Food Information Day

November 15, 2011, Johns Hopkins School of Public Health

CAAT and Orange House Partnership co-sponsored a one-day event focused on risk assessment and management for food. An interesting set of presentations compared and contrasted regulations and approaches to food safety and sustainability issues on both sides of the Atlantic. Speakers represented industry, government, and academia, both EU and US, and addressed concerns regarding animal health, international regulations, and 3Rs approaches, as well as food safety. Approximately 40 people attended.

CAAT Advisory Board Meeting

November 16-17, 2011, Johns Hopkins School of Public Health

CAAT members provided updates on all major CAAT programs (Research Projects; CAAT Grants; Evidence-Based Toxicology; CAAT Policy Program; Refinement Program; and CAAT-Europe Activities). In addition, the Board carried out its annual grant review, which included 19 applications – 16 new and 3 renewals, and 2 extensions of first-year funding.

The new grants will be posted on the CAAT site at: http://caat.jhsphs.edu/programs/grants/index.html

CAAT Board member Mark Lafranconi of Procter & Gamble gave a very well received presentation on “Looking Beyond Endpoint Alternatives.” He described P&G’s Animal Alternatives and Welfare Strategy, which incorporates, in brief:

1. Developing alternatives
   – Mechanistically based
   – Employing 3Rs
2. Maximizing use of existing information
3. Fostering acceptance of alternatives

CAAT-Europe – ecopa cooperation

It was officially announced at ecopa’s (European consensus platform for alternatives) general assembly on November 10 in Madrid that CAAT-Europe and ecopa have decided to collaborate closely and synergistically. As ecopa represents the national platforms for alternatives in 13 European countries and CAAT-Europe acts as a transatlantic communication hub between the US and Europe, this collaboration promises to enhance the flow of information, improve the quality of communication, and promote a joint effort that may serve as a role model for other NGO’s in this field.

CAAT-Europe’s role in this enterprise will be to organize the information flow from the national platforms to the interested public via the ecopa news corner in ALTEX. CAAT-Europe also will share expertise, supporting the ecopa website and providing internationally relevant news from the field of alternatives in testing and research, as well as contributing to the communication and representation of ecopa to interested parties via the ecopa Messenger.

Evidence-Based Toxicology Collaboration (EBTC) program

CAAT serves as the secretariat for the EBT Collaboration, which seeks to translate the principles and approaches of evidence-based medicine (EBM) to 21st century toxicology, so that new and traditional methods and the data generated from them can be critically evaluated. A workshop on Evidence-based Toxicology for the 21st Century: Opportunities and Challenges, was held on January 24-25, 2012 at the United States Environmental Protection Agency, Research Triangle Park, North Carolina. In addition to the website (http://ebtox.com), a newsletter and flyer are being planned. A parallel effort, led by CAAT team member Sebastian Hoffmann, will be publicly launched in Europe as a satellite to eurotox on June 17, 2012, Stockholm, Radisson Blu Royal Viking Hotel. We anticipate that these trans-Atlantic efforts will accelerate the paradigm shift already underway in toxicology towards pathway-based methods. For more information contact Sebastian Hoffmann (sebastian.hoffmann@seh-cs.com).

The Human Toxicology Project consortium

The HTP consortium, a coalition of several companies and organizations, seeks to accelerate the transition to a pathways-based approach in toxicology, as exemplified in the National Academy of Sciences’ report on Toxicity Testing in the 21st
The Humane Society of the United States serves as the Consortium’s secretariat. CAAT senior research associate Martin Stephens served as the secretariat’s director in his former position at the HSUS. With his recent move to CAAT, Stephens will serve as CAAT’s representative to the Consortium, and CAAT status within the Consortium has been elevated from “partner” to full-fledged member.


CAAT Director Thomas Hartung was a member of the NAS committee that published the NAS report, *Animal Models for Assessing Countermeasures to Bioterrorism Agents* on December 1, 2011. The report shows the limitations of animal models in this area and calls on novel technologies. CAAT plans to follow up with an information day. For key findings of the report, please see: [http://dels.nas.edu/Report/report/13233](http://dels.nas.edu/Report/report/13233)

**Refinement Working Group**

The first meeting of the CAAT-hosted Refinement Working Group was held on November 18, 2011 to discuss the industry use of microsampling and dried blood spot (DBS) analysis for drug metabolism and pharmacokinetic studies. Representatives from six companies presented the current practices in their respective organizations, which stimulated much discussion and information sharing. Dr. David Jacobson-Kram, a CAAT Advisory Board member and Associate Director for Pharmaceuticals in the Center for Drug Evaluation and Research at the US Food and Drug Administration, also attended the meeting, providing comments about the use of data from DBS in drug submissions. The presenters agreed to work together to publish a manuscript based on their talks, and a follow-up workshop will occur in 2012. CAAT was invited to organize a similar meeting in Europe in conjunction with Roche in Basel, Switzerland. This will take place in spring, 2012. CAAT also will convene a meeting in the US in conjunction with the spring Advisory Board meeting highlighting progress on the Three Rs in the pharmaceutical industry.

