sup> March 2013), the need for reliable and validated *in vitro* alternative testing methods for risk assessment, is more

## Highlights

Milestone in animal-free testing strategies: two *in vitro* methods accepted for the first time for the identification of non-irritant chemicals in the field of eye irritation

A major milestone has been achieved in the search of animal-free testing strategies: revised OECD test guidelines extending the applicability domain of two *in vitro* methods - the Bovine Corneal Opacity and Permeability (BCOP) test and the Isolated Chicken Eye (ICE) test - have been adopted by the OECD for the purpose of eve irritation testing.

This is the first time that *in vitro* methods are accepted for the identification of non-irritant chemicals in the field of eye irritation. Both *in vitro* methods are using *ex-vivo* isolated eyes from animals slaughtered for human consumption and will contribute to the substitution of the Draize eye irritation test performed on the eyes of living rabbits.

The revision of two OECD Test Guidelines based on organotypic methods for eye irritation testing was adopted at the OECD meeting of the Working Group of National Coordinators of the Test Guideline Programme held in Paris on 9 to 11 April 2013.

The two test guidelines had originally been adopted in 2009 for the identification of serious eve damage/eye irritation chemicals further to retrospective validation the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) in collaboration with EURL ECVAM and the Japanese Center for Validation of Alternative Methods (JaCVAM). Additional validation of the two tests showed their usefulness also for the identification of chemicals not requiring classification for serious eye damage/eye irritation (i.e. non-irritant chemicals), thus leading to the revision of the test guidelines under the co-lead of EURL ECVAM and the Netherlands.

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urgent than ever before. NOTOX is one of the building block projects of the SEURAT-1 (safety evaluation ultimately replacing animal testing) initiative, jointly funded by the European Commission and Cosmetics Europe for a period of five years. The main focus of the NOTOX project is to develop a based systems strategy for assessment of human relevant repeated dose toxicity using organotypic cultures. As such, NOTOX aims at establishing a systems biology platform for long-term toxicity prediction with closely linked experimental and computational technologies comprising of physiological and structural data. Data from "-omics" such as epigenomics, transcriptomics, proteomics, metabolomics and fluxomics will be integrated for studying and toxicity pathways at the modelling molecular, cellular and tissue levels. Experiments are designed to investigate physiologically relevant, repeated low doses of test compounds on human cellular systems which resemble the in vivo situation. Biokinetics is given due importance in these test systems. The strategies developed in this project will be of great benefit to not only cosmetics industry but also to the chemical and pharmaceutical industry. The ultimate goal is to provide animal free and more ethical, scientifically based strategies for repeated dose toxicity in order to meet European legislative demands.

For the information of general public and stakeholders, NOTOX has produced an 8 minutes film describing the main aims of the project. With a statement from Dr Ruxandra Draghia-Akli, head of the Health Directorate General of the European Commission, the film how leading underlines academic experts from various research fields. along with representatives from small and medium sized enterprises collaborate successfully to provide safe solutions to replace animal testing for safety assessment. Hard copies of the film can be sent to those interested upon request.

The NOTOX film is available on the project website: http://www.notox-

sb.eu/film

# Mapping the Human Toxome: Human Toxome Project Website Launched

The website for the Human Toxome Project was launched on April 11th, 2013. The Human Toxome Project was established comprehensively map pathways of endocrine disruption (ED), representing a first step towards mapping the human toxome. The consortium is led by Principal Investigator Thomas Hartung and co-investigators Melvin E. Andersen, Kim Boekelheide, Albert J. Fornace. Jr.. David J. Dix. Rosenberg, and Jim Yager.

More info at: <a href="http://humantoxome.com">http://humantoxome.com</a>

## Reviews of Health Research that Identify Opportunities to Focus on Disease Pathways and Human Biology-Based Research Modalities

Health research aims to discover the causes of human illness and to prevent or treat them. but the returns on today's investment in health research are becoming harder to see. The average time and cost to develop a drug continue to escalate, vet fewer new medicines reach the market. A key reason is the inability of animal models to sufficiently reflect human diseases, leading to failures in translation and late stage attrition. The problem is recognised by researchers, pharmaceutical companies and regulatory authorities, inspiring the Innovative Medicines Initiative in Europe, the Critical Path Initiative in the United States, and other similar efforts to overcome scientific bottlenecks, improve success and reduce costs, time-to-market, and overall waste associated with current drug attrition rates.

## **Funding opportunities**

The Humane Society International (HSI) to offer grants to credentialed scientists to prepare in- depth reviews including proposals for future research 'roadmaps' for three human disease areas, to be published in peer-reviewed journals.

