

The European Society of Toxicology *In Vitro* Official Journal: Toxicology *In Vitro* (published by Elsevier Science)

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Editorial

Dear ESTIV members,

I would like to begin by wishing everyone a very happy 2014.

I am looking forward to meeting you in Egmond aan Zee, The Netherlands at the ESTIV Congress from June 11-14, 2014, to share scientific information and ideas. Then in August, at the 9th World Congress on Alternatives and Animal Use in Life Sciences in Prague, it will be my pleasure to update you on recent activities in the field of *in vitro* toxicology.

In Newsletter 35 you will find details of many international events: the *"IVTIP* **ESTIV CAAT Meeting**" in the UK; the "t4 workshop on Integrated Testing Strategies for safety assessment" in Italy; the "High Content Imaging Technology Safetv in Sciences" in Germany; the ASCCT meeting in Maryland; the IPAM annual conference in Italy and the 29th SSCT workshop "Frontiers in Cell Toxicity Testing" in Denmark. You will also find the Report on the ESTAF PARERE Meeting, held in June in Ispra, Italy.

I appreciate the efforts of all those who contributed to making this a significant and informative issue. Please check the Newsletter for a long list of upcoming events.

I look forward to continuing to work with you this year and hope to see you in The Netherlands.

Best wishes,

Francesca Caloni, ESTIV

Message from the President

Dear ESTIV members,

First of all let me extend to you all, our best wishes for a successful 2014, both personally and for your professional activities related to toxicology *in vitro* !

This year is an exciting year rich in events in the field of toxicology *in vitro*, with the upcoming 18th ESTIV Congress taking place in Egmond-aan-Zee, The Netherlands, from 10 to 13 June (<u>www.estiv2014.org</u>) and the 9th World Congress on Alternatives and Animal Use in Life Sciences, taking place in Prague, Czech Republic from 24 to 28 August (<u>http://www.wc9prague.org/</u>).

The ESTIV 2014 Congress proposes an inspiring program in which the latest advancements and state of the art of new and emerging areas of toxicology *in vitro* will be addressed. The Congress will be organized in a 'back to its roots' format where all participants are gathered at the same conference centre, fostering communication and networking between our members.

In addition, the 9th World Congress will provide a broad view of the various applications of alternative test methods focusing not only on toxicology assessment but also training, efficacy assessment and policy making decisions.

The ESTIV board is working with dedication to support these and other events in which *in vitro* toxicology is promoted, such as the SCCT, CAAT and IVTIP meetings described in this newsletter. Our society is also engaged in establishing and reinforcing its network by liaising with European and overseas associations dedicated to toxicology *in vitro*, including Brazil, Japan and Latin-America. We hope such an enlarged network and the support and reporting of outreaching activities related to toxicology *in vitro* can be informative to your related activities.

Finally, the ESTIV board is committed to promote and support education and training in toxicology *in vitro* and is co-organizing the Seurat summer school which will take place as a satellite to the ESTIV 2014 Congress, as well as a practical training course on *in vitro* test methods accepted for regulatory use during the 9th World Congress. More information on the two education and training courses will be given in due course in the dedicated websites as cited above.

Briefly, we are committed to actively contribute and promote various activities related to toxicology *in vitro* within Europe and abroad, scientifically and educationally. We look forward to discussing such activities in more detail with you during our General Assembly meeting at the ESTIV 2014 Congress in Egmond-aan-Zee, The Netherlands. We hope to see many of you there and hope you enjoy reading the Newsletter.

With best regards,

Chantra Eskes President of ESTIV

IVTIP ESTIV CAAT Meeting 15–16 May 2013, Southampton, UK

On May 15–16, 2013, the *In Vitro* Testing Industrial Platform (IVTIP), in collaboration with ESTIV and CAAT, held an open meeting in Southampton, UK, hosted by British American Tobacco, to discuss the state of the art in alternative methods, how companies have, can and will need to adapt, and what drives and hinders regulatory acceptance and use. Several key messages arose from the meeting, including:

- In spite of partial replacement of methods in testing strategies, in no area can animal testing yet be completely replaced
- Substantial progress is needed in the development of methods to replace, reduce and refine animal experiments (the 3Rs approach)
- The emphasis on mechanisms and modes of action will be crucial to minimize animal studies in toxicological evaluation
- All stakeholders must not only promote the use of alternative tests, but also take responsibility to find pragmatic ways to change
- Sharing of information, harmonization, standardization and collaboration will help to improve the quality of tests and speed of validation

The outcome of the meeting will be published in a peer reviewed journal in 2014.

