



European Society of Toxicology *In Vitro*

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Newsletter

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Editorial

Dear ESTIV members,

I would like to congratulate to all ESTIV members receiving awards for their achievements in the field of toxicology *in vitro*. Helena Kandárová, Dagmar Jírová, Manfred Liebsch, Margit Heinlaan, Anne Kahru, Sarah Snykers and Eugenio Vilanova are among them.

In September we will meet again at the ESTIV2008 congress, to enjoy more personal scientific discussions and to meet new members. Cecilia Clemedson and Barbro Ingemarsson are doing great work in coordinating all the members involved in the organisation of this event. I would like to invite you to join the meeting presenting your work and bringing with you enthusiastic young scientists and fresh ideas. The scientific program and invited speakers are promising interesting and exciting sessions.

I wish you all great success at your research work and I am looking forward to hear from you soon.

Thank you all for your contribution,

Sonja Jeram

Message from the President

Dear colleagues,

A few important events have happened since we have published our last Newsletter in July. Most importantly we have held the 6th World Congress on Alternatives and Animal Use in the Life Sciences (WC6) in Tokyo last August. It was a remarkable event and all of you, who participated, will agree that this was the highlight for the 3Rs movement in the past year. I have tried to capture some of the atmosphere in my description in the

Newsletter. I am particularly happy that I have received some very impressive photographs from colleagues to illustrate the specific ethical, cultural and religious importance of animals that are being used for scientific purposes. In Japan, a country in which every stone and tree is respected as an individual, animals are even more respected as the closest companions of humans.

Quite unexpectedly almost 1000 participants attended WC6. This is, of course, good news and shows that the 3Rs concept is getting accepted around the world. In particular in Japan, the success of WC6 had a high impact on the scientific community and, as a consequence on February 23 a "Follow-up Conference to WC6" will be held in Tokyo by the Japanese Science Foundation and the Japanese Society for Alternatives to Animal Experiments (JSAAE) in order to implement the 3Rs concept into the scientific practice in Japan. Our Japanese colleagues want to learn from the current practice in the USA and in Europe, e.g. the EU Directive 86/609/EEC "On the protection of animals used for experimental and other scientific purposes". This is really a more positive result of WC6 than we expected. On behalf of the organisers I therefore want to thank all of you who came and made it happen!

Last September (19-22) Hasso Seibert, Vice-President of ESTIV, hosted the 25th Workshop of the Scandinavian Society of Cell Toxicology SSCT in Salzau (Germany). All of the participants agree that Hasso did an excellent job and praised the high scientific standard of all of the presentations and posters. In this ESTIV Newsletter Parvinder Kaur gives a nice description of the highlights of the SSCT 25 in Salzau.

The highlight of this year will be the [15th International Congress on *in vitro* Toxicology ESTIV2008 \(www.estiv2008.org\)](http://www.estiv2008.org), which will be hosted by our Swedish colleagues at the Djurönäset Conference Center, close to Stockholm, in Sweden. In this ESTIV Newsletter you will find the Second Announcement of ESTIV2008. Since this is the official bi-annual ESTIV conference, the local organising committee (LOC) in

Sweden has in close contact with the ESTIV Board drafted a scientifically challenging program. We will have speakers from all of the on-going Integrated Projects (IP) funded by FP6 of DG Research on development and validation of *in vitro* toxicity tests. The IPs are covering all fields of toxicology that are required for the safety testing of cosmetic ingredients and chemicals according to REACH. Most of the FP6 IPs have more than 20 groups of participants from all over Europe and they are managed in cooperation with ECVAM and ECOPA. So don't miss this opportunity to meet the leading scientists in the field of toxicology *in vitro* and join us at ESTIV2008.

From my perspective a most important step forward for the field of toxicology *in vitro* is the recent initiative in the USA by NIH, EPA and NIEHS to collaborate to improve the safety testing of chemicals with non-animal methods. Two NIH institutes have formed collaboration with the EPA to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals: "The New Strategy Aims to Reduce Reliance on Animal Testing". It is an important goal of this enterprise to provide regulators with new tools for risk assessment, which will no longer be based on animal experiments. Details are given in the joint press release of NIH and EPA, which you will find in this ESTIV Newsletter.

More details are given in the February 15, 2008, edition of Science (Transforming Environmental Health Protection 319, 906-907) in which the authors Francis S. Collins (NIH), George M. Gray (EPA) and John R. Bucher (NIEHS) are proposing on behalf of the consortium "*We propose a shift from primarily in vivo animal studies to in vitro assays, in vivo assays with lower organisms, and computational modeling for toxicity assessments.*" We are also providing you with this important publication, which actually demonstrates a shift of paradigm from *in vivo* to *in vitro* toxicology. This is a development most of us have dreamt of for the past 20 years. The institutions involved clearly indicate that from the scientific perspective this is a major scientific enterprise, which can only be achieved when these major institutions will cooperate effectively. Although I am not sure that Europe will be able to compete effectively with our US colleagues, I do appreciate that it finally going to happen: *Within a few years in vitro toxicology will be the basic approach in safety testing!*

I want to introduce you to another important activity in the field of alternatives, which is also starting from the

USA, the AltTox website (<http://www.alttox.org>) which is dedicated to promoting non-animal tests in toxicity testing. This website has an active AltTox-Forum to discuss upcoming new developments in all fields of *in vitro* toxicology. The forum is managed by moderators and you are invited to register and join. AltTox also provides a Toxicity Testing Resource Center (TTRC), which is covering all aspects of toxicity testing. The AltTox website is online since December 6, 2007, three months ago, and it is managed by Marty Stephens from the HSUS and George Daston from Procter and Gamble, which is also the main sponsor of the website.

In the current issue of the ESTIV Newsletter we are again publishing the portrait of a successful, young member of ESTIV, Sarah Snykers from Belgium. Sarah gives a good example that scientist can today build their careers on toxicology *in vitro*! This is encouraging for PhD students in Europe! Francesca Caloni from Milano is reporting on an activity to evaluate implementing the 3Rs in teaching in veterinary medicine in Italy. She and her colleagues are encouraging students in other European countries to join their initiative.

