European Society of Toxicology *In Vitro*

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Newsletter

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Editorial

Dear ESTIV members,

The 2010 Linz Congress,held in cooperation with ESTIV and EUSAAT was really succesfull. With more than 300 participants from 30 nations it was the **16th** ESTIV International Congress on In Vitro Toxicology, the **13th** Annual Congress of EUSAT and the **16th** Linz Congress on Alternatives to Animal Testing.
I would like to congratulate to the students who won the ESTIV awards: **Nathalie Lambrechts** (VITO-CARDAM) from Belgium for winning the ESTIV/Elsevier Young Scientist Award with the best oral presentation, **Mariliis Sihtmäe** (National Institute of Chemical Physics and Biophysics) from Estonia, for ESTIV/Elsevier best poster presentation and **David Pamies,** Bioengineering Institute, Miguel Hernandez University, Spain for winning the ESTIV award Student Session 2010 for the best presentation.
I hope the students' meeting, organised by Margit Heinlaan and Maria Laura Scarino, who presented the session, strengthened the connections between students and encouraged them all to continue with their research and studies in the field of *in vitro* toxicology and also find motivation to be active in organising new activities with other ESTIV members.
Moreover I want to wellcome the new ESTIV board members: Leonora Buzanska, Erwin Roggen, Asa Svenningsen, Laura Suter-Dick and Mathieu Vinken.
Erwin Roggen will organize the ESTIV 2012 Congress. Before this event we will have several opportunities to discuss the progress of our work. See the long list of future events in this Newsletter. Thank you very much to all of you who contributed to make this issue more informative and interesting.

I am looking forward to hearing from you,

Francesca Caloni

Message from the president

Dear colleagues

The turnover of the year gives us the opportunity to look back on what we left behind in 2010. Improved safety assessment of chemicals with the use of less animals remains the driving force of ESTIV. ESTIV has contributed in 2010 as an exchange platform among scientists. We organized a workshop on the use of serum free cultures in Denmark and the ESTIV2010congress in LINZ was organized jointly with the colleagues from EUSAAT and LINZ2010. Enjoying the Austrian hospitality, we have witnessed the scientific progress made in different areas of test development and implementation. We can also look forward to promising future developments such as use of stem cells, "system wide-omics" and computational toxicology. We should however remain alert for the need of quality control and harmonisation, validation of alternative methods should be speeded up and, where possible , the use of alternatives eg. for antibody production or for the use of animalserum in cultures, should be a further priority. One of the most important evolutions is that *in vitro* toxicology is being transformed into an upfront science which attracts young scientists and builds bridges to other scientific disciplines. ESTIV will strongly support these movements by encouraging involvement of young and talented scientists.
We feel the need to extend our collaborations in Europe and also towards other disciplines. ESTIV plans active engagement in different international and national initiatives within the EU. The joint workshop at LINZ that we organized together with the AXLR8 consortium actively seeked exchange with US colleagues. At the last general assembly we have renewed the membership of the executive committee of ESTIV. We are grateful to the members that left and did an excellent job : Dr. Van der Valk (vice president), Dr. Sjeram (Newsletter), Dr. Heinlaan (students representative). We welcomed the new board members: Dr. Buzanska, Dr. Vinken (student's

issues), Dr. Roggen (organizer of ESTIV2012), Dr. Svenningsen and Dr. Suter-Dick. Dr. Eskes will be our new vice- president and as you notice Dr. Caloni takes care of the newsletter. This team is committed to the ESTIV society and looks forward to work with you and further stimulate the growth of *in vitro* toxicology.
Greet Schoeters

President of ESTIV

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LINZ AWARDS 2010

ESTIV award for the best presentation in the ESTIV Students Session

The **ESTIV award** for the best presentation in the ESTIV Students Session was given to **David Pamies** (Bioengineering Institute, Migel Hernandez University, Alicante/Spain) for his presentation "*Silencing of neuropathy target esterase (NTE) causes changes in gene expression during the early stages of differentiation*". The prize was 250 Euros

ESTIV *and* Elsevier Young Scientist Award

ESTIV and Elsevier Young Scientist Award for the best oral presentation went to **Nathalie Lambrechts** (VITO-CARDAM, Mol/Belgium) for the lecture on "*Assessment of chemical skin sensitizing potency by an in vitro assay based on human dendritic cells*". The prize was 500 Euros and one year prescription to the Elsevier journal *Toxicology in vitro*.
ESTIV and Elsevier Young Scientist Award for the best poster presentation went to **Mariliis Sihtmae** (National Institute of Chemical Physics and Biophysics, Tallinn/Estonia) for the Poster Mariliis Sihtmäe, Irina Blinova, Villem Aruoja and Anne Kahru: "Toxicological information on REACH-relevant chemicals published in Russian language". The prize was 500 Euros and one year prescription to the Elsevier journal *Toxicology in vitro*.

