European Society of Toxicology *In Vitro*

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Newsletter

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Editorial

Dear ESTIV members
I am very much looking forward to meeting you "physically" in Lisbon for the ESTIV Congress and sharing scientific information and ideas. It is a pleasure to learn about the increasing activities in the field of toxicology *in vitro*: meetings, workshops, projects and publications.
I am honoured to inform you that **Professor Dr. med. Horst Spielmann**, our Past-President, is the recipient of the Björn Ekwall Memorial Award 2012, for his outstanding contribution to *in vitro* Toxicology and 3Rs.
On March 2012 ESTIV took part in the organization of the meeting on *Scientific roadmap for the future of animal-free systemic toxicity testing*, in Belgium, in collaboration with other organizations. More information is available on page 4 of this Newsletter.
The European Toxicology Risk Assessment Training Programme (Trisk) project has successfully concluded, and comments have been reported by **Bas Blaauboer** (TRISK organizer) and **Mathieu Vinken** (TRISK trainee). Updated information has been reported by **Chantra Eskes** on the Applicability of Validated and Adopted Skin & Eye Irritation *In Vitro* Methods to Assess and Classify Detergent Mixtures under EU CLP.
In the month of July, I hope you all enjoy your holidays and use this Newsletter to plan your future scientific meetings!

Best wishes,

Francesca Caloni

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Message from the President

Dear colleagues
It is our pleasure to present to you our newsletter which provides you with news of our society and connected networks. It is clear that *in vitro* toxicology becomes more and more part of a big scientific project towards more safety and improved human health. This will be further extensively taken up and discussed at ESTIV 2012 in Lisbon, Portugal, October 16 -19, 2012. The ESTIV 2012 conference is being prepared by our colleagues from the Portuguese Toxicology Association (AP Tox). You will read more on this in this newsletter. We will emphasize the strong European roots of *in vitro* toxicology thanks to the European framework projects and the many national projects and national organizations which support the research and implementation of alternative tests. Europe is establishing close links with the international community. ESTIV stimulates this and actively takes part as you will notice in a special session on transatlantic activities. New aspects such as the economics of alternatives will be covered, giving an opportunity to reflect on different societal challenges. One of the main goals of ESTIV is stimulation of young scientists, giving them further perspectives and the necessary scientific challenges. Students are very welcome and a special student session and a training session are being organized for them. Students can apply for travel grants and the best student's oral and poster presentation will be recognized by a joint ESTIV/ELSEVIER award.
We hope to welcome many ESTIV members in Lisbon.

Greet Schoeters
President of ESTIV

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Mark your calendar for ESTIV2012 !

ESTIV2012, will be hosted by the Portuguese Toxicology Association (AP Tox) in Lisbon, Portugal, 16th -19th October, 2012.

As is tradition, this congress will bring together researchers and students from academia and industry, involved in the development and use of *in vitro* methods in toxicology. The scientific program includes state-of-the-art lectures, workshops, and original communications and poster sessions that will explore challenges and successes of non-animal approaches for toxicity testing.

This year the congress will have a special emphasis on the following themes: Dermal toxicity, Ocular toxicity, Dermal sensitization, Innate immune responses in toxicity, Carcinogenicity testing, Reproductive & developmental testing, Systemic toxicity, and Computational toxicity & toxicokinetics. As with previous ESTIV congresses, a special student session will also be organized, where young researchers will be invited to briefly present their work;there will be an award for the best presentation.

A pre-congress workshop on "The Economics of Alternatives" will be co-organized by ESTIV, CAAT & IVTIP. This workshop will focus on the benefits versus costs balance related to *in vitro* testing, as well as on strategies to make the way forward regarding the application of *in vitro* tests and testing strategies.

In addition to the cutting-edge topics that will be covered in ESTIV2012, for the first time, a practical workshop will be organized on the 20th October. The purpose of this workshop is to gain hands-on experience with computerized *in vitro* – i*n vivo* extraplotation strategies.

In addition to the scientific program, you can count on the warm hospitality, excellent climate, rich culture and great food that Lisbon has to offer. The congress venue is located in the new part of the city, close to the airport and the Expo waterfront.

The ESTIV2012 organization committee is looking forward to seeing you in Lisbon.