In this issue Eugenio Vilanova provides information from the work of the Spanish platform on alternatives REMA and Falvia Zucco is updating us on 2 EU FP6 projects, EuroBioFund and LIINTOP.

The ESTIV Board has held a meeting in October 2007 at ECVAM. In order to manage the activities of ESTIV we need such meetings, since many problems can be solved more effectively in face to face meetings without time pressure from our jobs. The ESTIV Board needs engaged young scientists, who want to promote the field of toxicology *in vitro*. Taking into account the encouraging activities in our field around the world, we want to encourage you to volunteer to join us on the ESTIV Board. In particular since I and some of my colleagues will have to retire later this year during ESTIV2008.

Although we have already reached February, the ESTIV Boards wishes all of our members a successful and happy year 2008 and we are looking forward to seeing you at ESTIV 2008 in September in Sweden.

With the best wishes,



New Strategy Aims to Reduce Reliance on Animal Testing

14 Feb 2008: NIH Collaborates with EPA to Improve the Safety Testing of Chemicals

Testing the safety of chemicals ranging from pesticides to household cleaners will benefit from new technologies and a plan for collaboration, according to federal scientists from the National Institutes of Health (NIH) and the U.S. Environmental Protection Agency (EPA), who today announced a new toxicity testing agreement.

The collaborative research program is outlined in the jointly authored *Science* paper Feb. 15, 2008.

The co-authors - Francis S. Collins, M.D., Ph.D., NHGRI director; George M. Gray, Ph.D., assistant administrator for EPA's Office of Research and Development which houses the NCCT; and John R. Bucher, Ph.D., NTP associate director — describe the possibility of shifting from reliance on animal testing to biochemical- and cell-based assays, as well as those using lower organisms, such as zebrafish and roundworms. *"We propose a shift from primarily in vivo animal studies to in vitro assays, in vivo assays with lower organisms, and computational modeling for toxicity assessments."*

NIH Director Elias A. Zerhouni, M.D.

"I launched the NIH Roadmap for Medical Research five years ago to create collaborations between institutes and centers on big projects that none of them could do alone. But I never envisioned a trans-agency collaboration testing for environmental toxins. This research collaboration has the potential to make crucial discoveries that will protect the public health by identifying and understanding chemical toxicants to which people are exposed."

Two NIH institutes have formed a collaboration with the EPA to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. This new, trans-agency collaboration is anticipated to generate data more relevant to humans; expand the number of chemicals that are tested; and reduce the time, money and number of animals involved in testing. Full implementation of the hoped-for paradigm shift in toxicity testing will require validation of the new approaches, a substantial effort that could consume many years. This collaboration is being made possible through a newly signed, five-year Memorandum of

Understanding (MOU), which leverages the strengths of each organization.

http://www.niehs.nih.gov/news/releases/2008/docs/ntpncgce_pamou.pdf

Dr. Collins:

"A central component of federal effort will explore the use of high-throughput screening assays in toxicology. Such assays allow for the testing of thousands to hundreds of thousands of chemicals a day to determine their possible toxic effect."

NCGC is part of a larger Molecular Libraries Imaging Program within the NIH Roadmap for Medical Research. It was designed to advance research on molecules from which most medicines marketed today are derived.

Dr. Collins:

"We now are seeing tools newly available to us for chemical genomics research deployed for greater refinement, speed and capacity in chemical toxicity screening,"

Dr. Bucher:

"The experimental and computational expertise required to transform toxicology is an enormous undertaking and too great for any of our existing organizations to accomplish alone. This collaborative approach allows us to draw on our individual strengths and establishes a long-term, multiple U.S. federal agency commitment."

NTP will contribute thousands of compounds for testing. NTP's animal toxicology expertise will be utilized, along with a large database of the chemicals' effects on animals, with which the new cell-based data will be compared.

Dr. Bucher:

"As our detailed research strategy continues to develop, we will welcome the participation of other federal partners, as well as interested public and private sector organizations, to make this vision of 21st century toxicology a reality."

The EPA's engagement in this collaboration is part of its ToxCast™ program—an initiative launched in 2007 to revolutionize the agency's chemical toxicity evaluation procedures. ToxCast™ will use advances in computers, genomics and cellular biology to speed up toxicity testing and enhance capacity to screen new compounds.

For more information:

<http://www.niehs.nih.gov/news/releases/2008/toxrelease.cfm>

The 6th World congress (WC6) on alternatives and animal use in the life sciences

WC6 was held in Tokyo, Japan, on 21 -25 August 2007 with the support of the Japanese Society for Alternatives to Animal Experiment (JSAAE), the Alternatives Congress Trust (ACT) and the Science Council of Japan. After the previous World Congresses had been held in Baltimore (1993), Utrecht (1996), Bologna (1999), New Orleans (2002), and in Berlin 2005, WC6 was a very successful move to implement the Three Rs in Eastern Asia.

Although the organizers had anticipated that WC6 may not be attended by a representative number of participants, more than 1000 colleagues from around the world contributed to the success of this conference. Most importantly the elegant opening ceremony in a Shinto shrine in honour of animals used in research contributed significantly to the positive atmosphere of WC6. In a very emotional ceremony, which has basically not changed over the past 800 years, Shinto priest invited the souls of experimental animals into the shrine and offered to them food and water.



An old Shinto ceremony in honour of experimental animals, which is usually held once a year in many animal facilities in Japan.

Then members of the organizing committee from Europe, America and Japan donated branches and written prayers to the souls of the animals to apologize for the suffering through which they had gone. Finally the Shinto priests thanked the souls of the experimental animals for attending the ceremony before they left.

