

### The European Society of Toxicology In Vitro

Official Journal: Toxicology In Vitro

### **Newsletter No. 42**

**July 2018** 

#### Dear ESTIV Members,

Here is the latest edition of the ESTIV newsletter, where you will find some inspiring insights on a number of activities that took place in the field of *in vitro* and *in silico* toxicology during the last few months. This issue includes, among others, the reports from the Applied *in Vitro* Toxicology Course, the JRC Workshop on Bridging Across Methods in bioSciences (BEAMS) and the Workshop on Animal-free Innovations in Safety Assessment of Chemicals.

You will also find information on many forthcoming activities. Please pay a special attention to the new section "Methods", which we would like to introduce to the future issues of the newsletter. You are all very welcome to provide your contribution.

The current issue of the newsletter contains also information regarding ESTIV Privacy Policy (in line with GPDR). Please have a closer look to know more about how we process your personal data.

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

We hope the information shared here will inspire you before a well-deserved summer break!

Iwona Wilk-Zasadna

#### **Message from the president**

Dear ESTIV Members,

At the start of this second newsletter of the year, I am happy to inform you that 2018 has been very productive and successful for ESTIV thus far. Indeed, during the 57th Society of Toxicology Meeting in San Antonio-Texas in March this year, a Memorandum of Understanding was signed between ESTIV and the American Society for Cellular and Computational Toxicology (ASCCT). signing this Memorandum of Understanding. both societies intend to strengthen their relationship through exchange of information relevant to their missions. Furthermore, ESTIV, in collaboration with the Dutch Society for Toxicology, organized the "Applied In Vitro Toxicology" course from 8 to 13 April 2018 in Utrecht-The Netherlands. The course was hosted by Utrecht University and was attended by 25 participants coming from 13 different countries. Because of its success, and as part of the ESTIV-ASCCT Memorandum of Understanding, the next course will be organized together with ASCCT in Bucharest-Romania on 14-19 April 2019 (https://estiv2019.com).

The most exciting ESTIV event of the year is yet to come, namely the 20th International Congress on *In Vitro* Toxicology (ESTIV2018) that will be organized together with the German Toxicology Society and the Center for Alternatives to Animal Testing-Europe on 15-18 October 2018 in Berlin-Germany (http://www.estiv2018.com/). The ESTIV2018 conference will be preceded by 2 workshops and followed by a hands-on training. The ESTIV2018 program consists 8 thematic

sessions, a continuous poster session, a keynote lecture, the Björn Ekwall award lecture, 2 student sessions, 2 European project sessions, 2 lunch sessions and 2 general assembly sessions. Regarding the latter, you, as ESTIV member, are cordially welcomed to attend the ESTIV general assembly that will take place in the Estrel hotel in Berlin on 17 October 2018 at 17h.

I hope to welcome you all in Berlin in autumn! Meanwhile, I wish you a pleasant summer.



Prof. Mathieu Vinken, Ph.D., Pharm.D., E.R.T. President of ESTIV



Stive stiv

#### ESTIV 2018 Congress 15-18 October 2018 Berlin, Germany



On behalf of the European Society of Toxicology *In Vitro* (ESTIV), the German Toxicology Society (GT) and the Center for Alternatives to Animal Testing-Europe (CAAT-Europe), we would like to invite you to attend the 20th International Congress on *In Vitro* Toxicology (ESTIV2018). It will take place on 15-18 October 2018 in Berlin-Germany.

The general theme of the Congress is "New approach methodologies for *in vitro* toxicology applications". The Congress program consists of a number of special sessions, covering

- 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 Congress will be preceded by complimentary workshops and will be followed by a hands-on workshop. 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.

The scientific program and logistics details are available at https://www.estiv2018.com/

We hope to see you in Berlin!



Prof. Mathieu Vinken ESTIV



Dr. Robert Landsiedel



Prof.
Thomas Hartung
CAAT Europe

#### Applied In Vitro Toxicology Course

ESTIV, in collaboration with the Dutch Society for Toxicology (NVT), organized the "Applied *In Vitro* Toxicology" course from 8 to 13 April 2018 in Utrecht-The Netherlands. The course was hosted by Utrecht University and was attended by 25 participants coming from 13 different European and non-European countries. Of those, 25%, 30% and 45% had a background in the regulatory field, industry and university, respectively. The program consisted of 14 lectures in the area of regulatory, investigative and screening *in vitro* 

toxicology. During the group exercise, the course attendees applied all theoretically acquired in vitro skills to real-life cases of toxicologically relevant chemicals. Furthermore, the participants were given the opportunity to gain hands-on experience, in particular regarding in vitro skin and eye irritation testing, being organized by the course sponsor MatTek In Vitro Life Science Laboratories. New in this fourth edition of the course was a computer practical focused on in vitro-in vivo extrapolation approaches. Based on a survey filled out by the participants, the course was rated to be of very high quality.



Course participants and some of the course speakers at the famous Dom Tower in Utrecht.

The next course will be organized together with The American Society for Cellular and Computational Toxicology (ASCCT) in Bucharest-Romania on 14-19 April 2019.



The scientific program and logistics details are available at https://estiv2019.com.

#### 



The 57th Society of Toxicology Annual Meeting took place 11-15 March 2018 at the Henry B. González Convention Center in San Antonio-Texas. The conference gathered more than 6500 attendees with varying backgrounds from all over the world. The program consisted of continuing education courses, plenary sessions, keynote lectures, workshops, symposia, platforms sessions, roundtable sessions, featured lectures, special sessions and poster sessions. As much as 2800 presentations were given with focus on a plethora of topics relevant to the fields of human toxicology and ecotoxicology. Started many years ago, more and more attention is paid during the Society of Toxicology Annual Meetings to in vitro and in silico toxicology, which was fully reflected in the program. In fact, several ESTIV members attended the 57th Society of Toxicology Annual Meeting, with many of them giving an oral or poster presentation. The ToxExpo™ was organized in parallel with the 57th Society of Toxicology Annual Meeting and included more than 330 exhibitors providing services, equipment and new career opportunities to attendees.



