Corners

CAAT*feed*

CAAT's Program Administrator Marilyn Principe retires

After 30 years of service with CAAT, and 37 years total at Johns Hopkins, staff member Marilyn Principe has retired from her role as Program Administrator. For over three decades Marilyn has coordinated all of CAAT's symposia, workshops, parties, board meetings, and all special events, and many friends and supporters of CAAT will remember her for her meticulous attention to detail, her warm smile, always helpful demeanor, and tireless dedication to the center and its programs. She will be greatly missed by all of us, and we wish her the best on her renewed forays into art and a life of leisure and adventure.

Fourth International Conference on Alternatives for Developmental Neurotoxicity Testing (DNT)

May 12-14, 2014
The Inn at Penn, Philadelphia, PA

Developmental neurotoxicity from chemical exposures is a growing concern. The developing human nervous system is susceptible to pharmaceuticals and environmental contaminants, and exposure during development is known to cause lasting neurological deficits. This conference will bring together diverse stakeholders from around the globe, including research scientists, regulators, industry representatives, academics, and pediatricians.

Full details and registration: http://caat.jhsph.edu/programs/workshops/DNT4/index.html

CAAT-Europe workshop *Non-animal models of epithelial barriers (intestine, skin, lung) in research and industrial applications*

February 19-21, 2014
Saarbruecken, Germany

The biannual *International Conference and Workshop on Biological Barriers* has become an international landmark since its launching in 1997. In cooperation with CAAT a dedicated workshop was organized with Prof. Dr Claus-Michael Lehr. The epithelial barriers are the first instance protective biobarriers of the human body. They prevent and control the entrance of microorganisms, substances, and particles into the systemic circulation and organs. The effect of pharmaceuticals, chemicals, cosmetics, and food ingredients is highly dependent on their distribution at the cellular, organ, and whole system level. Some compounds are able to cross biobarriers by diffusion or active transport. Biobarriers themselves may be targets for therapeutic intervention, or may be exposed to toxic and other adverse effects. For examination and evaluation of the role of epithelial barriers various *in vitro*, *ex vivo*, and *in silico* systems have been developed. These models were discussed in this workshop with regard to their functionality and fitness-for-purpose from academic, industrial and regulatory points of view.

Thomas Hartung gave a series of lectures in Australia and New Zealand

CAAT Director Thomas Hartung undertook an extended tour of these countries in February, 2014 with eight lectures in seven cities (Sydney, Canberra, Melbourne, Perth, Adelaide, Auckland, and Wellington). This tour was prompted by the inauguration of a 3Rs center at the Australian National University in Canberra and organized by the Royal Society for the Prevention of Cruelty to Animals (RSPCA).

Among those lectures he addressed the Australian Government's National Health and Medical Research Council (NHMRC): His talk, *Look Back in Anger: What Clinical Trials Tell Us About the Quality of Preclinical Work*, explained the importance of alternatives in drug development and clinical trials. A complete webcast of the presentation can be found at: http://webcast.gigtv.com.au/Mediasite/Play/c8246b3f7b164e3899d4edf4d2a0e1c61d?catalog=c3021f42-2b1b-42bf-b937-eb8082376cc5

Five radio interviews were part of this tour. An example Up Close can be heard or read as transcript at: http://upclose.unimelb.edu.au/episode/289-fur-and-against-scrutinizing-efficacy-animal-testing-and-its-alternatives

Marcel Leist and Thomas Hartung presented at the Italian Senate in Rome

The two CAAT-Europe co-directors presented in January and February invited by different political parties in the Senate in Rome. The presentation by Thomas Hartung in Italian can be found at: https://www.youtube.com/watch?v=DkCL-56GOZs

EU Workshop: Animal Testing – Science or Tradition? At European Parliament

Francois Busquet, CAAT-Europe Policy Coordinator, spoke at the European Parliament in Brussels on February 19, 2014 at the expert meeting, "*Animal Testing – Science or Tradition?*" High-level experts presented the current state of legislation as well as the scientific achievements regarding alternatives to animal testing.

Paul Locke editorial on West Virginia Chemical Spill and the US Toxic Substances Control Act (TSCA)

CAAT US Policy Director Paul Locke penned an editorial on the chemical spill on the Elk River in West Virginia, urging the need for an update to the 38-year-old Toxic Substances Control Act to create better toxicological data through advances in alternative methods. The op-ed appeared in The Charleston Gazette and may be found here: http://www.wvgazette.com/Opinion/OpEdCommentaries/201401170145

CAAT at SOT

CAAT and the The Human Toxicology Project Consortium (HTPC) held a satellite meeting at the 2014 Society of Toxicology Meeting in Phoenix, Arizona on March 27, 2014. "*21st Century Toxicology*" provided an informal setting for the discussion of in vitro, pathway-based testing and related approaches.

