# News from the American Society for Cellular and Computational Toxicology

This spring the ASCCT webinar series hosted Dr Raymond Tice of the National Institute for Environmental Health Sciences, who presented an update of the Tox21 program, a collaborative effort between the US Food and Drug Administration, the National Institutes of Health, and the Environmental Protection Agency to use hundreds of cell-based assays to predict human health effects. Members can view a recording of past webinars on the ASCCT web site. Members will also enjoy two cutting-edge presentations this summer: June 21, Dr Nicole C. Kleinstreuer, Postdoctoral Fellow at EPA's National Center for Computational Toxicology, will present her work on the Virtual Embryo Project, and August 16 Dr Russell S. Thomas, Director of the Institute for Chemical Safety Sciences and the Center for Genomic Biology and Bioinformatics at the Hamner Institutes for Health Sciences will present his work on the use of high-throughput *in vitro* screens for hazard and risk assessment.

The ASCCT is also pleased to announce the First Annual Meeting of its membership. The meeting will feature a plenary lecture by Dr Melvin E. Andersen of the Hamner Institutes for Health Sciences, poster and lecture presentations by other ASCCT members, a business meeting with election of new Board of Directors members, and an evening social event.

The meeting will take place September 21 at the Lister Hill Auditorium, on the National Institutes of Health Campus in Bethesda, Maryland. Abstracts are accepted until July 15, and early bird registration rates are offered until September 1. Reduced rates for students are also offered. More information is available on the ASCCT web site, www.ascctox.org. All are invited! We hope to see you in September.

# CAAT*feed*

## CAAT-led consortium to receive $ 800,000 funding for novel (developmental) neurotoxicity cell model from NIH

The NCATS (National Center for Advancing Translational Sciences) and NINDS (National Institute of Neurological Disorders and Stroke) advisory councils have recommended grant application "*A 3D Model of Human Brain Development for Studying Gene/Environment Interactions*" for funding support. The call for proposals was in the context of developing novel predictive tools for the assessment of medical countermeasures for biological and chemical terrorism and warfare. The collaboration of PIs Thomas Hartung and Helena Hogberg with Johns Hopkins Medicine (Hongjun Song) and Kennedy-Krieger (Joe Bressler) will establish and characterize an *in vitro* model of the developing human brain for the purpose of testing drugs and chemicals.

The complexity of neur(odevelopment) al disorders and the interference of substances requires organotypic human cell cocultures: Astrocytes participate in synapse formation and regulate synaptic activity and chemicals that specifically target them have the potential to interfere with synaptic reinforcement and/or pruning. The PI's laboratory has successfully employed rat primary cell-based mini-brains, which shall be humanized and evaluated at CAAT by using induced pluripotent stem cells (IPSC). Partner Song has established IPSC to be employed and characterized for the neural cultures. The use of IPSC allows addressing genetics in human neurodevelopmental processes: Polymorphisms and epigenetic mechanisms involved in neurodevelopment are known to modify sensitivity to substances. Additionally, assays for testing toxicity in the developing brain must consider differences in sensitivity and susceptibility associated with the stage of development at which the organism is exposed. The model will reflect critical targets of substance actions such as proliferation, apoptosis, migration, axonal growth and dendritic arborization, synaptogenesis, as well as myelination, which will display differences in sensitivity to different types of chemicals. Functional endpoints are used to evaluate the complex cell-to-cell interactions that are affected in neurodevelopment, its perturbation and drug intervention.

The model to assess effects on human neurodevelopment leverages human stem cells from diverse genetic backgrounds, different cell types, and endpoints that assess the unique processes occurring during brain development. In this grant application, the main goal is to demonstrate the feasibility of the personalized model using IPSC derived also from individuals with neurodevelopmental disorders caused by known mutations and chromosomal aberrations.

Such human mini-brains will represent a versatile tool for more complex testing platforms and strategies as well as research into CNS physiology and pathology.