The famous "River Walk" in San Antonio-Texas provided a pleasant surrounding for the 57th Society of Toxicology Annual Meeting (picture courtesy of Mathieu Vinken).

The next Society of Toxicology Annual Meeting will take place 10-14 March 2019 in Baltimore-Maryland. More information can be found at www.toxicology.org/2019. The

deadline for submission of abstracts is 19 October 2018.

#### **ESTIV-ASCCT**

#### **Memorandum of Understanding**





During the 57th Society of Toxicology Meeting in San Antonio-Texas, a Memorandum of Understanding was signed between ESTIV and the American Society for Cellular and Computational Toxicology (ASCCT). signing this Memorandum of Understanding, both societies intend to strengthen their relationship through exchange of information relevant to the missions of the societies and by fostering an environment to expand the development, use and regulatory acceptance of predictive human-relevant non-animal approaches for toxicology. The goal of the Memorandum of Understanding is to provide members of each society a greater platform in which to develop and share their expertise.



ASCCT President David Allen (left) and ESTIV President Mathieu Vinken (right) signing the Memorandum of Understanding on 12 March 2018 during the 57th Society of Toxicology Meeting in San Antonio-Texas.

The societies wish to promote information exchange between the organizations and their

membership in many mutually beneficial ways, including (i) arranging or supporting respective annual meetings or other related symposia, workshops and trainings, (ii) encouraging members of each society to share their work and expertise in these methodologies through newsletter articles. webinars or corresponding communication with the membership, (iii) promoting the attendance and participation, through oral or poster presentations, at the annual meetings of both societies, and (iv) publicizing potential research collaborations, career opportunities relevant information between both societies.

#### 7th Annual Meeting of ASCCT



The 7th Annual Meeting of the American Society for Cellular and Computational Toxicology (ASCCT), ESTIV's sister society, will take place 11 September 2018 at the Lister Hill Auditorium of the National Library of Medicine NIH Campus, Bethesda-Maryland, USA. The general theme of the meeting is "Predictive toxicology: strategies for implementing approaches". new More information be can found at https://www.ascctox.org/meeting/38

#### 

Switzerland establishes a New Competence Centre to limit the use of animals for experimentation.



The Swiss 3R Competence Centre (3RCC) will subsidize scientific projects of quality and establish an educational program and communication strategy to promote the refinement, reduction and replacement of animal experimentation.

The Swiss legislation on the protection of animals requires that all person taking care of

animals, takes as much as possible into account their needs and ensure their wellbeing as far as the scope of their use allows it. Considerable progress took place in the last decade for the refinement, reduction and replacement (principles of 3Rs) of animal experimentation for regulatory purposes. On the 27 March 2018, Switzerland did an additional step by founding a 3R Competence Centre (3RCC) to further promote the principles of 3R in Switzerland in the areas of research and education.

Under the presidency of Dr. Kathy Riklin, member of the Swiss National Council, the 3RCC represents an association of academia, industry, regulators, government and animal welfare association including the eleven most important Universities and Higher Education Institutions from Switzerland, the Swiss association of pharmaceutical industry (Interpharma), the Swiss Federal Food Safety and Veterinary Office (FSVO) and, the Swiss Animal Protection. The 3RCC also benefits from an important support from the Swiss State Secretariat for Education, Research and Innovation (SERI), as it represents a scientific centre of national importance working on a non-commercial basis according to article 15 of the Federal Act on the Promotion of Research and Innovation (RIPA).

Situated in Bern, one of the main objectives of the 3RCC is to subsidize scientific projects related to the principle of 3Rs within Switzerland, with a first call for projects foreseen by the end of 2018. In addition, the centre aims to develop an educational program and communication strategy so that all those interested can have access to up-todate information on alternative methods to animal experimentation. Finally, the 3R Competence Centre aims to monitor progress made regarding the implementation of the principles of 3Rs in Switzerland and to offer its services to all authorities, teaching bodies and interested parties willing to gain additional information on the principles of 3Rs and methods alternative to animal experimentation.

For more information:

Dr. Chantra Eskes
Director 3RCC
Hochschulstrasse 6, Bern
chantra.eskes@rektorat.unibe.ch

## The Slovak National Platform for 3Rs (SNP 3Rs)



The idea for establishment of 3Rs center in Slovakia was under the discussion amongst the Slovak scientist, regulators and industry already since 2015. Strategy concept of a national 3Rs center was presented at the TOXCON 2016 Conference, organized by the Slovak Toxicology Society SETOX in High Tatras, and further discussed between several members of the National Committee for Alternative Methods (NOVS) at the EUROTOX 2017 Congress in Bratislava.

As a follow up, the Ministry for Agriculture and Rural Development of Slovak Republic organized in February 2018 an informal meeting of NOVS members, invited experts in toxicology and pharmacology, representatives of Slovak Academy of Science and academia, industry representatives and governmental organizations involved in the implementation of the EU legislation on animal welfare and protection in order to discuss the collaboration amongst the parties and to express an interest and formal support to the national 3Rs center. The attendees of that meeting fully endorsed an establishment of the Slovak National Platform for Three Rs (SNP 3Rs) that should stimulate development and implementation of the alternative methods in Slovakia."