– Thomas Hartung presented a talk at the In Vitro Microphysiological Systems Symposium on *Good Cell Culture Practices and Their Application to iPSC for Neurotoxicity*.
– Martin L. Stephens co-chaired and spoke in a Historical Highlights Session on "A History of the 3Rs in Toxicity Testing: From Russell and Burch to 21st Century Toxiology." His talk is entitled "A History of 3Rs Activity in Toxicology: Phases, Impacts, and Future Challenges."

The center also presented three poster/abstracts at the conference:

– Helena Hogberg et al.: Developmental Neurotoxicity Assessment in a 3D Organotypic Neuronal Model Using a Metabolomics Approach
– Lena Smirnova et al.: MiRNomics, Metabolomics, and 3D Neuronal Differentiation of LUHMES Progenitor Cells As an In Vitro Model for DNT Studies
– David Pamies et al.: Characterization of a Brain Microphysiological System for Studying Gene/Environmental Interactions
– Vanessa Sarocha et al.: Probabilistic Hazard Assessment for Skin Sensitization Potency Using Machine-Learning to Design Integrated Testing Strategies

David Pamies, PhD, Post Doc, Environmental Health Sciences (EHS), received two awards at the 2014 53rd Annual Meeting of the Society of Toxicology. The awards of *In Vitro and Alternative Methods Specialty Section MB Research* and the *In Vitro and Alternative Method Specialty Section* were granted for the poster "Characterization of a brain microphysiological system for studying gene/environment interactions" by Pamies, D., Makri, G., Bressler, J, et al.

Recent publications by CAAT/CAAT-Europe team

Beck, N. B., Becker, R. A., Boobis, A., et al. (2014). Instruments for assessing risk of bias and other methodological criteria of animal studies: Omission of well-established methods. *Env Health Perspect 122*, A66-A67.

Bouhifd, M., Hogberg, H. T., Kleensang, A., et al. (2014). Mapping the human toxome by systems toxicology. *Basic Clin Pharmacol Toxicol*, Epub ahead of print. http://dx.doi.org/10.1111/bcpt.12198

Pamies, D., Sogorb, M. A., Fabbri, M., et al. (2014). Genomic and phenotypic alterations of the neuronal-like cells derived from human embryonal carcinoma stem cells (NT2) caused by exposure to organophosphorus compounds paraoxon and mipafox. *Int J Mol Sci 15*, 905-926. http://dx.doi.org/10.3390/ijms15010905

Rivera-Mariani, F. E., Vysyaraju, K., Negherbon, J., et al. (2014). Comparison of the interleukin-1-inducing potency of allergenic spores from higher fungi (basidiomycetes) in a cryopreserved human whole blood system. *Int Arch Allergy Immunol 163*, 154-162.

Sogorb, M. A., Pamies, D., De Lapuente, J., et al. (2014). An integrated approach for detecting embryotoxicity and developmental toxicity of environmental contaminants using in vitro alternative methods. *Toxicology Letter*, Epub ahead of print. http://dx.doi.org/doi:10.1016/j.toxlet.2014.01.037

Waldmann, T., Rempel, E., Balmer, N. V., et al. (2014). Design principles of concentration-dependent transcriptome deviations in drug-exposed differentiating stem cells. *Chem Res Toxicol 27*, 408-420.

EUSAAT

European Society for Alternatives to Animal Testing

News from EUSAAT

Due to the significance of this topic for 3Rs methods, EUSAAT participated at the *10th International Conference and Workshop on Biological Barriers* (10th ICWBB) that took place in Saarbrücken, Germany, from 16 to 21 February 2014 (c.f. Information Box – Conference Summary 10th ICWBB). Our vice president Dr Eleonore Haltner, representing EUSAAT, held the final lecture speaking about the possibility to replace human studies by validated *in vitro* models, providing the example of *in vitro* studies as a basis for the EU marketing authorization for a pharmaceutical product. For the first time, conference participants had the opportunity to take home information about EUSAAT in the form of our new flyer, which the EUSAAT board had created in advance. Later this spring, EUSAAT will attend the annual conference of the *European Society for Toxicology in Vitro*, which will take place from 10-13 June 2014 in the Netherlands.

