

European Society of Toxicology In Vitro

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Newsletter

Issue No 31 January 2012

Editorial

Dear ESTIV members, I would like to begin by wishing everyone a very Happy New Year. This year the ESTIV Congress will take place in Lisbon from October 17-20. Please save the date!

Newsletter 31 you will find many listed: international events workshop/seminar "Towards toxicity animals" assessment without iointly organized by SSCT and FINCOPA, the roundtable at the CELLTOX Congress 2011, "The 3Rs today: from basic research to regulatory tests" and the 99th Indian Science Congress "Alternatives Toxicity Teaching, Testing, and Education" held in Bhubaneswar, India.

Please check the Newsletter for long list of future events.

I appreciate the efforts of all those who contributed to making this a significant and informative issue and would like to take this opportunity to congratulate **Dr. Päivi Myllynen from the University of Oulu, Finland**, who won the 2011 Björn Ekwall Memorial Award.

I would also like to inform you that an agreement has been signed for a collaboration between the Institute for Health and Consumer Protection of the Joint Research Centre in Ispra and the University of Milano Bicocca. Cooperation between CAAT Europe and Ecopa has also been officially announced.

I look forward to continue working with you this year and thank you again for your valuable input.

Best wishes.

Francesca Caloni

Message from the President

Dear colleagues A warm welcome in 2012. 2012 announces itself as a year of reality and truth. Also the in vitro sciences matured and it is time to point to the advances which have been made over the years. Some expectations are met: there are new tests which replace animal testing but not all relevant endpoints are yet covered. In vitro science also improves mechanistic understanding and provides better science for safety evaluation. This information should be further incorporated in the risk assessment process, which is still a big challenge. ESTIV intends to contribute to these goals in 2012. In 2012 we will have the ESTIV conference which will be hosted by the Portuguese Toxicology Association (AP Tox) in Lisbon, Portugal, October 17-20, 2012. You will read more about this in this newsletter. In vitro science and safety evaluation is receiving renewed worldwide interests. In 2011 ESTIV strengthened the links with organizations and stakeholders which support in vitro science each from their own perspective. We had a joint meeting with the In Vitro Testing Industrial Platform (IVTIP) and the Centre of Alternatives to Animal Testing –Europe (CAAt-Europe) in Monaco. We made a bridge towards our transatlantic partners by a joint session with the American Society for Cellular and Computational Toxicology at the World Congress in Montreal, Canada. ESTIV became member the ECVAM stakeholder form (ESTAF).

We invite our members to actively take advantage of these opportunities in 2012. The ESTIV executive committee looks forward to work with all of you in 2012.

Greet Schoeters
President of ESTIV

DIOXIN 2011

From 21 to 25 August 2012 the 31st International symposium on halogenated persistent organic pollutants(POPs) - DIOXIN2011 – took place in Brussels.

The congress was attended by more than 900 participants and addressed persistent organic pollutants such as dioxins and PCBs but also newer emerging chemicals such as flame retardants and musks. Advances were presented on exposure assessments in the environment and in biological tissues, progress in chemical analytical techniques and bioassays, toxicology in vitro, in vivo and computational tools, population studies on environmental health relations.

Novel toxicology approaches using nonanimal studies contributed substantially to the field. This was highlighted by the ESTIV award which was given to excellent contributions form young investigators.

Anna Pereira-Fernandes from the University of Antwerp, Belgium received an award for her excellent presentation and work on "The Environmental Obesogen Hypothesis: A Mechanistic Evaluation of the Hypothesis and the Development of a Screening System for Obesogenic Substances" as well as Karine Audouze from the Department of Systems Biology of the Technical University of Denmark her Denmark, for poster presentation on "Computational Systems Biology to Explore Environmental Chemical Toxicity Hazards". We look forward to meet these scientists at ESTIV2012.