## CAAT Information Day: New Approaches to Assessing Countermeasures to Bioterrorism Agents

This Information Day was held on May 22 at the Johns Hopkins Bloomberg School of Public Health, Baltimore Maryland. See: http://caat.jhsph.edu/programs/workshops/countermeasures.html

As discussed in this issue's *Food for thought* article, the need for evaluating medical countermeasures (MCM) for biological terrorism and warfare is emerging as a new driving force for alternative approaches, mainly as a *Human on a Chip* approach. Speakers included George Korch (JHSPH and HHS Assistant Secretary for Preparedness Response, Co-chair of NRC committee animal models for MCM), Lisa Hensley (FDA), Judy Hewitt (NIAID), William C. Florence (DTRA), David Gibson (US Army), William Warren (Sanofi-Pasteur), Sonia Grego (RTI International), Marti Jett (US

Army Center for Environmental Health Research), Anthony Bahinski (Wyss Institute, Harvard University), and Jennifer Sekowski (US Army) as well as Joanne Zurlo, and Thomas Hartung from CAAT.

## Why Europe needs the human toxome project

In his *Euro Biotechnology News* editorial Francois Busquet (CAAT-Europe policy program) summarizes the May 15 program presented at the European Parliament in Brussels on the "Human Toxome Project – A New European Horizon for Risk Assessment". http://www.eurobiotechnews.eu/people/editorial/2012/francois-busquet.html

The European Parliament workshop, prompted by the CAAT-Europe policy program started in February 2012, was introduced by Vittorio Prodi, MEP. Speakers included Troy Seidle (Humane Society International), Roberto Dall' Aglion (University of Milan Italy), Simona Bussi (Bracco Group), Maurice Whelan (Head of Unit Systems Toxicology, and Validation of Alternative Methods responsible for EURAL ECVAM, DG JRC), Jos Kleinjans (Maastricht University), Gernot Klotz (CEFIC), Jim Bridges (Chair of the Scientific Committee on Emerging and Newly Identified Risks (SCENIHR) of DG SANCO), Roberto Bertollini (WHO), and Philippe Martin (DG SANCO) as well as Thomas Hartung (CAAT). Speakers embraced the concept of the Human Toxome and discussed its opportunities and role relative to a variety of related European projects.

## Kick-off meeting of Evidence-Based Toxicology Collaboration (EBTC) Europe

Following the US effort that resulted in the 2011 creation of an Evidence-based Toxicology Collaboration (EBTC), a European counterpart to EBTC was initiated to adapt Evidence-based Medicine (EBM) principles to toxicology. Evidence-based Toxicology (EBT) seeks to systematically implement transparency, objectivity, and consistency in toxicology. The EBM toolbox (e.g., systematic reviews and test assessment methodology) is available for translation to toxicology, as are the approaches of the Cochrane Collaboration, which applies and fosters systematic reviews. CAAT is running the joint secretariat for the US and EU branch. The meeting, held June on 17, 2012, was held in conjunction with the Eurotox Congress 2012 (Stockholm, Sweden). See also the revamped EBTC website: http://ebtox.com/home.html. The European steering group includes Sonja Beken (FAMHP), Alan Boobis (Imperial College), Neil Carmichael (ECETOC), Jan Hengstler (Leibniz Research Centre), Philippe Hubert (INERIS), Joanna Jaworska (P&G), Ian Kimber (University of Manchester), Annette Kopp-Schneider (German Cancer Research Centre), Jean-Roch Meunier (L'Oréal), Bennard van Ravenzwaay (BASF), Kai Savolainen (Finnish Institute of Occupational Health), Thomas Singer (Hoffmann-La Roche), Nigel Skinner (Agilent), and Carl Westmoreland (Unilever) as well as Marcel Leist, Martin Stephens, Sebastian Hoffmann (seh consulting + services), and Thomas Hartung for CAAT.

