

### The European Society of Toxicology In Vitro

Official Journal: Toxicology In Vitro

### **Newsletter No. 41**

#### February 2018

Dear ESTIV Members,

First, let me extend to you all the best wishes for a successful 2018, both personally and professionally.

The year 2017 was marked by a number of highlights for our society and the present newsletter provides some inspiring insights on a number of activities that took place during the last few months.

This issue includes information on many past events, including reports from the 53th EUROTOX Congress, IC-3Rs symposium, launching of the FCS-free Database and few others. You will also find information about forthcoming activities.

We would like to thank everyone who contributed to this newsletter and encourage those, who have any news from the *in vitro* toxicology field, comments or questions about ESTIV and its activities to contact us directly at the e-mails given in this newsletter.

Iwona Wilk-Zasadna

#### Message from the president

Dear ESTIV Members,

In this first newsletter of 2018, I want to start by wishing you a very happy new year, a good health and lots of joy for you, your family and your beloved ones. At the professional level, I hope this may be a very productive and prosperous year for each of you.

2017 has been a successful year for ESTIV. On 8-13 January 2017, ESTIV organized for the second time the 'Applied *in vitro* toxicology

course'. This fully booked course took place in Belvaux-Luxembourg and was attended by 25 participants from 11 different European and non-European countries. ESTIV was also represented at major conferences in 2017, including at the 10th World Congress Alternatives and Animal Use in the Life Sciences (20-24 August 2017, Seattle-USA) and the 53th EUROTOX Congress (10-13 September 2017, Bratislava-Slovakia), some which are reported in this newsletter. In addition, ESTIV has supported several international workshops, has granted poster awards during relevant conferences, has been represented in a number organizations and regulatory bodies and has been, and still is, involved in European research and training projects.

You, as ESTIV member, are undoubtedly the main driver of ESTIV's success in these initiatives. However, all of this would not have been possible without the efforts of a very committed team of ESTIV board members. I would like to cordially thank each of the regular members and board members for your involvement in ESTIV.

2018 will be a challenging year for ESTIV. Indeed, given the overwhelming success of the previous 2 courses, it has been decided to organize the 'Applied in vitro toxicology course' as of now on a yearly basis. The next course will take place 8-13 April 2018 in Utrecht-The Netherlands in collaboration with Dutch Society for Toxicology (http://estivnvt2018.webs.com/). Furthermore, ESTIV, together with the German Toxicology Society and the Center for Alternatives to Animal Testing-Europe (CAAT-Europe), will organize the 20th International Congress on In Vitro Toxicology (ESTIV2018) on 15-18 October 2018 in Berlin-Germany (http://www.estiv2018.com/).

I hope to see you during these events and I hope you will enjoy reading this newsletter!



Mathieu Vinken
President of ESTIV



ESTIV 2018 Congress 15-18 October 2018 Berlin, Germany



The next ESTIV congress will be organized in collaboration with CAAT-Europe and the German Toxicology Society on 15-18 October 2018 in Berlin-Germany.

Abstracts can be submitted for oral or poster presentations fitting in one or more of the following sessions:

- Bio-engineering and stem cell models
- Toxicokinetics and *in vitro in vivo* extrapolation
- Models, biomarkers and assays for systemic toxicity testing
- Disease models and translational toxicology
- New developments in local toxicity and skin sensitisation testing
- In silico modelling and read-across approaches
- Updates and developments in regulatory toxicology
- New developments in inhalation toxicity testing

The scientific program and logistics details are available at www.estiv2018.com. There are ample opportunities for acquiring student travel bursaries as well as for sponsorship and exhibition.

We hope to see you in Berlin!

#### Applied In Vitro Toxicology Course

ESTIV will organize the third 'Applied In Vitro Toxicology Course' in collaboration with the Dutch Society of Toxicology (NVT) on 8-13 April 2018 in Utrecht-The Netherlands. The course consists of a series of lectures and 2 hands-on exercises on skin irritation and biokinetics. This will be taught by experts in 3 areas of *in vitro* toxicology, namely regulatory in vitro toxicology, screening in vitro toxicology and investigative in vitro toxicology. Earlycareer scientists from industry, regulatory agencies and academia, including doctoral and postdoctoral candidates, interested in in vitro toxicology are encouraged to apply. Applicants should have a background in toxicology, biology, chemistry, (veterinary) medicine. bio(medical), pharmaceutical sciences or equivalent. English proficiency is required. A maximum of 25 participants will be enrolled in the course on a first-come firstserved basis. For more information, program and registration, please see the course website www.estivNVT2018.webs.com

We hope to see you in Utrecht!



The course organizers Nynke Kramer, Bas Blaauboer and Mathieu Vinken.

11th World Congress on Alternatives and Animal Use in the Life Sciences



The 11th World Congress on Alternatives and Animal Use in the Life Sciences will be organized in Maastricht-The Netherlands on 23-27 August 2020. The general theme of the

congress is "3Rs in transition: from development to application". For more information and submission of topic proposals, please see the congress website http://www.wc11maastricht.org/.