Nobody, who attended this impressive ceremony in honour of the experimental animals, will ever forget it. It helped participants from around the world to get an understanding of the deep commitment of our Japanese colleagues to our fellow companions. Moreover, it also shows that they pay respect to animals that is much closer to their hearts and emotions than ever experienced either in Europe or the USA. It was, therefore, the most important message of WC6 that scientists in parts of the world who may never have experienced the 3Rs principle are emotionally

more deeply committed to the suffering and death of experimental animals than scientists outside Asia.



Members of the Alternatives Congress Trust and organisers of the WC6 Satellite Meetings in Beijing, Seoul and Kyoto taking part in a traditional sake barrel opening ceremony at the WC6 banquet.

Attendants from academia, industry as well as regulators appreciated the unique hospitality of our Japanese hosts, who tried to make the conference most memorable for everyone. Even the most skeptic colleagues, who had never been to Japan before and who were afraid of the foreign language, food and culture, enjoyed Tokyo and Japan throughout the entire conference. In the end everybody was happy that the positive momentum from WC5 in Berlin was kept alive in Tokyo.

Taking into account the challenges of animal welfare aspects in the European legislation, e.g. the seventh amendment of the EU Cosmetics Directive and the new chemicals policy REACH, the lectures at WC6 were dominated by participants from industry and regulatory agencies while the percentage of students and colleagues from academia was lower than at the previous World Congresses. Due to the expensive costs of traveling and accommodation the number of representatives from animal welfare organizations in Europe was lower than previously.

In addition to the scientific program, which focused on all important scientific issues of previous World Congresses, e.g. education, ethics, animal welfare, regulatory issues, validation, advanced techniques and international exchange of ideas, the social program was the highlight of WC6. In particular the opening of the farewell banquet added to the local flavour, when members of the Alternative Congress Trust and the local organizers participated on stage in a traditional Japanese sake barrel opening ceremony (Figure 2).

In order to bring the 3Rs concept to more than one Asian country, satellite meetings of WC6 were held in Beijing (China) and Seoul (South Korea) before and in the old Imperial city Kyoto in Japan after WC6. From Europe Coenraad Hendriksen was an invited speaker at the Beijing satellite meeting, Thomas Hartung in Seoul and Horst Spielmann in Kyoto.

The Japanese hosts were quite impressed both by the high number of participants from around the world and by the high scientific standard of the lectures, sessions and workshops. The Science Council of Japan (SCJ) has in particular expressed its sincere thanks to the organizer of the World Congresses, the Alternative Congress Trust (ACT), and the SCJ wants to continue to support conferences on the 3Rs in Japan in collaboration with the ACT. To start this important activity, the SCJ will host a conference in February 2008 in Tokyo. To show their appreciation of the support in organizing the first World Congress on Alternatives in Japan the Japanese Society for Alternatives to Animal Experiments (JSAAE) awarded the honorary membership of the Society JSAAE to Horst Spielmann.

The next World Congresses on Alternatives and Animal Use in the Life Sciences will be held in 2009 in Rome, where Thomas Hartung (ECVAM) and Herman Koeter (EFSA) will be the organizers, and in 2011 colleagues from Canada made an offer to host WC8 in Vancouver.

Horst Spielman

The 25th SSCT Workshop on *In Vitro* Toxicology



September 19-22, 2007, Salza, Germany

The Scandinavian Society for Cell Toxicology celebrated its twenty-fifth anniversary at Salza, Germany. The aim of the SSCT workshops has been to further basic scientific knowledge in cell toxicology and to promote the use of *in vitro* models as substitutes to animal research. Participants from more than 12 countries came together for this cause and attended the comprehensive 4 day workshop.

The workshop began with the BMEF award lecture by Dr. Curren which necessitated the approach from an open mind for the success of alternative methods. The workshop included a special session on 'Methods of Cell Toxicology'.

The course lectures during this special session were oriented towards neurotoxicology and its approach by the use of *in vitro* techniques. Special emphasis was laid on the use of cell culture models for investigating the mechanisms behind neurotoxicity.

The experimental data presented at the workshop highlighted the importance of *in vitro* models to provide answers to basic scientific questions such as identification and prediction of toxicity and their mechanistic pathways. The course also paid special attention to the current promising technology of fluorescent probes. The advantages as well as disadvantages of a variety of fluorescent probes for functional studies were discussed.

The workshop was organized at the Landeskulturzentrum which is a castle and an estate in Salza. The culture, architecture and landscape of the place motivated the attendees of the conference to come together for a short walk around the area which was arranged by the organizing committee. This provided ample time for informal discussions among the participants.

Later, several talks and poster presentations described simple yet novel *in vitro* modeling systems for analysis of a range of useful endpoints. Awards for the best oral and poster presentation were given to encourage the young scientists in the field of cell toxicology. The winners were Helena Hogberg (ECVAM, Ispra, Italy) and Anne Jess (Institute of Toxicology, Kiel, Germany). The program was organized at a high scientific level and several speakers addressed the issue of reducing animal studies with multifaceted approaches and multidisciplinary expertise. The course lectures from the special session are accessible at the SSCT webpage: <http://www.ssct.net/salzaucourse.html>

Parvinder Kaur
Board Member, SSCT

Department of Neuroscience, Norwegian University of
Science and Technology

Students “validate” alternative teaching

The 3Rs concept in research and education is very well known, but it is important to evaluate the “student’s point” of view, especially in disciplines where practical teaching is fundamental like in Veterinary Medicine and Science and Production Animals Curricula.

The following “evaluation questionnaire” was submitted to the students at the University of Milan, Faculty of Veterinary Medicine, during the academic year 2006/2007 (Course in of Veterinary Toxicology in Wild Animals and Veterinary Toxicology in Reproduction 5th year, Vet Curriculum and Veterinary toxicology 3rd year in Science and Production animals Curriculum).