Professor Dr. med. Horst Spielmann is the recipient of the Björn Ekwall Memorial Award 2012

Professor Dr. med. Horst Spielmann is the recipient of the Björn Ekwall Memorial Award 2012. He was selected by the board of the Björn Ekwall Memorial Foundation (BEMF) together with the board of the Scandinavian Society for Cell Toxicology (SSCT). The Björn Ekwall Memorial Award will be handed over to Prof. Spielmann during the ESTIV 2012 congress 16 – 19 October, Lisbon, Portugal. The title of the Björn Ekwall Memorial Lecture which will be given by Prof. Spielmann is: *Today Björn Ekwall would endorse the concept "Toxicology in the 21st Century*".

The BEMF wants to honour the outstanding scientific work of Prof. Spielmann. He has significantly promoted the research in the field of *in vitro* toxicology by developing non-animal tests aiming to replace and to reduce animal experiments in regulatory toxicology. The *in vitro* models developed by Prof. Spielmann are used world-wide, e.g. for the estimation of phototoxicity, to test skin irritation, and for the detection of embryotoxicity *in vitro*. The studies of Prof. Spielmann have led to validated tests, and also acceptance into the regulatory guidelines. Horst Spielmann (born April 3, 1942, in Lublin, Poland) defended his PhD thesis in 1969 and became Dr. med. at the Department of Pathology, Medical School of the Freie Universität Berlin where he continued as a postdoctoral student and assistant professor at the Institute for Toxicology 1969-1980. From 1981 he has been the Head of the Department for Pharmacology and Toxicology at the Battelle Institute, Frankfurt on Main, and 1983-1989 director and professor at the Federal Health Institute Berlin.

He has been the Head of ZEBET 1989 -2007, the Head of the Federal Institute for Risk Assessment (BfR) 2004 – 2007. Horst Spielmann retired in 2007 from ZEBET, and is currently a Honorary Professor for Regulatory Toxicology at the Freie Universität Berlin, and the consultant of the President of the BfR. Since 1987, Prof. Spielmann has been the chairperson and member of several management teams of German and international validation studies funded by the German Ministry for Education, by the European Commission, by European Centre for the Validation of Alternative Methods (ECVAM) and by European Cosmetic, Toiletry and Perfumery Association (COLIPA). Prof. Spielmann is the member of several national and international boards and advisory committees involved in the validation of *in vitro* tests, e.g. the coordinator of EU/ECVAM project called "Validation study to evaluate *in vitro* tests using reconstituted human skin models for assessing the skin irritation potential of test chemicals", which has led later to regulatory acceptance.

The recent coordination activity of Prof. Spielmann is the FP7 project AXLR8, which started in 2010 and focuses to accelerate the transition to a toxicity pathway-based paradigm for chemical safety assessment through internationally coordinated research and technology development.

Prof. Spielmann has published over 240 articles in peer reviewed journals, 99 articles published in books, and is the author or editor of 18 books.

During many years Horst Spielmann collaborated with Dr. Björn Ekwall. He participated in the international Multicenter Evaluation of *In vitro* Cytotoxicity (MEIC) project (1989-1999) being head of one of the laboratories at ZEBET that provided data for the MEIC reference chemicals. H. Spielmann was an associate editor of ATLA, which published all papers about MEIC project.

Ada Kolman, PhD, Assoc. Professor
President of the BEMF
Hanna Tähti, PhD, Professor emer.
Board member of the BEMF

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Transnational Access at VITO through FP7 QNano Research Infrastructure – call for proposals

QNano aims to establish a pan-European analytical research infrastructure whose purpose is to drive high quality research and testing practices for assessment of the potential risks posed by nanomaterials. The Transnational Access (TA) component of the FP7 QNano Research Infrastructure is dedicated to providing Users from the European nanosafety community access to nanomaterials processing, characterisation and exposure assessment facilities. Access to 15 major European research sites is via a single application and evaluation process. The central principle of access provision is to offer the Users a full range of services from standard nanomaterials, tuition in best practice, laboratory support and training, and a suite of protocols for all aspects of nanomaterial processing and characterisation in a biological context.

VITO will enable Users to access equipment and facilities for nanoparticle exposure assessment, including *in vitro* biological assays, proteomics and transcriptomics platforms, and occupational exposure measurements, and for *in-situ* and *ex-situ* nanoparticle characterisation (material characterisation and imaging, mass spectrometry, and chemical analysis).