The congress organizers are active on different social media, including Facebook, Twitter and LinkedIn ("WC11Maastricht"), on which regular updates are posted.

in3:an integrated interdisciplinary approach to animal-free nanomaterial and chemical safety assessment



The in3 project (pronounced "in three") is funded by the EU's Marie Skłodowska-Curie Action - Innovative Training Network (MSCA-ITN for short). The project long title is "An interdisciplinary integrated approach animal-free nanomaterial and chemical safety assessment" and aims to drive the synergistic development and utilisation of integrated in vitro and in silico tools for human chemical and nanomaterial (NM) safety assessment. Hence in three (in3). The project will focus on differentiation of human induced Pluripotent Stem Cells (hiPSC) to toxicologically relevant target tissues including; brain, lung, liver, vasculature and kidney. The tissues, from the same genetic backgrounds, will be exposed to several compounds and the data generated will be used to develop safety assessment approaches by integrating cheminformatics, mechanistic toxicology and biokinetics into computational models. The project has hired 15 PhD students to carry out these activities in a coordinated and highly collaborative fashion. The scientists trained within in 3 will acquire a unique multidisciplinary skill set giving them a competitive employment advantage in safety assessment sciences either in industry, governmental bodies or academia.

The core scientific activities of include:

- Differentiation of well-characterised human iPSC into brain, lung, liver, kidney and vascular cells
- Delineation of tissue specific and donor specific effects of compound exposures

(uptake, metabolism, extrusion, and mechanistic toxicity)

- Development and optimisation of quantitative adverse outcome pathways (qAOPs) for each target organ which will be unified in an organism-level model
- Optimisation of QSAR and read-across tools for safety assessment
- Ultimately to create a unified expandable integrated testing strategy for chemical and NM safety assessment

The project is coordinated by Prof. Dr. Paul Jennings at the Vrije Universiteit Amsterdam. In October 2017, the project had a successful kick off meeting with the majority of the ESRs, Pls and the scientific advisory team. We will look forward to providing updates and highlights over the next 3 years.

Web page: <a href="http://estiv.org/in3/index.php">http://estiv.org/in3/index.php</a>



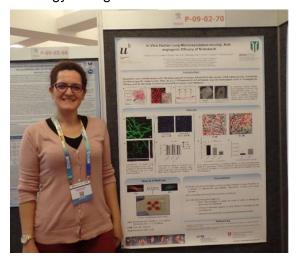
# ESTIV poster award during the 53rd EUROTOX Congress



September 10–13, 2017

The 53rd Congress of the European Societies of Toxicology (EUROTOX) took place in Bratislava-Slovakia on 10-13 September 2017 and was organized by the Slovak Toxicology Society. The theme of the congress was "Connecting for a safer future" and the scientific program highlighted significant developments and achievements in the field of toxicology, including *in vitro* and *in silico* toxicology, ESTIV has granted the best poster award, including a prize of 500€ and 1-year free ESTIV membership, during the congress to Soheila Zeinali from the ARTORG Center of the University of Bern-Switzerland for the

poster entitled "*In vitro* human microvasculature-on-chip: anti-angiogenic efficacy of Nintedanib". The poster was selected by a jury consisting of ESTIV board members Chantra Eskes, Laura Suter-Dick, Anne Marie Vinggard, Paul Jennings and Mathieu Vinken based on originality. complexity, presentation, rationale relevance to the field of in vitro and in silico toxicology. Congratulations to Soheila!



# ESTIV GIVIMP/GCCP session during the 53rd EUROTOX Congress



September 10–13, 2017

Sandra Coecke (European Commission Joint Research Centre, Ispra-Italy) and Bas Blaauboer (Utrecht University, Utrecht-The Netherlands) organized an excellent session on "Good *In Vitro* Method Practices/Good Cell Culture Practice" (GIVIMP/GCCP) on behalf of ESTIV at the 53rd EUROTOX Congress in Bratislava-Slovakia.



Coecke first discussed recent Sandra developments regarding an OECD guidance document on GIVIMP. This was followed by a presentation of Bas Blaauboer highlighting the requirements for publication of *in vitro* toxicity data. Next was a talk by David Pamies (CAATat John Hopkins University, Baltimore-USA) on GCCP for stem cells and stem cellderived in vitro models. The session was closed by a lecture by Jan van der Valk (Utrecht University, Utrecht-The Netherlands) focused on the use of serum-free cell culture media and serum alternatives. The session was greatly appreciated by the audience as evidenced by the crowded meeting room. ESTIV would like to thank all 4 speakers and in particular Sandra Coecke and Bas Blaauboer for organizing this session.