The platform was officially launched at the annual meeting of the Slovak Toxicology Society SETOX on June 21st 2018 at the Toxicology Conference TOXCON 2018. The SNP 3Rs will operate with support of SETOX and its mission will be to provide information, resources, and practical guidelines on the 3Rs principles of Russell and Burch in science, education, research and development.

For more information: Dr. Helena Kandarova Vice-president, SETOX kandarova@centrum.sk

#### **Nordic 3R Centers**

### In several Nordic countries there are now established 3R centers:

#### **Finland**

Finland has recently (in 2018) established a Finnish 3R Consortium. The consortium is coordinated by Finnish Centre for Alternative Methods to Animal Experimentation (FICAM). It consists of universities, other institutions and industry performing animal experiments and developing non-animal methods and approaches. The main aims are to:

- act as a national focal point of the 3 Rs,
- promote 3Rs on national level in many ways e.g. share information through electronic media, organize education and training courses, give presentation to public, announce a 3R prize
- promotes co-research projects

For more information:

Dr. Tuula Hainonen

tuula.heinonen@staff.uta.fi

#### Sweden



In Sweden a 3R Center was established by the end of 2016 together with support from the government of 15 Mill. SEK for the period 2017 to 2020. Since then the Swedish 3Rs Center has been under construction and has from January 2018 transcended to active administration.

For more information:

http://www.jordbruksverket.se/swedishboardo fagriculture/engelskasidor/animals/swedish3r scenter/aboutus/historyoftheswedish3rscente r.4.5593fa9915fcd5f0f543e112.html

#### **Denmark**



In 2013 the Danish 3R-Center was established and is supported by the Danish Animal

Welfare Society, LEO Pharma, Lundbeck and Novo Nordisk. The Danish Ministry of Food offers operational and research funding. The main tasks cover:

- promotion the development of alternatives to animal testing
- minimising the use of laboratory animals in specific experiments
- improvement conditions of laboratory animals
- collection and dissemination knowledge on alternatives to animal testing
- initiation and support research in laboratory animal studies and the development of alternatives
- cooperation with similar centres abroad The Danish 3R-Center is hosting an annual 3R-symposium.

For more information: <a href="https://3rcenter.dk/">https://3rcenter.dk/</a>

#### Norway



norecopa

Norecopa is the Norwegian Consensus Platform for the advancement of "the 3 Rs" (Replacement, Reduction, Refinement) in connection with animal experiments. It was founded on 10 October 2007. Norecopa involves all stakeholders interested in animal research, including:

- Government and regulators.
- Research and teaching,
- Industry,
- Animal welfare organisations,

and whenever possible, seeks consensus, between them.

For more information: <a href="http://norecopa.no/">http://norecopa.no/</a>

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



The MSCA-ITN project in 3 (pronounced "in three") with grant no. 721975 is now in its second year and all of the 15 ESRs are in place. We had our second general assembly meeting in Milan in April 2018, hosted by Prof. Emilio Benfenati at the Istituto di Ricerche Farmacologiche Mario Negri. This was an exiting meeting which incorporated an in silico training course for the ESRs and a Science Day where the ERS presented their projects, work conducted and plans for the next 6 months. We also had a nice viewing of the Da Vinci's, The Last Supper (see picture) as part of our social activities. Our training program is now in full swing, with regular online lectures on aspects related to regulation, toxicology, and developmental assessment biology. In a few weeks the ESRs will meet in Liverpool for a workshop on Adverse Outcome Pathways hosted by Prof. Mark Cronin at the School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, United Kingdom. Finally, we will have an in3 session at the upcoming ESTIV 2018 meeting in Berlin, where all of the ESRs will give a 5 min presentation of their projects. Looking forward to meeting you there.

Best Regards, Prof. Dr. Paul Jennings in3 coordinator

Web page: http://estiv.org/in3/



JRC Workshop on Bridging Across Methods in bioSciences (BEAMS) and new section in ESTIV Newsletter – open to members!

Advances in science go hand in hand with technological innovation. In the biosciences, new methods employing 'omics, stem cells, tissue-on-chip devices, and computational modelling are emerging alongside novel animal models and techniques to refine animal experiments. Progress in understanding biological systems and disease, developing new drugs and advancing toxicology are just some areas that depend on how scientific methods develop, integrate and compete.

In order to facilitate the effective translation and application of new scientific methods for addressing societal challenges, on 19-20 June 2018 the European Commission's Joint Research Centre (JRC) organized a workshop with the aim to discuss the utility and feasibility of establishing a knowledge sharing forum specifically for bridging across scientific methods in the biosciences (BEAMS).

The workshop was intended to start off a conversation among a small group representing key organisations which have an interest in advancing basic, applied and translational bioscience research by championing the best scientific methods available. Three inter-related questions were addressed:

- how will knowledge sharing help to bridge across different scientific methods?
- what means of knowledge sharing can accomplish this?
- how can effective forms of knowledge sharing be supported?

ESTIV (represented by Mathieu Vinken) was invited to the workshop to share our experience on communication on methods in life sciences/biosciences with other representatives of relevant societies. It was acknowledged that ESTIV already does an excellent job in terms of sharing knowledge regarding methods (e.g. conferences, Applied *In Vitro* Toxicology course, etc.).

However, in order to improve it even more we intend to have <u>an open section in our newsletter on methods, which can be used</u>

by our members. The contents of this section can be very diverse (e.g. a concise summary of a method, own experiences, a reference to a methodology paper, etc.). In case you are interested to share your testing approaches within our society, you are very welcome to send your contribution to newsletter@estiv.org.