An overview of equipment per category is available at http://www.qnano-ri.eu/access.html.

The second call will open on May 1st, 2012 and close on July 31, 2012. Dates of the next calls will be published at the website.

Contact VITO-TAF: Inge Nelissen, vito-ta@qnano-ri.eu

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TRISK

In January 2012, the European Toxicology Risk Assessment Training Programme (TRISK) was successfully completed. The TRISK project was funded by the European Union in the framework of the Second Programme of Community Action in the field of Health (2008-2013). The main goal of this project was to provide a comprehensive training in toxicological risk assessment that could serve as a model for future European training in risk assessment for accredited European risk assessors. The training programme was specifically intended for individuals who had previous training or experience in toxicology and who would like to pursue a career in risk assessment in Europe in industry, regulatory authorities, consultancy or academia. TRISK was organized by 5 European universities (University of Utrecht-The Netherlands, Karolinska Institutet-Sweden, University of Surrey-United Kingdom, University of Düsseldorf-Germany and University of Milan-Italy) and one research consortium (Technoalimenti SCpA-Italy). As such, the TRISK programme consisted of 8 one-week course modules, an applied training period and a final examination. Following advertisement and application, 25 young TRISK trainees from 15 different European countries were selected in November 2009. In 2010, the trainees attended the theoretical modules that were alternately organized at the different TRISK academic host institutions around Europe. Each module comprised a number of state-of-the-art lectures, hands-on training and/or a group exercise and an examination. The different modules covered a broad spectrum of topics, including (*i*) an introduction to risk assessment and management, with special attention to chemical risk assessment, (*ii*) the role of ADME in risk assessment, (*iii*) the identification and assessment of genotoxic and non-genotoxic carcinogens, (*iv*) exposure analysis in risk assessment, (*v*) identification and assessment of organ toxicity, including neurotoxicity and immunotoxicity, (*vi*) epidemiology and statistics in toxicological risk assessment, and (*vii*) identification and assessment of reproductive toxicity and endocrine disruption. In an additional module, the trainees were asked to attend a one-week European course focussed on a topic of personal interest in the area of risk assessment or toxicology. In 2011, 450 hours of applied training at different European institutions performing risk assessments was foreseen. The trainees submitted their applied training reports by November 2011 and presentation of these reports took place in Brussels-Belgium early December 2011. All trainees successfully defended their applied training report and received a certificate of the TRISK training.

Mathieu Vinken (TRISK trainee) and Bas Blaauboer (TRISK organizer).

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Metabolomics in Toxicology and Preclinical Research, State-of-the-Art and Potential Application- a joint CAAT Europe and BASF Symposium and Expert Workshop, 13-15 February 2012, Berlin

This symposium, attended by 130 registered participants, brought together opinion leaders in toxicometabolomics from all over the world. As part of the transatlantic think tank for toxicology (t^4), it was sponsored by the Doerenkamp-Zbinden Foundation. State-of-the-art use of the technology, both *in vivo* and *in vitro*, was presented. The following one-and-a-half-day workshop prepared a consensus report, to be published in *ALTEX*, regarding opportunities for using the technology *in vitro*, *in vivo*, and for regulatory purposes.

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Consensus Workshop: Quality Standards for Publications Dealing with *In Vitro* Test Systems

The consensus workshop, held March 13, was organized by CAAT-Europe as a SOT satellite meeting. The quality of *in vitro* data presented in scientific publications, particularly in the field of toxicology, is of great importance—regarding reproducibility, for example, and as the basis for evidence-based toxicology (EBT). The goal of the workshop was to engage experts in the process of assembling a comprehensive set of guidelines for authors, referees, editors, and regulators. The experts worked out a set of recommendations covering different aspects of the topic prior to the meeting. A

draft document was generated and discussed during the workshop. The public feedback was very positive. Work on the subject is ongoing, and the consensus report with all contributors will be published soon.

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Open Forum, on 21st Century Toxicology and Evidence-based Toxicology

SOT, 11-15 March 2012 San Francisco

CAAT, the Evidence-based Toxicology Collaboration (EBTC), and the Human Toxicology Project Consortium hosted an open forum on 21st century toxicology and evidence-based toxicology as a satellite meeting to the Society of Toxicology annual conference March 11 in San Francisco. The forum offered participants an opportunity to provide informal updates on work they are doing to advance the new toxicology.

