



Corners



News from the American Society for Cellular and Computational Toxicology

The American Society for Cellular and Computational Toxicology (ASCCT) released its second newsletter to its membership in June. To increase visibility about the activities and plans of the Society, this newsletter, together with the first issue, released in March, is being made available to the general public via the ASCCT website (www.ascctox.org). Subsequent newsletters will be available only to members.

This summer the ASCCT has added many individual members and one new Founding Sponsor: S.C. Johnson. Organizations that contribute \$ 1000 by Aug. 31, 2011 will be considered Founding Sponsors and will receive a lifetime complimentary individual membership, display of their logo on the ASCCT website, and other advertising benefits over the life of the Society.

Individuals, students, and organizations had the opportunity to join the So-

ciety in Montreal at the ASCCT booth at the 8th World Congress on Alternatives and Animal Use in the Life Sciences.

During the Congress, the ASCCT also co-hosted a lunch session with the European Society for Cellular and Computational Toxicology (ESTIV), i.e. Session I-14: Comparing the Challenges of Implementing New Non-animal Methods in the U.S. and Europe.

Four speakers (two ESTIV and two ASCCT members) discussed the challenges in implementation and use of alternative methods within corporate and academic sectors.

Topics included:

- Factors driving the search for and development of alternative methods
- Resources available for development and validation (or lack thereof)
- Comparison of processes for the development of methods, whether the de-

velopment and use will be in-house or external

- Challenges to the regulatory acceptance of data from alternative methods
- Recommendations for making the implementation and use of alternative methods more efficient

In July ASCCT members enjoyed the first in what will be a series of educational webinars on topics in *in vitro* and *in silico* toxicology, including regulatory agency, member, and OECD activities and emerging research and tools. The first webinar was given by Dr. Patricia Schmieder of the EPA's National Health and Environmental Effects Research Laboratory, describing MetaPath, a Metabolism Pathway Database and computational tool. The next webinar will be in September and will be given by Dr. Gilman Veith of the International QSAR Foundation, on Effectopedia.

Become a member to find out more!



CAATfeed

CAAT at the 8th World Congress on Alternatives and Animal Use in the Life Sciences Montreal, Canada. August 21-25, 2011

- On Sunday, August 21, CAAT and the Human Toxicology Project Consortium co-hosted a satellite meeting on implementation of the NAS Report: “21st Century Toxicology: Updates on Current Efforts.”
- CAAT observed its 30-year anniversary Monday evening as part of the opening Get-Together Party at the magnificent Bonsecours Market overlooking the St. Lawrence River.
- CAAT again organized a meeting of representatives of the various 3Rs organizations world-wide, as well as a separate Altweb Project Team Meeting.

CAAT collaboration with IVTIP and ESTIV

CAAT joined forces with the In Vitro Testing Industrial Platform (IVTIP) and the European Society of Toxicology In Vitro (ESTIV) to offer a meeting that addressed “In vitro reconstructed human tissue models as alternatives to animal testing: applications and limitations.” The meeting was held in Monaco April 26-28. The meeting also was sponsored by EPAA and Cefic.

The highlight of the first day was the official announcement of the ALEXAN-

DRA Association. ALEXANDRA (Alternatives to Experiments on Animals Destined to Research Applications) is a Monaco-based initiative headed by Dr. Bart de Wever and Dr. Constantin Turchina. The Association (<http://www.alexandra-project.org>) aims to stimulate research and development in the area of alternative methods to animal experimentation by providing financial support to researchers and entrepreneurs worldwide. The ALEXANDRA Association will work in collaboration with other international centers of excellence including CAAT, ESTIV, ZET and IVTIP. ALEXANDRA also will provide a platform for discussion and exchange of information on the selected R&D projects between scientific opinion leaders, industry, regulatory bodies and the public, organizing regular international conferences in Monaco.

During the Monaco meeting, IVTIP, ESTIV and CAAT-Europe officially announced their decision to collaborate closely in the future. Networking is the principal tool implemented by each organization to reach our goals. The common denominator for the three organizations is the genuine interest in *in vitro* testing and the objective to actively promote *in vitro* toxicology in product development, hazard identification and safety assessment.

The goals of this collaboration among the three societies include:

- Optimize the exploitation of the synergies with the objective of improving the flow of relevant knowledge be-

tween academia, industry and regulatory bodies.