The Hessian Animal Welfare Research Award

Hessischer Tierschutzforschungspreis

This year, the Hessian State Ministry for the Environment ("*Ministerium für Umwelt und Klimaschutz, Landwirtschaft und Verbraucherschutz*") will grant again the Hessian Animal Welfare Research Award (for further information, c.f. http://www.tierschutz.hessen.de). Excellent scientific work which offers new methodology to the 3Rs principle or which continues with an existing basic approach can be granted with up to € 15,000. The Hessian Minister for the Environment Priska Hinz will carry out the awarding based on the nomination of a judging panel. EUSAAT feels honored that for the 7th time, our vice-president Dr Eleonore Haltner, as CEO of a company developing and standardizing alternative methods, has been appointed member of this jury.

Upcoming World Congress on Alternatives and Animal Use in the Life Sciences

EUSAAT is a supporting society of the *9th World Congress on Alternatives and Animal Use in the Life Sciences* (WC9; http://www.wc9prague.org/supporting-societies/). Since there are no EUSAAT-Linz conferences during years in which World Congresses take place, we invite our EUSAAT members and all supporters of the EUSAAT-Linz conferences to actively participate at the WC9: Calls for abstracts are open with the abstract submission deadline April 15, 2014: http://www.wc9prague.org/call-for-abstracts/. To re-ceive the most recent updates on WC9, please visit the WC9 NEWS website: http://www.wc9prague.org/wc9-news/

Information Box – Conference Summary 10th ICWBB

The 10th International Conference and Workshop on Biological Barriers was organized by the *Helmholtz-Institute for Pharmaceutical Research in the Saarland and the Saarland University* with *CAAT-Europe* serving as co-organizer. *Prof. Claus-Michael Lehr* (University of Saarland; GER) and *Prof. Ulrich F. Schäfer* (University of Saarland, GER), both long-lasting members of EUSAAT, initiated the conference in the year 1997 under the nickname "cell culture course". Meanwhile the conference has turned into a well-recognized international meeting where scientists from around the world present their latest research results in the scientific disciplines of nanomedicine and *in vitro* alternative methods to study biological barriers, including the gastro-intestinal tract, the skin, and the respiratory tract.

This year, the program was more streamlined than the years before by condensing the conference and subsequent workshop from previously 10 days to 6 days. The popular weekend program with soft skill courses and social program in the German-French-Luxembourgian "Saar-Lor-Lux" region was sacrificed, but most of the yearlong regular participants accepted this necessary change.

The 2014 conference's special focus on epithelial barriers was supplemented by scientists putting this topic into a broader scientific perspective. Thereby the "Bio-Barriers" conference bridged the gap between nanomedicine and nanotoxicology. The Sunday sessions were chaired by Prof. C.-M. Lehr, Prof U. F. Schäfer, *Prof.*

David Grainger (University of Utah, USA) and *Prof. Steven Schwendeman* (University of Michigan, USA). *Prof. Patrick Couvreur* (University Paris Sud, FR) held the opening lecture addressing the "hot topic" of how to overcome resistance to treatments. Further lectures covered special drug delivery systems, such as tropoelastine-based hydrogels microfluidics for microencapsulation, particles for delivery of large molecules, and the interaction between nanomaterials and the immune system. Monday morning lessons covered the topic of bacterial barriers. There, as during the afternoon, possible roles of mucus and surfactants were discussed intensively. *Prof. Jesus Perez-Gil* (University of Madrid, ES) raised the question whether the lung surfactant serves as a barrier or a shuttle for drug delivery.

On Monday evening, the participants were invited to a "get together" party at the so-called "*Saarländischer Abend*" (Saarland evening), sponsored by Across Barriers GmbH, to continue the lively daytime discussions in a casual atmosphere at the Sciencepark Saar.

On Tuesday, the skin barrier was topic number one. Presentations covered the broad spectrum of topics from hair follicles as targets for drug delivery to computational modeling of the skin barrier, and additional themes like analytic techniques to visualize the transport of substances across the skin. On Wednesday, *Dr Mardas Daneshian* (CAAT Europe, GER) opened the scientific sessions on *in vitro* models of biological barriers. *Prof. Joke Bouwstra* (University Leiden, NL) gave a comprehensive overview on human skin models, and EUSAAT's vice-president *Dr Eleonore Haltner* held the final lecture. Additionally, eighty scientific research posters covering the spectrum of topics addressed at the conference were presented. The three lab courses, which took place after the conference, were designed to provide instruction in advanced analytical techniques and methods relevant to skin research and nanomedicine.