**CAAT activities in India**

On January 6, 2012 the 99th Indian Science Congress in Bhubaneswar hosted a plenary session on “Alternatives in Teaching, Toxicity Testing, and Education” organized by the Mahatma-Gandhi-Doerenkamp Center (MGDC) and supported by the Doerenkamp-Zbinden-Foundation. The program brought together three Doerenkamp-Zbinden Chairs, i.e., M. A. Akbarsha, M. Leist, and T. Hartung, among others. The Science Congress was attended by 19,000 participants.

In conjunction with this Congress, the International Conference on Alternatives to Animal Use in Research, Education and Toxicity Investigations was held in Chennai on January 4, 2012. The Conference, organized by MGDC and the International Institute of Biotechnology and Toxicology, included the three Doerenkamp-Zbinden Chairs as speakers. Thomas Hartung also presented at the MGDC, as well as in collaboration with the Humane Society International and the Federation of Indian Animal Protection Organisations (FIAPO) at the Indian Institute of Toxicological Research, Lucknow, and at the National Institute of Nutrition, Hyderabad. The various initiatives aim to gather critical mass in India, supporting self-organization aimed at the creation of 3Rs Centers, a consensus platform, and possibly a validation center (such as InCVAM). CAAT has offered further support for such initiatives.

**Upcoming meetings**

**Save the date:**

*February 13–15, 2012*

Metabolomics in Toxicology and Pre-clinical Research, State-of-the-art and Potential Applications – a joint CAAT-Europe and BASF Symposium and expert Workshop (Berlin, Germany). For more information contact: caat-eu@unikonstanz.de

**Save the date:**

*February 21, 2012: EBTC webinar*

EBTC director, Martin Stephens will present an ASCCT (The American Society for Cellular and Computational Toxicology) webinar on Evidence-based Toxicology. For more information contact: [http://ascctox.org/meetings.cfm](http://ascctox.org/meetings.cfm)
Open Forum on 21st Century Toxicology and Evidence-based Toxicology

Sunday, March 11, 2012, 1:00-4:00 pm at the Marriott Marquis Hotel, San Francisco, CA

CAAT and the Human Toxicology Project Consortium will host an open forum on 21st century toxicology and evidence-based toxicology as a satellite meeting to the Society of Toxicology annual conference this March in San Francisco. The forum is an opportunity for participants to provide informal updates on work they are doing to advance the new toxicology. CAAT and the HTP Consortium hosted similar meetings on 21st century toxicology last year at both the SOT conference and the World Congress on Alternatives and Animal Use. This year we are adding evidence-based toxicology to the mix, given the work of the newly formed Evidence-based Toxicology Collaboration (see www.ebtox.com), for which CAAT serves as secretariat. The HTP Consortium comprises several companies and organizations – including CAAT – seeking to accelerate implementation of the National Research Council’s 2007 report on “Toxicity Testing in the 21st Century.” Registration requested. Contact mprincipal@jhsph.edu

CAAT-Europe Workshop on “Quality standards for publications dealing with in vitro systems”

Monday, March 12, 2012, 5:00-9:00 PM, at the Marriott Hotel in San Francisco, CA

CAAT-Europe will host a workshop on “Quality standards for publications dealing with in vitro systems.” The quality of the data presentation in scientific publications is of critical concern in the scientific world. For animal experiments in general, the ARRIVE guidelines have been worked out for minimum publication standards, and the specific problem of underpowered studies has been discussed. For in vitro models, recommendations are available for good cell culture practice and for system validation (OECD GD34). This workshop aims to produce a comprehensive set of guidelines that should help authors, referees, and editors dealing with data gathered with in vitro systems. Recommendations will be made for points to consider with respect to statistical planning and presentation of data on alternative methods in the field of toxicology.

Participation is by invitation. Contact: M. Daneshian (caat-eu@uni-konstanz.de)

US FDA, CAAT, and MARTA to Co-sponsor Workshop on Reproductive and Developmental Toxicology

April 16, 2012 at the US Food and Drug Administration

The FDA initiative on “Advancing Regulatory Science” focuses on developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA regulated products. To this end, the Office of the Commissioner, Food and Drug Administration (FDA), the Johns Hopkins Center for Alternatives to Animal Testing (CAAT), and the Middle Atlantic Reproduction and Teratology Association (MARTA) have agreed to cosponsor the training workshop entitled “Reproductive and Developmental Toxicology: From In Vivo to In Vitro.”