- Stimulate the application of *in vitro* tests by industry and the acceptance of these tests by regulatory authorities.

CAAT-Europe holds workshop on dog use in biomedical research and testing

The workshop, held in Budapest, Hungary, drew representatives from universities, pharmaceutical companies, NGOs, and other stakeholders who discussed where dogs are currently being used and how the Three Rs might be applied to their use. A summary and outcomes of the meeting will be published in ALTEX. The meeting was covered by *Nature* in a recent article titled: “Call to curb lab tests on dogs. Canine remains the default option in outdated pharmaceutical toxicology.” See <http://www.nature.com/news/2011/110628/full/474551a.html>. Although there were some minor errors in the article, the basic focus and discussion of the meeting were presented accurately.

Nature article on CAAT study analyzing phase one of REACH

In Europe the REACH legislation aims to fill the large information gaps we have on chemicals in current use. This massive effort has a large impact



on animal use and its alternatives. We previously published an estimation of the animal numbers required to achieve the REACH goals if we apply the first guidance for testing (<http://www.nature.com/nature/journal/v460/n7259/full/4601080a.html>). The outcome was that this approach is clearly not feasible. The first 200 publicly available summary reports were now analyzed focusing on reproductive and developmental toxicity, which will require 90% of the animals and 70% of the testing costs of REACH (<http://www.nature.com/news/2011/110712/full/475150a.html>). 20% more substances were registered than expected (final count 3242) in the first phase and it appears that more information on reproductive and developmental toxicity is available than we expected. However, only few dossiers suggest new animal experiments be done, despite large data gaps remaining in these areas. Therefore, the proposed completeness check of 5% of dossiers not proposing new animal experiments by ECHA will not suffice to ensure the information needs required by REACH are met. Extrapolating only the tests that have been suggested in these first 200 proposals to the full dossier count will already exceed European testing capacities. We clearly need to integrate alternative approaches, especially in reproductive toxicity testing, where the one-generation study already accepted by OECD reduces animal use and costs by over 60%, but is not yet accepted for REACH (<http://www.nature.com/>

[news/2010/100113/full/463142b.html](http://www.nature.com/news/2010/100113/full/463142b.html)). The full study has been expanded to 400 dossiers and is under peer-review at ALTEX.

Upcoming CAAT events

CAAT t⁴ Workshop

Roadmap for Systemic Toxicity Testing
October 10-12, 2011
Konstanz, Germany
Contact: caat-eu@uni-konstanz.de

CAAT-Europe Workshop and Information Day

Status and Future of Cosmetics Safety Testing
October 13, 2011
Konstanz, Germany
Contact: caat-eu@uni-konstanz.de

CAAT-US t⁴ Workshop

Testicular Toxicology In Vitro Models
October 26-27, 2011
Baltimore, MD, USA
Contact: mprincip@jhsp.edu

CAAT-US Information Day

Food Information Day
November 15, 2011
Baltimore, MD, USA
Contact: mprincip@jhsp.edu

For up-to-date listings and information about CAAT programs and events:

<http://caat.jhsph.edu/programs/>

Recent publications by CAAT/ CAAT-Europe Faculty

Bressler J., O'Driscoll C., et al. (in press). P19 embryonic carcinoma cell line: A model to study gene-environment interactions. In Michael Aschner, et al. (eds.). *Cell Culture Techniques (Neuromethods 56)*, Heidelberg: Springer Science+Business Media.

Hartung, T., and Sabbioni, E. (2011). Alternative in vitro assays in nanomaterial toxicology. *Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol.*, doi: 10.1002/wnan.153.

Stiegler, N., Krug, A., Matt, F., and Leist, M. (2011). Assessment of chemical-induced impairment of human neurite outgrowth by multiparametric live cell imaging in high-density cultures. *Toxicol. Sci.* 121, 73-87.



News from ecopa

The European Consensus-Platform for Alternatives – ecopa – welcomes the opportunity to inform ALTEX readers of our activities in a regular corner.