EUROTOX 2017 Continuous Education
Course: Human immortalized and induced

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CONNECTING FOR A SAFER FUTURE

pluripotent stem cells

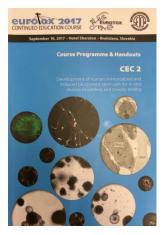
September 10–13, 2017

ESTIV and CAAT have jointly promoted a Continuous Education Course on the "Development of human immortalized and induced pluripotent stem cells for *in vitro* disease modelling and toxicity testing" that took place during EUROTOX 2017. Participants came from the pharmaceutical, food and agrochemical industry as well as regulatory agency and academia.

The combination of cell culture with geneticand bio- engineering has led to a number of technologies to make cell culture more human- and organotypic- like, such as human stem cell-derived systems, 3D culture, perfusion, co-cultures, combinations with scaffolds and sensors that can lead to multiorgan "human-on-chip" solutions. By recreating human cells and organ architecture, homeostasis of the cell environment and organ functionality, these models mirror more closely the species of interest and its physiological situation.

However, these technologies also bring a number of challenges in order to ensure reproducibility and quality of the systems used. These include cell identity, characterization of pluripotency,

differentiation, functional potential, genetic stability, windows of use and microbiological controls as well as non-homeostatic and non-physiological culture conditions. The poor or lack of implementation of quality control and reporting standards can contribute to the current reproducibility crisis in the life sciences.



The presentations given during the CEC addressed:

- Immortalization of human cells by Regina Grillari (BOKU, Austria)
- Neuronal differentiation of human pluripotent stem cell lines by András Dinnyes (Biotalentum, Hungary)
- Human pluripotent stem cells for cardiac disease and safety pharmacology by Robert Passier (Leiden University Medical Centre, Netherlands)
- Induced pluripotent stem cell-derived cellular systems for in vitro disease modelling and toxicity testing by Giorgia Salvagiotto (Cellular Dynamics, UK)
- Bioengineering next-generation stem cell culture technology by Nikolce Gjorevski (EPFL, Switzerland)
- Good cell culture practices on human stem cells by Thomas Hartung (CAAT, USA).

These presentations aimed at providing insights on the challenges encountered in developing and culturing standardized and reproducible human immortalized and induced pluripotent stem cells from different organs, and on possible tools for ensuring their quality for *in vitro* disease modelling and toxicity testing applications. Furthermore, it addressed the concept of Good Cell Culture Practice (GCCP) applied to the fast-paced developments of new technologies such as

human stem-cell-derived models and organotypic cell cultures, based on an international collaboration started in 2015 and carried out in the US and Europe.

Finally, the following issues were addressed during the round-table discussions:

- The need to have well characterized human immortalized / induced pluripotent stem cells;
- The need to define what is the level of characterization required (e.g., cellular/neuronal types present, functionality, etc.);
- The need to ensure quality control throughout the differentiation protocol;
- The issue of donors: need for interindividual differences versus single donor for e.g. personalized medicine, and what is meant by 'healthy' donor' when he/she may develop a disease later on in life?

These issues represent some examples of the possible issues to be addressed in order to ensure the robustness of human-based cell lines and their related *in vitro* testing outcomes.

Chantra Eskes ESTIV past-president

# ESTIV survey on the use of alternative test methods for animal experimentation

An ESTIV survey was conducted from 19 July to 10 August 2017. Comprised of ten questions, it aimed at understanding the current uses and possible bottlenecks in using alternatives to animal testing for both, R&D and regulatory purposes. The survey was sent to all ESTIV members, out of which 53 responses were received. The respondents worked in academia (49%), industry (36%) and government (15%). Most of respondents (out of 51) had experience with *in vitro* methods (96%), followed by computational models (24%), animal models (18%), nontesting methods (16%) and refinement alternatives (12%).

Interestingly to the question on 'why did you start working with/on alternative methods', a majority of answers (out of 52) related to scientific/human relevance (79%) and mechanistic understanding (71%), followed by ethics (50%), and regulatory needs (25%). The main cited means used to retrieve information on alternative methods (out of 52)

were scientific publications (92%) and congress/conferences (88%), followed by regulatory texts (48%), internet/commercial sources (40%) and training courses (31%).

The main purposes for using alternative methods were reported to be (out of 51 answers): R&D (75%), regulatory (41%), validation (37%), policy/advocacy (12%) and education and training (2%). To the question on whether regulatory requests on use of alternative methods had an impact on the respondent's activities, a majority of yes was obtained (63% out of 51 answers), and stated to mainly impact the implementation (6 answers), development (3 answers) and investment (2 answers) on alternative methods.

A total of 50 out of 50 respondents believe the use of alternative methods in R&D could be improved, and the following main obstacles were reported to currently exist:

- The conservative approach (e.g., animal studies considered as gold standard) by regulatory authorities, scientists and/or journal reviewers (15 of 28 answers);
- The non-availability of methods for some endpoints/physiological functions (6 of 28 answers);
- The lack of funding and personnel (6 of 28 answers);
- The limited understanding about the potential of (combined) alternative methods (6 of 28 answers).