The 28th workshop of SSCT and FINCOPA seminar: "Towards toxicity assessment without animals"

21-23September 2011, Tampere, Finland

The 28th Workshop of the Scandinavian Society for Cell Toxicology (SSCT) was jointly organised with the Seminar of the Finnish Consensus Platform for Alternatives (FINCOPA). The Finnish Graduate School of Toxicology also took part in the organisations. Dr Tuula Heinonen, the chairman of both societies, was the president of the meeting. The personnel of FICAM (the Finnish Centre for Alternative Methods, www.ficam.fi) were

responsible for the practical arrangements.

The meeting provided different stakeholders (academy, government, industry) with an excellent platform to share new knowledge and ideas among over 100 participants from 15 different countries. There were 23 invited speakers, 7 free oral, and 23 poster presentations. The abstract book contained abstracts. and advanced technical solutions were presented by 12 companies in an interesting exhibition. The title of the "Towards toxicity assessment without animals" reflects the background and scheme of the scientific programme well. The safety of chemicals to humans, and the risks the environment have only been determined for a fraction of all the chemical substances currently in use. The pressure to perform toxicity assessment without animals comes from various stakeholders: European Commission's goal is to decrease the use of laboratory animals, regulatory guidelines such as Cosmetics directive prohibits the use of animals in assessing the safety of cosmetics or cosmetic ingredients, REACH is calling for non-animal tests to be performed whenever possible, and the industry requires test methods which are cheaper and more relevant than animal experiments. These issues were discussed in connection with the lectures in five oral sessions as well as in the Poster session:

- 1. Status of EU projects and new developments to replace animal experiments
- 2. Impact of the council adopted updated Directive 86/609/EEC, 2010/63/EU
- 3. A new paradigm. Away from histopathology-based toxicity assessment
- 4. Optimal *in vitro* cellular model
- 5. Significance of biological barriers in toxicity risk assessment
- Poster session: The abstracts are available at the home page of FICAM, and the Proceedings will be published in Toxicology in Vitro. The Björn Ekwall Award was given to an excellent young scientist Dr Päivi Myllynen (University of Oulu, Finland). The title of her lecture was "Placental transporters: models and mechanisms in toxicology". Two other prizes were also given at the meeting: the Gambro prize to Dr. Line (University of Copenhagen, Mathiesen Denmark) for the best oral presentation ("Placental transport of large molecules studied using human ex vivo placental perfusion"), and the best poster prize to Dr Dorothée Hallier-Vanuxeem (Artois

University, France) whose title was "Ready-To-Use *in vitro* blood-brain barrier model adapted to repeated dose toxicological screening".

The Björn Ekwall Memorial Award

The Björn Ekwall Memorial Award was established by the Scandinavian Society for Cell Toxicology (SSCT) to honour the memory of Dr. Björn Ekwall (1940-2000), an outstanding Swedish cell toxicologist and the founder of the SSCT.

The Björn Ekwall Memorial Foundation (BEMF), initiated by the SSCT in 2001, awards its annual prize to a scientist working actively in the field of *in vitro* toxicology and who contributes to the replacement/reduction of animal experiments, by the development of *in vitro* tests, or by validation and implementation of *in vitro* tests.

Ten years have passed since the founding of the BEMF, and 11 scientists from different countries have received the Björn Ekwall Memorial Award so far (Walum et al., The tenth anniversary of the Björn Ekwall

Memorial Foundation, ATLA 39, 389-402, 2011, and the BEMF home page, under the address:

www.bemf.eu).

The year 2011 Björn Ekwall Memorial Award was given to the excellent young scientist, Dr. Päivi



Myllynen, from the University of Oulu, Finland. Dr. Myllynen, graduated from Medical school 1999, and completed her Ph.D. in 2003.

She is now an associate professor at the Department of Pharmacology and Toxicology at the Institute of Biomedicine, University of Oulu. She built her scientific career with great determination and enthusiasm, starting her own research group of younger scientists and doctoral students.