## t[4] Workshop Toxicity Testing in the 21st Century – Beyond Environmental Chemicals

CAAT hosted a workshop as part of the Transatlantic Think Tank for Toxicology ($t^4$) in Ranco, Italy on June 4-6, 2012. The invited participants from FDA, EPA, EMA, EFPIA, and industries addressed the needs of the pharmaceutical, biological, and food industries for more predictive methods of assessing the effects on humans of various therapeutics and food additives. Discussion focused on the major points addressed in the NRC report, *Toxicity Testing in the 21st Century – A Vision and a Strategy*, which was tailored to testing of environmental chemicals. Participants addressed ways to adapt the principles developed in the report to the specific needs of other industries and regulatory agencies. A workshop report reflecting the discussions and recommendations of the participants will be published in *ALTEX*.

## CAAT Pharmaceuticals Information Day – Scientific and Animal Welfare Innovations In Drug Development and Safety Assessment

This Information Day was held May 7, 2012. Speakers included Brian Berridge (GlaxoSmithKline), Marilyn Brown (Charles River Laboratories), Wayne Buck (Abbott Laboratories), Myrtle Davis (National Cancer Institute), Oliver Flint (BristolMyers Squibb), Douglas Keller (Sanofi), William Pennie (Pfizer), and Manisha Sonee (Johnson & Johnson) as well as Joanne Zurlo and Thomas Hartung from CAAT.

More details are available at: http://caat.jhsph.edu/programs/workshops/pharmainfoday.html

## CAAT Special Lecture by Jesse L. Goodman, MD, MPH, Deputy Commissioner for Science and Public Health of US Food and Drug Administration

Linked to the pharmaceuticals Information Day and the CAAT-US board meeting, CAAT organized on May 7 a lecture by FDA chief scientist Jesse Goodman at Johns Hopkins: *Advancing Regulatory Science to Protect and Promote Health – Opportunities and Challenges*. Dr Goodman stressed several collaborations between FDA and CAAT.

## Award to former CAAT coworker

Erwin van Vliet (at the time CAAT, Johns Hopkins University, Baltimore, USA; currently Hospital Clinic – Universitat de Barcelona, Department of Maternal-Fetal Medicine, Fetal and Perinatal Medicine Research Group, Barcelona, Spain) was awarded the 2012 ALTEX Award for his 2011 article "Current standing and future prospects for the technologies proposed to transform toxicity testing in the 21st century" in *ALTEX* 28, 17-44 (freely available on the ALTEX and CAAT AltWeb websites).

## Upcoming events

*Organotypic behavior of 3D-cell culturing models to maintain functional capacity: moving from phenotyping to mechanisms*
October 22-25, 2012
Konstanz, Germany

The workshop on October 22-24 (by invitation only) is co-organized with the Alexandra Foundation, Monaco, ecopa, and BASF. It will be linked to the CAAT-EU board meeting (24 Oct) and a public information day (25 Oct) on the same topic.
Contact: Mardas Daneshian (caat-eu@uni-konstanz.de)

*Pharmaceutical Industry Refinement Working Group*
October 26, 2012
Konstanz, Germany

This collaboration of so far 12 pharmaceutical companies and CROs with regulators brokered by CAAT aims to exchange best practices and discuss their acceptability for regulatory studies. The group will meet for the first time in Europe to expand to this side of the Atlantic. By invitation only.
Contact: Joanne Zurlo (jzurlo@jhsph.edu)

*Alternative in vitro methods to characterize the role of Endocrine Active Substances (EASs) in human hormone-targeted tissues*
December 17, 2012
Rome, Italy

A joint symposium of Istituto Superiore di Sanità, the Italian Platform for Alternative Methods (IPAM), and CAAT-EU.
Contact: Stefano Lorenzetti (stefano.lorenzetti@iss.it).

## New CAAT staff, faculty, board members, and sponsors

Some new staff members have joined the CAAT team: Sean Clarkson (Associate Director of Development), Jaimie Derita (Administrative Secretary), Dr Annamaria Rossi (part-time Scientific Project Officer, so far Pfizer, UK), and Dr Lena Smirnova (Research Associate, so far ZEBET, Germany). Annamaria Rossi aims among others to establish a working group of pharmaceutical industry for the safety assessment of biologicals.
Contact: Annamaria Rossi (roam60@alice.it).