CAAT and the HTP Consortium hosted similar meetings on 21st century toxicology last year at both the SOT conference and the World Congress on Alternatives and Animal Use in the Life Sciences. This year we added evidence-based toxicology to the mix, given the work of the newly formed Evidence-based Toxicology Collaboration (EBTC) (see www.ebtox.com), for which CAAT serves as secretariat. The HTP Consortium comprises several companies and organizations, including CAAT, seeking to accelerate implementation of the NRC's 2007 report on "Toxicity Testing in the 21st Century."

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Scientific roadmap for the future of animal-free systemic toxicity testing

March 20-21, 2012 Brussels, Belgium

The European REACH regulations, together with testing bans for cosmetic ingredients in Europe and a possible US TSCA reauthorization, point to the desire for a transition to an animal-free strategy for systemic toxicity testing. Other areas and novel products could similarly benefit from humane predictive approaches. A recent stocktaking (Adler et al. 2011, Toxicol 85, 367-485) and its expert review (Hartung et al. 2011, ALTEX 28, 183-209) identified gaps in the science available.

An expert workshop, presented and discussed in a multi-stakeholder forum, was held to promote the development of a roadmap to close these gaps (Basketter et al 2012, ALTEX 29:3-89). The event was hosted by CAAT and CAAT-Europe, ecopa, EUSAAT, Doerenkamp-Zbinden-Foundation, ESTIV, IVITIP, ESTIV, IIVS, Humane Society International, and ToxCast (US EPA), together with Cefic and Cosmetics Europe. This event also benefited from the advisory comments of Eurogroup for Animals and ecopa, as well as from the contributions of the SEURAT-1 consortium and the European Chemicals Agency (ECHA).

The convention included 140 registered participants. The public expert responses were constructive, and the discussions on the recommendations of the presented report were lively. A summary of this event has been published in *ALTEX*.

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CAAT EUROPEAN POLICY PROGRAM

The CAAT European Policy Program will be supervised by Dr. Paul Locke, who has directed CAAT's US policy program since 2004. The European Policy Program will help cement CAAT's role as a transatlantic bridge for the 3Rs and alternatives and as a global scientific voice for bringing the 3Rs and humane science into law, regulations, and guidance. François Busquet will be the CAAT representative in Brussels. Dr. Busquet, an expert in the field of zebrafish embryo and its applicability to toxicity and safety testing and research, worked for ECVAM, European Commission until January 2012. CAAT has been active in transatlantic policy issues for some time. In June 2010, it sponsored a symposium in Washington, DC entitled "International harmonization in toxicity testing: An EU perspective on the way forward." CAAT is also an active member of the American Consortium on European Studies (ACES) and an EU Centre for Excellence supported by DG RELEX of the European Commission, and it organizes many information days through CAAT-Europe in Konstanz. One of the goals of the European Policy Program is to serve as a voice of science to political decision makers in the EU and to act as a conduit so that cutting edge humane science is available to make policy on both sides of the Atlantic.

The objective of the policy program is to enhance and extend CAAT's visibility at the EU legislator level and to provide information, primarily to the EU Parliament but also to other EU and National institutions as appropriate. In order to accomplish this objective, the following activities will be undertaken:

- Dissemination and support of CAAT's innovation and scientific activities in Europe by arranging face-to-face meetings with Members of the European Parliament (MEPs) and CAAT representatives
- Catching MEPs' attention on CAAT's rational, science-driven approach to chemical safety testing and animal welfare issues
- Attending specific European Parliamentary (EP) related events
- Close follow-up on the MEPs' work at the Committee level and at Plenary Sessions at the Parliament in Brussels and Strasbourg.
- Communicating CAAT's position to MEPs on draft EU legislation for amendments when proposed by the European Commission or MEPs
- Informing CAAT on first-hand news from the EP and EC on future EU policy programs (e.g. Horizon 2020), available EU funding, or potential EU collaborations with CAAT
- Development of IT tools to keep policy makers and CAAT informed of their respective agendas
- Identifying partnerships with lobbying organizations, especially CAAT sponsors and partners, to create synergies
- Providing scientific and policy perspectives of the EU to the US, and vice versa

Contact: François Busquet <caat-eu-policy@uni-konstanz.de>

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Applicability of Validated and Adopted Skin & Eye Irritation In Vitro Methods to Assess and Classify Detergent Mixtures under EU CL

In 2008, the EU adopted the Regulation on Classification, Labelling and Packaging of substances and mixtures (EU CLP), which introduces the UN Globally Harmonized System for classification (GHS). While this regulation fully applies to chemical substances since December 2010, companies will have until 1 June 2015 to reclassify their mixtures according to the GHS system. Amongst other requirements, a new calculation method for default classification of mixtures was implemented in the CLP regulation.