EUSAAT Poster Awards

The Linz 2010 **EUSAAT Poster Awards** were given to the authors of 3 posters: **Felix Spöler** (Institute of Semiconductor Electronics, RWTH Aachen University, Aachen/Germany), **Markus Frentz** and **Norbert F. Schrage** (Aachen Centre of Technology Transfer in Ophthalmology (ACTO), Aachen/Germany), for their poster: "*Improving the sensitivity of organotypic in vitro assays for eye irritation testing: The Ex Vivo Eye Irritation Test (EVEIT)*"

Michael Gülden and **Hasso Seibert** (University Hospital Schleswig-Holstein, Kiel/Germany) for their poster: "*Concentration or dose: What is the proper measure for quantitative in vitro - in vivo extrapolation of toxic potency?*"

Daniel Mueller, **Saskia Mueller**, **Georg Tascher** (Saarland University, Biochemical Engineering, Saarbruecken/Germany), **Daniel Knobeloch** (Department of General, Visceral and Transplantation Surgery, Charité Campus Virchow Clinic, Berlin/Germany), **Andreas K. Nuessler** (Dept. of Traumatology, TU Munich, MRI, Munich/Germany), **Elmar Heinzle** and **Fozia Noor** (Saarland University, Biochemical Engineering, Saarbruecken/Germany) for their poster: "*Sensitive assessment of drug-induced changes in primary human hepatocyte metabolome using a combination of GC-MS and multivariate statistics*".

ALTEX AWARD 2009

The ALTEX award fort he 2009 main article in ALTEX was given to **Costanza Rovida** for the article "Reevaluation of animal numbers and costs for *in vivo* tests to accomplish REACH legislation requirements for chemicals – a report by the Transatlantic Think Tank for Toxicology (t4)".

The Dieter Lütticken Award

The Dieter Lütticken Award for development of *in vitro* bovine respiratory tract organ culture model goes to **Dr. A.W. (Dan) Tucker**, Department of Veterinary Medicine, University of Cambridge, Cambridge/United Kingdom.

The Award of the Doerenkamp-Zbinden Foundation

The Award of the Doerenkamp-Zbinden Foundation was given to **Prof Dr Michael Balls**, CBE MA DPhil FIBiol, Zoologist and Emeritus Professor of Medical Cell Biology at Nottingham University, Nottingham/UnitedKingdom.

The Doerenkamp-Zbinden Medal of Honour

The Doerenkamp-Zbinden Medal of Honour was awarded to **Prof. Dr. Walter Pfaller**, MD, Innsbruck Medical University, Department of Physiology and Medical Physics, Innsbruck/Austria, and Vice-President of EUSAAT.

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REPORT FROM TOXCON 2010

The Slovak Toxicology Society SETOX and the Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, organized the 15th Interdisciplinary Toxicology Conference TOXCON 2010. The Conference with the motto "Borderless Toxicology" was held at the High Tatras, at Stará Lesná – Hotel Academia, Slovakia, from September 6 to 10, 2010.
TOXCON 2010 was held under the auspices and support of the Federation of European Toxicology Societies EUROTOX and Visegrad Fund. Meetings of Slovak and Czech toxicologists which have been organized since 1996 changed to real international conference with more than 170 participants from Visegrad countries (Slovakia, Czech Republic and Poland), further Germany, Austria, Italy, Lithuania, Iran, India and USA.

TOXCON Participants

TOXCON 2010 was dedicated to the memory of **Prof. Helena Rašková**, doyen of Czech and Slovak pharmacology and toxicology.
An integral part of the conference was the educational course for young toxicologists called "Advanced Toxicology Course".
Excellent European toxicologists gave lectures on various topics. **Prof. Horst Spielmann** (Free University, Berlin, Germany) dealt with basic principles and methods in toxicology with emphasis on necessity to regulate production and use of chemicals which could have unfavorable effects on living organisms. **Prof. Emanuela Corsini** (University of Milan, Italy) gave lecture on immunotoxicology, immunosuppression, cancer sensitivity and use of *in vitro* procedures in immunotoxicology. **Dr. Helena Kandárová** (MatTek, In Vitro Life Sciences, Bratislava, Slovakia) concerned with validated and pre-validated alternative methods in toxicology.