Ecopa is a non-governmental organization that promotes the 3Rs at the European level. It brings together 14 European national consensus platforms on alternative methods: the Austrian Centre for Alternative and Complementary Methods to Animal Testing (zet), the Belgian Platform for Alternative Methods to Animal Testing (BPAM), the Czech Consensus Platform for 3R Alternatives to Animal Experimentation (CZECOPA), the Danish Consensus Platform for Alternatives (DACOPA), the Finnish National Consensus Platform for Alternatives (Fin-copa), the French *Plateforme Nationale pour le développement des Méthodes alternatives à l'expérimentation animale*, the German Foundation for the Promotion of Alternate and Complementary

Methods to Reduce Animal Testing (Stiftung set), the Hungarian Consensus Platform for Alternatives (HUCOPA), the Italian Platform on Alternative Methods (IPAM), the Netherlands Organization for Health Research and Development (ZonMw), Norwegian Reference Centre for Laboratory Animal Science & Alternatives (norecopa), the Spanish *Red Española para el Desarrollo de Métodos Alternativos a la Experimentación Animal* (Rema), the Swedish Platform for the 3Rs alternatives to animal experiments (Swecopa), the 3R Research Foundation Switzerland, and associated platforms in Poland and Ireland.

Ecopa's major stakeholders are animal welfare organizations, industry, academia and governmental institutions, which are all equally represented. The aims of ecopa are exchange of scientific information, expertise and experience, development and implementation of 3R-methods and

improvement of public, governmental and scientific awareness toward alternative methods. Ecopa is active in science, education and also in ethical issues with respect to alternative approaches. The tools ecopa involves for its aims include organization of conferences and seminars, dissemination of information also via scientific publications, scientific and educational initiatives, membership in relevant bodies, preparing reports, and critical and scientific political statements (e.g. "impact of REACH 2006"), organization of workshops (e.g. annual ecopa workshop and ecopa Science Initiative – eSI-workshops), and participation in EU projects. Ecopa was involved in several FP6 and FP7 projects, i.e. CONAM, PREDICTOMICS, A-CUTE-TOX, RE-PROTECT, SENS-IT-IV, BIOSOM, carcinoGENOMICS, LIINTOP, FORIN-VITOX and START-UP. The registered office of ecopa is located in Brussels.



Zet (Austria):

New teaching material for schools

Alternatives to animal testing need support! Therefore, it is crucial that juveniles learn about them already in school. In cooperation with Dr Klaus Schröder from “Zet” (*Zentrum für Ersatz- und Ergänzungsmethoden*), the Austrian Association for Animal Welfare Education “*Tierschutz macht Schule*” developed an educational magazine for college students and young people interested in studying

at university. The mascot rat “Rita 3R” guides readers through the teaching resource, explaining important terms such as the “3Rs in science” and showing ways to improve the life of research animals. In order to provide first hand data and impressions “Rita 3R” also interviews Prof. Dr Hanno Würbel (Institute of Veterinary Physiology, Justus-Liebig-University of Giessen, Germany) and Dr Jan Lund Ottesen (Veterinarian, Head of the Animal Facility of Novo Nordisk). This educational magazine can be read individu-

ally or used in class without preparatory time according to the approach of holistic learning. Next to interviews with experts, “Rita 3 R” informs on the history of animal testing as well as on the European Cosmetics Directive. The practical aspects of the development of alternatives to animal testing are shown through a portrait of the work of Dr Schröder and his team at Zet. The magazine “Animal pro – research animals” can be ordered at: www.tierschutzmachtschule.at



Norecopa (Norway):

International Consensus Meeting on Farm Animals

Norecopa regularly arranges international meetings on the application of the 3Rs. Previous meetings have focused on fish and wildlife research. The upcoming meeting will be on “Harmonization of the Care and Use of Farm Animals in Research”, to be held September 26-28, 2012 at Oslo airport Gardermoen.

The revised EU Directive on animal research will come into effect just 3 months after this meeting, and last year a new edition of the *FASS Guide for the Care and Use of Agricultural Animals in Research and Teaching* was issued in the United States. The consensus meeting will serve as a forum to discuss the implications of

these new documents, as well as providing continued professional development for all those involved in the use of farm animals in research.

For more information visit www.norecopa.no/sider/tekst.asp?side=21 or contact Adrian Smith (adrian.smith@vetinst.no).

Care and Use of Fish in Research

One of the new items in the revised EU Directive is that all procedures are to be classified according to their severity (Article 15). An expert group commissioned by the EU has produced guidelines for the severity classification of procedures used on animals in research. This report

focused on procedures used on the traditional laboratory animals. A number of procedures commonly used in fish research were not mentioned.