We are looking forward to knowing more about methods you are using in your daily life

#### 

# Animal-free innovations in safety assessment of chemicals – joint BfR and RIVM workshop

How can the process of validation, acceptance and use of animal-free innovative approaches to assess the safety of chemicals be facilitated? This was the topic of the second joint workshop of the German Federal Institute for Risk Assessment (BfR) and the Dutch National Institute for Public Health and the Environment (RIVM) (13th and 14th June 2018, Bilthoven). International experts governmental institutes, regulatory agencies, industry, academia and animal welfare organisations discussed this topic interactive sessions.

#### Towards Animal-free testing

Validation is a procedure used to assess the reliability and relevance of a new test method. It is an important step towards regulatory acceptance, implementation and use of a new method for chemical safety assessment. Current validation procedures are designed for single test methods. These procedures are not fully compatible with progress made in the field of animal-free innovations, in which often information from multiple methods needs to be combined to assess the safety of a chemical.

#### Two scenarios

Two scenarios can be followed towards an animal-free safety assessment framework. Firstly, an evolutionary scenario in which the current animal test-based system is modernised step by step as new animal-free approaches become available. Secondly, a revolutionary scenario that starts from scratch by describing the human biology and how this can potentially be affected by chemicals. Insight in the mechanisms involved in toxicity

can subsequently be used to develop novel test methods. Ultimately, a framework combining different animal-free approaches covering human biology can be developed. The current validation procedures need to be adapted to be able to assess the reliability and relevance of such a revolutionary scenario.

#### Recommendations

International experts exchanged their points of view on how the process of validation. acceptance and use of animal-free innovations can be facilitated along the scenarios for evolution and revolution. They discussed a human biology-driven approach mechanistic validation. recommendations were the need to define the biological relevance and uncertainties of new test methods and to use these aspects to evaluate their scientific validity. The need to increase experience and confidence was recognised. This can be achieved, for example, through case studies with defined sets chemicals in which multiple stakeholders collaboratively participate. A workshop report will be published soon.

#### Collaboration with BfR

For years, BfR and RIVM have been dedicated to replace, reduce and refine animal testing for regulatory safety assessment. The Joint Declaration of Intent between both organisations the has strengthened collaboration in this area. This and future workshops aim to bring together stakeholders to achieve acceptance, implementation and use of animal-free methods for safety assessment.



Experts attending BfR and RIVM workshop

#### **Altertox Academy**



Altertox is organising more than five laboratory trainings after the summer! Join us in KU Leuven to learn about PBPK modelling or stop by in Vienna to attend our first training on Good Cell Culture Practice. We are also slowly extending to the pharmaceutical field in Montpellier focusing on 3DTissue Engineering Quality Control - From the bench to the bedside.



Altertox is expanding its activity in congress organisation. We co-organised this year with Epithelix the <u>LIVe conference</u> in Nice for more than 100 of participants.

For the next three years, Altertox will provide trainings on knowledge management for policy to the European Commission Joint Research Centre.

Altertox will be at <u>European Science Open Forum</u> (ESOF) in Toulouse in July to present a poster about skills4science. Skills4science intends to provide young scientists key elements about research integrity, sexual harassment in science, avoiding misconducts, social media communication and science collaboration for their career. Some pictures and videos from our 1st training at VUB are available on our Facebook page.

#### **Highlights**





#### **3Rs Science Prize 2018**

The European Partnership for Alternative Approaches to Animal Testing (EPAA) is proud to announce that a call for submissions is now open for its 2018 3Rs Science Prize.

The EPAA aims to promote the development, validation and acceptance of 3Rs alternative approaches (replacement, reduction and refinement of testing on animals). The 3Rs science prize is granted every other year to a scientist with an outstanding contribution to 3Rs. This way, positive contributions from industry or academia are promoted and more scientists are encouraged to focus their research on the 3Rs goals. Scientists working on methods for regulatory testing (e.g. safety, efficacy, batch testing) and applying the 3Rs to those methods may apply for the prize.

An EPAA jury (made up from 2 industry, 2 European Commission and 2 EPAA mirror group representatives) evaluates the submissions and provides the EPAA steering committee with the results of the evaluation and a recommendation on the ranking of the submissions. Based on this recommendation, the steering committee should then endorse the winner, and grant a €10,000 prize.

The prize will be granted to the institution of the winner to be announced at the EPAA annual conference, on 20 November 2018.

### Application deadline: 3 September 2018 at 12:00 (noon) Brussels time

More information at:

https://ec.europa.eu/growth/content/3rsscience-prize-2018-call-submissions\_en



# 15th International Symposium on Persistent Toxic Substances 6-9 November 2018, FHNW, Basel

The International Symposium on Persistent Toxic Substances (ISPTS) is a well-known international conference series hosted in prominent academic institutions around the globe.

Persistent Toxic Substances (PTS) are receiving worldwide attention due to their high resistance to degradation from abiotic and biotic factors. high mobility. bioaccumulation, and long-term toxicity to the environment and human health. The ISPTS provides the primary platform for scientists, experts and students working on PTS to discuss and exchange information on environmental processes and toxicity, as well as on the development of innovative technologies for contamination control and remediation of PTS.

More information at:

https://www.ispts2018.ch/





#### Call for Expression of Interest: P4M— Public Private Partnership for Performance Standards for Microphysiological Systems

Organo-typic cultures with elements of organ architecture and functionality are flourishing, increasingly moving even to multi-organ systems. They promise to boost the relevance of *in vitro* work, fueled also by the increasing availability of high quality human cells due to stem cell technologies. CAAT has been part and actively promoted these developments. In various stakeholder discussions, we perceived the need to complement the technical developments with quality assurance aspects. Our ongoing efforts toward Good Cell Culture

Practice (GCCP), *in vitro* reporting standards and *in vitro* risk-of-bias assessments already go in this direction.