Dr H. Kandarova

Within the practical training, Dr. Kandarová together with her colleague **Dr. Silvia Letašiová**, demonstrated *in vitro* skin corrosion test (OECD 431). **Dr. Michal Dubovický** (Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Bratislava, Slovakia) gave lecture on basic principles in developmental neurotoxicology and use of laboratory animals in evaluation of adverse effects of chemicals on developing brain. Lectures presented within the educational course were issued by the Slovak Toxicology Society SETOX in the form of textbook named "Advances in Toxicology". The textbook is an appropriate study material not only for young toxicologist but also for scientists from other related biomedical subjects.
In the Conference Opening Ceremony, **Prof. Daniela Ježová**, vice-president of the Slovak Academy of Sciences, **Prof. Radomír Nosáľ**, director of the Institute of Experimental Pharmacology and Toxicology, **Dr. Mojmir Mach**, member of Executive Committee of EUROTOX and **Dr. Jana Navarová**, president of SETOX, welcomed all participants of the Conference. Delegates of Middle European toxicology societies, i.e. **Dr. Věra Štetinová** from Czech society, **Prof. Wojciech Wasowicz** from Polish Toxicology Society and **Prof. Wilfried Bursch** on behalf of Austrian Toxicology Society ASTOX welcomed participants and thanked to organizers for kind invitation. Organizers and participants of the Conference were pleased by participation of **Prof. Ivan Raška**, a son of Prof. Rašková, who is a head of the Institute of Cell Biology and Pathology, Charles University and Institute of Physiology, Czech Academy of Sciences, Prague. He was giving lecture dedicated to his mother on Hutchinson-Gilford Syndrome. Lectures and posters presented at the Conference showed up-to-date results and knowledge from the field of toxicity mechanisms, alternative *in vitro* methods, xenobiotic metabolism, pharmacotoxicology, cytotoxicity, carcinogenicity and genotoxicity,

environmental, military, occupational and developmental toxicology as well as recent analytical methods used in toxicology. An excellent and challenging lecture on detection of xenobiotics by means of HPLC-MS method was giving by **Ing. Robert Mistrik,** a laureate of the prize of the Head of the Year 2008 in Slovakia. **Prof. Manfred Liebsh** from the Federal Institute for Risk Assessment (ZEBET), Berlin, Germany, concerned with alternative methods in toxicology. Military toxicology represented a significant part of the Conference. In session chaired by **Prof. Jiří Kassa**, recent knowledge from the field of development and use of protection against chemical warfare agents were presented and discussed. Abstracts of presented lectures and posters were published in the journal Interdisciplinary Toxicology issued by SETOX and the Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences in Bratislava. Thanks to support of Visegrad Fund, the best young scientists were awarded. Main award for the best oral presentation went to young toxicologist from India, **Dr. Tamanna Jahangir.** Prize for the best poster presentation went to **Dr. Tomáš Perečko** from the Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Bratislava.

Fist time in history of TOXCON, official meeting of the delegates from Middle European Toxicology Societies (Slovakia, Czech Republic, Poland and Austria) was held at the Conference. Representatives of individual societies presented profiles and activities of their societies. Platform for further international cooperation and common applying for financial support in the form of scientific and mobile projects has been established.

Social program was an important part of the Conference. Social evening, barbeque as well as hiking to the High Tatras mountains created an atmosphere for informal discussions, scientific and friendly contacts as well as for nice relax after tiring scientific sessions. More information about the conference and it program is available at: http://www.toxcon.sav.sk/

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Workshop on Regulatory Assessement of *in vitro* data on Skin Corrosion and Irritation within the European framework

14-15 September, Bern, Switzerland

Participants of the Bern Workshp

On the 14 & 15 September 2010, the Swiss Federal Office of Public Health and SeCAM organized together with ECVAM, BfR and the OECD the workshop on "Regulatory Assessment of *In Vitro* Data on Skin Corrosion & Irritation within the European framework".