Dr. Myllynen has significantly contributed to in vitro toxicology by evaluating placental transfer and metabolism of environmental contaminants and food-borne carcinogens in the human placental perfusion model. She has also taken part in the evaluation of the placental perfusion model as a test method for the detection of reproductive toxicity in the ReProTect project, an integrated project under the EU 6th Framework Programme. The title of the Björn Ekwall Memorial Lecture delivered by Dr. Myllynen at The 28th Workshop of SSCT and FINCOPA seminar, 21-23 September, 2011, Tampere, Finland, was: "Placental transporters: models and mechanisms in toxicology".

Ada Kolman, PhD, Assoc. Professor President of the BEMF

EUROECOTOX: European Network for Alternative Testing Strategies in ecotoxicology

In October 2011 more than 40 international experts with a background in research, industry or regulation met at the Helmholtz Centre for Environmental Research, Leipzig, Germany to discuss the perspectives of alternatives to animal experiments in environmental risk assessment. Although many regulations principally encourage the use of alternative approaches such as QSAR, read across or alternative test systems such as cells or embryos, their practical application is limited. Main reasons are not a principal unavailability of methods but the lack of international acceptance, i.e. by availability of appropriate OECD guidelines.

The outcome of the Expert Meeting will be published as a commentary paper where the potential areas for alternative approaches in environmental risk assessment, including present limitations as well as perspectives for further development and improvements are highlighted. The outcomes are based on the discussions held during eight breakout sessions, where acute and chronic toxicity in fish and birds, endocrine disruption in fish and amphibians, bioaccumulation in fish, nonapproaches, testing alternative approaches and sublethal/alternative endpoints have been discussed under the aspects of limitations of methods and for regulatory acceptance, research needs and overall recommendations.



details: Contact www.euroecotox.eu; email: info@euroecotox.eu



European Network for Alternative Testing Strategies in Ecotoxicology

Roundtable REPORT: The 3Rs today from basic research to regulatory tests **CELLTOX 1991-2011**



ISS, Rome 19-21 October 2011

From 19 to 21 October Italian 2011 the Association for In Vitro Toxicology CELLTOX celebrated its 20th anniversary by organizing an International Meeting in Rome: "CELLTOX 1991-2011: Twenty in vitro years of

Toxicology: Achievements and Future Challenges".

During the course of the conference a roundtable was organized to discuss "The 3Rs today: from basic research to regulatory tests".

The speakers invited to contribute to the roundtable discussions were: Prof Lucio Costa (Professor of Toxicology in the Department of Environmental and Occupational Health Sciences at the University of Washington), Prof Thomas Hartung (Director of CAAT, Center for Alternatives to Animal Testing), Dr Joachim

Kreysa (Head of In Vitro Methods Unit at Joint Research Centre Institute for Health and Consumer Protection), Dr Greet Schoeters (Scientific director of CARDAM, the Centre of Advanced Research and Development of Alternative Methods and President of ESTIV), and Dr Flavia Zucco (former Research Director at CNR and coordinator of several EU projects focussing on alternative methods). Dr Anna Laura Stammati, former President of CELLTOX, coordinated the roundtable. The speakers contributions and the discussion that followed addressed some important points and problems faced by today's research on alternative methods and the efforts to implement the 3Rs principles in basic research and in regulatory testing. The discussion started with the impact of the recent Directive 63/2010 (on the protection of animals used for scientific purposes). Then moved on to the application of the 3Rs in basic research and in the development of alternative regulatory testing. It was noted that the Directive is important but not sufficient. There is a strong need for better information to those involved in basic research. The referees responsible for evaluating new grant proposals, and the members of the ethical committees need to better informed about the existing alternatives and the limitations of animal experiments, to avoid the overestimation of their power for extrapolation to human exposure. Considering the advancement of the 3Rs, the two first; Refinement and Reduction are already realities. Replacement, however, is far behind, depending on the widespread belief is that if not tested in vivo it cannot be predictive for humans. Further implementation of the 3Rs principles will depend on the availability of research grants for alternative methods, but also, the development of new tests and new models that can be applied in the regulatory field. The way towards a reduction of animal experiments in regulatory testing depends on the development of integrated approaches. involving batteries of in vitro tests and in silico modelling, that will allow better extrapolation to human in vivo exposure effects. The role of databases is extremely important as they favour the spreading of information on the best and more appropriate models, tests and methods to address basic research questions.