As a next step, we would like to invite all stakeholders to join us starting a discussion about performance standards for microphysiological systems (MPS). This will encompass questions like:

- · What makes a cell culture an MPS?
- What is a good MPS, e.g. fit-for-purpose, reproducibility, relevance, validity?
- How does an MPS need to be documented and reported?
- How can a lab show proficiency in testing with an MPS?
- What quality assurance and management need to be in place?

This call for expression of interest wants to identify possible partners from academia, regulatory agencies, industry (users and technology providers), and others (e.g., NGOs). You are invited to contact us at <a href="mailto:caat@jhu.edu">caat@jhu.edu</a>. Letter of motivation and referrals to relevant activities in this area you are part or aware of are most welcome. We will start organizing the dialogue with the exact form depending on the responses received.

Become part of an exciting process helping to revamp the relevance of *in vitro* work!



Training on advanced cell culture and data management systems 3-4 October 2018, Douglas Connect Lab, Technology Park Basel, Switzerland

Joint workshop and hands-on training on Quasi-Vivo cell culture flow system by Kirkstall Ltd. (United Kingdom) and best practices in data management by Douglas Connect GmbH (Switzerland).

This training is dedicated to scientists interested in the application of advanced cell culture systems and to get familiar with the latest approaches related to experimental data management and integrated *in vitro - in silico* testing and assessment.

The training includes both theory and practices of advanced cell culture techniques and data management practices through a combination of lectures, demonstrations and practical hands-on experience.

The Quasi Vivo® system developed by Kirkstall Ltd. is an advanced interconnected cell culture flow system, engineered to provide in vivo like conditions for cell growth.

Further, the resources available at Douglas Connect GmbH and the achievements towards making *in vitro* experimental data findable, accessible, interoperable and reusable (FAIR data principles) will be presented and demonstrated during the training.

More information at:

http://www.douglasconnect.com/training-on-advanced-cell-culture-and-data-management-systems



### Toxicology 21: Scientific Applications: New Course on Coursera

This course familiarizes students with the novel concepts being used to revamp regulatory toxicology in response to a breakthrough National Research Council Report Toxicity Testing in the 21st Century: A Vision and a Strategy. We present the latest developments in the field of toxicology—the shift from animal testing toward human relevant. high content, high-throughput integrative testing strategies. Active programs from EPA, NIH, and the global scientific community illustrate the dynamics of safety sciences.

The course is taught by CAAT's Thomas Hartung and Lena Smirnova.

Course Info and Registration: <a href="https://www.coursera.org/learn/toxicology-21/home/welcome">https://www.coursera.org/learn/toxicology-21/home/welcome</a>



# UL, CAAT, and ToxTrack Scientists Train US FDA and Health Canada on Novel Computational Toxicology Tools

Scientists from Underwriters Laboratories (UL), Johns Hopkins' CAAT, and ToxTrack LLC, a Hopkins spin-off created by CAAT's Tom Luechtefeld, provided separate in-depth training meetings at Health Canada and the US Food and Drug Administration in February 2018. The meetings provided an overview of UL's Cheminformatics Suite and an in-depth training on the science underpinning the REACHacross Module, which implements CAAT research into automated read-across. analyzing By billions of chemical combinations, REACHacross software can predict chemical hazards, including skin sensitization, acute oral- and dermal-toxicity, eye- and dermal-irritation, mutagenicity, and acute- and chronic-aquatic toxicity. The training was designed to assist these agencies in adopting non-animal methods as a means to evaluate chemicals for a variety of regulatory programs.

The US FDA has recently released a strategic plan for using non-animal methods in its reviews. The training was provided in conjunction with a beta-user program designed to provide REACHacross users with an opportunity to use the software and provide feedback for further design enhancements. Through the beta-user program, users of REACHacross will gain confidence for using the hazard predictions in their regulatory activities avoiding animal testing and provide valuable insights to better develop the tools that regulators need.

ToxTrack website: <a href="https://toxtrack.com">https://toxtrack.com</a>



## Thomas Hartung Receives Hellenic Society of Toxicology Award

CAAT Director Thomas Hartung received the Hellenic Society of Toxicology Award in recognition for his contributions to toxicological sciences. The award was presented at the Greek Congress of Toxicology, held February 2nd-4th in Larisa Greece. Hartung gave the plenary lecture on "Making alternatives the new normal—the continuing paradigm shift in toxicology."



#### Open Access Journal Frontiers in Big Data Launches with Thomas Hartung as Specialty Chief Editor for Medicine and Public Health

Thomas Hartung has been named Specialty Chief Editor for Medicine and Public Health for the new open access journal, Frontiers in Big Data. Frontiers in Big Data will help researchers in this move to data-driven science. As a multidisciplinary, open-access hub of information on data-driven solutions, the journal will identify ground-breaking discoveries and communicate these to academics, policy-makers, industry and the public worldwide. As an open-access journal, big data solutions published in Frontiers in Big Data will be freely and universally available empowering researchers. citizens companies to rapidly and efficiently combine knowledge and so drive the big data revolution.



#### Lena Smirnova Receives \$20,000 ARDF AiR Challenge Grant for Testing for Autism Toxicants by Gene Environmental Interaction

Alternatives Research and Development Foundation's (ARDF) AiR Challenge Grants

are intended to accelerate alternatives development in biomedical research.

The AiR challenge program is intended not only as a means of rewarding scientists, advancing biomedical progress, and sparing animals from suffering. It is also intended to help dispel the outdated notion that an interest in medical progress and a concern for animals are inexorably in opposition; indeed, finding better non-animal approaches to researching human disease is a win-win for humans and animals. The ARDF is also seeking to broaden the understanding and appreciation for alternative methods not only among scientists, but also among the general public, thought-leaders, media representatives, and patients and patient-advocates.