The workshop took place in Bern, Switzerland and comprised 40 participants coming from various European countries. Representatives of the major stakeholders involved in the process going from the testing to the assessment of *in vitro* data for hazard identification were present including regulatory agencies, ECVAM, OECD, industries from various sectors, CROs, European associations and scientists with expertise on skin irritation & corrosion *in vitro* methods. Main agreements were achieved and key recommendations were made regarding:

- the information requirements considered useful for the assessment of *in vitro* data on skin corrosion & irritation,
- the applicability of *in vitro* skin corrosion data to the Globally Harmonised System for Classification and Labelling as introduced in the new EU CLP Regulation;
- the applicability of integrated testing strategies for determining skin corrosion & irritation hazards, and
- the applicability of adopted *in vitro* tests to assess mixtures, preparations and dilutions.

Overall the 'Bern Workshop' represented a forum for truly open discussions of stakeholders who expressed and exchanged their points of views with a real open mind. In particular, discussions no longer addressed the regulatory acceptance but the regulatory assessment of *in vitro* data demonstrating there is already full acceptance of alternative methods to identify skin irritancy and corrosion hazards. Some countries have

pioneered by appointing National Coordinators dedicated to *in vitro* data assessment.

Unfortunately, such initiatives are still seldom if not unique, albeit they would benefit the new generation to be prepared to the new way of hazard and risk assessment approaches with no animal data.

Chantra Eskes
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CAAT's Europe Workshop on Teaching and Education of 3Rs approaches 25-27 October 2010, Kostanz

Participants to the Workshp on Teaching and Education of 3Rs

The workshop **on Teaching and Education of 3Rs approaches** organized by the Center for Alternatives to Animal testing –Europe (CAAT) and the Transatlantic Think Tank for Toxicology, aimed to bring together academic teachers indifferent areas of 3rs for exchange of knowledge to support collaboration, to exchange experiences, lecture contents as well as didactic strategies.

Teaching is today even more important because of the rapid development of new *in vitro* and *in silico* methods and the evolution of the idea of the 3rs in the context of the paradigm shift in toxicology according National Academy of Sciences vision for a toxicology for the 21st century.

Teaching 3Rs today should address alternative methods, risk assessment, critical discussion of the predictive power of current approach and the ethics underling the 3Rs. The three chairs for alternative methods established at the Universities of Konstanz, Utrecht and Johns Hopkins established by the Doerenkamp-Zbinden Foundation have put forward a vision of a collaboration of academic teachers in the field, building up a communication platform sharing contents of lectures and creating a central depository of teaching material disseminating methodical and theoretical concepts, addressing regulatory as well as technical obstacles and contributing thereby 3Rs research.

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WORKSHOP Toxicity Testing in the 21st Century and Alternative Methods Milan November 26th, 2010

Toxicity testing is posing increasing challenges to health care, industry, and research communities, as well as the society as a whole. The complexity of issues at stake is matched by the recognition of theoretical, operational, methodological, and economical constraints that may hamper the efficacy of current procedures in toxicity testing. Likewise, the same constraints have been a powerful drive for the development of new methods, technologies, and scientific approaches to tackle difficulties and overcome bottlenecks. The importance of understanding the possible adverse consequences of human and other living systems exposure to new agents, the recognition that individuals are exposed to complex mixtures of toxic compounds in the real world, the implementation of the REACH regulation in the EU, are just a few examples of the challenges that demand further developments in toxicity testing at many levels. Initiatives are ongoing worldwide to support the advancements of our theoretical and technological tools for the evaluation of the hazards posed by the large number of existing agents. One such initiative, representing a key contribution owing to its wide scientific perspective and societal oversight, is the report entitled "*Toxicity testing in the 21st century - A vision and a strategy*", issued by the US National Research Council. Building up on recent advances in bio-medicine and biotechnology, the report describes a transformative paradigm shift in toxicity testing, "...(1) to provide broad coverage of chemicals, chemical mixtures, outcomes, and life stages, (2) to reduce the cost and time of testing, (3) to use fewer animals and cause minimal suffering in the animals used, and (4) to develop a more robust scientific basis for assessing health effects of environmental agents." (Report, p. 3). In order to

contribute to discussions aimed at supporting thinking, research activities and action in the area of toxicity testing, the Italian Platform on Alternative Methods (IPAM) organized a workshop entitled "***Toxicity Testing in the 21st Century and Alternative Methods***".