A total of 49 out of 49 respondents believe the use of alternative methods could be improved also for regulatory purposes, and the following main obstacles were reported to currently exist:

- The lack of acceptance / harmonization / willingness to change / familiarity from e.g. regulators and/or toxicologists (11 of 26 answers);
- The long validation and legal implementation processes (5 of 26 answers);
- A well-defined applicability domain, even if restricted (4 of 26 answers);
- The complexity and costs of using multiple tests / testing strategies (3 of 26 answers).

The following areas received the higher number of responses as areas, where alternative methods could be further implemented (out of 43 answers):

- Carcinogenicity (n=55 answers, including 29 for R&D and 26 for regulatory purposes);
- Reproductive & developmental toxicity (n=53 answers, including 28 for regulatory purposes and 25 for R&D);
- Pharmacokinetics (n=52 answers, including 28 for R&D and 24 for regulatory purposes);
- Systemic toxicity (n=49 answers, including 26 for R&D and 23 for regulatory purposes);
- Disease modelling (n=44 answers, including 28 for R&D and 16 for regulatory purposes);
- Skin sensitization (n=41 answers, including 24 for regulatory purposes and 17 for R&D).

the respondents believe alternative methods can be further improved (out of 49 answers) by having: dedicated funding (80%), improved legislation (71%), better cross-sectors communication (69%), professional training courses (57%)congresses (51%),workshops (49%),dedicated university degrees (47%).

These questions have been shared with the American Society for Cellular Computational Toxicology (ASCCT), and with the Japanese Society for Alternative to Animal Experimentation (JSAAE). Furthermore, the results of the survey were presented during the 10th World Congress on Alternatives and Animal Use in the Life Sciences (WC10) that took place on 20-24 August 2017 in Seattle, Washington, USA. The audience was very pleased about the outcome, and ASCCT informed that a similar outcome had been obtained from their members.

Further details on the survey outcome can be found at the ESTIV website.

Chantra Eskes ESTIV past-president

"New Scientific Impulses Towards 3R Alternatives"
Symposium Report
25th September 2017



The Innovation Centre 3Rs (IC-3Rs), an initiative of the Vrije Universiteit Brussel (VUB), aims to shine a spotlight on alternative methodologies that incorporate the 3Rs

principle of Refinement, Reduction and Replacement. The platform was launched on the 25th September 2017 with an inaugural symposium at VUB's Health Campus, Jette-Brussels.

Among the introductory addresses, the State Secretary, Bianca Debaets highlighted that, while complete replacement of animal usage in biomedical, medical and toxicological research is not yet possible today, timely investment in alternative methodologies and new *in vitro* technologies are essential now. In this way, methods to reduce and refine can be progressed so that the goal of complete replacement may be achievable in the future, even if only in a limited area.



In addition, the important role of platforms, like IC-3Rs, in disseminating new technologies towards 3R alternatives was elaborated by the event's moderator, Bernward Garthoff, Chair BiO.NRW. One such key task is the creation of a databank that details all alternative methodologies in use and under development. For Belgium, this will represent a valuable, searchable resource, that provides visibility to the alternative methodologies available in Flanders, Brussels and, if possible, also in the Wallonia region.



The scientific content of the symposium featured cross-disciplinary talks from key VUB experts. Through this program, the 180 plus attendees of the symposium heard about

advances in alternative methodologies. Recent innovations in stem cell research that utilize human rather than animal source tissue was discussed. Innovative 3D-culture models, that aim to achieve a better reflection of *in vivo* physiology in *in vitro* systems were introduced to the audience. Furthermore, interesting talks were given on the potential of the latest gene editing strategies to achieve unprecedented gene targeting both *in vitro* and *in vivo*. Finally, the emergence of *in silico* approaches to limit the reliance on animal models in screening for human safety was discussed extensively.



The symposium program was punctuated by a walking lunch and closing reception, providing the opportunity for participants to network and discuss their perspectives on the day's themes. The organizers offered participation in the full day's events free of charge, thanks to the generous support of 20 local and international sponsors, including ESTIV. The interaction with key industry sponsors, who are active in alternative methodologies, was facilitated by 8 exhibition stands at the venue. Following the success of this first event, it is envisaged to broaden future activities under the IC-3Rs platform: more young-researcher and student involvement; wider input from other Belgian universities; and content from various industries where increasing commitments to the 3Rs are also stimulating innovation.

# Launch of the FCS-free Database: fcs-free.org



On the 15th of August, the 3Rs-Centre Utrecht Life Sciences (ULS) and Animal Free Research UK launched the FCS-free Database: fcs-free.org, as new addition to the 3Rs Database programme. The website

allows researchers to identify FCS-free media for specific cell types and to exchange information on the applicability of FCS-free media. This website will contribute to the replacement of animals used for research and to the reproducibility of *in vitro* methods. Dr. Jan van der Valk introduced the topic by explaining why cell culture media are supplemented with fetal calf serum.