For more information: http://www.ivtip.org

Bart de Wever, IVTIP

ESTAF PARERE Meeting Report, 5–6 June 2013, Ispra, Italy

The meeting was held the 5^{th} and 6^{th} June 2013.

ESTAF update

The ESTAF sharepoint is accessible to ESTIV members only via the restricted members webpage <u>http://estiv.org/membonly/membonly.php</u>. A username and password is required, which can be obtained only by ESTIV members by clicking on the corresponding link to ensure the documents are not made publically available.

The ESTIV board would like to thank its members who contributed during the last commenting rounds. As representatives of ESTAF, the opportunity to contribute toward ECVAM strategy and activity is a unique opportunity and one upon which ESTIV invests efforts, to ensure our contribution and visibility remains active. We rely on the varied expertise and support of our members in order to offer this valuable input. Therefore your comments are greatly appreciated.

Commenting rounds completed and coming soon

Published recommendations

- Three Cell Transformation Assays for In Vitro Carcinogenicity Testing using Syrian Hamster Embryo Cells (SHE) and the BALB/c 3T3 Mouse Fibroblast Cell Line (March 2012).
- 3T3 NRU cytotoxicity assay for the identification of substances not requiring classification for acute oral toxicity (May 2013)
- DPRA for skin sensitisation testing (December 2013)
- Bhas Cell Transformation Test for carcinogenicity testing (December 2013)
- Keratinosens[™] test method for skin sensitisation testing (February 2014)

Under consultation or coming soon

- Zebrafish Embryo Toxicity Test for acute fish toxicity testing
- h-CLAT for skin sensitisation testing
- EpiOcular[™] reconstructed tissue for eye irritation testing
- CYP induction (hepatic enzyme induction / biotransformation)
- MELN (Estrogen-receptor transactivation assay)

ESTAF meeting 5th/6th June.

The first day consisted of a one day workshop on "Establishing the Relevance and Ensuring the Acceptance of Alternative Methods for Regulatory Safety Assessment" that addressed the current issues and strategies with the participants from various organizations. Presentations included: Sonja Beken (BLG) Update Validation of New Technology for Use in Drug Discovery in Europe; S. Casati (EURL ECVAM) Update on the Implementation of the EURL ECVAM Skin Sensitisation Strategy; M. Whelan (IHCP) Using an Adverse Outcome Pathway (AOP) Framework for establishing relevance of methods; M. Paparella (AUT) Reliability, Relevance and Adequacy – what is good enough; K. Louekari (ECHA) Relevance and Acceptability of Alternative Methods used under REACH Regulation; Emily McIvor (HSI) Humane Society International implementation and ambition; H. Tyle (DMK) Some remarks on alternative methods and their relevance to

G. Schoenfelder (BFR) Facilitating the uptake of alternatives in biomedical research; A. Worth (EURL ECVAM) Validation of QSAR models for regulatory purposes - principles and practice and A. Gourmelon (OECD) Possible options to address the validation and regulatory acceptance of HTS assays at OECD. The second day was the ESTAF /PARERE meeting and included updates on current activities. Susanne Belz presented ECVAM's

ensure acceptance for regulatory safety assessment; H. Schweinfurth (EFPIA) ICH

development of alternative testing paradigms;