The workshop was intended to meet the interests of the scientific community at large, the industrial world (both providers and end-users of technologies), as well as decision-makers and political consultants..

The opening session was devoted to setting the frame of the workshop, by presenting key elements of its scope and contents. This session included an introduction by the President of IPAM, a presentation of the report issued by the US NRC, the description of challenges and opportunities for alternative methods in toxicity testing, as well as the bottlenecks of toxicity testing within the perspective of alternative methods. The first session was devoted to the core scientific and technological issues, with presentations of tools available for the paradigm shift in toxicity testing. The talks focused onto the use of most recent technologies and approaches of systems biology in toxicity testing (transcriptomics, proteomics, metabolomics as well as *in silico* computational approaches). The second session was devoted to selected existing cases of toxicity testing. A round table completed the workshop, and was aimed at gathering key stakeholders, to discuss perspectives and difficulties in implementing the paradigm shift in toxicity testing approached in the workshop.

Isabella De Angelis

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Third OSIRIS Training Course

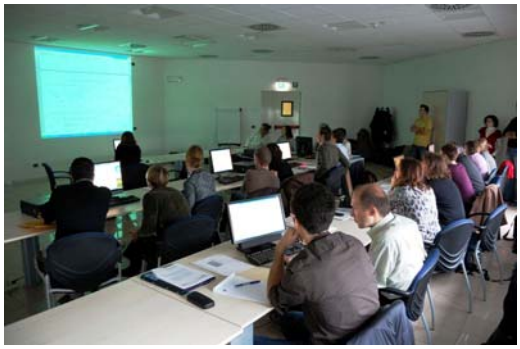
OSIRIS aims to develop Integrated Testing Strategies (ITS) for the risk assessment of chemicals, increasing the use of non-testing information for regulatory decision making and thus minimising the need for animal testing. ITS shift risk assessment from a "box-ticking" approach with extensive animal testing to a more efficient, context-specific and substance-tailored approach. the OSIRIS ITS Training Courses specifically target professional end-users in industry and regulatory agencies involved in the submission and review of chemical risk assessments.

They aim to introduce the main concepts underlying the design of ITS, giving particular emphasis on non-testing methods such as QSAR (qualitative or quantitative structure-activity relationships), chemical grouping and read-across, as well as to provide training on the practical application of software tools that facilitate the optimisation and application of ITS.

The Third OSIRIS Training Course has been held on 3-5 November 2010 at the Mario Negri Institute for Pharmacological Research in Milan, Italy. The first day started with an introduction on risk assessment, risk analysis, risk management and ITS within the REACH regulatory framework. The approaches of read-across and exposure-based waiving, components of the ITS, were explained and decision analytic modelling under REACH was introduced for the case of genotoxicity. The concept and functions of the OSIRIS ITS Webtool and the integrated Chemical Space Navigation Tool were presented.

The OSIRIS Webtool implements the ITS components developed within the project and will be made available to the public.On the second day, different aspects of ITS for the environmental endpoint bioconcentration factor (BCF) and the human health endpoint genotoxicity were addressed. An overview was given of different types of alternative (chemistry-driven and *in silico*) modules for environmental bioaccumulation assessment in the ITS framework. Different tools for BCF prediction were compared – including the software ChemProp –, emphasising uncertainty and applicability domain issues. The use of *in vitro* methods in bioaccumulation assessment was analysed. Moreover, the OSIRIS ITS on BCF implemented in the Webtool was demonstrated. Regarding the endpoint genotoxicity, an overview was given of the use of bacterial and mammalian *in vitro* test methods and *in silico* methods for industry in house decision making as well as of the regulatory use of genotoxicity data. Available *in vitro* and *in silico* tools to assess mutagenicity and cancerogenicity and new future perspectives were analysed. The new DNA-binding profiler in the OECD (Q)SAR Application toolbox was demonstrated and the ITS scheme for genotoxicity developed within OSIRIS was presented. The third day was devoted to the practical application of QSAR and expert systems tools. Hands-on experience was provided to the course participants for different *in silico* tools to predict the BCF. The results were compared and aspects of uncertainty were discussed. After an introduction on the principles of QSAR and available software tools, a workflow for the assessment of the genotoxic potential of

chemicals by means of in silico methods was presented. A case study provided hands-on experience on using different in silico prediction tools for genotoxicity. More information on OSIRIS is available at www.osiris-reach.eu .