The bioethical aspects were also discussed, emphasizing the importance of addressing the animal welfare issue in basic research and in education, since implementation of the 3Rs needs more than it is written in the new Directive. It was recalled that some EU funded projects on bioethical issues (i.e. Anim.Al.See) resulted in guidelines and recommendations that are now endorsed and adopted by the European Commission.

A general conclusion of the roundtable was that further spreading of information and education on alternative methods and the scientific and ethical issues that accompany them is still one of the major priorities, and like this one organized meetings CELLTOX fulfil this need. It is also important to expand the 3Rs and reach beyond the field of toxicology, looking for new models and approaches from the life sciences and the clinical fields with an open mind to the integration of these models in the attempt to further reduce animal experiments.

Dr Stammati closed the roundtable recalling the early days of in vitro toxicology research in Italy with the Workshop organized by herself and Dr Zucco in Urbino in 1984, well before the birth of the Italian Association for in vitro Toxicology CELLTOX whose 20th birthday was celebrated in this meeting. This congress and the roundtable demonstrate how far we have gone since those early days and promise a bright future for this field of research and for the advancement of the 3Rs principles in research, education and regulatory testing.

Yula Sambuy INRAN -National Research Institute on Food and Nutrition, Rome - Italy sambuy@inran.it

SIGNED A COLLABORATION AGREEMENT BETWEEN THE EUROPEAN UNION AND UNIVERSITA' DEGLI STUDI DI MILANO BICOCCA







The Institute for Health and Consumer Protection of the Joint Research Centre in Ispra (VA), Italy, and the University of Milano Bicocca (UniMIB), Milan, Italy, have recently signed a Collaboration Agreement.

The general objective of this Agreement is to collaborate more effectively in the field "Environmental and Biomedical Sciences".

The aim of the Collaboration Agreement is to join forces on a "multiscale characterization of *in vitro* systems for hazard identification, and environmental system monitoring, to address *in vitro* processes at the following levels:

- Molecular level (gene and protein expression)
- Subcellular level (structural and functional proteins, organelles organization and function)
- Single cell and cell aggregates.

The comparison and correlation of biological data. to identify toxicological mechanisms and pathways will also be addressed.

Several lines of actions will be taken to achieve the objectives of the Collaboration Agreement. In particular:

- Exploring possibilities for joint projects
- Exchange of scientific and technological information
- Carry out joint research projects
- Joint organization of seminars and conferences
- Take part in the execution of on-going programmes, projects, and related activities of mutual interest of the JRC and UniMIB
- Exchange of research personnel, including students (e.g., graduate, post-graduate, PhD, fellowship holder)

Dr. Laura Gribaldo of the Molecular Biology and Genomics Unit will be the coordinator for the JRC and Dr Chiara Urani, Department of Environmental and Territory Sciences will be the coordinator for UniMIB.

CAAT-Europe-ecopa cooperation

At ecopa's (European consensus platform for alternatives) general assembly on November 10 in Madrid, it was officially announced that CAAT-Europe and ecopa will start to collaborate more closely and synergistically than before. As ecopa represents the national platforms for alternatives in 13 European countries and CAAT-Europe acts as a transatlantic communication hub between the USA and Europe, this collaboration will enhance the flow of information, improve communication, and promote a joint effort

that may serve as a role model for other NGO's in this field. The role of CAAT-Europe will be to organize the information flow from the national platforms to the interested public via the ecopa news corner in *ALTEX*. CAAT-Europe will also support the ecopa website and provide internationally relevant news concerning alternatives in testing and research. They will also contribute to the communication and representation to interested parties via the *ecopa Messenger*.