Van der Valk: "Cells that are grown outside the body (in vitro), need, among others, nutrients, proteins and growth factors to stay alive and multiply. Fetal calf serum (FCS) contains these necessary components, but there are moral and scientific concerns associated with FCS." FCS is harvested, with a high chance of suffering, from unborn calves. Furthermore, since it is a natural product, the composition of the commercially available FCS varies from which to batch, impedes reproducibility of results. FCS is a universal supplement that works for most cells. FCSfree culture media, though, have to be developed for every cell type. To facilitate the search for available FCS-free media that can be used to successfully grow cells in the lab, the FCS-free Database is developed".

Afterwards, Dr. Alpesh Patel of Animal Free Research UK explained why they have invested time and money in the development of this database. Patel: "Animal Free Research UK funds and promotes research without the use of animals, and with human relevance. This was a great project to get involved in, since it reflects our vision on how human research should be carried out without the need for any animals in any form to be used."

After the presentations, Ted van den Bergh, director of Triodos Foundation and one of the partners of the 3Rs Database programme, was invited forward. Together with Dr. Patel,

he pushed the red button that officially launched <u>fcs-free.org</u>.

The fcs-free database facilitates the identification of serum-free media for specific cell types. It provides information on commercial sources and extracts information from publications with formulations. Each record contains a review function, like TripAdvisor, where researchers can review and describe experiences with particular media.



Furthermore, the website is expanding its information with a list of publications that review the use of serum-free media.

If you have published about serum-free chemically defined media, preferably with formulations, and wish to be included in the database, please use the form at: <a href="https://fcs-free.org/contact/update-the-database">https://fcs-free.org/contact/update-the-database</a> to submit your information.

#### **Altertox Academy – upcoming trainings**



Altertox was founded in 2012 in Brussels, Belgium and qualifies as a SME (Small Medium Enterprise) with two full time employees and two free-lance. Altertox has two main activities: public affairs and trainings both linked with 3Rs (replacement, reduction and refinement).

The organizing of training activities in laboratories with a particular focus on *in vitro* 

and in silico methods started in 2016 and was subcontracted exclusively to CAAT-Europe under the brand name CAAT Academy. Under CAAT Academy brand, Altertox has organised more than 15 hands-on laboratory trainings all over Europe. The topics ranged from in vitro skin & eye irritation models to in silico methods such as read-across. Migration of the old (https://www.caat-academy.org/) to the new website (https://academy.altertox.be) took place at the end of 2017. It now solely operates under the name of Altertox Academy with the same team, same concept, and same standards of deliverables as it was with the previous brand name. Moreover, another goal of Altertox Academy is to become work package leader for training for EU calls.



All the hands-on trainings are performed in English and limited to a maximum number of 15 participants for the laboratory or 20 participants for *in silico* training divided to a maximum of 4 people per group. The unique concept of Altertox Academy is to always have at least 3 different suppliers within one session. Participants shall generate data with the methods demonstrated and being guided with the interpretation of data.

With Altertox being the unique interface with the participants, it allows the co-host and the suppliers to focus only on the content of the training while Altertox focuses on any miscellaneous external requests from the participants (e.g. dietary restrictions, travel arrangements, payments, training expectations etc.). Due to the fact that Altertox provides guidance to the suppliers, the latter can promote in the best conditions their tools to their prospects.

Altertox Academy upcoming events agenda:

 Hands-on training on the use of weight of evidence with non-testing methods for cosmetics ingredients

May 22-23, 2018
Mario Negri Institute – Milano, Italy
Registration Link:
https://altertox2018-marionegri.eventbrite.com

Hands-on training on in silico and in vitro liver models

May 31 and June 1, 2018 Biopredic International - Paris, France

Registration Link: <a href="https://altertox2018-biopredic.eventbrite.com">https://altertox2018-biopredic.eventbrite.com</a>

Congress: Lung In Vitro
July 5-6, 2018
Nice, France
Registration Link:
http://www.epithelix.com/support/LIVe2018

 Hands-on training on PBPK modelling for quantitative in vitro-in vivo extrapolation October 5-6, 2018 KU Leuven - Leuven, Belgium Registration Link: https://altertox2018-kuleuven.eventbrite.com

 Hands-on training on stem cells and 3D tissue engineering October 25-26, 2018

IRBM – Montpellier, France

 Hands-on training on culture of human highly relevant cells according to Good Cell Culture Practice (GCCP)

October 30-31, 2018
Evercyte – Vienna, Austria
Registration Link:
https://altertox2018-evercyte.eventbrite.com

Hands-on training on in vitro lung models
 November 15-16, 2018
 Epithelix – Geneva, Switzerland
 Registration Link:
 https://altertox2018-epithelix.eventbrite.com

Hands-on training on skin sensitization
 November 22-23, 2018
 BASF – Ludwigshafen, Germany
 Registration Link:
 <a href="https://altertox2018-basf.eventbrite.com">https://altertox2018-basf.eventbrite.com</a>

Highlights



**LUSH Prize** rewards the most effective projects and individuals, who have been working towards the goal of replacing animals in product or ingredient safety testing across five strategic areas: I) Lobbying, II) Public Awareness, III) Science, IV) Training, V) Young Researcher Awards.