Eleonore Haltner
Vice President of EUSAAT
the European 3Rs Society
on behalf of the Board

NTP
National Toxicology Program
U.S. Department of Health and Human Services

UNITED STATES
ICCVAM
Advancing Alternatives to Animal Testing

News from NICEATM and ICCVAM

ICCVAM elects chairs

At ICCVAM's January meeting, the principal representatives from the 15 ICCVAM agencies elected Dr Abby Jacobs, U.S. Food and Drug Administration (FDA), and Dr Anna Lowit, U.S. Environmental Protection Agency (EPA), to serve as co-chairs of ICCVAM for the coming year. Drs Jacobs and Lowit served as acting co-chairs of ICCVAM during 2013 and will continue to lead ICCVAM as it defines new procedures and sets goals and priorities for the near future. We encourage ICCVAM stakeholders to join NICEATM and ICCVAM in thanking Drs Jacobs and Lowit for taking on this responsibility and supporting them as they lead ICCVAM in its future activities.

Casey appointed director of NICEATM

National Toxicology Program Director Dr John Bucher announced the appointment of Dr Warren Casey as Director of NICEATM on January 7. Casey had been serving as Acting Director of NICEATM since January 2013. In his announcement, Bucher commented, "*I congratulate War-*

ren on an outstanding first year, and look forward to many more successful years of service to NICEATM, ICCVAM and ICATM (the International Cooperation on Alternative Test Methods)."

Murine Local Lymph Node Database available on NICEATM website

On behalf of ICCVAM, NICEATM has conducted a number of analyses to evaluate the usefulness of the murine local lymph node assay (LLNA) to identify potential skin sensitizers. NICEATM is making this data publicly available as reference material for developing and evaluating alternative methods that replace, reduce, or refine the use of animals for skin sensitization testing. The database is available at http://ntp.niehs.nih.gov/go/40498.

NICEATM supporting Workshops on Alternatives for Pertussis Vaccine Testing

A recent report summarizing the conclusions from a workshop on alternatives to the murine histamine sensitization test (HIST) for acellular pertussis vaccine testing was published in the January issue of *Biologicals*. The November 2012 workshop was organized by NICEATM and ICCVAM. A link to the report and other information about the workshop are available at http://ntp.niehs.nih.gov/go/HISTwksp.

Workshop participants reviewed and discussed data generated by an international study that compared the performance of 12 *in vitro* assays. Participants concluded that no alternative method was sufficiently developed for harmonized validation studies at this time, and agreed that no single *in vitro* assay would be applicable to all vaccine formulations. Two cell-based assays were recommended for further development and optimization as the most promising for future acceptance or adoption. Workshop participants also agreed that a harmonized Chinese hamster ovary cell aggregation assay should be assessed as an alternative to the HIST for calibration of pertussis toxin reference standards.

An international collaborative study of the Chinese hamster ovary cell assay is in progress. Data from this study and other recent advances in method development will be reviewed at an international workshop planned for mid-2015. In addition, a workshop to consider implementation and regulatory acceptance of *in vitro* alternatives to the HIST will be convened as a satellite meeting of the Ninth World Congress on Alternatives and Animal Use in the Life Sciences in August 2014. Information on this meeting is available on the World Congress website at http://www.wc9prague.org/satellite-meetings/. NICEATM will be providing support for both upcoming workshops.

NICEATM and ICCVAM activities at recent scientific meetings

In January, NICEATM presented five posters at the Society of Toxicology (SOT)-sponsored workshop "FutureTox II: Pathways to Prediction – *In Vitro* Data and *In Silico* Models for Predictive Toxicology." NICEATM poster presentations from this workshop are available at http://ntp.niehs.nih.gov/go/41295.

Highlights of NICEATM and ICCVAM activities at the SOT Annual Meeting in March included:

- Dr Nicole Kleinstreuer of the ILS NICEATM contract support staff was a presenter at an SOT Continuing Education Course on Elucidating Adverse Outcome Pathways for Developmental Toxicity.
- ICCVAM co-chair Dr Abby Jacobs of the FDA's Center for Drug Evaluation and Research co-chaired a session on non-animal approaches to photosafety testing of pharmaceuticals.
- ICCVAM member Dr Pertti (Bert) Hakkinen of the National Library of Medicine presented a poster describing NLM's toxicology education resources.
- NICEATM Director Dr Warren Casey and eight members of the ILS NICEATM contract support staff contributed to 14 posters presented in sessions on Alternatives to Mammalian Models, Computational Toxicology and Data Integration, Risk Assessment, and other topics.