Alternatives in Teaching, Toxicity Testing and Education-

99th Indian Science Congress in Bhubaneswar, India

The 99th Indian Science Congress in Bhubaneswar, on January 6, 2012, hosted a plenary session on "Alternatives in Teaching, Toxicity Testing, and Education". This session was organized by the Mahatma-Gandhi-Doerenkamp Center (MGDC) and supported by the Doerenkap-Zbinden-Foundation. The Science Congress was attended by 19,000 participants and the program included the three Doerenkamp-Zbinden Chairs, i.e. M.A. Akbarsha, M. Leist, and T. Hartung. The International Conference on Alternatives to Animal Use in Research. Education and Toxicity Investigations, in Channai was held in conjunction with the Indian Science Congress on January 4, 2012. The Conference, organized by MGDC and the International Institute of Biotechnology and Toxicology, also included the three Doerenkamp-Zbinden Chairs as speakers.

Thomas Hartung presented at the MGDC, as well as in collaboration with the Humane Society International and the Federation of Indian Animal Protection Organisations (FIAPO) at the Indian Institute of Toxicological Research, Lucknow, and at the National Institute of Nutrition, Hyderabad.

The various initiatives aimed to gather a critical mass in India, to support self-organization and the creation of 3Rs Centers, a consensus platform, and possibly a validation center (such as InCVAM). CAAT has offered further support for such initiatives.

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Meetings calendar

SOT's 51st Annual Meeting, March 11–15, 2012, at the Moscone Convention Center in San Francisco, California

http://www.toxicology.org/ai/meet/am2012/

INVITROM and Kirkstall Ltd will organize the 2012 Spring Symposium on: Advances in in vitro cell and tissue culture and 4th annual quasi vivo user group meeting 22-23 May 2012 Utrecht. The Netherlands

http://www.invitrom.org/kirkstall/kirks.html Contact Conference Technical Chair Dr Kate Darley

Email: kdarley@kirkstall.org

48th Congress of the European Societies of Toxicology **(EUROTOX 2012)** 17-20 June 2012

Stockholm. Sweden www.eurotox2012.se

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Eawag, the Swiss Federal Institute of Aquatic Science and Technology, will host the

European Conference the on Replacement, Reduction and Refinement animal experiments Ecotoxicology, organized by the European Network for Alternative Testing Strategies in EUROECOTOX Ecotoxicology (www.euroecotox.eu). Date: 28th-29th of June 2012Venue: Eawag, Dübendorf (close to Zürich), SwitzerlandThis conference will focus on the current state and future directions of the implementation and application of the to acceptance, 3Rs. from bench ecotoxicology. Save the date! Call for abstracts for presentations will be sent out in January 2012

Local organiser:

Prof. Dr. Kristin Schirmer Head Department - Environmental Toxicology Eawag, Swiss Federal Institute of Aquatic Science and Technology Überlandstrasse 611 8600 Dübendorf Box Switzerland Phone: +41 (0)44 823 5266 Fax: +41 (0)44email: 823 53 11 kristin.schirmer@eawag.ch

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ESTIV 2012 October 17-20, 2012 Lisbon Portugal http://www.estiv2012.com/

Why should you go on 17-20 October to ESTIV2012 in Lisbon, Portugal?

- Because of the cutting-edge topics
- on non-animal approaches for toxicity testing
- on physiologically relevant biomarkers profiles
- on molecular mechanisms and pathways
- > to participate in the special student session
- to win the student's award for the best poster/oral presentation
- to get hands -on experience with computerized in vitro – in vivo extrapolation strategies
- to discuss with colleagues
- > to meet senior scientists in the field
- to enjoy the Portugese hospitality and beautiful Lisbon

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The 9th World Congress on Alternatives and Animal Use in the Life Sciences 24-28 August 2014, Prague, Czech Republic www.wc9prague.org