meeting and included updates on current activities. Susanne Belz presented ECVAM's communication strategy and their policy on providing transparent information to stakeholders and the general public in a concise and timely manner via twitter, websites and news items. Annette Roi dissemination ECVAM's discussed of information via the ECVAM DataBase service on Alternative Methods (DB-ALM) which currently has 3154 subscribers, the (Q)SAR Inventory, Tracking Model System for Alternative methods towards Regulatory acceptance (TSAR) and the ECVAM Search guide, with a view to promote the practical acceptance and use of alternatives, to help committees. governmental to support academia & industry when preparing projects, to contribute to registrations of chemicals, to report about ECVAM validation activities and to inform the animal welfare community. The ECVAM Search Guide is available at http://bookshop.europa.eu. This free handbook contains a 7 step check list to help users to make full use of the various information retrieval tools available to them and an inventory of relevant resources, to support the project authorization process of animal experiments (Directive 2010/63/EU (Art.37 annex VI). Claudius Griesinger reported on the status of published and pending test method recommendations and their applicability. **ECVAMs** modular approach to validation and appointment of the new ESAC committee. Raffaella Corvi gave an account of the EURL ECVAM strategy to reduce animal use in genotoxicity testing by a combination of computational models, enhanced in vitro performance (new in vitro tests and review of existing in vitro methods) and intelligent in vivo follow up testing (reducing testing and end point integration into a single study). Patric Amcoff

reviewed international acceptance activities by ICATM partners (ICCVAM. OECD. JaCVAM, KoCVAM, ECVAM, Health Canada - ChiCVAM and BraCVAM have expressed interest in joining) which was set up to promote consistent and enhanced voluntary international cooperation, collaboration and communication among validation organizations in order to support timely adoption of alternative methods and achieve greater efficiency by avoiding duplication and provide biannual input to ICCR (International Cooperation on Cosmetics Regulation) on progress. ECVAM consults with these groups harmonised recommendations, on peer reviews and validations. Understanding how each other work, prioritise and synchronise is very valuable. ECVAM wants to improve their own visibility in this sector. Finally, Valerie Zuang gave an update on ECVAM activities and current status including test method submissions, the ECVAM validation work flow and validation studies led by ECVAM or other validation bodies and the establishment of NETVAL for validation ring trials. She also reviewed the current status of regulatory acceptance.

Alison Gray, ESTIV

t⁴ Workshop: Integrated Testing Strategies (ITS) for Safety Assessment 8-10 July 2013, Ranco, Italy

CAAT-Europe organized, with the support of ESTIV, a workshop on "Integrated Testing Strategies (ITS) for Safety Assessment" to discuss how to make ITS a practical tool that may help toxicologists in risk assessment of chemicals by using data from different tests and sources.

Risk assessment should be ruled by evidence and not by fear. In fact, for the determination of science-based, high-throughput and human-relevant approaches for safety assessment of chemicals, an objective decision-making process is required and needs to be accepted for regulatory purposes. It is increasingly recognized that the future of chemical risk assessment is not with animal tests alone but rather through a combination of approaches (including in vitro,

ex vivo, *in silico*, *in chemico*), i.e. an Integrated Testing Strategy (ITS).

Each component necessarily has a distinctive applicability domain and should address functional endpoints relevant to the the mechanisms underlying adverse outcome. In spite of this common awareness. the way toward this goal is still unclear as there are controversies starting from the definition and construction of an ITS, how it can be optimized and finally validated. Last, but not least, there are no computational tools that can be used for these purposes.

Those were the topics for discussion during this three days workshop, that included about 30 brought together 30 experts from the US and Europe, coming from various areas of expertise and organisations, including governmental bodies (EFSA, EURL-ECVAM, FDA) and scientific associations (ESTIV, EPAA, CEFIC).

Three breakout groups focused the discussion on ITS composition, validation and its relation to the US approach of Tox21c, i.e. how ITS may help the paradigm change of toxicology.

Taking skin sensitization as a case study to explain and understand the potential of the approach, a lively debate took place, which was evidence of the current interest and importance that ITS will play in the future of risk assessment. A detailed report from the workshop will be published soon in ALTEX.

Costanza Rovida, CAAT EU

29th Workshop of Scandinavian Society for Cell Toxicology "Frontiers in Cell Toxicity Testing", 25 - 27^h September 2013, Charlottenlund, Denmark

The 29th SSCT Workshop, organized by Prof. Lisbeth E. Knudsen and Dr. Line Mathiesen (Department of Public Health, University of Copenhagen) with the help of an International Scientific Advisory Committee took place in Denmark on 25-27 September 2013. During the opening ceremony, Prof. Knudsen noted that the most pragmatic approach to reduce experiments on animals is the introduction of alternative methods (Replacement alternatives) in accordance to the Directive/63/EU on the protection of animals used for scientific research.