The reviews will critically evaluate the contributions and limitations of animal-based models of human diseases, and identify opportunities for progress through the application of 21st-century paradigms, including understanding disease pathways using the growing toolbox of human biology-based models and technologies.

Applicants will have a scientific PhD (or equivalent) and current or recent research experience in the academic, private or public sectors, as well as publications relevant to the disease area they propose to address. HSI has already published a critical review of asthma research [1] and reviews on Alzheimer's and Parkinson's diseases and motor neuron disease are in preparation.

HSI is now interested in further disease areas where the current research paradigm can be critically reviewed on a scientific basis and where a draft 'roadmap' can be envisaged using mainly contemporary human-specific models and technologies. With the aid of systems biology, disease pathways and networks can increasingly be researched by means of advanced clinical and *ex vivo* studies and sophisticated *in vitro* models using human cells (including induced pluripotent stem cells).

For these 21st-century techniques to achieve their full potential, HSI believes that a new paradigm will be needed in medical research and drug discovery: one that is less dependent on animal models, conceptually and in practice. A similar transition is already well underway in chemical toxicology [2].

Three grants of up to US\$10,000 (or equivalent) will be payable to the successful applicants for writing and publishing each review. Further grants will be available for disseminating the work at scientific conferences and workshops.

In early September 2013, HSI will circulate a Request for Proposals relating to this project (closing date for applications will be mid-October).

For further information contact Dr Gill Langley: glangley@hsi.org.

[1] Buckland GL. Harnessing opportunities in non-animal asthma research for a 21st-century science. Drug Discovery Today. 2011; 16(21-22):914-27.

[2] Stephens M, Barrow C, Andersen M, Boekelheide K, Carmichael P, Holsapple M. Accelerating the development of 21st century toxicology: Outcome of a Human Toxicology Project Consortium workshop. Toxicol Sci. 2012; 125(2):327-34.

# New fellowship scheme from the *In Vitro* Toxicology Society (IVTS)

As part of our ongoing support to early career scientists, 2013 saw the launch of the IVTS mini-fellowship scheme. The scheme has been set up to aid research training opportunities for scientists in techniques which are not available at their home institution. The fellowships are designed to allow early career scientists to set up collaborations with established scientists, learn new techniques useful for their own research, and to promote further career development particularly in the field of in vitro toxicology research. The scheme is open to IVTS members that are either students currently enrolled on a PhD Programme or Post-doctoral Scientists within 10 years of obtaining their PhD. More details about this new scheme can be found on our website: http://www.ivts.org.uk/site/early-career-

<u>support/</u>. Although the closing date for this year's submission has passed, we intend to make this an annual scheme.

#### **Awards**

# 2014 CAAT Science-based Refinement Awards: Call for Proposals

Attention veterinarians, lab technicians, animal technicians, and all who work with laboratory animals: The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) now is accepting proposals for the 2014 Science-based Refinement Awards (formerly the Animal Welfare Enhancement Awards).

The focus of these awards is to elicit scientific evidence to support the enhancement of the

housing, handling and/or experimental situations for laboratory animals.

Deadline for Submission is September 30, 2013.

PDF Poster Available for download and distribution at: <a href="http://altweb.jhsph.edu/news/2012/sci">http://altweb.jhsph.edu/news/2012/sci</a> based refinement awards%20201
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More information can be found at: <a href="http://caat.jhsph.edu/programs/awards/AWE/2014/index.html">http://caat.jhsph.edu/programs/awards/AWE/2014/index.html</a>.

### EPAA 3R Laboratory technician Prize

In 2013, the EPAA will grant a €3000 prize to a laboratory technician involved in implementing and raising awareness of Replacement, Reduction and Refinement of animal testing.

While most of the current Three Rs prizes and awards target scientists, much of the processes using animals for safety science performed actually by laboratory technicians and animal care takers. The purpose of this prize is to target those actually implementing alternative approaches to animal testing and raise awareness of their role for the day to day implementation of Three Rs principles and, in particular, for seizing opportunities for further Refinement. Animal technicians mainly contribute to one main 'R' - Refinement and this is what the should focus on. Most animal prize technicians are not working on replacement or reduction. In addition there are few prizes for the neglected R of refinement. It is the hardest R to provide sound scientific evidence on. Therefore, this prize is an opportunity to first, recognise technicians as opposed to scientists and second, promote refinement – the R that has the benefit for the animals that still need to be used in experiments. Refinement refers to improvements to scientific procedures and husbandry which minimise actual or potential pain, suffering, distress or lasting harm and/or improve animal welfare in situations where the use of animals is unavoidable.