Workshops

Workshop "Quality **CAAT-Europe** on standards for publications dealing with invitro systems" Monday, March 12, 2012, 5:00-9:00 PM, at the Marriott Hotel in San Francisco CAAT-Europe will host a workshop on "Quality standards for publications dealing with in-vitro systems." The quality of the data presentation in scientific publications is of critical concern in the scientific world. For animal experiments in general, the ARRIVE guidelines have been worked out for minimum publication standards, and the specific problem of underpowered studies has been discussed. For in vitro models, recommendations are available for good cell culture practice and for system validation (OECD GD34). This workshop aims to produce a comprehensive set of guidelines

that should help authors, referees, and editors dealing with data gathered with *in vitro* systems. Recommendations will be made for points to consider with respect to statistical planning and presentation of data on alternative methods in the field of toxicology. Participation is by invitation.

Contact:

Mardas Daneshian (Mardas.Daneshian@uni-konstanz.de)

FDA Workshop on in vivo & in vitro Reproand Developmental Tox. 16 April 2012 On April 16, 2012, the US Food and Drug Administration will sponsor a 1-day Workshop on "Reproductive and Development Toxicology Testing - From In Vivo to In Vitro" at the White Oak Campus of the US Food and Drug Administration in Silver Spring, MD.

Recent publications of ESTIV members

Gulden, M, Jess, A, Kamman J, Maser E, Seibert, H (2010) Cytotoxic potency of H_2O_2 in cell cultures: impact of cell concentration and exposure time. Free Radic Biol Med 49, 1298-1305

Pöltl D, Schildknecht S, Karreman C, Leist M (2011) Uncoupling of ATP-depletion and cell death in human dopaminergic neurons. NeuroToxicology. *in press*

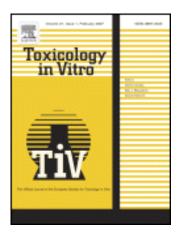
Procaccianti C, Stefanini FM, Urani C (2011)The Cell Transformation Assay: Toward a Statistical Classification of Mixed and Intermediate Foci Images. ATLA 39, 23-36.

Scholz, D., Pöltl D, Genewsky A, Weng M, Waldmann T, Schildknecht S and Leist M (2011) Rapid, complete and large-scale generation of post-mitotic neurons from the human LUHMES cell line. J Neurochem 119(5), 957-971

Seibert, H, Maser, E, Schweda, K, Seibert, S, Gulden, M (2011) Cytoprotective activity against peroxide-induced oxidative damage and cytotoxicity of flavonoids in C6 rat glioma cells. Food and Chem Toxicol 49, 2398 – 2407

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Toxicology in Vitro



Official Journal of the European Society of Toxicology in Vitro

Editors: Daniel Acosta, Bas J. Blaauboer, Daniel Dietrich

ESTIV membership fee

Membership fee

The membership for an individual member for 2011 is € 30,00. If you are also a member of one of the affiliated societies (CellTOX, SSCT, INVITROM, IVTS), the membership amount to € 18,00.

Method of Payment

Bank Transfer
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Attention of: ESTIV
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Due to the high costs of applying for and cashing EuroCheques, please do not use this means of payment.

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

Sieng Horbach

ESTIV e-mail list

ESTIV has an e-mail list, which has the potential to be a very valuable resource. There are many types of questions that you could pose to the list, whether you are a junior or a senior scientist. To send a message to all ESTIV members on the list (presently more than 200 colleagues), simply address your e-mail to estiv@freelists.org

Please do not be concerned about security. This is a "closed" list, which means the "list-owner" (Jan van der Valk) is able to select who is allowed to join. Only

ESTIV members could receive the message. The ESTIV secretary advises the "list-owner" of eligible members. If you have never received a message from the ESTIV list, it is because you have not informed us of your e-mail address. Please correct this immediately by sending a message to me at i.b.f.vandervalk@uu.nl, and your name will be added.

Jan van der Valk

ESTIV Corporate member



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



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

http://www.novozymes.com/en



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

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



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http://www.thor.com/

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ESTIV Affiliated Societies

CellTox, Italy

Scandinavian Society for Cell Toxicology

INVITROM

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

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For more information on ESTIV and membership application contact

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

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