1. How the topic of alternatives to animal use is generally included in Veterinary Medicine /Science and Production animal curriculum?
2. Did you receive a practical education with alternatives in the different disciplines like Anatomy, Biochemistry, Physiology or Toxicology?
3. How would you introduce tomorrow’s veterinary students to the alternative methods in education?
4. Compulsory and/or elective?
5. Are you satisfied with the practical learning with alternative models presented in your module related to Toxicology?
6. Do you think it is important to implement the use of alternative models in education in your curriculum and specifically Veterinary Toxicology?
7. Could you describe the possible advantages using alternatives in teaching?
8. Do you consider useful and stimulating for your education to set up with your student group alternative models for education in Veterinary Toxicology?

Totally 56 questionnaires have been collected: 21 from Vet and 25 from Science and Production animals curricula and the final answers to the questions reported in the table were the following:

- In both curricula the concept of alternative methods to animal use is new for students, and in all disciplines the students have received specific education on it.

- Students received practical learning with methods that could be defined as alternatives, in biochemistry or anatomy, with videos or computer data-bases.
- The students, especially from Vet curriculum, were very interested in alternatives and suggested an elective course, with lectures related their application in teaching and research.
- They found the alternatives used during the Veterinary Toxicology course very interesting, useful and educative. The computer-based models permit interaction between students and students and the teacher. Students think it is important to implement their use, involving also other disciplines. They also think that alternative models have to be implemented in Veterinary Toxicology.
- The first answer related the advantages of alternatives were related to the ethical aspect that alternative model could also be more explicative and permit good and repetitive practice for the students. Moreover the costs of practical courses are reduced.
- The possible development of an alternative model was found by the students an active way of learning, and they suggested some possible new models.

In conclusion the principal end-points were the following:

- a) Evaluation of alternatives related to learning objectives: improvement of learning, student-teacher interaction etc.
- b) Definition of the teaching “value” of alternatives in veterinary curriculum and if supported by an elective course
- c) Priorities on the use of alternatives in practical classes in veterinary curriculum
- d) Risks-benefits of using alternatives in veterinary education
- e) “State of the art” of alternatives in the curriculum and comments
- f) Setting up working group to develop alternative models in veterinary education: is it a stimulating approach?

Teaching with 3Rs, under student evaluation, was really approved and “validated” for practical, economical, ethical and learning reasons with the suggestion of post-academic training (master) and continuous education course (teachers and professionals) and from this year this project has been enlarged involving some European Veterinary Universities.

Francesca Caloni
University of Milan, Faculty of Veterinary Medicine

The best paper published in Toxicological Sciences during the past year

Sarah Snykers was born on September 20, 1979 in Heusden-Zolder, Belgium. She attended secondary school at the Onze-Lieve-Vrouw Lyceum, Genk, where she majored in Latin-Mathematics with highest distinction. In 1997 she started the study of Pharmaceutical Sciences at the Vrije Universiteit Brussel (VUB).



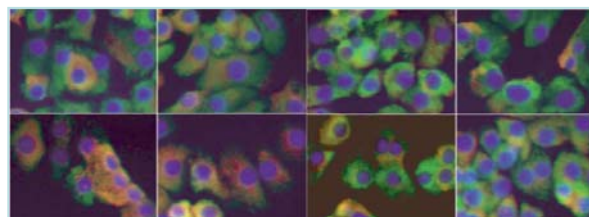
Sarah Snykers, Dept. Toxicology, Vrije Universiteit Brussel, Belgium.

Her Master's thesis, entitled 'Effect van Trichostatine A op apoptose in primaire culturen van rathepatocyten' was carried out at the Department of Toxicology, Dermato-Cosmetology and Pharmacognosy (FAFY), VUB, under supervision of Prof. T. Vanhaecke and promotorship of Prof. V. Rogiers. In June 2002, she graduated with highest distinction and received the price of best student (2nd cycle of Pharmacy studies). She subsequently started a PhD (IWT-bursary) in Pharmaceutical Sciences on 'The *in vitro* hepatic potency of postnatal progenitor cells' at the Department of Toxicology, VUB under promotorship of Prof. V. Rogiers and Prof. T. Vanhaecke. Her core scientific interests and experience are situated in the field of molecular toxicology, *in vitro* toxicology, cell signalling, biotransformation, developmental biology and stem cell technology. In May 2007, she successfully defended her PhD thesis and received the title of Doctor in

Pharmaceutical Sciences. Currently, she continues her initiated research work on postnatal stem cells at the Department of Toxicology, VUB as a postdoctoral fellow of the FWO-Vlaanderen Belgium. The postdoc project is focused on the establishment of standardised protocols to isolate and differentiate plastic progenitor cells from human sources, and unraveling the mechanisms that underlie the hepatic differentiation of human postnatal progenitor cells.

She has 7 publications in international peer-reviewed journals and books as first author and 12 as co-author, and was invited speaker at several national and international congresses. Her research work also resulted in 2 patents concerning the production of mature and functional hepatocyte-like cells out of (1) adult bone marrow cells [PCT/EP2004/0012134] and (2) neonatal rat liver epithelial cells [PCT/EP2006/005622] by application of the developed 'sequential' differentiation protocol, including co-exposure to histone deacetylase inhibitors.

One of her papers, i.e. "Snykers S, Vanhaecke T, Papeleu P, Luttun A, Jiang Y, Vander Heyden Y, Verfaillie C, Rogiers V. (2006) Sequential exposure to cytokines reflecting embryogenesis: the key for *in vitro* differentiation of adult bone marrow stem cells into functional hepatocyte-like cells. *Toxicol Sci* 94(2): 330-341" has been selected by the SOT Board of Publications as **the best paper published in Toxicological Sciences during the past year**. The official Awards Ceremony will be held on Sunday, March 16, 2008, in conjunction with the 2008 SOT Annual Meeting in Seattle, Washington.



Detailed view of expression of phase I biotransformation enzymes at days 24 and 30 upon sequential or simultaneous exposure to liver-specific factors.