#### Meetings and workshops calendar

### PAN-AMERICAN CONFERENCE FOR ALTERNATIVE METHODS 2018

August 23-24, 2018
Rio de Janeiro, Brasil
<a href="http://caat.jhsph.edu/programs/workshops/PanAm">http://caat.jhsph.edu/programs/workshops/PanAm</a>
erican2018/index.html

### 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/

#### 7<sup>th</sup> ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELLULAR AND COMPUTATIONAL TOXICOLOGY (ASCCT)

September 11, 2018 Bethesda-Maryland, USA

### WORKSHOP ON PYROGEN TESTING METHODS

September 18-19 Bethesda, Maryland https://ntp.niehs.nih.gov/go/mat-2018

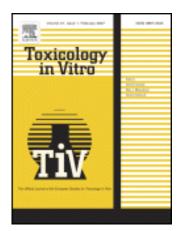
### 20<sup>th</sup> INTERNATIONAL CONGRESS ON *IN VITRO* TOXICOLOGY (ESTIV2018)

October 15-18, 2018
Berlin, Germany
<a href="https://www.estiv2018.com/">https://www.estiv2018.com/</a>

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

November 6-9, 2018 Basel, Switzerland https://www.ispts2018.ch

#### Toxicology in vitro



Official Journal of the European Society of Toxicology in vitro

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

#### **ESTIV Privacy Policy**

Dear ESTIV members,

We value the importance of protecting your privacy and personal data. To ensure transparency and security, our privacy statement as set forth below will inform you about the nature, scope and purpose of the personal data processed by us. We have updated our privacy policy as part of our ongoing commitment to be transparent about how we use your data and keep it safe. We have included changes to address the new standards introduced by the European data protection law known as the General Data Protection Regulation (GDPR).

## 1. Purposes of the information collection and data processing

ESTIV collects and processes your personal data in order to provide you with the information and services linked to your ESTIV membership. ESTIV is the sole owner of the information collected and will not sell, share or rent this information to others in ways different from what is disclosed in this statement.

#### 2. Categories of personal data

Personal information refers to any information that you voluntarily submit to us and that identifies you. This information includes:

- Name and surname, email, phone, address, job title and company.
- Other data that you have provided while contacting us, especially using the contact, download or signup forms on our website.

• Data that you have sent to us through an online survey or email.

Personal information can also include information about any transactions, both free and paid, that you enter into the website and information about you that is available on the internet, such as from Facebook, LinkedIn, Twitter and Google, or publicly available information that we acquire from service providers. For marketing purposes and to improve our website and services, we also may collect data sent by your web browser, such as information about your browser, your IP address and your

operating system.

#### 3. Data recipients and processing parties

We do not sell or rent your personal information to third parties. We do not share your personal information, except as provided in this privacy policy. We use third party data processors to process personal data on our behalf if needed. Such service providers support ESTIV, especially relating to hosting and operating the website, marketing, analytics, improving the website and sending email newsletters. These processors may be located outside the European Union. Our website may also include social media features, such as share or like buttons. Such features are provided by third party social media platforms, such as LinkedIn, Twitter or Facebook. Where data is collected this way, its processing is governed by the privacy policy of the respective social media platforms. Our content may link to third party websites to provide relevant references. We are not responsible for such external content, which may contain separate privacy policies and data processing disclosures.

We may disclose your personal information if required by law, regulation or other legal subpoena or warrant. We may also disclose your personal information to a regulatory or law enforcement agency if we believe it to be necessary to protect the rights, property or personal safety of ESTIV, its members or any third party.

#### 4. Webpage and cookies policies

When you visit our website, our system may automatically collect information about your visit, such as your browser type, your IP address and the referring website. This collection may be done in conjunction with our vendors responsible for the functionality of the website. ESTIV uses performance cookies or

analytics cookies to collect information about your use of the website and enable us to improve the way it works. You may refuse to accept cookies from the website at any time by activating the setting on your browser, which allows you to refuse cookies. Further information about the procedure to follow in order to disable cookies can be found on your internet browser provider's website via your help screen.

#### 5. Email communications and newsletters

If you have given us your email for purposes of communication or promotion, we will use your data to contact you or send emails relating to your interests. You may revoke your consent to being contacted by email any time, by stating your wish to unsubscribe to the ESTIV secretary. Users who no longer wish to receive the ESTIV newsletter may opt out of receiving these communications by informing the ESTIV secretary. Furthermore, with your consent, we may make use of email tracking technology to obtain data if you open an email or if you click on links in an email. This data will be used only in automated ways to help improve future marketing messaging and/or to prioritize follow ups based on perceived communications relevance. Without your consent, we will not make use of personal data unique to you, such as your IP address, your device and browser information or the time and number of times you open an email or click on a link.

### 6. Technical and organizational data protection and retention

ESTIV operates using commercially reasonable technical and organizational measures to protect your personal data against abuse and loss. We store such data in secure environments.

We provide guidance to ESTIV board members having access to personal data and data protection best practices, and require them to consent to the confidentiality standards. While we use all reasonable efforts to protect your personal information, we cannot guarantee the absolute security of your data submitted through our website. We will retain your information for the period necessary to fulfill the purposes outlined in this privacy policy unless a longer retention period is required or allowed by law.

#### 7. Rights and contact information

Upon request, we will provide you with information as to whether and what personal

data we store in relation to you. Should your personal data be incorrect, you may have it rectified. You may also revoke your consent to use your personal data in the future, in whole or in parts, or request deletion of your personal data. Please feel free to direct such requests, or other questions and comments regarding this privacy statement or the privacy practices of gdpreu.org to the ESTIV secretary, who is your primary contact for the GDPR issues, or the ESTIV president.