In order to support young scientists, in parts of the world where animal-free science is not so well accepted, regional Young Researcher Awards have been founded. 2017 LUSH prize awardees are as follows:

#### YOUNG RESEARCHER AMERICAS

**Carolina Catarino** (Rensselaer Polytechnic Institute, USA) for her work on animal-free approaches for engineering physiologically relevant humanized skin models using 3D bioprinting technology.

**Zhen Ma** (Syracuse University, USA) for her work on developing human heart model for animal-free embryotoxicity drug screening

**Kamel Mansouri** (Scitovation, USA) for his work on *in silico* screening of chemicals for estrogen and androgen receptor activity

Renato Ivan de Ávila Marcelino (Federal University of Goiás, Brazil) for his work on applicability of the association of micro-DPRA and photo-micro-DPRA to identify the photosensitization potential of "real-life" mixtures.

**David Pamies** (Center for Alternatives to Animal Testing, USA) for his work on development of a dysmyelination test to study developmental neurotoxoicity of environmental chemicals in a human brain microphysiological system.

#### YOUNG RESEARCHER ASIA

**Jiabin Guo** (Institute of Disease Control and Prevention, China) for his work on toxicity pathway-based assessment of chemical-

induced mitochondrial toxicity using *in vitro* assays and computational modeling.

**Kenry** (National University of Singapore, Singapore) for his work on development of a biomimetic intravascular thrombosis-on-chip model for elucidating thrombosis mechanism and evaluating the thrombolytic efficacy and toxicity of therapeutic nanomaterials.

**Satoshi Koyama** (Takasaki University of Health and Welfare, Japan) for his work on development of HepaRG system for evaluation of toxicity variation based on metabolic induction.

#### YOUNG RESEARCHER REST OF WORLD

**Nathalie Bock** (Queensland University of Technology, Australia) for her work on all-human bioengineered *in vitro* models as platforms for cancer research.

**Sandra Heller** (Ulm University, Germany) for her work on animal-free diabetes modelling on an iPSC chip platform.

Vanessa Kappings (Karlsruhe Institute of Technology, Germany) for her work on vasQchip: a novel vascularized microchip platform to save animals' lives.

**Anna Monzel** (University of Luxembourg – Luxembourg Centre for Systems Biomedicine, Luxembourg) for her work on novel toxininduced human *in vitro* organoid model of Parkinson's disease.

**Rebecca Payne** (Newcastle University, UK) for her work on bringing single-cell technology to the paediatric bedside to aid diagnosis and inform treatment of immune dsyregulation.



Lena Smirnova won the Green and Open Neuroscience Award for her outstanding contributions to forwarding human-based neurotoxicity research that saves human lives and replaces the use of animal in research. The honour is awarded by the Green Neuroscience Laboratory and The Physicians Committee for Responsible Medicine (PCRM).



#### **EURL ECVAM 2017 Status Report**

The JRC hosted EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) has published its Status Report 2017 presenting an update on the development, validation and regulatory acceptance of alternative methods to animal testing.

Among the topics featured in the report, the reader can find information on research and development projects, test method submissions, validation studies, peer reviews, EURL ECVAM recommendations, test guidelines and guidance documents, and a range of initiatives to share information on alternatives and promote their acceptance and use across the globe.

Read more at: Zuang et al., (2017), <u>EURL ECVAM Status Report on the Development, Validation and Regulatory Acceptance of alternative Methods and Approaches (2017).</u>



The ECHA report on Non-animal approaches - Current status of regulatory applicability under the REACH, CLP and Biocidal Products regulations, is available on ECHA's website under <a href="https://echa.europa.eu/publications/technical-scientific-reports">https://echa.europa.eu/publications/technical-scientific-reports</a>.

The report was written in response to ECHA's management board request to have an objective report on the current non-animal approaches and their applicability within the regulatory framework, as part of the overall approach of ECHA to avoid unnecessary animal testing.

The report highlights the need to continuous development of alternatives to animal testing and their consideration for chemical safety assessment under the EU legislation. It describes how non-animal approaches should be used to fulfil legal requirements and what is realistically achievable with the current methods. The report states there have been significant scientific developments in the past 10 years regarding the replacement of animal testing for chemical safety assessment with non-animal approaches, in particular for lower tier endpoints. For more complex endpoints, a full replacement of animal testing is not yet foreseeable but options to reduce animal testing exist and should be used.