Several new methods based on the use of human cells or tissue models were presented. In addition, high throughputmethods, *in silico* methods, and QSAR's for the evaluation of toxic hazards were also addressed. The adverse outcome pathway (AOP) approach was highlighted in many presentations together with integrated testing strategy to evaluate chemical toxicity *in vitro*.

During this Workshop SSCT celebrated its 30-year anniversary. Prof. Erik Walum, the first president of SSCT gave a lecture about the history of SSCT, established in 1983, October 21, in Uppsala. The first meeting was held on the initiative of Björn Ekwall, and after that the SSCT workshop has been organized every year with exception of the year 2010, when the meeting intended to take place in Norway was cancelled. The important mission of SSCT has been to promote the study of effects of chemicals in cellular models. This mission was concretized in the Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) programme (1989-1999), initiated and guided by Dr. Björn Ekwall. The main goal of the project was the evaluation of the predictive value of in vitro cytotoxicity tests for human toxicity.

The Björn Ekwall Memorial Lecture was given by Prof. Per Artursson (Uppsala University, Sweden) who received the Björn Ekwall Memorial (BEM) Award 2013. The President of BEM Foundation, Ada Kolman presented the motivation for the award and handed out the diploma to Per Artursson. In his "Towards presentation quantitative predictions of ADMET properties in vitro" Prof. Artursson very interestingly discussed the 40% failure rate of drug candidates during clinical trials caused by unpredictable pharmacokinetic events. He noted that the application of new methods based on advanced cell and molecular biology in early drug discovery resulted today in almost complete elimination of clinical failure due to unpredictable pharmaceutical events. In some cases these methods have been regulatory accepted by agencies as surrogates for in vivo studies. He also

addressed some weaknesses of the current methodologies in vitro as composed pharmacodynamics properties such as drug exposure and adverse effects remain difficult to predict in vitro. To overcome these difficulties he presented recent approaches towards more quantitative predictions of drug exposure: e.g. models for estimation of free concentration, proteomics-informed drug quantification of drua transport and metabolism, and in vitro predictions of drug induced liver injury.

Overall the SSCT Workshop "Frontiers in Cell Toxicity Testing" consisted of 5 sessions, 28 oral presentations and 12 poster presentations. It counted a total of 71 participants from 9 countries. It was delightful that there were many young scientists participating. The posters were presented in the lecture hall, and shortly also to the whole auditorium short summaries. as The workshop was very well organized and both scientifically and socially interesting and successful.

Speakers were invited by the organizers to submit their presentations issued as mini reviews to the Journal of Basic and Clinical Pharmacology and Toxicology. The topics of the oral sessions were:

- 1. New technologies in cell toxicity testing
- 2: Pathways of toxicity
- 3: In vitro/ in silico analysis for risk assessment
- 4: 3D and ex vivo tissue models
- 5: In vitro tests for Human Biomonitoring

At the end of the Workshop three prizes to young scientists were granted: the prize for the best oral presentation to Thit Aarøe Mørck, and for the two best posters to Henrik Johansson and Jonas Christoffersson, sponsored by the Danish Animal Welfare Society, the Committee for Experimental animals.

Hanna Tähti, FICAM

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LatinFARMA – 20th Latin-American congress, 5th Ibero-American and 11th Cuban Congress of Pharmacology 21-25 October 2013, La Habana, Cuba

The LatinFARMA Congress comprised 700 delegates from 39 countries, to exchange the latest advancements in various areas of pharmacology. A specific session was dedicated to the implementation of alternative methods in pharmacology in which key speakers coming from Switzerland, Spain, Argentina, Israel, UK, Colombia and Mexico presented some of the latest advancements in the area.

In addition, a specific session was organized to discuss the constitution of a Latin-American / Ibero-American Network for 3Rs alternatives. In this session. ESTIV's president, Chantra Eskes, presented the functioning, aims and objectives of ESTIV. Furthermore, presentations were given on the Brazilian Association on Alternative methods. on the Argentinean approaches for implementation of alternative methods and on the Cuban approaches in the development of 3Rs alternatives in the field of toxicology and metabolism. Finally, Mario Landys Chovel Cuervo, vice-president of the Cuban Society of Pharmacology, presented the need for creating a Latin-Ibero-American Network of alternatives. The organizers allocated sufficient time for the participants to have very open and active discussions about the constitution of such networks and the opportunities and difficulties each participant saw in their respective regions for the implementation of 3Rs. A Steering Group comprising the main interested parties in the constitution of such a network has been established in order to formalize such constitution. ESTIV, in particular, was proposed to act as a the God-Father for such a network. The next practical activity of this network will be the organization of the 2nd Latin-American Congress dedicated to Alternative Methods, which shall take place in Cuba.