Following the international consensus meeting entitled “Harmonisation of the Care and Use of Fish in Research,” a complementary report on procedures used in fish research was published:

Hawkins, P., Dennison, N., Goodman, G., et al. (2011). Guidance on the severity classification of scientific procedures involving fish: report of a Working Group appointed by the Norwegian Consensus-Platform for the Replacement, Reduction and Refinement of animal experiments (Norecopa). *Lab. Anim.*, Epub ahead of print.



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 by law with evaluating the usefulness and limitations of new, revised, and alternative safety testing methods with regulatory applicability and providing recommendations on their scientific validity to U.S. Federal agencies, which must respond to ICCVAM within 180 days. ICCVAM promotes the scientific validation and regulatory acceptance of safety testing methods that more accurately assess the health hazards of chemicals and products while reducing, refining (decreasing or eliminating pain and distress), and replacing animal use.

NICEATM 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 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.

Peer Panel Report available on a new method to identify potential endocrine active substances

In a public meeting on March 29-30, 2011, an independent international peer review panel agreed with ICCVAM draft test method recommendations stating that an *in vitro* test method may be used as an initial screen to identify substances with the potential to enhance or inhibit activation of the estrogen receptor. More than 40 scientists representing industry, academia, and U.S. Federal regulatory agencies attended the peer panel meeting at the National Institutes of Health. The meeting was open to the public.

NICEATM convened the peer review panel meeting as part of the ICCVAM test method evaluation process. The panel, which included expert scientists from seven countries, reviewed data from a NICEATM-sponsored validation study to assess the accuracy and reliability of an *in vitro* estrogen receptor (ER) transcriptional activation (TA) test method. This test method, the BG1Luc ER TA, was considered for qualitative identification of substances with *in vitro* ER agonist or antagonist activity. The BG1Luc ER TA test method uses human ovarian cancer cells to measure whether and to what extent a substance induces or inhibits TA activity via the ER-mediated pathway. Also known as the LUMI-CELL[®] ER assay, this method was developed by Xenobiotic Detections Systems, Inc., with support from a Small Business Innovation Research grant from the NIEHS.

The report of the peer review panel meeting was made available in May, and

NICEATM invited public comment on the report via email announcements and a notice in the *Federal Register*. ICCVAM will consider the peer review panel's report, comments from the public, and comments from the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) as it develops final test method recommendations that will be forwarded to U.S. Federal agencies later this year.

Exposure to substances that interfere with the normal function of hormones in the endocrine system can lead to abnormal growth, development, or reproduction. The U.S. Environmental Protection Agency initiated the Endocrine Disruptor Screening Program to screen pesticides and environmental contaminants for their potential to affect the endocrine systems of humans and wildlife. The BG1Luc ER TA test method may be appropriate for use as an initial screen of substances tested in this program.

The peer review panel report, which contains a detailed summary of the panel's discussions and conclusions, along with all of the documents considered by the peer review panel, are available on the NICEATM-ICCVAM web site at: <http://iccvam.niehs.nih.gov/methods/endocrine/PeerPanel11.htm>

ICCVAM Working Group proposes test guideline changes to improve animal welfare

While alternative test methods are now available to evaluate some chemical eye hazards, regulatory testing still often re-



quires the use of animals. Fortunately, U.S. Federal agencies now have accepted ICCVAM recommendations for pain management procedures that can eliminate most if not all pain and distress when it is necessary to use animals for eye safety testing of chemicals and products.

NICEATM and the ICCVAM Interagency Ocular Toxicity Working Group (OTWG) recently proposed updates to the current Organization for Economic Co-operation and Development (OECD) test guideline for *in vivo* ocular safety testing to incorporate the ICCVAM-recommended pain management procedures. An updated test guideline will allow these procedures to be used worldwide, resulting in improved animal welfare for those situations where *in vivo* testing is necessary for ocular safety testing. The current test guideline, "Acute Eye Irritation/Corrosion" (Test Guideline 405) was issued in April 2002.

A draft revised Test Guideline 405 was circulated to OECD member countries for comments in June 2011. The updated draft test guideline is expected to be considered by the international Working Group of National Coordinators of the OECD Test Guidelines Program at their spring 2012 meeting.

The ICCVAM recommendations include procedures for using topical anesthetics (similar to those used in human eye surgeries) and systemic analgesics prior to and after test article administration in order to avoid animal pain and distress. The recommendations also identify specific clinical signs and le-

sions that can be used as humane endpoints to allow the early termination of studies in order to lessen or avoid pain and distress.