#### BETTER POLICIES FOR BETTER LIVES

The OECD has published a number of new Test Guidelines (TG) and Guidance Documents (GD) related to *in vitro* methods for human health hazard assessment, including:

- DECD TG 442E on in vitro assays addressing the Key Event on activation of dendritic cells on the Adverse Outcome Pathway for Skin Sensitisation. The TG addresses the following assays: i) the human cell Line Activation Test or h-CLAT method, (ii) the U937 Cell Line Activation Test or U-SENS and (iii) the Interleukin-8 Reporter Gene Assay or IL-8 Luc assay.
- Revised **OECD** TG 492 on Reconstructed human Cornea-like Epithelium (RhCE) test method identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage. The revised TG addresses the following test methods: EpiOcularTM Eye Irritation Test (EIT) and SkinEthicTM Human Corneal Epithelium (HCE) EIT.
- Approach on Testing and Assessment (IATA) for Serious Eye Damage and Eye Irritation. The IATA is composed of well described and characterised "Modules", each of which contain one to several individual information sources of similar type. The strengths and limitations as well as the potential role and contribution of each

Module and their individual information sources in the IATA for the identification of serious eye damage, eye irritation and no need for classification are described in the GD 263 with the purpose of minimizing the use of animals to the extent possible, while ensuring human safety.

- Updated OECD TGs 405, 437, 438, 460 and 491 to include mention to the newly adopted GD 263 on an IATA for Serious Eye Damage and Eye Irritation.
- OECD GD 278 presenting the report of the OECD Workshop on Intellectual Property issues in OECD TGs.

For more information on the OECD TGs, please consult:

http://www.oecd-

ilibrary.org/environment/oecd-guidelines-forthe-testing-of-chemicals-section-4-healtheffects\_20745788

For more information on the OECD GDs, please consult:

http://www.oecd.org/env/ehs/testing/series-testing-assessment-publications-number.htm



3RS-CENTRE UTRECHT LIFE SCIENCES NEWSLETTER, JANUARY 2018

**3Rs-Centre ULS** stimulates the development, acceptance and implementation of methods which can Replace, Reduce and Refine (the 3Rs) animal experiments. The centre facilitates the 3Rs in education and animal research in many ways, by providing information and advice about 3Rs models.

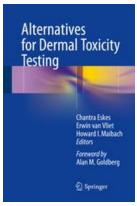
The monthly newsletter of the 3Rs/Centre ULS is available at newsletter.

## Alternatives for dermal toxicity testing Eskes C., van Vliet E., Maibach H.I. Eds.

Dermal toxicity is one of the pioneer areas in which alternative methods to the use of animal testing has gained scientific, industrial and regulatory acceptance. Several alternative methods for dermal toxicity have been optimized, scientifically validated and gained international regulatory acceptance.

In view of the considerable progress made, the book aims at providing up-to-date comprehensive information on the most advanced alternative test methods available for the assessment of dermal toxicity with particular emphasis in the areas of skin

irritation, skin corrosion, skin sensitization, UV-induced effects and skin genotoxicity. For each test method, a description of the currently available protocol is given including highlights of its critical steps, applicability, limitations, potential role and use within testing approaches and correlation with the traditional animal data and when available, also to human data.



Furthermore, the book addresses exploratory areas that may be of relevance for the future of dermal toxicity safety testing, including the use of human progenitor skin cells, integration of in vitro and clinical methodologies, and application of high throughput screening techniques.

The editors warmly acknowledge all authors that contributed to make the project of this book a reality, and to Springer for their support in the project. Albeit attempting to be comprehensive, new and/or additional methods and authors that could not be involved in the present book will be invited to contribute to the next editions to come, for which any comments and/or suggestions are welcomed.

The book is available at: <a href="http://www.springer.com/us/book/978331950">http://www.springer.com/us/book/978331950</a> 3516

#### Meetings and workshops calendar

### INAUGURAL FRANCQUI LECTURE BY MAURICE WHELAN

"Moving away from animal use in basic and applied science-the way forward"

February 27, 2018

VUB. Brussels, Belgium

http://www.vub.ac.be/events/2018/inaugural-francqui-lecture-2017-2018-replacing-animals-in-science-impossible-or

## EFSA - IPAM DAY - 3 RD LIFE-EDESIA WORKSHOP on

"Endocrine Disruptors and alternative methods to animal testing – a scientific and regulatory perspective

February 28, 2018 Parma, Italy

http://www.iss.it/life/

#### SOT 57th ANNUAL MEETING AND TOXEXPO

March 11-15, 2018 San Antonio, Texas, US

http://www.toxicology.org/events/am/AM2018/index.asp

## 23<sup>rd</sup> INTERDYSCIPLINARY TOXICOLOGY CONFERENCE - TOXCON 2018

June 20-22, 2018
The High Tatras, Stará Lesná, Slovakia http://konferencia.uef.sav.sk/

## 52<sup>nd</sup> CONGRESS OF THE EUROPEAN SOCIETY OF TOXICOLOGY (EUROTOX 2018)

September 2-5, 2018 Brussels, Belgium

http://www.eurotox-congress.com/2018/

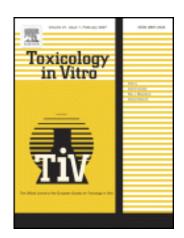
## 15<sup>th</sup> INTERNATIONAL SYMPOSIUM ON PERSISTENT TOXIC SUBSTANCES