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

Al-Saleh I, Al-Rajudi T, Al-Qudaihi G, Manogaran P (2017) Evaluating the potential genotoxicity of phthalates esters (PAEs) in perfumes using *in vitro* assays. Environ Sci Pollut Res Int 24:23903-23914. doi: 10.1007/s11356-017-9978-1

Al-Saleh I, Elkhatib R, Al-Rajoudi T, Al-Qudaihi G (2017) Assessing the concentration of phthalate esters (PAEs) and bisphenol A (BPA) and the genotoxic potential of treated wastewater (final effluent) in Saudi Arabia. Sci Total Environ 1, 578:440-451. doi: 10.1016/j.scitotenv.2016.10.207

Brinchmann BC, Skuland T, Rambøll MH, Szoke K, Brinchmann JA, Gutleb AC, Moschini E, Kubátová A, Kukowski K, Le Ferrec E, Lagadic-Gossmann D, Schwarz PE, Låg M, Refsnes M, Øvrevik J, Holme JA (2018) Lipophilic components of diesel exhaust particles induce pro-inflammatory responses in human endothelial cells through AhR dependent pathway(s). Particle Fibre Toxicol 15:21. doi:10.1186/s12989-018-0257-1

Callegaro G, Forcella M, Melchioretto P, Frattini A, Gribaldo L, Fusi P, Fabbri M, Urani C (2018) Toxicogenomics applied to *in vitro* Cell Transformation Assay reveals mechanisms of early response to cadmium. Toxicol in Vitro 48:232-243 doi: 10.1016/j.tiv.2018.01.025

Chary A, Hennen J, Klein S, Serchi T, Gutleb AC, Blömeke B (2018) Respiratory sensitization: toxicological point of view on the available assays. Arch Toxicol 92:803-822. doi:10.1007/s00204-017-2088-5

Chaudhari U, Nemade H, Sureshkumar P, Vinken M, Ates G, Rogiers V, Hescheler J, Hengstler JG, Sachinidis A (2018) Functional cardiotoxicity assessment of cosmetic compounds using human-induced pluripotent stem cell-derived cardiomyocytes. Arch Toxicol 92:371-381. doi: 10.1007/s00204-017-2065-z

Clippinger AJ, Allen D, Jarabek AM, Corvaro M, Gaça M, Gehen S, Hotchkiss JA, Patlewicz G, Melbourne J, Hinderliter P, Yoon M, Huh D, Lowit A, Buckley B, Bartels M, BéruBé K, Wilson DM, Indans I, Vinken M (2018) Alternative approaches for acute inhalation toxicity testing to address global regulatory and non-regulatory data requirements: an international workshop report. Toxicol In Vitro 48:53-70. doi: 10.1016/j.tiv.2017.12.011

Colaianna M, Peterson H, Ilmjärv S, Kern I, Julien S, Baquiè M, Hengstler JG, Pallocca G, Bosgra S, Leist M, Krause KH (2017) Fingerprinting of neurotoxic compounds using a mouse embryonic stem cells dual luminescence assay. Arch Toxicol 91:365-391. doi: 10.1007/s00204-016-1690-2

Desprez B, Dent M, Keller D, Klaric M, Ouédraogo G, Cubberley R, Duplan H, Eilstein J, Ellison C, Grégoire S, Hewitt NJ, Jacques-Jamin C, Lange D, Roe A, Rothe H, Blaauboer BJ, Schepky A, Mahony C (2018) A strategy for systemic toxicity assessment based on non-animal approaches: The Cosmetics Europe Long Range Science Strategy programme. Toxicol In Vitro 50:137-146. doi: 10.1016/j.tiv.2018.02.017.

Edwards A, Roscoe L, Longmore C, Bailey F, Sim B and Treasure C (2018) Adaptation of the human Cell Line Activation Test (h-CLAT) to Animal-Product-Free Conditions. ALTEX.doi:10.14573/altex.1710051 [Epub ahead of print]

Efremova L, Chovancova P, Adam M, Gutbier S, Schildknecht S, Leist M (2017) Switching from astrocytic neuroprotection to neurodegeneration by cytokine stimulation. Arch Toxicol 91:231-246.

doi: 10.1007/s00204-016-1702-2

Friis Berntsen H, Granum CB, Audinot JN, Hofer T, Verhaegen S, Gutleb AC, Ropstad E (2017) The neurotoxicity of perfluorinated compounds in isolated cerebellar granule neurons is related to carbon chain length and functional group attached. Neurotoxicol 63:70-83. doi:10.1016/j.neuro.2017.09.005

Hakkola J, Bernasconi C, Coecke S, Richert L, Andersson TB, Pelkonen O (2018) CYP induction and xeno-sensing receptors PXR, CAR, AHR and PPAR $\alpha$  at the crossroads of toxicokinetics and toxicodynamics. A Minireview. Basic Clin Pharmacol Toxicol; doi: 10.1111/bcpt.13004.

Hirsch C, Striegl B, Mathes S, Adlhart C, Edelmann, M, Bono E, Gaan S, Salmeia KA, Hölting L, Krebs A, Nyffeler J, Pape R, Bürkle A, Leist M, Wick P, Schildknecht S (2017) Multiparameter toxicity assessment of novel DOPO-derived organophosphorus flame retardants. Arch Toxicol 91:407-425. doi: 10.1007/s00204-016-1680-4

Jacques-Jamin C, Duplan H, Rothe H, Vaillant O, Eilstein J, Grégoire S, Cubberley R, Lange D, Ellison C, Klaric M, Hewitt N, Schepky A (2017) Comparison of the Skin Penetration of 3 Metabolically Stable Chemicals Using Fresh and Frozen Human Skin. Skin Pharmacol Physiol 30:234-245. doi: 10.1159/000475472.