OSIRIS Workshop

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AXLR8 2010: progress report

The EU-sponsored coordination project *AXLR8* is pleased to announce the availability of the publication *Alternative Testing Strategies: Progress Report 2010*. This report includes:
An introduction to the *AXLR8* project
An update on the activities and achievements of 3Rs-oriented research funded under the Health theme of the European Union's 6th and 7th Research Framework Programmes during the year 2009. Contributions from EU member state 3Rs centres and from international colleagues who participated in the 2010 *AXLR8* Scientific Workshop and public Info Forum
Observations by the independent *AXLR8* Scientific Panel on the status of EU and international 3Rs research and development activities. Suggestions for near-term research priorities to advance the science of toxicity testing, as well as EU legislative mandates in relation to the 3Rs. Given the substantial and increasing global investment in research aimed at developing new safety assessment methods and implementing the 3Rs in toxicology, there is a recognised need for better information exchange and transparency in this research area. *AXLR8* provides the tools for effective real-time dialogue, information exchange, problem solving, and international cooperation.

The *2010 Progress Report* may be downloaded electronically from **AXLR8.eu/publications**. In addition, a limited number of hard copies are available upon request from the **AXLR8 secretariat**

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Video of CAAT Workshop "21st Century Validation Strategies for 21st Century Tools" Available Online

The CAAT workshop, 21st Century Validation Strategies for 21st Century Tools, was held July 13th and 14th, 2010, in Baltimore, Maryland. The full listing of speakers and topics, along with Quicktime video of the event is available on the CAAT website at:
http://caat.jhsph.edu/programs/workshops/july13validation.htm.

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American Society for Cellular and Computational Toxiology now accepting new members

ASCCT – a new scientific society - is seeking the participation and support of institutions, companies, and organizations with an interest in promoting non-animal toxicology. The ASCCT was formed in 2010 to capitalize on a recent surge in the demand for more human-relevant methods to assess hazards of chemical exposure, and to provide a complement to well-established *in vitro* societies around the world such as ESTIV.

The society aims to provide an organized forum for discussion of cellular (*in vitro*) and computational (*in silico*) toxicology approaches especially as replacements for animal-based methods. Through its meetings and activities, the Society will promote collaboration among scientists and regulatory professionals working in different fields to facilitate the development, acceptance and routine use of these methods. The goal of bringing together expertise from a variety of backgrounds is reflected in the selection of the Board of Directors, which comprises President Rodger Curren and Treasurer Erin Hill of the Institute for In Vitro Sciences and Secretary Kristie Sullivan of the Physicians Committee for Responsible Medicine. Thomas Hartung of Johns Hopkins University and CAAT, Melvin Andersen of The Hamner Institute for Health Sciences, Chihae Yang of Altamira, LLC, and Chad Sandusky of PCRM rounding out a diverse and dynamic group. The board is currently considering activities for 2011 and would welcome new member's input.Individuals can join ASCCT at its web site, www.ascctox.org. Memberships are offered for students, individuals, and Founding Member organizations. All members will receive a quarterly e-newsletter, a discounted subscription rate to the

journal ALTEX, and discounted registration for ASCCT events. Founding Member organizations will also receive a space for their logo on the ASCCT site and other advertising materials, and one lifetime membership within their organization. Please consider joining to help build a strong, active society and contribute to the future of toxicology.

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Meetings calendar

6th conference of Predictive human toxicity and ADME/Tox studies from the Mondial Research Group January 27th-28th, 2012 in Sheraton Hotel, Airport Zaventum, Brussel
http://www.mondialresearchgroup.com/index.php?whereTo=humt11

IVTIP Spring 2011 meeting in collaboration with ESTIV and CAAT on"*In vitro* reconstructed human tissue models as alternatives to animal testing: applicability and limitations"
26-28 April 2011, Novotel, Monte Carlo, Monaco

The meeting aims at having test users to present their experiences with the available test that could help define the applicability and limitations of the tests.
www.ivitip.org; www.estiv.org; caat.jhsph.edu

Third International Conference on Alternatives for Developmental Neurotoxicity Testing (DNT)
11-13 May, 2011
Ispra, Italy

http://ihcp.jrc.ec.europa.eu/events_workshops/dnt3conference

SETAC Europe 21st Annual Meeting
Ecosystem Protection in a Sustainable World: a Challenge for Science and Regulation
Milan, Italy, 15-19 May 2011,
http://milano.setac.eu/?contentid=291