More information about the ICCVAM recommendations for the use of anesthetics, analgesics, and humane endpoints in ocular safety testing may be found on the NICEATM-ICCVAM web site at: <http://iccvam.niehs.nih.gov/methods/ocutox/pretreat.htm>

NICEATM-ICCVAM International Workshop on Rabies Vaccine Testing: Preliminary agenda available and call for abstracts

NICEATM and ICCVAM will convene an "International Workshop on Alternative Methods for Human and Veterinary Rabies Vaccine Testing: State of the Science and Planning the Way Forward" on October 11-13, 2011, at the U.S. Department of Agriculture Center for Veterinary Biologics in Ames, Iowa. The workshop is co-organized by the European Centre for the Validation of Alternative Methods, the Japanese Center for the Validation of Alternative Methods, the Korean Center for the Validation of Alternative Methods, and Health Canada.

This workshop will bring together international scientific experts from government, industry, and academia to review the available methods and approaches that reduce, refine (decrease or eliminate pain and distress), and replace animals used in human and veterinary rabies vaccine potency testing. Participants then will develop an implementation

strategy to achieve global acceptance and use of these alternatives.

A preliminary draft agenda for the workshop is now available on the NICEATM-ICCVAM web site. Planned sessions will include reviews of current practices and regulations for rabies vaccine potency testing, opportunities for reduction and refinement of animal use in currently available *in vivo* assays, and available non-animal methods and strategies for rabies vaccine potency testing. Breakout sessions will allow discussions leading to recommendations on how to achieve the acceptance and use of available alternative methods.

A poster session planned for the upcoming workshop will feature presentations on current research, development, validation, and regulatory acceptance of alternative methods that may reduce, refine, or replace the use of animals in rabies vaccine potency testing. NICEATM and ICCVAM invite the submission of abstracts for scientific posters to be displayed during this workshop; abstracts should be submitted by August 17, 2011.

Rabies in humans is a uniformly fatal disease, with infections killing more than 55,000 people worldwide each year. Rabies vaccines serve a vital role in preventing further deaths and controlling the disease in certain animal populations. According to the World Health Organization, an estimated 15 million people receive post-exposure vaccine prophylaxis annually due to actual or suspected exposures to the rabies virus. In the U.S. and other developed countries, rabies vaccines have effectively eliminated do-



mestic canine rabies virus strains. However, determining the safety and effectiveness of rabies vaccines requires large numbers of laboratory animals and involves significant pain and distress. New methods and approaches are sought that: 1) are more humane and use fewer or no animals, 2) are faster, cheaper, and more accurate, and 3) are safer for laboratory workers.

A recent international workshop organized by NICEATM, ICCVAM, and its international partners identified rabies vaccines as one of the three highest priorities for future research, development, and validation of alternative test methods that could further refine, reduce, and ultimately replace animal use for potency and safety testing. One of the highest priority implementation activities was the organization of an international workshop on alternative methods for rabies vaccine potency testing. Based on recent scientific and technological advances, several alternative approaches have been proposed or are currently available.

Participants in the October workshop will review these approaches and define efforts necessary to achieve global acceptance and implementation. The workshop will identify critical components of manufacturing processes necessary to demonstrate batch-to-batch consistency and how monitoring these components can be used with *in vivo* and *in vitro* potency tests in an integrated approach to reduce and replace animal use for rabies batch release. Workshop participants also will identify the most appropriate source(s) for reference reagents to ensure standardization of *in vitro* rabies potency testing methods.

A link to online registration, a preliminary draft agenda, abstract submission guidelines, and other information is available on the NICEATM-ICCVAM

website at <http://iccvam.niehs.nih.gov/meetings/RabiesVaccWksp-2011/RabiesVaccWksp.htm>. Those planning to attend the workshop are asked to preregister by October 1, 2011. Please note that late registration at the workshop will not be available, as U.S. Department of Agriculture security requires that all attendees preregister for the workshop.

If you have questions about the workshop or would like more information, please contact NICEATM at: niceatm@niehs.nih.gov

Nominations received for validation studies on four *in vitro* test methods

ICCVAM recently received nominations for validation studies on four *in vitro* test methods. Public comments were requested and will be considered by ICCVAM as it finalizes its recommendations for the priority of these proposed studies. These test methods may have the potential to reduce or replace animal use for detecting and quantifying botulinum neurotoxins and for identifying non-endotoxin pyrogens. NICEATM also seeks data generated using *in vitro* test methods relevant to the nominations, as well as relevant *in vivo* reference data.