Chantra Eskes, ESTIV

Joint Information Day on "High Content Imaging Technology in Safety Sciences" 24 October 2013, Mainz, Germany

The advent of digital imaging has allowed microscopy to be integrated into objective analyses techniques. High Content Imaging (HCI) allows automated microscopy and multi-parametric, objective image analysis in real time, in higher-throughput and in situ, whereas other cell analysis techniques may involve isolating the cells or other preparatory techniques which induce stress and potentially obscure the data.

This information day was organised to focus on the possibilities of the HCI technology for examination of damage mechanisms and toxic effects of chemicals on specific cellular processes by using reporter systems and, mechanistic dyes. Its application to toxicological analysis and computational methods of analysis were also explored in a range of presentations by expert groups from the pharmaceutical industries and academic research establishments

Prof. Marcel Leist, University of Konstanz, discussed Germanv 'the unbiased characterisation of cell differentiation and neurotoxicity'. He described how HCI can be used to view cell migration, orientation, change in shape and distribution and how such endpoints could be quantified with sophisticated automated analysis software. demonstrated in an example where human ESC differentiated into sensory neurons could be targeted by neuro-specific compounds independently of viability. In this example, the software was used to define the nucleus and 'punch out' the cell body. so that only the area of the neurite was measured. Compounds leading to neuro-specific effects such as neurotoxicants, as opposed to compounds inducing non-specific toxic effects, could be identified.

Prof. Bob de Water, Leiden university, The Netherlands addressed a 'high throughput imaging based pathways of toxicity GFP reporter platform' which described a strategy that aims to create a platform of predictive reporters by using cell imaging, related to acute liver injury. The approach integrates multi-parametric 2D and 3D HCI with functional genomics by incorporating markers of oxidative stress, ER stress, inflammation and DNA damage by a number of predictive pathways modelled in a HepG2 stable reporter cell line.

Dr. Peter Macko, ECVAM, in his presentation entitled 'non-invasive HCI methods for studying dynamic cellular processes and bioenergetics' described how the redox state cell processes, in particular of the mitochondria, can be monitored by the auto fluorescence that is emitted according to their energetic state. This was measured by pixel number according to the intensity of redox and could be influenced by exposure to toxic compounds. Combined with other parameters such as cell number and morphology this contributed to a multi-parametric analysis package for the assessment of toxicity.

Marianne Uteng gave a technical Dr. description of the Novartis approach to studying some types of mitochondrial toxicity by HCI using the Cellomics Array Scan combined with the potentiometric fluorescent dye tetramethylrhodamine methyl ester (TMRM) to detect mitochondrial permeability membrane depolarization. and As а suggested measurement of cell number, Marianne described the use of mitotracker green-fluorescent mitochondrial stain which localize mitochondria appears to to regardless mitochondrial membrane of covalently binding potential by to mitochondrial free thiol groups. To measure apo-necrosis, the Apo-one caspase-3/7 Assay was employed, which contains (Z-DEVD)2-R110 as the substrate, which upon cleavage by caspase present in the cytoplasm, migrates to the nucleus emitting fluorescence. Using this approach, her group was able to determine the toxicity of a drug candidate suspected of causing pancreatitis.