We are happy to welcome two new sponsors to the CAAT family, i.e., Novartis and ThermoFisher. They will be represented on the CAAT board by Dr Markus Schmutz (Global Animal Welfare Officer Novartis Pharma) and Dr Martin L. Pietila (Global Manager of New Markets Life Science Research – Cellomics). Furthermore, David Dix (EPA), Eric Hutchinson (JHMI), David Jacobson-Kram (FDA) have joined our US board.

## Recent publications by CAAT/ CAAT-Europe Faculty

Leist, M., Hasiwa, N., Daneshian, M., and Hartung, T. (2012). Validation and quality control of replacement alternatives – current status and future challenges. *Toxicology Research*. doi: 10.1039/c2tx20011b, available at: http://cl.ly/0l163l0X2e0A0i1j3J1m

Rovida, C., Ryan, C., Cinelli, S., et al. (2012). The Local Lymph Node Assay (LLNA). *Current Protocols in Toxicology, Supplement 51*, 20.7.1-20.7.14.

Hartung, T. (2012). 21st century toxicology – 88 years left? *Chemistry World June 2012*, p. 39, available at: http://www.rsc.org/chemistryworld/2012/05/21st-century-toxicology


# News from NICEATM and ICCVAM

We are pleased to provide this update on recent and planned activities of the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and its Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). ICCVAM is composed of representatives from 15 U.S. Federal regulatory and research agencies that require, use, or generate toxicological and safety testing information. ICCVAM is charged with evaluating the usefulness and limitations of new, revised, and alternative safety testing methods and integrated testing strategies with regulatory applicability. ICCVAM then provides recommendations on the scientific validity of evaluated methods and strategies to U.S. Federal agencies.

U.S. Federal law established ICCVAM as a permanent interagency committee under NICEATM. NICEATM, which is located within the National Institute for Environmental Health Sciences (NIEHS), administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. Consistent with the NTP mission, NICEATM also conducts and coordinates international validation studies on high-priority improved safety testing methods and strategies.

NICEATM and ICCVAM promote the scientific validation and regulatory acceptance of safety testing methods that more accurately assess the health hazards of chemicals and products while reducing, refining (enhancing animal welfare and decreasing or eliminating pain and distress), and replacing animal use. NICEATM and ICCVAM collaborate to evaluate new and improved test methods and strategies applicable to the needs of U.S. Federal agencies and work to achieve national and international harmonization of safety testing methods.

## Updated Five-Year Plan for 2013-2017 available for comment

NICEATM and ICCVAM are requesting public comment on a draft NICEATM-ICCVAM Five-Year Plan, which will provide strategic direction for NICEATM and ICCVAM during 2013-2017. The plan outlines how, consistent with ICCVAM's statutory duties and purposes, NICEATM and ICCVAM will contribute to the transformation of safety testing by fostering and promoting the incorporation of scientific advances and innovative technologies into new improved test methods and integrated testing and decision strategies.

Recent advances in emerging science and technology innovations are driving transformative changes in toxicology and how safety testing is performed. The field of toxicology is evolving from a practice based largely on animal testing towards one based on the integration of data from a wide range of sources, including *in vitro* methods that evaluate changes in biological pathways predictive of adverse outcomes and *in chemico* and *in silico* methods.