DIOXIN 2011 - 31st International Symposium on Halogenated Persistent Organic Pollutants. DIOXIN 2011 will take place from 21-25 August 2011, in the beautiful city of Brussels, Belgium. DIOXIN 2011 will focus on the science of persistent organic pollutants and will include the entire pathway from environmental exposures until health effects and impact assessment. ESTIV will organise a specific session on the use of alternative methods for toxicological assessment of important environmental chemicals such as POPs. If you are interested , invitations for abstracts will be sent out soon. News on DIOXIN 2011 can be followed on the web site http://www.dioxin2011.org/ and a link will be available soon at the ESTIV web site

8th World Congress on Alternatives & Animal Use in the Life Sciences 21-25 August, 2011
Montréal, Quebec, Canada
http://www.ccac.ca/en/CCAC_Main.htm

47th Congress of the European Societies of Toxicology (EUROTOX 2011) Palais des Congrès, Paris, France,
August 28th to 31st.
http://www.eurotox2011.com

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Workshops calendar

Critical Evaluation of the Use of Dogs in Biomedical Research & Testing:
A CAAT Workshop
On January 12 and 13, 2011, CAAT will hold a workshop bringing together investigators who use dogs as disease models to present their research while fostering dialogue on the implementation of alternative models. Representatives from the US Food and Drug Administration (FDA) will be invited to review data obtained from dogs submitted in support of drug submissions. Veterinarians and experts in dog behavior will be invited to discuss the welfare issues associated with research and testing on dogs.
The workshop will take place at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. Further details will be posted on the CAAT website: http://caat.jhsph.edu
For more information contact Joanne Zurlo, CAAT Director of Science Strategy (jzurlo@jhsph.edu)

CAAT-EU / *ecopa* – Workshop: Implementation of the new EU Directive 2010/63/EU on the protection of animals used for scientific purposes: Opportunities for the 3Rs January 31 – February 2, 2010 in Berlin, Germany.

On 8-9 March 2011, an **OSIRIS Stakeholder Workshop** will be held at the Helmholtz Centre for Environmental Research – UFZ in Leipzig, Germany. Key stakeholders and experts from regulatory authorities, industry and academia are invited to test the methods and ITS developed within the project.

Courses calendar

Course in Statistics for toxicologists 21/11/2011
Focus on dose response The objective of the course is to provide knowledge on dose response modelling in toxicology, including benchmark dose analysis, for risk assessment of chemicals. The course is intended for PhD students, post docs, senior scientists and other professionals. Funding for travel, subsistence and course fee is available for PhD students and post docs. The course is organised by RA-COURSES, a project funded by European Union Marie Curie Actions. For application and further information: **Application deadline is January 21, 2011**
www.cascadenet.org/~RA-COURSES

XCellR8 Cell Culture Training Calendar 2011
Introductory Cell Culture Techniques:
A strong foundation in core techniques;latest best-practice; troubleshooting tips. . 1-2 March; 7-8 June; 29-30 November
Primary Cell Culture:
Key techniques including isolation , culture conditions,3-D systems and extracellular matrices..
12-13 July
Introduction to Bioreactors:
Includes clonal selection and expansion; key procedures in bioreactor set-up and optimal use. 22-23 March; 11-12 October
Fast Train Events:
1-day essential overview of key topics: seminars, practical demonstrations; targeted exhibition. Ideal introduction or update.
Further information on www.x-cellr8.com

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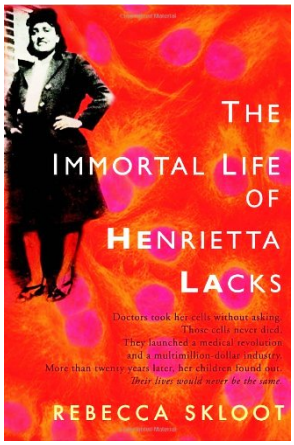
Book REVIEW

The immortal life of Henrietta Lacks
by Rebecca Skloot, Crown Publishers, New York, 2010