November 6-9, 2018 Basel, Switzerland

https://www.ispts2018.ch

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#### Toxicology in vitro



Official Journal of the European Society of Toxicology in vitro

Editors: Frank A. Barile Bas J. Blaauboer Paul Jennings

#### **Recent publications of ESTIV members**

Adriaens E, Alépée N, Kandarova H, Drzewiecka A, Gruszka K, Guest R, Willoughby JA Sr, Verstraelen S, Van Rompay AR (2017) CON4EI: Selection of the reference chemicals for hazard identification and labelling of eye irritating chemicals. Toxicol *In Vitro* 44:44-48. doi: 10.1016/j.tiv.2017.06.001

Adriaens E, Guest R, Willoughby JA Sr, Fochtman P, Kandarova H, Verstraelen S, Van Rompay AR (2017) CON4EI: Slug Mucosal Irritation (SMI) test method for hazard identification and labelling of serious eye damaging and eye irritating chemicals. Toxicol *in Vitro*, doi: 10.1016/j.tiv.2017.08.020 [Epub ahead of print]

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### **ESTIV** membership fee

#### Membership fee

The membership for an individual member for 2017 is 30€ If you are also a member of one of the affiliated societies (CellTOX, SSCT, INVITROM, IVTS, EUROTOX), the membership amount to 18€.

#### **Method of Payment**

Secure online credit card payment *via* PayPal:

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> > **Erwin Van Vliet**

### **ESTIV Corporate Members**



MatTek *In Vitro* Life Science Laboratories, an European subsidiary of MatTek Corporation (USA) produces since 2011 reconstructed 3D human tissue models for the EU and Asia market in Bratislava, Slovakia. MatTek is at the forefront of tissue engineering and is a world leader in the production of innovative 3D reconstructed human tissue models.

MatTek's skin and ocular tissue models are used in regulatory toxicology (OECD, EU guidelines) and address toxicology and efficacy concerns throughout the cosmetics, chemical, pharmaceutical and household product industries. MatTek Corporation celebrates 30 years anniversary in 2015. www.mattek.com



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. www.epithelix.com



Altertox Academy is a SME (Small Medium Enterprise) with tailor made trainings as main activity. It provides hands-on training in human-relevant alternative methods and technologies for toxicologists, from a 3R perspective (replacement, reduction and refinement). Among other services, Altertox Academy also provides support as work package leader in training for EU calls. https://academy.altertox.be/



As independent and customer-oriented research organisation, VITO provides innovative technological solutions as well as scientifically based advice and support in order to stimulate sustainable development and reinforce the economic and social fabric of Flanders.

https://www.vito.be

#### **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 (SSCT).

#### 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. This is a "closed" list, which means that only ESTIV members will receive the message. However, please note that this list should not be used to send confidential messages or attachments as these are uploaded to the archive that can be accessed by the general public.

#### Important!

The procedure of sending messages to the ESTIV e-mail list have changed.

To send a message to all ESTIV members on the list (presently more than 250 colleagues), simply address your e-mail to ESTIV Secretary secretariat@estiv.org. Your message will be further distributed to ESTIV 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 at secretariat@estiv.org and your name will be added.

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

In addition, ESTIV has a Facebook page, where relevant events are announced by the Board and ESTIV members.

#### **ESTIV Executive Board Members 2016-2018**

EXECUTIVE BOARD	POSITION	E-Mail
Mathieu Vinken	President	mvinken@vub.ac.be
Elsa Casimiro	Vice president	ecasimiro@infotox.pt
Laura Suter-Dick Iwona Wilk-Zasadna	Secretary/ Newsletter	secretariat@estiv.org laura.suterdick@fhnw.ch lwona.wilkzasadna@gmail.com
Erwin van Vliet	Treasurer	treasurer@estiv.org vanvliete@gmail.com
Helena Kandárová	Communication	hkandarova@mattek.com
Paul Jennings	EC grants and website	p.jennings@vu.nl
Chantra Eskes	Training courses	chantra.eskes@secam-ce.eu
João Barroso	Sponsors	Joao.BARROSO@ec.europa.eu
Anne Marie Vinggaard	Affiliations	annv@food.dtu.dk
Leonora Buzanska	Students	buzanska@cmdik.pan.pl
Philippe Bourrinet	ESTIV 2016	Philippe.Bourrinet@guerbet-group.com
Mardash Daneshian	ESTIV 2018	mardas.daneshian@uni-konstanz.de

#### **ESTIV Honorary Members**

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

#### **Further information**

For more information on ESTIV and membership application contact Laura Suter-Dick (ESTIV Secretary) e-mail: <a href="mailto:secretariat@estiv.org">secretariat@estiv.org</a>