Information on NICEATM and ICCVAM activities at the SOT Annual Meeting is available at http://ntp.niehs.nih.gov/go/41297.

Upcoming workshops on alternatives

A "Collaborative Workshop on Aquatic Models and 21st Century Toxicology" will be held May 5-6 at the Hunt Library at North Carolina State University in Raleigh, NC. The purpose of the workshop will be to explore and discuss how aquatic models may be used to (i) screen and prioritize compounds for further in vivo testing and (ii) assess mechanisms of chemical toxicity and how this knowledge can impact the environment and human health. Information about the workshop is available at http://ntp.niehs.nih.gov/go/41308.

A workshop on "Adverse Outcome Pathways: From Research to Regulation" will be held September 3-5 in the William H. Natcher Conference Center, National Institutes of Health, Bethesda, MD. Information and a registration form for this workshop will be available on the NTP website in the near future.

Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together

IIVS News & Views

NociOcular Assay: A novel *in vitro* assay to assess eye stinging potential

The NociOcular Assay, developed by Dr Anna Forsby at Stockholm University, is a novel neuronal model with high expression of functional TRPV1 channels. The TRPV1 channel is a well characterized pain receptor that is expressed in sensory nociceptors, which can be activated by chemical stimuli. Corneal and mucosal tissue in the conjunctiva are rich in innervations which express TRPV1 channels. Therefore, TRPV1 channel activation is thought to be a general mediator of chemically induced pain on the surface of the eye.

In this cellular model, a TRPV1 expressing clone of the human SH-SY5Y neuroblastoma cell line was obtained by stable transfection. TRPV1 channel activation is measured by acute increases in the intracellular free Ca^{2+} using the fluorescent probe Fura-2AM. Prior to Ca^{2+} measurements the TRPV1 expressing SH-SY5Y cells are cultured in 96-well plates. The mean value (% increase of basal Ca^{2+} level) from triplicate wells is then monitored for each concentration from each independent experiment. The TRPV1 antagonist capsazepine is added simultaneously with each concentration to confirm the specificity of TRPV1-mediated Ca^{2+} influx.

Although several *in vitro* eye irritation models exist, none of them has demonstrated the ability to predict the human sting potential of products that may come in contact with the eyes. Therefore, an assay capable of detecting eye sting potential would be a beneficial pre-clinical screening tool. IIVS participated in a collaborative study with Johnson & Johnson Consumer and Personal Products Worldwide and Dr Forsby's laboratory to test 19 baby cleanser formulations in the NociOcular Assay and compare the results to existing human clinical eye sting data. Our data, published in Toxicological Sciences (http://dx.doi.org/10.1093/toxsci/kfs198), support that the TRPV1 channel is a principle mediator of eye stinging sensation induced by baby bath and shampoo formulations and that the NociOcular test may serve as a simple bioassay to ascertain this sensory response in the eye.

IIVS is pleased to introduce the NociOcular Assay as a new addition to our suite of *in vitro* assays. The current prediction model for the assay is based on studies with surfactant ingredients and formulations, but we seek to expand the applicability of the assay by performing additional investigation into other product types. If you would like more information about the NociOcular assay, please contact Dr Kimberly Norman at: knorman@iivs.org or Dr Anna Forsby at annaf@neurochem.su.se

Practical Methods for *In Vitro* Toxicology training workshop and custom training program for BTBU scientists

A key educational program at IIVS is our annual training course, Practical Methods for *In Vitro* Toxicology. For over 17 years IIVS has instructed scientists from industry, government/regulatory, and academic institutions on key laboratory techniques for conducting *in vitro* assays, and has assisted them in learning how to interpret the resulting data. During the multi-day program, participants are exposed to a variety of *in vitro* methods through lectures and hands-on activities with our highly trained biologists and Study Directors.

Held in January each year, the course features hands-on instruction on the Bovine Corneal Opacity and Permeability Assay (BCOP), 3T3 Phototoxicity assay, and use of 3D tissue constructs for dermal irritation testing. Participants are provided with demonstrations of a number of other assays during the 3 and a half day course including the KeratinoSens assay for skin sensitization testing, the Cytosensor Microphysiometer assay for eye irritation testing, and the Corrositex assay for determining DOT packing groups and hazard classification. Lectures on the assays include case studies to discuss data interpretation. Presentations on global acceptance of *in vitro* methods, the use of good laboratory practices, the US Tox 21 program, and new technologies for organ cultures round out the program. The success of this course has led to requests from individual companies and organizations for IIVS to create custom-designed workshops for their specific needs.