The detergents and maintenance products industry has carefully assessed the impact of the EU CLP Regulation on consumer product labels and came to the conclusion that consumers will face several label changes in particular regarding irritant effects. Indeed, the use of the default calculation method for irritant / corrosive effects might result in the over-labelling of many products currently not requiring classification according to consistent animal, *in vitro* and human experience data. Such over-labelling could confuse end-users and lead to the underestimation of real risk when this is merited due to trivialization of labelling.

On the other hand, the EU CLP provides the opportunity to make use of testing strategies to classify mixtures which include the use of weight-of-evidence and of validated and suitable alternative methods, in order to ensure accurate classification and avoid unnecessary animal testing. Although several *in vitro* tests for eye and skin irritation and/or corrosion have been validated and/or adopted at the OECD level, many of them, especially in the area of skin irritation and corrosion have undergone validation studies based mostly on single entities substances, so that their suitability to assess mixtures has not been addressed or only to a limited extent.

In order to ensure appropriate product classification, the European Detergent Association A.I.S.E. initiated in 2010 a scientific program to investigate the applicability of validated and adopted *in vitro* skin & eye irritation/corrosion methods to

reliably classify detergent and cleaning product formulations. The program addresses skin irritation, eye irritation/corrosion, and skin corrosion & eye effects for extreme pH products. Each area includes a review of existing literature and existing data shared by A.I.S.E. member companies, and the practical testing in selected *in vitro* test methods of representative formulations supported by existing animal and/or human data. The knowledge gained through the program will be used to develop guidance on the use of the most suitable *in vitro* methods / strategies for classification and labelling of detergent and cleaning products and/or make recommendations on future investigations and/or developments.

Chantra Eskes, SeCAM and Elodie Cazelle, A.I.S.E.

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Meetings calendar

INTERDISCIPLINARY TOXICOLOGY CONFERENCE TOXCON 2012 & ADVANCED TOXICOLOGY COURSE

The Slovak Toxicology Society SETOX in cooperation with the Institute of Experimental Pharmacology & Toxicology, Slovak Academy of Sciences invites you to The Interdisciplinary Toxicology Conference TOXCON 2012 & Advanced Toxicology Course that will be held in The High Tatras, Slovakia from August 27 to August 31, 2012. The meeting will start with the "Advanced Toxicology Course" in which toxicological experts will impart their knowledge to young scientists. The participants of the course will receive comprehensive information on Intracellular signalling pathways and cell death, Immunotoxicology, Toxicity testing using alternative methods and will be trained in a practical exercise in the work with *in vitro* reconstructed human tissue models.

The main topics of the following TOXCON 2012 conference will be environmental and industrial toxicology, experimental and clinical toxicology and important problems of military toxicology. The individual conference contributions (lectures, poster presentations, working groups) will be spread over 3 days of the rich scientific program. Each day will be dedicated to one central topic presented by a highly experienced key-note speaker.
: http://www.toxcon.sav.sk/

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ESTIV 2012
October 16-19, 2012
Lisbon Portugal
http://www.estiv2012.com/

Why should you go on 16-19 October to ESTIV2012 in Lisbon , Portugal?

- Because of the cutting-edge topics on:
  - non-animal approaches for toxicity testing
  - physiologically relevant biomarkers profiles
  - molecular mechanisms and pathways
- to learn more about the economics of alternative methods
- to get hands -on experience with computerized *in vitro – in vivo* extrapolation strategies
- to meet senior scientists in the field and discuss with colleagues
- to participate in the special student session and/or win the student's award for the best poster/oral presentation
- to enjoy the Portuguese 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

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May 14-15, 2013, IVTIP organizes a 2 day open meeting in Southampton, UK
"2013: State of the art on in vitro alternative methods from an industrial point of view: ready for regulation? "

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Recent publications of ESTIV members

AXLR8 Public Service Review:
http://axlr8.eu/assets/axlr8-update-2012.pdf

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

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