The draft plan describes four broad strategic opportunities for NICEATM and ICCVAM to foster and promote development, validation, and regulatory acceptance of scientifically sound alternative test methods by the U.S. Federal government and other organizations:

– *Promote the Application and Translation of Innovative Science and Technology* to develop predictive alternative test methods and integrated testing and decision strategies
– *Advance Alternative Test Methods and Testing Strategies* through new evaluation activities for focus areas initially identified in the 2008-2012 Five-Year Plan and new focus areas for 2013-2017
– *Facilitate Regulatory Acceptance and Use of Alternative Methods* through high quality test method evaluations and effective outreach and communication
– *Develop and Strengthen Partnerships* with the broad range of ICCVAM stakeholders

NIEHS and NICEATM invite comments on the draft 2013-2017 Five-Year Plan from all ICCVAM stakeholders for consideration by ICCVAM and ICCVAM member agencies' program offices. In addition, comments are sought on how NICEATM and ICCVAM can most effectively contribute to the evolving transformation of safety testing. Stakeholder comments will be considered in finalization of the draft plan.

The draft updated Five-Year Plan is available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/docs/5yearplan.htm

A link to an online comment form is also available on this page. Comments may also be submitted to NICEATM via email at niceatm@niehs.nih.gov. Individuals submitting comments are asked to include appropriate contact information, and all comments received will be posted on the NICEATM-ICCVAM website and identified by the individual's name, affiliation, and sponsoring organization.

## ICCVAM 2010-2011 Biennial Report now available

The *Biennial Progress Report 2010-2011: Interagency Coordinating Committee on the Validation of Alternative Methods* is now available on the NICEATM-ICCVAM website. The Biennial Progress Report describes activities and progress by NICEATM and ICCVAM during 2010 and 2011.

During the past two years, NICEATM, ICCVAM, and ICCVAM member agencies contributed to the national and/or international endorsement and adoption of 14 new and updated alternative safety testing methods. Since ICCVAM was established, NICEATM, ICCVAM, and the ICCVAM member agencies have contributed to the acceptance of over 50 alternative methods to protect the health of people, animals, and the environment while reducing, refining, and replacing animal use.

Selected highlights from the *Biennial Progress Report* include:

– On behalf of NICEATM and ICCVAM, NIEHS signed an agreement to add the Republic of Korea to the International Cooperation on Alternative Test Methods (ICATM). ICATM was established in 2009 by the United States, the European Union, Japan, and Canada to expedite the worldwide validation and regulatory acceptance of improved alternative test methods.
– The Organisation for Economic Co-operation and Development (OECD) adopted an international guidance document prepared by NICEATM and ICCVAM for two *in vitro* test methods that can be used to reduce animal use for identifying potentially poisonous substances. NICEATM led the international validation studies for the two cytotoxicity test methods, which can reduce animal use by up to 50% for each test.
– U.S. Federal agencies and the OECD adopted several new versions and applications of the murine local lymph node assay (LLNA), an alternative method recommended by ICCVAM to assess whether substances may cause allergic contact dermatitis. The recommendations reduce animal use for each test by 20-40% and support expanded use of the LLNA for nearly all testing situations. Two new "green" versions of the LLNA were adopted that do not require radioactive reagents and that will allow laboratories worldwide to take advantage of animal welfare benefits provided by the LLNA.
– U.S. Federal agencies adopted ICCVAM-recommended alternative test methods and procedures that will further reduce, refine, and replace animal use for eye safety testing. These include the routine use of medications to avoid most if not all pain and distress when it is necessary to use animals for required safety testing, and the first *in vitro* test method that can be used in a "bottom-up" approach to identify substances that are not considered eye hazards.
– NICEATM, ICCVAM, and their ICATM partners convened the first international workshop on alternative methods for human and veterinary vaccine potency and safety testing. The workshop recommended priority research needed to develop improved and more efficient test methods that can also reduce, refine, and replace animal use. A focused workshop on human and veterinary rabies vaccine test methods was held in 2011, and additional focused workshops are planned for 2012 (see announcements below) and 2013.
– ICCVAM completed international evaluation of an *in vitro* test method proposed as a screening test to identify substances with potential endocrine activity. The test method uses engineered human cells to identify substances that induce or inhibit activation of the human estrogen receptor. Use of this test method may reduce the number of animals necessary for endocrine disruptor screening.
– NICEATM and ICCVAM convened two workshops on *Best Practices for Regulatory Safety Testing* to promote the use of improved and more efficient test methods that can also reduce, refine, and replace animal use. Participants learned how to select and use approved alternative methods to assess the safety or potential hazards of chemicals and products.