Dr. Eugenio Fava from the German Centre for Neurodegenerative Diseases (DZNE), described approaches at the High Content Screening Facility to study causes and mechanisms leading to neurodegenerative disease. Through collaboration between basic, health care and clinical researchers, knowledge obtained in laboratories can be rapidly translated into therapeutic applications. This is achieved by evolving a sophisticated mathematical model by using high content and high-throughput screenings quantitative multiparametric image with analysis to identify not only single responses in the cell metabolism, but also complete signal transduction pathways and characteristic cellular phenotypes. Combined with clinical data, side effects, metabolites, gene identification, and computation, a network of compounds interacting with the desired target has been produced. From 36 compounds, 250 interaction pathways have been generated at the DZNEDr Mario Beilmann, Boehringer, Germany described how HCI can be used as a screening tool for non-clinical drug safety investigations in complex cell models. Investigations included i) measuring the accumulation of phospholipids using various dyes and performing analyses based on spot count, spot intensity and spot area: ii) using it as a screening tool to rank kinase inhibitors in lung epithelial cells as a measure of toxicity; and iii) performing the combined measurement of cell membrane, mitochondrial and DNA damage in cardiotoxicity.

Anthony Davies, reviewed the work being conducted at INCHSA, the High Content Screening and automation technology core, Trinity college, Dublin, and in particular, the development of *in vivo* mimetic bioreactor technologies as a basis for improved *in vitro* models for drug discovery and safety testing. The facility is also being used for gene silencing and nano-biology for studying the biocompatibility of a range of advanced nanomaterials which have potential therapeutic and diagnostic applications.

Manfred Kansky and Dr Stefan Dr. Kustermann, Roche are also using HCI for the early assessment of drug candidates, in target organ toxicity. The team uses Cellciphr high content screening technology and concedes that with sensitivity /specificity ranging from 52-96%, HCS has the potential to deliver some background information to guide further mechanistic studies. HCI can be used as a mechanistic tool to analyse specific processes in single cells, to make kinetic assessments of drug candidates in real time or to analyse early events before gross toxic phenotype becomes apparent. HCI is therefore useful for complex multiplexed analysis of rare events (less than 3% of the population).

Prof. Yvon Jule, from Biocellvia, University of Provence, France, is using in house developed image analysis technology in histological tissue sections, dual stained with chromogenic or fluorescent immunostaining to discriminate cell components and biomarkers from human explant or 3D models.

Roland Fleck, head of the Biological Imaging and Assay Development Section at the National Institute for Biological Standards and Control (NIBSC), UK, reviewed the current status of electron microscopy.

Concluding remarks were given by Thomas Hartung, CAAT Europe, who described the technology as state of the art, moving toward 3 dimensional, ultrastructures, functionality and higher integration with other technologies / assay types. That there is much cross talk between genomics, HTS and HCI and that now we are data rich but all of which are exposed to the same issue since they are dependent upon the quality of the biological system they are analysing. Therefore it is important to focus our research efforts into substance delivery, identification of the most appropriate reference substances. data mining and interpretation. A workshop report will be prepared highlighting the main issues to be addressed. Actions for the future include the creation of a task force. replicating this workshop in the US and identifying gaps that need to be filled in order to support progress in this field.

Alison Gray, ESTIV

Second Annual Meeting of the American Society for Cellular and Computational Toxicology (ASCCT) 31 October 2013, Bethesda, Maryland

The American Society for Cellular and Computational Toxicology (ASCCT) wrapped up a successful 2nd Annual Meeting October 31, 2013. The meeting was held at the Lister Hill Auditorium on the NIH campus in Bethesda, Maryland. Meeting attendees enjoyed top-notch presentations by two plenary speakers and four ASCCT members, as well as a panel discussion, poster session, and social hour.

Donald E. Ingber, Founding Director of the Wvss Institute for **Biologically-Inspired** Engineering at Harvard University, presented his lab's work developing biomimetic "organs on chips," which are miniaturized platforms of cultured cells with applied mechanical forces that form small working models of the human or animal lung, small intestine, or kidney. One major finding of the Wyss team's work is the importance of mechanical force on the cells; for example, cells from the Caco-2 cell line grown on these chips and subjected to peristaltic force exhibit a more in vivo-relevant phenotype than statically-seeded Caco-2 cells. A key motivation of this work is the current difficultv experienced bv pharmaceutical companies testing potential therapies for human toxicities using animal tests; according to the FDA, 92% of drugs passing pre-clinical safety and efficacy tests fail in clinical tests or shortly after entering the market.