Korotkov S, Konovalova S, Nesterov V, Brailovskaya I (2018) Mersalyl prevents the TI+-induced permeability transition pore opening in the inner membrane of Ca2+-loaded rat liver mitochondria. Biochem Biophys Res Commun. 495:1716-1721.

doi: 10.1016/j.bbrc.2017.12.023

Korotkov S, Sokolova T, Avrova N (2017) Gangliosides GM1 and GD1a normalize respiratory rates of rat brain mitochondria reduced by tert-butyl hydroperoxide. J Evolut Biochem Physiol 53:200-207.

doi: 10.1134/S0022093017030048

Lacroix G, Koch W, Ritter D, Gutleb AC, Larsen ST, Loret T, Zanetti F, Constant S, Chortarea S, Rothen-Rutishauser B, Hiemstra P, Frejavon E, Hubert P, Gribaldo L, Kearns P, Aublant JM, Angeloni S, Diabaté S, Weiss C, de Groot A, Kooter I (2018) Air-liquid interface *in vitro* models for respiratory toxicology research: consensus workshop and recommendations. Appl In Vitro Toxicol 4:1-16. doi:10.1089/aivt.2017.0034

Nyffeler J, Chovancova P, Dolde X, Holzer AK, Purvanov V, Kindinger I, Kerins A, Higton D, Silvester S, van Vugt-Lussenburg BMA, Glaab E, van der Burg B, Maclennan R, Legler DF, Leist M (2017) A structure-activity relationship linking non-planar PCBs to functional deficits of neural crest cells: new roles for connexins. Arch Toxicol 92:1225-1247. doi: 10.1007/s00204-017-2125-4

Nyffeler J, Dolde X, Krebs A, Pinto-Gil K, Pastor M, Behl M, Waldmann T, Leist M (2017) Combination of multiple neural crest migration assay to identify environmental toxicants from a proof-of-concept chemical library. Arch Toxicol 91:3613-3632. doi: 10.1007/s00204-017-1977-y

Pallocca G, Nyffeler J, Dolde X, Grinberg M, Gstraunthaler G, Waldmann T, Rahnenführer J, Sachinidis A, Leist M (2017) Impairment of human neural crest cell migration by prolonged exposure to interferonbeta. Arch Toxicol 91:3385-3402. doi: 10.1007/s00204-017-1966-1

Piersma AH, Burgdorf T, Louekari K, Desprez B, Taalman R, Landsiedel R, Barosso J, Rogiers V, Eskes C, Oelgeschläger M, Whelan M, Braeuning A, Vinggaard AM, Kienhus A, Van Benthem J, Ezendam J. (2018) Workshop on acceleration of the validation and regulatory acceptance of alternative methods and implementation of testing strategies. Toxicol In Vitro, 50, 62-74.

Pop A, Drugan T, Gutleb AC, Lupu D, Cherfan J, Loghin F, Kiss B (2018) Estrogenic and anti-estrogenic activity of butylparaben, butylated hydroxyanisole, butylated hydroxytoluene and propyl gallate and their binary mixtures on two estrogen responsive cell lines (T47D-Kbluc, MCF-7). J Appl Toxicol 38:1-14. doi:10.1002/jat.3601

Rothe H, Obringer C, Manwaring J, Avci C, Wargniez W, Eilstein J, Hewitt N, Cubberley R, Duplan H, Lange D, Jacques-Jamin C, Klaric M, Schepky A, Grégoire S (2017) Comparison of protocols measuring diffusion and partition coefficients in the stratum corneum. J Appl Toxicol 37:806-816. doi: 10.1002/jat.3427.

Secker P, Beneke S, Schlichenmaier N, Delp J, Gutbier S, Leist M, Dietrich D (2018) Canagliflozin mediated dual inhibition of mitochondrial glutamate dehydrogenase and complex I: an off-target adverse effect. Cell Death Dis 9:226. doi: 10.1038/s41419-018-0273-y

Shemarova I, Nesterov V, Korotkov S, Sobol' K (2017) Involvement of Ca2+ in the development of ischemic disorders of myocardial contractile function. J Evolut Biochem Physiol 53:368-379.

doi: 10.1134/S0022093017050027

Silkin Yu, Korotkov S, Silkina E (2017) The study of the bioenergetic characteristics of the red blood cells of black sea fish: the common stingray (Dasyatis pastinaca L.)

and Black Scorpionfish (Scorpaena porcus L.). Biophysics 62: 434–439.

doi: 10.1134/S0006350917030204

Sobol C, Nesterov V, Belostotskaya G, Korotkov S (2017) The Effects of TI+ ions on the dynamics of intracellular Ca2+in rat cardiomyocytes. Biophysics 62: 68–74. doi: 10.1134/S0006350917010201

Vinken M (2018) Taking adverse outcome pathways to the next level. Toxicol In Vitro 50:A1-A2. doi: 10.1016/j.tiv.2018.03.017

Vinken M (2018) *In vitro* prediction of drug-induced cholestatic liver injury: a challenge for the toxicologist. Arch Toxicol 92:1909-1912. doi: 10.1007/s00204-018-2201-4

#### **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:

Please visit our website:

http://www.estiv.org/payment.html

Bank Transfer: RABOBANK

IBAN #: NL20 RABO 0101 4857 51

BIC: RABONL2U Attention of: ESTIV

Regentenland 35, 3994TZ, Houten, The Netherlands

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).

estive stive sti

#### **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.

estives tives ti

#### **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>