Nomination for the detection and quantification of botulinum neurotoxins

NICEATM seeks information and data from alternative test methods used for detecting and quantifying botulinum neurotoxins (BoNT), including but not limited to three test methods nominated by BioSentinel Pharmaceuticals, Inc. (BioSentinel). Data from the standardized mouse LD₅₀ assay currently used for these endpoints are requested for comparison.

Participants in a 2006 NICEATM-ICCVAM international workshop on alterna-

tive methods for botulinum toxin testing noted that some available methods might be useful as replacements for the standard mouse LD₅₀ assay in the future, given additional development and validation efforts. Following appropriate validation and demonstration of adequate performance, the three test methods nominated to ICCVAM by BioSentinel may have the potential to meet regulatory requirements for detection and quantification of BoNTs in a range of applications, thus reducing or replacing animal use in the standard assay.

Nomination for the detection of non-endotoxin pyrogens

In addition, NICEATM seeks information and data from alternative test methods used to identify non-endotoxin pyrogens, including but not limited to the monocyte activation test (MAT), which was nominated to ICCVAM by Biotest AG. Data on non-endotoxin pyrogens tested in the rabbit pyrogen test are requested for comparison.

A 2008 ICCVAM evaluation report recommending five *in vitro* methods proposed for assessing the potential pyrogenicity of pharmaceuticals and other products noted that the test methods appeared also to have the potential for identifying a wider range of pyrogens than endotoxins. Accordingly, ICCVAM recommended future studies that could expand the applicability of the test methods. In response to these recommendations, Biotest AG has nominated a commercialized version of one of the tests for additional validation studies to evaluate its usefulness for identifying non-endotoxin pyrogens.

Public comment invited

Based on the information provided by the test method sponsors, ICCVAM proposes that the recently nominated activities are of sufficient interest and applicability to



warrant further evaluation. ICCVAM's preliminary recommendation is that both nominations should have a high priority for further discussion to assess what information is needed to adequately characterize the usefulness and limitations of the proposed test methods and any other similar *in vitro* test methods for these endpoints.

As part of the nomination review process, NICEATM invited public comments on these nominations and on the appropriateness and draft relative priority assigned by ICCVAM to the nominated activities. The preliminary ICCVAM recommendations were discussed by the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) at its meeting in June. SACATM agreed with ICCVAM that the nominations should receive a high priority for continued activity. ICCVAM will consider public and SACATM comments as it finalizes its recommendations on the priority of these nominations.

NICEATM staff presented at international meeting

NICEATM staff and ICCVAM committee members delivered presentations on recent NICEATM-ICCVAM activities and accomplishments at the Eighth World Congress on Alternatives and Animal Use in the Life Sciences in Montreal, Canada August 21-25. The theme of the Eighth World Congress (WC8) was "Together It's Possible," reflecting the specific goal of bridging the distance between science and policy and to identify opportunities for collaboration.

NICEATM and ICCVAM delivered five presentations at WC8 summarizing recent ICCVAM recommendations on the use of new versions and applications of the murine local lymph node assay to

identify substances with the potential to cause allergic contact dermatitis. Other presentations highlighted recent ICCVAM recommendations on ocular safety testing methods as well as conclusions and recommendations from the 2010 NICEATM-ICCVAM workshop on alternative methods for vaccine potency and safety testing.

NICEATM-ICCVAM requests nominations and submissions of test methods with potential regulatory applications

NICEATM and ICCVAM welcome nominations and submissions from the public for new or revised alternative safety testing methods with the potential to improve the accuracy of safety assessments and the potential to reduce, refine, or replace the use of animals. Test methods that incorporate advances in science and technology are especially encouraged.

Nominations can be submitted for proposed test method validation studies, specific test method or validation issues, or requests for test method evaluations. Such nominations typically are addressed with international validation studies, workshops, conferences, or test method independent scientific peer review meetings.

When validation studies have been completed that adequately characterize a test method's usefulness and limitations for a specific proposed regulatory requirement or application, a submission can be sent to ICCVAM for review and technical evaluation of the test method. ICCVAM then develops a test method evaluation report and formal recommendations that are forwarded to U.S. Federal agencies for acceptance consideration.