The *Biennial Progress Report* is available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/about/ICCVAMrpts.htm

## International Workshop on Alternative Methods for *Leptospira* Vaccine Potency Testing to be held in September: Agenda now available

NICEATM, ICCVAM, and their ICATM partner organizations will convene an "International Workshop on Alternative Methods for *Leptospira* Vaccine Potency Testing: State of the Science and the Way Forward" on September 19-21, 2012. The workshop will be hosted by the U.S. Department of Agriculture (USDA) Center for Veterinary Biologics at the National Centers for Animal Health in Ames, Iowa.

Leptospirosis is a bacterial zoonotic disease caused by spirochetes of the genus *Leptospira*. An estimated 500,000 human cases of leptospirosis occur worldwide each year with a fatality rate

of up to 25% in some regions. Designated as a Neglected Tropical Disease by the U.S. National Institutes of Health and a Neglected Zoonotic Disease by the World Health Organization, leptospirosis is a global public health priority.

In the United States and other countries, *Leptospira* vaccines are used in cattle, swine, and dogs to protect them from disease and to reduce the risk of animal-to-human transmission. Human vaccines are also available in some countries outside the United States. Manufacturers test the potency of vaccine lots prior to their release to ensure their effectiveness. However, methods currently used to test the potency of *Leptospira* vaccines involve large numbers of laboratory animals that experience significant pain and distress, accounting for over one third of the animals reported to the USDA in this category.

This workshop will bring together international scientific experts from government, industry, and academia to review recent advances in science and technology, in addition to available methods and approaches for *Leptospira* vaccine potency testing. The workshop will focus on methods and approaches that will provide improved accuracy, efficiency, and worker safety and that are more humane and use fewer or no animals. Participants will develop a strategy to achieve global acceptance and implementation of scientifically valid alternative methods.

Registration information and a workshop program are now available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/meetings/LeptoVaccWksp-2012/LeptoVaccWksp.htm

The workshop is open to the public with no charge for attendance, but all attendees must preregister by September 7, 2012. NICEATM and ICCVAM also invite the submission of abstracts for scientific posters to be displayed during this workshop; abstracts should be submitted by August 13, 2012. If you have questions about the workshop or would like more information, please contact NICEATM at: niceatm@niehs.nih.gov

## Hold the date: International Workshop on Alternative Methods for the Detection of Pertussis Toxin in Acellular Pertussis Vaccines, November 28-29, 2012

NICEATM and ICCVAM will convene an "International Workshop on Alternative Methods for the Detection of Pertussis Toxin in Acellular Pertussis Vaccines: State of the Science and the Path Forward" on November 28-29, 2012. The workshop will be held at the William H. Natcher Conference Center at the U.S. National Institutes of Health headquarters in Bethesda, Maryland. NICEATM and ICCVAM are organizing the workshop in collaboration with partner organizations in the International Cooperation on Alternative Test Methods.

Pertussis, also known as whooping cough, is a highly contagious bacterial disease that was a major cause of childhood mortality until vaccines became available.

Regulatory authorities require safety, potency, and purity testing prior to release of pertussis or pertussis-containing vaccines. The murine histamine sensitization test (HIST) is a key safety test performed to ensure that pertussis toxin in these vaccines has been effectively inactivated. However, such testing may involve large numbers of mice, some of which can experience significant unrelieved pain and distress. An international workshop organized in 2010 by NICEATM, ICCVAM, and their international partners identified the HIST as a priority for future research, development, and validation of alternative test methods that could further reduce, refine, or replace animal use for acellular pertussis vaccine safety testing.