OTHER AWARDS

Prof. Eugenio Vilanova, member of STIV and member of the Committee of the Spanish Platform on Alternatives (REMA), from the University "Miguel Hernandez" of Elche, has been named member of RAC-ECHA (Risk Assessment Committee of the European Chemical Agency) which is a critical body in the Agency in the implementation of the REACH. This

Committee may be a critical entity in the acceptability of toxicological results obtained from alternative methods and strategies. The RAC is starting activities since January 2008, is formed by independent experts and will have key role in the evaluation of dossiers registered for substances requiring authorizations under REACH Regulation and other functions in assessing ECHA in decision process in the development and implementation of REACH. Prof. Vilanova has also been awarded with the recognition of **EUROTOX 2007 Honorary Member** and is the chairperson of the next IUTOX-2010 Congress to be held in Barcelona-Spain 10-15 July 2010 (www.iutox2010.org).

Margit Heinlaan participated at the 14th Congress on Alternatives to Animal Testing in Linz, Austria. She presented a poster: "Ecotoxicological hazard of ZnO, TiO₂ and CuO (nano)powders: effects on bacteria, crustaceans and protozoa" (Heinlaan, M., Blinova, I., Ivask, A., Mortimer, M., Dubourguier, H-C. Kahru, A.). The poster won 2007 **Bo Holmstedt Poster Award** for having shown a feasible link between toxicology and the 3R principle.

At the same meeting another award (ZET poster award 2007) went to Hana Bendová, David Basketter, Helena Kandárová, Marie Marriott, Kristina Kejlová, Dagmar Jírová, Erin Spiller, Marek Malý and Manfred Liebsch for the presented work "Comparison of human patch test and 3D human skin model results with classification of chemicals based on rabbit Draize test."

For further information on 14th Congress on Alternatives to Animal Testing in Linz see: <http://www.zet.or.at/subnode,3,147,de,poster,kongress.php>

REMA - Spanish Platform of Alternatives

REMA, the Spanish Platform of Alternatives is participating in European projects on alternatives in close collaboration with ECOPA:

CONAM. Participation in "Workpackages" of Education and Ethic developing educational and training activities oriented to introduce alternative methods in the considerations and requirement in the activities in Ethic committees in research-education institutions.

ForInViTox (Forum for researchers and regulators to meet manufacturers of toxicology test methods). The project intend to analyse the applicability of results of *in vitro* and *in silico* methods in European Project under 5FP and 6FP, evaluating the results that have not been

transferred to potential users and to facilitate this transfer by facilitating collaboration between researchers, potential users and developers of commercial methods.

Other projects are under evaluation process to identify the difficulties to apply alternative methods in developmental process.

Eugenio Vilanova

EuroBioFund

EuroBioFund is a strategic initiative of the European Science Foundation and the European Commission. Its objective is to catalyse the development of large scale pan-European life science research programmes by bringing together key stakeholders from research, industry and funding organisations, at an annual networking event, EuroBioForum.

Following an open Call, the ASAT proposal (Assuring Safety without Animal Testing, original proposal has been attached) has been selected to be presented, together with five other proposals, at EuroBioForum, 5-7 December, 2007 in Lisbon, Portugal.

The aim of the meeting was to discuss the potential opportunities for developing a collaboration which will bring Europe a future with reduced animal testing, by conducting research on the implementation of the applied systems biology approach based on risk assessment needs, by means of building on and expanding of existing networks of research groups.

The next EuroBioForum for is planned to be held in Strasbourg, France. Please refer to the website <http://www.esf.org/activities/eurobiofund> for further information.

Flavia Zucco
CNR, Istituto di Neurobiologia e Medicina Molecolare

The LIINTOP project

The LIINTOP project (www.liintop.cnr.it) had the second meeting at the University of Rennes by the end of January. About 40 researchers attended the meeting.

The previous year has been spent in integrating the competences, in building interfaces among the different institutions, in setting up the structural aspects, and in starting the collaborations. The administrative and the preliminary management aspects have also been accomplished.

From now on the different partners will be involved mainly in the scientific activity and technical dialogue. The first meeting in Rome, one year ago, was devoted to introducing the various partners and groups and to establish fruitful collaborations. In Rennes the work performed in 2007 has been presented by the different partners and WPs, with the aim to assess the state of the art and to establish a stronger and more productive integration in and among the WPs. The discussion has been very alive and productive and the research appears now well implemented on his way on. Several research support activities have also been planned such as subgroup meetings, teleconferences, better use of the web-forum, wider dissemination. The next general meeting is schedule for January 2009 in Valencia, Spain.

Flavia Zucco

CNR, Istituto di Neurobiologia e Medicina Molecolare

12.00-12.15	Discussione generale
12.15-13.30	Pausa pranzo (Mensa ECVAM)
13.30-16.30	EPISKIN - Esercitazioni pratiche
16.30-17.00	Discussione generale e chiusura del corso

Theoretical and practical course: EPISKIN, an alternative to dermal irritation study

4 Marzo, 2008, Ispra, Italy.

Comitato organizzatore

Francesca Caloni (Università degli Studi di Milano)

Isabella De Angelis (ISS - Roma)

Simonetta Gemma (ISS - Roma)

Pilar Prieto (CCR-Ispra, ECVAM)

PROGRAMMA

9.00 - 9.30	Registrazione dei partecipanti
9.30 - 9.45	Indirizzi di benvenuto
9.45 -10.15	Le procedure di validazione, principi generali - Pilar Prieto (ECVAM)
10.15-10.45	Percorso di validazione del modello EPISKIN - Valerie Zuang (ECVAM)
10.45-11.00	Pausa caffè
11.00-11.30	Conformità ai principi della BPL nell'utilizzo dei tessuti umani ricostruiti <i>in vitro</i> – Marisa Meloni (VitoScreen)
11.30 -12.00	Il Modello EPISKIN - Roland Roguet

ECVAM
*EC-Joint Research Centre,
Via Enrico Fermi 2749
Ispra (Varese)*

4 Marzo 2008

For more information see the website www.celltox.it

i-SUP2008

i-SUP2008 *Innovation for Sustainable Production 2008*

BRUGES, BELGIUM, APRIL, 22 - 25, 2008

We cordially invite you to attend the joint i-SUP2008 event that will be held from 22 till 25 April 2008 in Bruges, Belgium.