After many attempts, Mary Kubick, assistant of dr. George Gey, was finally able to keep human cells alive in culture. This happened in 1951 and the cells came, as later appeared, from a malignant adenocarcinoma from which a young black woman suffered. Despite treatment, she died shortly after because of many metastases from this aggressive tumour. From that moment in the book, two story lines appear; that of the success of the first human cell line, the HeLa cell line, and that of the family of the deceased donor, originally unaware of the effect of the cells on medical progress. The book discusses the lack of medical ethics at that time and the reason why the name was released of the donor: Henriette Lacks. The author also discovers that although many companies got rich through new therapies with the help of the HeLa cells, the family of Henriette Lacks lived in poverty and had, ironically, limited to no access to medical care. Only twenty years after the HeLa cells started their advance in research, Henriette Lacks' relatives discovered the details, which had a dramatic effect on their lives. The book further describes the danger of using the very immortal HeLa cells: already in 1966 dr. Stanley Carter presented the "HeLa bomb", the fact that many other cell lines were contaminated, or had been taken over by the HeLa cells, which are able to be passed on by air. A property of these cells that we still have to take into account, nowadays.I received this book as a good-bye present when I left the ESTIV board. I am very pleased with this book that at moments reads like a thriller. Actually, every *in vitro* scientist should have read this book, since it discusses not only the story of the first and probably mostly used human cell line, but also the practical aspects of culturing human cells, and the ethical aspects of procuring, using and making profits with these cells.

Rebecca Skloot has succeeded to write a book that is not only of interest to the scientific world, but is also accessible to the non-scientific reader who is interested in the background of cells that were unknowingly taken from a poor young black woman and have, since then, saved many lives.

Jan van der Valk

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MESSAGE FROM PhD STUDENTS

On November 22nd, I defended my PhD thesis at the University of Antwerp; entitled: **Towards a mechanism-based *in vitro* screening assay for chemical-induced skin sensitization**

My promotor is Prof Dr Greet Shoeters.
From now on, I will continue working on this topic as a post-doc on VITO, with the support of the Flemish Agency for Innovation through Science and Technology.
The *in vitro* assay on which the PhD was based upon, is called VITOSENS. The model consists of a human primary dendritic cell model, derived from CD34+ progenitors in cord blood. Before my PhD started, novel gene markers for chemical skin sensitizing exposure have been identified in these cells by microarray technology. The first major finding of the PhD project involves the establishement of a functional role of a selection of the VITOSENS markers in the skin sensitization process. Furthermore, the most discriminating VITOSENS markers, CREM and CCR2, appear to be non-responsive to an inflammatory, non-sensitizing stimulus such as Lipopolysaccharide S. These findings indicate that the markers might represent a sensitizing-specific signal.
The other main result that was obtained in the thesis, includes the potential of VITOSENS to rank sensitizing chemicals according to their skin sensitizing potency. The 2 parameters that allow this classification are the presumably sensitizing-specific gene expression fold changes of CREM and CCR2, and the concentration that induces 20% cytotoxicity. This might not be suprising since cytotoxicity *in vitro* is often called a measure to danger signals. To summarize, both the CD34+ dendritic cell model that closely reflects the human standard, and the novel discriminating markers for skin sensitization, which seem to be involved in the molecular mechanisms underlying skin sensitization, render VITOSENS highly specific for skin sensitizing substances. The assay allows to estimate both skin sensitizing hazard and potency, and therefore may contribute to further risk assessment. Based on these findings, VITOSENS is a promising, mechanism-based *in vitro* assay to serve in an integrated approach that mimics all aspects required to induce skin sensitization in susceptible individuals. During the next 2 years, we will try to further refine and quantify the parameters that are responsible for skin sensiting potency. As such, we want to construct dose-response curves for these variables from which we can then derive a human 'no-expected-sensitization-induction-level' for skin sensitizing chemicals.

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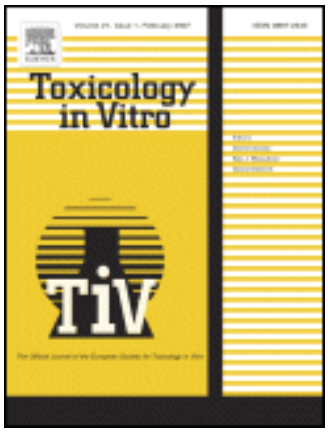
Toxicology *in Vitro*



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

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Sjeng Horbach

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ESTIV has an e-mail list, which has the potential to be a very valuable resource but so far has not been taken advantage of. There are many types of questions that you could pose to the list, whether you are a junior researcher, or a senior scientist. In order to send a message to all ESTIV members on the list (at present 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 j.b.f.vandervalk@uu.nl, and your name will be added.

Jan van der Valk

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