Creating a computational model of the developing embryo sounds complex, but the US EPA's National Center for Computational Toxicology is up to the challenge. Tom Knudsen, Developmental Systems Biologist, presented his team's work to create a working virtual model-a "vEmbryo" to then use to predict the toxicity of chemicals to the developing embryo. The model is built from known biological pathways, which can then be perturbed by "switching" genes on or off to investigate the effect of various pathway states on normal or chemical-affected development. The effort aims to integrate high-throughput predictive models, cell fate, and lineage, ADME models, cell behavior, Adverse Outcome Pathway (AOP) information, and information from high-level experimental validation using computational tools. Real-time behavior of "cells" within the model mimicked the observed biological cell behavior exposed to the same chemicals.

A panel featuring Drs. Knudsen and Ingber, plus Edward Carney from the Dow Chemical Company, Amy Clippinger from People for the Ethical Treatment of Animals, and Steven Bradbury from the US EPA, and moderated by John "Jack" Fowle, ASCCT Board Member, discussed how they were already, and could envision, applying these and other advanced tools to their sector of work. Finally, four talks and a poster session demonstrated the depth and breadth of the fields of cellular and computational toxicology. The oral presentations included:

- Cultured Porcine Cornea Assay Using Confocal Microscopy for High Resolution Detection and Quantification of Sub-Mild Ocular Irritation, Michelle Piehl, MB Research Laboratories
- Identification of Pathways of Developmental Neurotoxicity for High Throughput Testing by Metabolomics, Helena Hogberg, Center for Alternatives to Animal Testing, Johns Hopkins University
- Human Multi-cell Type 3D Liver Microtissues for Hepatotoxicity Testing, Jens Kelm, InSphero, Inc.
- RIFM's Framework for In Silico Evaluation of Fragrance Materials, Sneha Bhatia, Research Institute for Fragrance Materials, Inc.

ASCCT members can access some of the presenters' slides and other resources on the ASCCT web site; a more complete account of the proceedings will be available shortly. Please visit the <u>ASCCT web site</u> for more information.

ASCCT

IPAM Annual Conference 14th November 2013, Brescia, Italy

TALIAN FLATFORM ON ALTERNATIVE METHODS

IPAM, the Italian Platform on Alternative Methods, held its annual Conference in collaboration with the Reference Center for Alternative Methods, Care and Welfare of Animal, in Brescia on November 14th, 2013. The conference entitled "*Toxicology and Stem cells: new frontiers*" focused on stem cells as a promising tool for toxicology screening. Scientists and experts from the Industry, Academia and Research institutes presented their activity in this field.

The conference concluded with the Farmindustria AWARD 2013, given annually to a young scientist who published on the topic of alternative methods and drug research and development. This year the recipient was Dr. Nadia Ucciferri from Pisa National Research Council for her PhD thesis on "Functional and morphological study of cells in connected culture in response to interactions associated with nanoparticles".

IPAM

Meetings calendar

24–27, March 2014 **SOT's 53rd Annual Meeting,** Phoenix, Arizona. <u>http://www.toxicology.org/AI/MEET/AM2014</u>

12-14 May 2014

Fourth International Conference on Alternatives for Developmental Neurotoxicity Testing (DNT) The Inn at Penn, Philadelphia, PA

http://caat.jhsph.edu/programs/workshops/DN T4/index.html



11-14 June 2014 **18th Congress of the European Society of Toxicology In vitro** Egmond aan Zee, The Netherlands www.estiv2014.org



Satellite meetings:

SEURAT-1 & ESTIV Joint Summer School:

The SEURAT-1 & ESTIV Joint Summer School will be organised prior to the ESTIV conference, from 8 to 10 June, 2014.

1st NOTOX Satellite Meeting:

The NOTOX Satellite Meeting will be held on the 10th of June, 2014.

CAAT-ESTIV-IVTIP joint workshop on Industrial and Regulatory Implementation of Non-Animal Integrated Testing Strategies The CAAT-ESTIV-IVTIP joint workshop on ITS will be held on the 10th of June, 2014.

More information at: <u>http://www.estiv2014.org/satellite.html</u>



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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

23-24 October 2014 3rd Symposium on **Fish and Amphibian Embryos as Alternative Models in Teratology and Toxicology** Aulnay-sous-Bois, Paris, France <u>https://www.ufz.de/fish-frog-embryo/</u>

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Recent Publications of ESTIV members

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