This unique event covers the central theme "Innovation for Sustainable Production" by hosting five parallel conferences. To realize this organisation, VITO (Flemish Institute for Technological Research) has joined forces with Janssen Pharmaceutica, Umicore, essenscia and OVAM.

On Wednesday April 23, the plenary session will present viewpoints of prominent industrial and governmental key-note speakers.

For more details, please visit our website at www.i-sup2008.org

The conference on "Environment, Health and Safety" will certainly be of great interest to you.

Abstracts are solicited on the themes:

- Targeted toxicity testing
- Implemented test strategies in pharmaceutical, cosmetic and chemical product safety assessment
- The Regulatory Arena: challenges in method acceptance
- Industrial Centers of Excellence in in vitro services. Who does what?

Please note that the deadline for abstract submission is January 15, 2008.

Looking forward to meeting you in Bruges,

On behalf of the organising committee,

Greet Schoeters

INVITROM

INVITROM symposium

'Towards better reliable in vitro methods'



As a satellite to I-SUP2008, the Dutch-Belgian Society for In Vitro Methods (INVITROM) organizes the symposium *'Towards better reliable in vitro methods'* on the 22nd of April in Bruges, Belgium.

During the morning sessions, lectures will cover different aspects related to good *in vitro* practices:

- Good Cell Culture Practices - Sandra Coecke (B-ECVAM)
- Free Concentration Concept - Nynke Kramer (NL-IRAS)
- Predicting In Vivo Effect Levels - Miriam Verwei (NL-TNO)
- Cultured Cells and their Circadian Clock: Time is the Essence - Bert van de Horst (NL Erasmus University)
- Acceptation and Use of In Vitro Methods in Regulatory Testing - Sonja Beken (B-Federal Agency for Medicines and Health Products)

In the afternoon break-out groups will discuss *in vitro* methods related to:

- Human Tissue
- Mechanistic Based Models
- Serum free Cell Culture
- Slice Methods and Preservation
- In Vitro Disease Models

Up-to-date information and registration can be found on the INVITROM website: www.invitrom.org



Welcome to the 15th International Congress on *in vitro* Toxicology ESTIV2008

NEW DATES
25-28 September, 2008

Second Announcement ESTIV2008
Djurönäset Conference center, Stockholm, Sweden

www.estiv2008.org

Welcome

Welcome to the 15th International Congress on *in vitro* Toxicology, ESTIV2008 (former INVITOX Workshop), at Djurönäset in Stockholm 25-28 September, 2008. PLEASE NOTE that the Congress will be held earlier than former announced.

Djurönäset Conference Venue is located 40 km east of Stockholm City, in the Stockholm archipelago. The venue is easily reached by taxi or bus from the Stockholm City centre.

PhD students are especially invited to participate for a reduced fee.

The congress is a joint venture organised by European Society of Toxicology In Vitro (ESTIV), Scandinavian Society for Cell Toxicology (SSCT) and Experträdet.

The Björn Ekwall Memorial Foundation (BEMF) award winner will give a lecture during the Opening session 25 September 2008.

Aims and Purposes of ESTIV2008

- to stimulate the interest of young scientists to get involved in advanced molecular methods in toxicology
- to expand the knowledge of *in vitro* methods among the scientific community in the life sciences
- to increase the legitimacy of *in vitro* methods and their acceptance by the authorities for regulatory purposes
- to act as a platform for exchange of information and discussion
- to help with increasing the number of new methods that are suitable and ready to enter validation
- to serve as a scientific forum for research on and application of advanced *in vitro* methods in the life sciences with a focus on toxicology
- to promote an increased application of advanced *in vitro* methods in laboratories of academic institutions and industry
- to increase the adoption and acceptance of *in vitro* methods for regulatory purposes as, e.g. required by the new EU Cosmetics Directive and EU Chemicals Policy (REACH)
- to explore new technical and scientific challenges with respect to *in vitro* toxicology

Sessions

1. *Embryonic stem cells for developmental toxicology in vitro*
Invited speaker: **Dr. Martina Klemm**, Proteosys, Mainz, Germany
2. *In vitro models for aquatic ecotoxicology*
Invited speaker: **Dr. Kristin Schirmer**, UFZ, Leipzig, Germany
3. *Topical toxicity and in vitro tests for allergy-inducing compounds*
Invited speaker: **Dr. David Basketter**, Unilever, U.K. (to be confirmed)
4. *New in vitro models and strategies: Gene ontology categorization and bioinformatics processing in cell culture phenotyping and toxicity testing*
Invited speaker: **Prof. Roland Grafström**, Karolinska Institute, Stockholm, Sweden
5. *Toxicokinetics and metabolism-mediated toxicity*
Invited speaker: **Prof. Olavi Pelkonen**, Oulu University, Oulu University, Finland.
6. *In vitro models for tissue-specific toxicity: gastro-intestinal toxicity and hepatotoxicity*
Invited speaker: **Prof. Jürgen Borlak**, Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, Germany.
7. *Modelling of absorption, intracellular accumulation and excretion*
Invited speaker: **Prof. Per Artursson**, Uppsala University, Uppsala, Sweden.
8. *Predicting models for acute toxicity and new strategies in neurotoxicology*
Invited speaker: **Dr. Anna Forsby**, Stockholms University, Stockholm, Sweden.
9. *New approaches in validation*
Invited speaker: **Prof. Michael Sjöström**, Umeå University, Umeå, Sweden.
10. *Progress in implementation of alternative tests, future testing strategies, automatised screening, requirements of legislation*
Round table discussions

Satellite meeting - all day 24 September, 2008

A satellite meeting is organised by the EU-projects Vitrocellomics and Invitroheart in collaboration with the organizers of ESTIV2008 prior to the ESTIV2008, 24 September, 2008.