Organizations or individuals that wish to propose nominations or submissions of

promising test methods are encouraged to contact NICEATM for information and guidance on preparing proposals. Submission and nomination guidelines also are available on the NICEATM-ICCVAM website at: <http://iccvam.niehs.nih.gov/SuppDocs/submission.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 919-541-2384; fax 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



Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together

IIVS News

IIVS offers assay for skin sensitization

Developed by Givaudan, the KeratinoSens assay offers a cost effective way to screen ingredients for their potential as skin sensitizers. The assay is based on the Nrf2-Keap1-ARE toxicity pathway and utilizes a reporter cell line with a luciferase gene to detect electrophilic chemicals – a feature of skin sensitizers. The assay showed promising reproducibility and predictivity during a recent multi-laboratory study (Natsch et al., 2011) and is currently being considered for review by ECVAM. To learn more about the KeratinoSens Assay contact Dr. Kimberly Norman at knorman@iivs.org.

Dates for annual hands-on training course announced

Practical Methods for In Vitro Toxicology Workshop

On January 23-26, 2012, the IIVS' Practical Methods for *In Vitro* Toxicology Workshop will be held at the IIVS facility in Gaithersburg, MD. The course is comprised of both lecture and laboratory activities intended to provide a comprehensive introduction to *in vitro* toxicology techniques and the regulatory environment in which they are used. Past course participants have included representatives from industry, academia, and government agencies.

Course size is limited to 12 participants to allow for individual instruction in the laboratory. Registration fee includes lunch each full day and two evening events. For more information on the course including a sample agenda, please contact Amanda Ulrey at: aulrey@iivs.org

Chinese Symposia on Alternatives to Animal Testing

The growing international interest in non-animal testing methods was demonstrated recently during a series of symposia held in the People's Republic of China. Between April 11 and 15, Chinese scientists and regulators organized three major meetings which were held in Beijing and Guangzhou. Dr. Rodger Curren (IIVS) and Dr. Brian Jones (Mary Kay Cosmetics) were invited to the symposia and gave presentations on behalf of the IIVS Science Advisory Panel.

The *First International Symposium on Cosmetics – Alternatives to Animal Experimentation for Cosmetics* took place on April 11-12 in Beijing. The meeting was organized by the China Cosmetic Research Center with major support from the Food Licensing Department of the SFDA – the department which regulates cosmetics in China. The purpose of the symposium was to increase communication and cooperation within the international cosmetic community and to remove technology barriers to cosmetic safety assessment. The symposium had more than 100 attendees and speakers from the SFDA, Beijing Technology and Business University, China CDC, China Entry-Exit Inspection and Quarantine Bureau, and industry speakers from Asia, Europe and the United States. It was clear during the meeting that internationally recognized alternative methods would gradually be approved by the SFDA for evaluation of cosmetics.

Two days later the Center for Disease Control and Prevention (CDC) of Guangdong Province and the Laboratory Animal Center of Southern Medical University organized the *International*

Symposium on Technology and Application of Alternatives to Animal Testing. This meeting brought together more than 100 delegates from industry and several CDCs (where much of the safety testing of chemicals and cosmetics is conducted) to discuss the current state of the art of non-animal testing and research/validation efforts by the CDC in this area. The meeting also included a tour and laboratory demonstration of several assay systems by the CDC, as well as a demonstration of reconstructed human skin produced in China by L'Oréal.

The third meeting took place at the Food Lab of Guangdong Inspection and Quarantine Technology Center which supports the administrative functions overseeing import and export of cosmetics in China. This laboratory has been extremely active in helping set National Standards for alternative testing methods such as the 3T3NRU Phototoxicity Test, keratinocyte cytotoxicity, and the mouse Embryonic Stem Cell Test. The advantages of scientific collaboration between IIVS (and other industry laboratories) and the Technology Center was an important discussion topic.

At each of these venues, Dr. Curren presented the "Routine Use of Non-Animal Methods by Cosmetic and Personal Care Product Manufacturers in the United States" and Dr. Jones presented information on the Bovine Cornea Opacity and Permeability Assay. The discussions and interactions with numerous Chinese scientists and government regulators were extremely encouraging, and it would not be surprising to see China quickly become an important player in the growth of *in vitro* methods internationally.