The upcoming workshop will provide a forum to discuss and review protocols and available data from an ongoing study of *in vitro* alternatives to the HIST test. The workshop will also review recent advances and innovations in science and technology that can be applied to the development of new methods and approaches for acellular pertussis vaccine safety testing that are more humane, use fewer or no animals, and may provide greater accuracy, precision, and efficiency. Finally, the workshop will address the path toward validation, global acceptance, and implementation of scientifically valid alternative methods for acellular pertussis vaccines.

Registration information and a workshop program will be available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/meetings/HISTWksp-2012/HISTWksp.htm

The workshop is open to the public with no charge for attendance, but all attendees are encouraged to preregister by November 16, 2012. If you have questions about the workshop or would like more information, please contact NICEATM at: niceatm@niehs.nih.gov

## NICEATM requests nominations of High Throughput Assays for the Tox21 Program

The U.S. government's multiagency "Tox21" initiative aims to improve hazard assessment of substances potentially harmful to humans and the environment. This will be done using integrated high throughput screens that provide information on substances' effects on biological pathways related to toxicity.

NICEATM is accepting nominations of high throughput screening (HTS) assays on behalf of the Tox21 Consortium and its Assays and Pathways Working Group. Nominated assays determined to be compatible with the HTS program will support Tox21 by providing data on endpoints that serve as biomarkers for initiating or downstream events in toxicity pathways. Of particular current interest are assays that evaluate effects to the following pathways:

- Biological pathways: Wnt, SHH (aka SONIC hedgehog), Delta-notch, TGF-beta, receptor tyrosine kinase (aka RTK), and retinoid
- Endocrine pathways: estrogen, thyroid, adrenal, and androgen

Data collected in the Tox21 initiative will be used in the near term to prioritize uncharacterized substances for regulatory testing using both traditional and novel test methods. The eventual goal of Tox21 is to use HTS methods to generate data

that will allow risk assessors to more accurately predict the effects of regulated substances on human health and the environment.

Information about nominating assays and NICEATM support of Tox21 can be found on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/Tox21/Tox21.htm

### For more information

Questions about NICEATM and ICCVAM activities are welcomed and can be directed to Dr William S. Stokes, Director, NICEATM, at niceatm@niehs.nih.gov; phone +1 919 541 2384; fax +1 919 541 0947. Copies of documents mentioned in this update can also be obtained by contacting NICEATM.

Information on the availability of NICEATM and ICCVAM draft documents, requests for nominations of experts to participate at workshops and on peer review panels, and specific information about NICEATM-ICCVAM meetings are communicated via the ICCVAM-all e-mail list and in notices posted in the U.S. *Federal Register*.

Subscribers to the ICCVAM-all e-mail list are notified directly of NICEATM-ICCVAM activities. Subscribers receive e-mail notification of NICEATM-ICCVAM *Federal Register* notices, availability of NICEATM-ICCVAM reports, notices of upcoming meetings, requests for public comments or data, and other events of interest to our stakeholders. If you would like to subscribe to the ICCVAM-all list, or for more information, please visit the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/contact/ni_list.htm

IIVS
Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together

# IIVS News & Views

### British American Tobacco joins the IIVS Science Advisory Panel

IIVS is pleased to welcome Dr Marianna Gaca of British American Tobacco's (BAT) Group Research & Development Center to its Science Advisory Panel. BAT's research and development activities are principally focused on better understanding the harm caused by tobacco use and working to develop potentially less harmful products. Part of BAT's current research program is focused on developing *in vitro* models relevant to a number of tobacco related diseases and disease processes. BAT hopes that these models will enable them to understand further the biological effects of tobacco smoke and provide a tool for the assessment of prototype products. To learn more about BAT's research and development activities, please visit: www.batscience.com

### Validation services

IIVS has historically participated in a wide range of validations from small, single-stakeholder studies, to large, international multi-laboratory, regulatory validations. We have been involved in all aspects of these types of studies, including validation study design, optimizing the technical procedures and documentation systems, providing training to participating labs, executing the in-life activities, and final management evaluation of validation study data. Accordingly, we tailor our activities to meet the nature and scope of the stakeholders' expectations.