Anybody who is interested, are welcome to participate. Detailed program can be found on www.estiv2008.org

SSCT Special session – 9:00-12:00 25 September, 2008

Scandinavian Society of Cell Toxicology are hosting a special session on methods in cell toxicology, 9.00-12.00, 25 September, 2008

Registration

Registration for ESTIV2008, satellite meeting and SSCT Special Session will start in February 2008 at www.estiv2008.org

Sponsoring and exhibition opportunities

There are many sponsorship opportunities by which companies can contribute to the success of ESTIV2008. Sponsors may decide to become the Main sponsors or Gold or Silver sponsor or compile their individual sponsorship packages (official, printed matter, social events etc). An industrial exhibition will be organised in the lobby of the main building, where the coffee breaks will be held.

For specific information on the sponsorship opportunities and exhibition, please contact Karin Gabrielson Morton at sponsoring@estiv2008.org

Local Organising Committee

Cecilia Clemedson, Chair, Expertrådet, Sollentuna
Barbro Ingemarsson, Conference Secretariat, Expertrådet, Sollentuna
Ada Kolman, The Swedish Fund for Research without Animal Experiments, Stockholm
Per Artursson, Uppsala University
Anna Forsby, Stockholm University
Roland Grafström, Karolinska Institutet, Stockholm
Erik Walum, Biovitrum, Stockholm
Ian Cotgreave, AstraZeneca, Södertälje
Raimund Strehl, Cellartis, Gothenburg
Charlotta Berg, Gambro, Lund
Marika Nordin-Andersson, Swedish Chemical Inspectorate, Stockholm
Erik Ullerås, Swedish University of Agricultural Sciences, Uppsala

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Margit Heinlaan, NICPB, Estonia
Chantra Eskes, Sponsor coordinator, ECVAM, Ispra, Italy
Maria Laura Scarino, INRAN, Rome, Italy
Barbro Ingemarsson, Expertrådet, Sweden

Meeting calendar

SOT, Society of Toxicology's 47th Annual Meeting.
16-20 March, 2008.

Seattle, Washington, USA

<http://www.toxicology.org/AI/MEET/AM2008/housing.asp>

The 3Rs: From Fundamentals to Application

19 March, 2008

London, UK

<http://www.nc3rs.org.uk/downloaddoc.asp?id=649>

PRIM&R: 2008 Annual Institutional Animal Care & Use
Committee (IACUC) Conference

25-28 March, 2008

Atlanta, GA

<http://www.primr.org/>

Perspectives in Percutaneous Penetration

Eleventh International Conference

26-29 March 2008

La Grande Motte, France

<http://www.pppconference.org/>

INVITROM Symposium. Towards Better Reliable *In*

Vitro Methods

22 April, 2008

Bruges, Belgium

<http://www.invitrom.org/english/index.html>

i-SUP2008

Innovation for Sustainable Production 2008

22 – 25, April, 2008

Bruges, Belgium

Alternatives to Animal Testing: New Approaches in the
Development and Control of Biologicals

23-24 April, 2008

Dubrovnik, Croatia

<http://www.edqm.eu/site/Alternatives-to-Animal-Testing-Dubrovnik-Croatia-259.html>

High Level Workshop on "Predicting human adverse
effects from systemic exposure to substances without
the use of animals"

28-29 April 2008, Brussels

http://ec.europa.eu/enterprise/epaa/index_en.htm

Engineering Tissue Alternatives to Animals

30 April, 2008, London, UK

<http://www.nc3rs.org.uk/event.asp?id=830>

High level workshop on "Predicting human adverse effects
from systemic exposure to substances without the use of
animals"

28-29 April 2008, Brussels, Belgium

http://ec.europa.eu/enterprise/epaa/index_en.htm

13th Interdisciplinary Toxicology Conference
dedicated to doyen of czechoslovak pharmacology and
toxicology Prof. MUDr. Helena Rašková, DrSc. on her
beautiful anniversary and 60th anniversary of Institute of
Experimental Pharmacology SASc foundation Integration of
Toxicological Research Within V4

27–30 May, 2008

Trenčianske Teplice - SLOVAKIA

<http://www.toxcon.sav.sk>

Conference: Nanotechnology Towards Reducing Animal
Testing

28-29 May, 2008

London, England

<http://www.nano.org.uk/newsletter/animals/>

Coordination and Collaboration: International Conference on
Animal Research Policy

24-25 June, 2008

Washington, DC

<http://altweb.jhsph.edu/>

2nd International Congress on Stem Cells and Tissue
Formation

6-9 July, 2008

Dresden, Germany

<http://www.stemcellcongress-dresden.de/>

Reduced animal testing

25 -26 July, 2008, Zurich, Switzerland

<http://www.mondialresearchgroup.com>

15th International Congress on *in vitro* Toxicology
ESTIV2008 (former INVITOX workshop)

25-28 September, 2008, Djurönäset Conference Center,
Stockholm, Sweden.

<http://www.estiv2008.org>

45th Congress of the European Societies of Toxicology
EUROTOX 2008

5-8 Octobre, 2008, Crete, Greece

<http://eurotox2008.org>

AALAS National Meeting 2008

9-13 November, 2008, Indianapolis, Indiana, USA

<http://www.aalas.org/index.aspx>

46th Congress of the European Societies of Toxicology
EUROTOX 2009

September, 2009, Dresden, Germany

IUTOX 2010

11–15 July, 2010, Barcelona, Spain

Open call of proposal for IUTOX 2010 Congress. The
Congress Organisers want to encourage activities on
alternatives methods which involve interactions of academia-
industry as well as with regulators and social parties.
Proposal can be sent to the Chairperson of the scientific
Committee Dr. Ana Ferrer directly aferrerd@salud.aragon.es
or using the form in the Web of the Congress
www.iutox2010.org.