One such program was held in February when IIVS staff hosted two visitors from Beijing's Technology and Business University (BTBU) for an extended training on *in vitro* assays. BTBU is one of the few universities within China that has a cosmetics science academic program. One BTBU professor and a graduate student traveled to our facility to receive extended hands-on training in best practices for cell culture and non-animal toxicology assays such as the BCOP and phototoxicity assay using 3T3 cells. During

their time at our laboratory, they were also given training in the use of 3D tissue constructs for determining ocular and dermal irritation of chemicals and observed the performance of the KeratinoSens assay for determining skin sensitization potential. In addition to the hands-on performance of these assays in the laboratory in real time, they also received instruction on laboratory administration and spoke with our Study Directors about practical concerns such as equipment maintenance, ordering supplies, scheduling, and compliance with Good Laboratory Practices. IIVS gratefully acknowledges PETA for supporting this program through which a training laboratory at BTBU will be established for non-animal testing methods for cosmetics. IIVS staff will continue to provide remote support to the university as they launch their new program and open the laboratory.

International cooperation – EPAA

In the fall of 2012, IIVS and the European Partnership for Alternative Approaches to Animal Testing (EPAA) signed a Memorandum of Understanding to coordinate efforts in progressing the international use of non-animal testing methods. The two organizations agreed to combine resources and collaborate to promote international awareness and education of these methods, and to provide science-based advocacy to key stakeholders. Since the signing of the MOU, IIVS has engaged in several activities in China which provided direct contact with scientists and key decision makers on the implementation of *in vitro* methods.

Dr Quanshun Zhang, Manager of International Outreach at IIVS, attended the International Congress of Toxicology (ICT) in Seoul, Korea to interact with a delegation of scientists from China. These scientists came from major areas of government and academic institutions including the CFDA, CDC, Ministry of Environmental Protection, Chinese Academy of Science and Sun Yat-Sen University. Korea, with the formation of the Korean Center for the Validation of Alternative Methods (KoCVAM), serves as a model for the adoption of OECD Test Guideline methods and participation in international validation efforts. An "Alternatives Methods Section" of the Congress featured speakers from JaCVAM, ICCVAM, and ECVAM who further reinforced advantages of international harmonization of alternative methods.

At the Chinese Society of Toxicology (CSOT) in Guangzhou, China, Dr Zhang presented a poster on behalf of EPAA titled "International Sharing of Scientific Knowledge in Affecting Change in Regulatory Testing Approaches". Over 1,500 toxicologists attended the meeting from industry, government, and academic/research institutions. As China considers changes to its regulatory testing requirements it is critical to discuss the advantages of *in vitro* testing approaches with key decision makers and thought leaders within China.

In addition to annual conferences such as the ICT and SOT, IIVS represented EPAA's commitment to international outreach at less formal venues designed to introduce industry scientists and students to *in vitro* methods. For example, Dr Zhang was invited to speak at the Skin Biology Symposium organized by the Beijing Daily Chemical Association, an organization comprised of domestic cosmetic and ingredient manufacturers. The presentation focused on the application of 3D skin models in safety and efficacy assessment of cosmetics and ingredients. Dr Zhang also provided a lecture to graduate students at the Beijing Technology and Business University (BTBU). See more about BTBU in the previous story.

To broaden general awareness of alternatives in China, EPAA helped support the translation into Chinese and publication of *The Three Rs and the Humanity Criterions* by Prof. Michael Balls. This edition is an abridged version of The Principles of Humane Experimental Technique by William Russell and Rex Burch. This newly translated book will be distributed free of charge to many libraries and all major universities within China.

New book published: Reducing, Refining and Replacing the Use of Animals in Toxicity

In the words of editors David Allen and Mike D. Waters, the text describes the ever-expanding "toolbox" of test methods available to toxicologists. By combing *in silico*, *in vitro*, and *ex vivo* methods toxicologists are moving closer to using mechanistically based alternatives without requiring animals.

Chapters include the history of the 3Rs, regulatory testing, international harmonization, refinement, computational modeling, skin sensitization, and more. The chapter titled "*In Vitro* Toxicology Models for Acute Eye and Skin Irritation Assessment" was authored by Gertrude-Emilia Costin and Hans Raabe of IIVS (http://books.google.nl/books?isbn=1849736529).