IIVS has recently participated in a number of international assay validations for regulatory acceptance. Among these are:

- a three-laboratory validation of the InVitro International Ocular IRRITECTION® assay to be submitted to ECVAM
- the COLIPA-sponsored Eye Irritation Validation Study using the MatTek EpiOcular™ reconstructed human tissue model
- a three-laboratory Skin Irritation Test Validation of the CellSystems® EST1000 reconstructed human epidermis tissue model
- Ceetox SenCeeTox screen for identifying skin sensitizers using reconstructed human epidermis
- KeratinoSens Assay: A rapid human cell based screen for identifying skin sensitizers

### IIVS training: Safety Research Institute for Chemical Compounds, Hokkaido, Japan

In February 2012, IIVS was invited by the Japanese Center on the Validation of Alternative Methods (JaCVAM) to the Safety Research Institute for Chemical Compounds Co., Ltd (SRICC) in Hokkaido, Japan to provide training on

the Bovine Corneal Opacity and Permeability (BCOP) assay. Established in 1970, SRICC is a contract research organization which provides toxicology testing services for various industries such as pharmaceutical, agricultural, and chemical manufacturers.

The training was conducted over 4 days, and provided several staff members with the opportunity to perform the assay under the supervision of IIVS staff. The training focused on perfecting the technical details of the assay to provide their biologists with the experience to handle some of the unique challenges that can be encountered when working with the assay system. A lecture on histology was also provided by Hans Raabe, which demonstrated representative artifacts that may be observed in the analysis of bovine corneas.

At the end of the training, SRICC's lab team demonstrated their proficiency in the assay to members of JACVAM. SRICC aims to continue to gain experience with the assay and begin using it for commercial services in the near future. With the training received from IIVS, SRICC will be the first organization in Japan to offer BCOP for commercial testing services.

## Next IIVS webinar: July 19th, 10 am EDT Revising Skin Irritation Testing Strategies: Applying Non-Animal Test Methods

Join Hans Raabe of IIVS to discuss the integration of non-animal test methods into strategies for determining the dermal irritation potential of test materials. The skin irritation test (SIT) for R38 prediction (OECD TG 439), skin corrosivity assay (OECD TG 431), and a time-to-toxicity approach will be discussed. Both regulatory and non-regulatory uses of these methods will be highlighted along with basic protocol outlines and strategies to use non-animal test methods. Please visit: www.iivs.org to register

## IIVS staff outreach

Hans Raabe, Vice President, Director Laboratory Services, has been selected as Vice President-elect to the Society of Toxicology's In Vitro and Alternative Methods (IVAM) Specialty Section. The IVAM Specialty Section was founded in 1994 and consists of SOT members who have expertise or interest in the application of *in vitro* techniques to problems of cellular toxicity, with a special emphasis on product safety. IVAM holds regular meetings at the annual SOT meeting and sponsors continuing education courses as well as three student awards for posters on subjects related to *in vitro* toxicology. To become involved in IVAM please visit: www.toxicology.org

Erin Hill, Vice President, Director Program Development, has been elected to the board of the In Vitro Testing Industrial Platform (IVTIP). Member companies utilize IVTIP as a forum to further their interest in the use of *in vitro* methods for regulatory and safety testing and to network with experts in the field during two annual meetings. As a board member Erin will be involved in designing IVTIP programs and representing the organization at various conferences. For more information on the platform or to become a member, please visit: www.ivtip.org

Brian Jones, Director Education and Outreach Programs, has been awarded a professorship in the School of Science at Beijing Technology and Business University (BTBU). BTBU, awarded the rank of Excellence by the Ministry of Education, is a key state-run university in China with comprehensive disciplines covering Arts, Sciences, Engineering, Law and more. The School of Science currently has more than 300 undergraduates, 60 post graduates and 78 faculty members with 14 professors. Brian's responsibilities will be to provide a fall lecture series on skin biology, safety and efficacy testing of cosmetic products and ingredients, with a focus on non-animal methods, and to be a graduate student advisor.