More information can be found at: <a href="http://ec.europa.eu/enterprise/epaa/3\_4\_awar">http://ec.europa.eu/enterprise/epaa/3\_4\_awar</a> ds.htm

### Latinfarma 2013

La Havana, Cuba

www.latinfarma.com

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### **Meetings calendar**

1-4 September 2013

Eurotox 2013 - Interlaken, Switzerland

www.eurotox2013.com

20 September 2013

# 10<sup>th</sup> Anniversary Symposium of Fincopa – Implementation of the Directive 2010/63/EU in Finland

Tampere, Norway

www. uta.fi. jarjestot.ficopa/

25-27 September 2013

## SSCT 29th Scientific meeting

Charlottenlund, Denmark

www.ssct.se

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20-23 November 2013

# CIFARP – 9<sup>th</sup> International Congress of Pharmaceutical Sciences

Ribeirão Preto, Brazil

www.cifarp.com.br/site/

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10-11 December 2013

# In Vitro Medical Device Testing Symposium

Johns Hopkins Mt. Washington Conference Center Baltimore, MD

21-25 October 2013

4-5 November 2013

## **IVTS Annual meeting**

University of Leicester, UK

# http://www.ivts.org.uk/site/annual-meeting-2013/



11-14 June 2014

# 18<sup>th</sup> Congress of the European Society of Toxicology *In vitro*

Egmond aan Zee, The Netherlands

www.estiv2014.org





24-28 August 2014

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

Prague, Czech Republic

www.wc9prague.org

### **Recent Publications of ESTIV members**

Clotworthy M, Archibald K (2013) Advances in the development and use of human tissue-based techniques for drug toxicity testing. Expert Opin Drug Metab Toxicol. May 20. [Epub ahead of print]

Coecke S, Pelkonen O, Batista Leite S, Bernauer U, Bessems J, Bois F, Gundert-Remy U, Loizou G, Testai E, Zaldívar JM (2013) Toxicokinetics as a key to the integrated toxicity risk assessment based primarily on non-animal approaches. Toxicol In Vitro 27, 1570-1577.

Devreese M, Pasmans F, De Backer P, Croubels S (2013) An in vitro model using the IPEC-J2 cell line for efficacy and drug interaction testing of mycotoxin detoxifying agents. Toxicology in Vitro 27, 157-163

Fahy GM, Guan N, de Graaf IAM, Tan Y, Griffin L, and Groothuis GMM.(2013) Cryopreservation of precision-cut tissue slices. Xenobiotica 43(1), 113-132

Groothuis GMM and de Graaf IAM (2013) Precision-cut intestinal slices as in vitro tool for studies on drug metabolism. Curr Drug Metab 14(1), 112-119

Guan N, Blomsma SA, Fahy GM, Groothuis GMM and de Graaf IAM (2013) Analysis of gene expression changes to elucidate the mechanism of chilling injury in precision-cut liver slices. Toxicol in Vitro 27(2), 890-899

Gunness P, Mueller D, Shevchenko V, Heinzle E, Ingelman-Sundberg M and Noor F (2013) 3D organotypic cultures of human HepaRG cells: a tool for in vitro toxicity studies. Toxicol Sci 133 (1), 67-78

Hadi M, Westra IM, Starokozhko V, Dragovic S, Merema MT and Groothuis GMM. (2013) Human precision-cut liver slices as an ex vivo model to study idiosyncratic drug-induced liver injury. Chem Res Toxicol. 26(5), 710-720

Hadi M, Dragovic S, van Swelm R, Herpers B, van de Water B, Russel FGM, Commandeur JNM and Groothuis GMM. (2013) AMAP, the alleged non-toxic isomer of acetaminophen, is toxic in rat and human liver. Arch Toxicol 87(1), 155-165

Hamers T, Legler J, Blaha L, Hylland K, Marigomez I, Schipper CA, Segner H, Vethaak AD, Witters H, de Zwart D and Leonards PE (2013) Expert opinion on toxicity profiling-report from a NORMAN expert group meeting. Integr Environ Assess Manag 9(2), 185-191

Hoelting L, Scheinhardt B, Bondarenko O, Schildknecht S, Kapitza M, TanavdeV, Tan B, Lee QY, Mecking S, Leist M, Kadereit S (2013) A 3-dimensionalhuman embryonic stem cell (hESC)-derived model to detect developmental neurotoxicity of nanoparticles. Arch Toxicol 87(4), 721-733

Jennings P (2013) Stress response pathways, toxicity pathways and adverse outcome pathways. Archives of toxicology 87(1):13-4 doi:10.1007/s00204-012-0974-4

Juan-Garcia A, Manyes L, Ruiz MJ, Font G (2013) Applications of flow cytometry to toxicological mycotoxin effects in cultured

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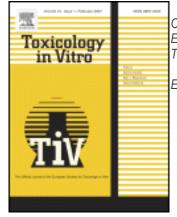
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