Recent publications of ESTIV members

- Carrera V, Sabater E, Vilanova E, Sogorb MA (2007). A simple and rapid HPLC-MS method for the simultaneous determination of epinephrine, norepinephrine, dopamine and 5-hydroxytryptamine: application to the secretion of bovine chromaffin cell cultures. *Journal of Chromatography B*, 847 (2007) 88–94.
- Cipak L, Letasiova S, Repicky A, Jantova S (2007). New [1,2,4]triazolo[4,3-c]quinazoline enhances cisplatin- and temozolomide-induced growth inhibition and apoptosis in HL-60 cells. *Neoplasma*. 54(1): 16-20.
- Combes, R. (2007). Reproductive toxicity testing under the REACH System – Time for a paradigm shift. *ATLA* 35, 1-4.
- Dvorak Z, Vrzal R, Henklova P, Jancova P, Anzenbacherova E, Maurel P, Svecova L, Pavek P, Ehrmann J, Havlik R, Bednar P, Lemr K, Ulrichova J (2008). JNK inhibitor SP600125 is a partial agonist of human aryl hydrocarbon receptor and induces CYP1A1 and CYP1A2 genes in primary human hepatocytes. *Biochem Pharmacol* 75(2):580-588.
- Gibbs S, van de Sandt JJM, Merk HF, Lockley DJ, Pendlington RU and CK Pease (2007). Xenobiotic metabolism in human skin and 3D human skin reconstructs: a review. *Current Drug metabolism* 8, 758-772.
- Gray AC, McLeod JD and Clothier RH (2007). A review of *in vitro* modelling approaches to the identification and modulation of squamous metaplasia in the human tracheobronchial epithelium. *ATLA* 35, 493–504.
- Heinlaan M, Ivask A, Blinova I, Dubourguier, H-C and A Kahru (2007). Toxicity of nanosized and bulk ZnO, CuO and TiO₂ to bacteria *Vibrio fischeri* and crustaceans *Daphnia magna* and *Thamnocephalus platyurus*. *Chemosphere* (in press).
- Jantová S, Čipák L, Letašiová S (2007): Berberine induces apoptosis through a mitochondrial / caspase pathway in human promonocytic U937 cells. *Toxicol In Vitro*. 21(1): 25-31.
- Kruse JJCM, Svensson JP, Huigsloot M, Water van de B, Vrieling H, Giphart-Gassler M, Polman J, Schoonen WGEJ, Horbach SJ (2007). A portrait of cisplatin-induced transcriptional changes in mouse embryonic stem cells reveals a dominant p53-like response. *Mutation research* 617, 58-70.
- Monroy-Noyola A, Rojas P, Vilanova E, Sogorb MA (2007). Comparative hydrolysis of O-hexyl O-2,5-dichlorophenyl phosphoramidate and paraoxon in different tissues of vertebrates. *Arch Toxicology*
- Monroy-Noyola A, Sogorb MA, Vilanova E (2007). Stereospecific hydrolysis of a phosphoramidate as a model to understand the role of biotransformation in the neurotoxicity of chiral organophosphorus compounds. *Toxicology Letters* 170: 157–164.
- Papouskova B, Bednar P, Frysova I, Styskala J, Hlavac J, Bartak P, Ulrichova J, Jirkovsky J, Lemr K (2007) . Mass spectrometric study of selected precursors and degradation products of chemical warfare agents. *J Mass Spectrom* 42:1550–1561.
- Piersma, AH, Janer G, Wolterink G, Bessems JGM, Hakker BC, Slob W. (2008). Quantitative extrapolation of *in vitro* whole embryo culture embryotoxicity data to developmental toxicity *in vivo* using the benchmark dose approach. National Institute of Public Health and the Environment (RIVM), 3720 BA Bilthoven, Netherlands. *Toxicological Sciences*, Volume 101, Issue 1, Pages 91-100.
- Quesada E, Castell JV, Vilanova E, Carrera V (2007). Over-expression of neuropathy target esterase activity in bovine chromaffin cell cultures by adenovirus-mediated gene transfer. *Toxicology Letters* 168: 286–291.
- Quesada E, Sabater E, Sogorb MA, Vilanova E, Carrera V (2007). Recovery of neuropathy target esterase activity after inhibition with mipafox and O-hexyl O-2,5-dichlorophenyl phosphoramidate in bovine chromaffin cell cultures. *Chemico-Biological Interactions* 165 (2007) 99–105.
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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 2008 is € 30.00. If you are also a member of one of the affiliated societies (CellTOX, SSCT, INVITROM), the membership amounts to € 18.00.

Method of Payment

Bank Transfer
RABOBANK, IBAN #: NL20 RABO 0101 4857 51
BIC: RABONL2U

Attention of: ESTIV
Polderkade 1, NL-5345 RR Oss, The Netherlands
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 (2CO). Due to processing costs an additional charge of € 1.50 is included. To use these services, please visit the ESTIV website at www.estiv.org.

Sjeng Horbach

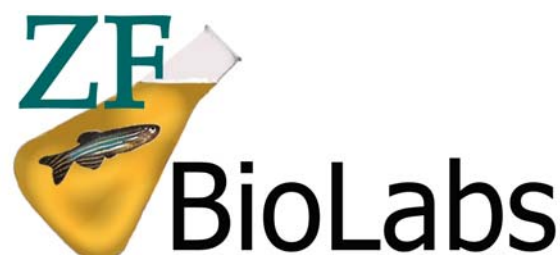
ESTIV e-mail list

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 question that you could pose via 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 150 colleagues), simply address your e-mail to ESTIV-L@NIC.SURFNET.NL

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. 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 secretary@estiv.org, and I will arrange for your name to be added.

Jan van der Valk

ESTIV Corporate member:



ZF BioLabs. Ronda de Valdecarrizo 41° B. 28760. Tres Cantos (Madrid). Spain. Website: www.zfbiolabs.com

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For more information on ESTIV and membership application contact

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