The overall objectives of this training program are to bring scientific information about new in vitro technologies for reproductive and developmental toxicology to the FDA, as well as to provide a forum for scientists from the FDA, academia, and industry to discuss how these new technologies could eventually be integrated into the FDA paradigm. No registration fees will be charged to any participants in the course.

Additional information regarding the workshop will be announced on Altweb (http://altweb.jhsph.edu), the CAAT website (http://caat.jhsph.edu), and other venues.

Recent publications by CAAT/CAAT-Europe Faculty


Fincopa was founded in 2003 in Tampere. The first president was professor (emerita) Hanna Tähti. Today Fincopa has approximately 40 members covering all the pillars of academia, animal welfare, industry and regulators. Fincopa has been and is active in promoting the 3Rs in many ways; the members are especially active in developing human cell-based, validated tissue/organ methods as alternatives to animal experiments, promoting refinement, participating in key committees, commenting draft laws and regulations, disseminating 3Rs information by web pages, leaflets, posters, and articles in national and international newspapers, giving interviews on television and in newspapers and by organizing national and international meetings. The most recent meeting held was the 28th Workshop of SSCT and the FINCOPA Seminar “Towards toxicity assessment without animals” organized in September 2011. Their strategy is to organize co-meetings with relevant other societies to reach a wider audience and scientific forum. The board meets four times per year; its current members are Tuula Heinonen (president), Päivi Alajuuma (secretary), Eila Kaliste, Hannele Huuskonen, Marika Mannerström, Heidi Diallo, Marianna Norring (finance) and Paula Hirşjärvi. Each person has a substitute.

Roman Kolar, Kristina Wagner, and Bettina Fach of the German Animal Welfare Federation have completed their project: “Analysis of EU-legislation in terms of consistency and state-of-the-art regarding the implementation of the 3Rs in the data requirements to identify potential for further improvement” funded by SET (Foundation for the Promotion of Alternate and Complementary Methods to Reduce Animal Testing, www.stiftung-set.de).

The background of the project was that present and future EU legislation on the protection of animals used for scientific purposes (Directives 86/609/EEC and 2010/63/EU) requires that alternative methods to animal tests must be used when they are recognised by EU legislation. This principle is not implemented to its full extent when it comes to risk assessment that chemicals and new products have to undergo prior to their authorisation and placing on the market.

In this project the German Animal Welfare Federation screened data requirements of relevant EU laws and provisions regarding chemicals (REACH), biocides, pesticides, and food safety and found that test methods that are part of the risk assessment do not reflect the state-of-the-art of science and technology. Most of the data requirements investigated still require testing on animals for many toxicological endpoints, even though 40 alternative testing methods accepted on EU- or OECD-level are at hand. The reasons here range from shortage of manpower to implement existing knowledge and expertise in the field of alternative methods to unclear and misleading statements on the applicability and state of validation of alternative methods. These results call for a homogeneous EU-wide strategy aiming an efficient implementation of the 3Rs to comply with Directives 86/609/EEC and 2010/63/EU for all areas involving risk assessment of substances. This would clearly simplify data requirements, save costs on various levels, and improve product safety for consumers.
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 a committee composed of representatives from 15 U.S. Federal regulatory and research agencies that require, use, or generate toxicological and safety testing information. The purpose of ICCVAM is to reduce, refine, and replace the use of animals in testing. To accomplish this, ICCVAM is charged 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. 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.

Guidance document developed by ICCVAM Working Group adopted by OECD

A guidance document developed and proposed by a NICEATM/ICCVAM working group has been adopted by the Organisation for Economic Co-operation and Development (OECD). The guidance document supports further development of the in vitro bovine corneal opacity and permeability (BCOP) and isolated chicken eye (ICE) test methods.

Guidance document developed by ICCVAM Working Group proposed for OECD

In 2006, ICCVAM recommended that the BCOP and ICE test methods were useful to screen for ocular corrosives and severe irritants in appropriate circumstances and with specific limitations. If either of these alternative methods yields a positive result, the product can be labeled as an ocular corrosive or severe irritant, and no live animal testing is required. This recommendation formed the basis for OECD Test Guidelines 437 (for the BCOP test method) and 438 (for the ICE test method).

The ICCVAM Interagency Ocular Toxicity Working Group then developed a guidance document for use with Test Guidelines 437 and 438. The goals of the guidance document are to (1) promote histopathology evaluation as an additional endpoint for ocular safety testing and (2) provide specific guidance on using the BCOP and ICE test methods to expand their respective databases and optimize the test methods’ usefulness for identifying all hazard categories.

The guidance document, “Supplement to Test Guidelines 437 and 438: The Bovine Corneal Opacity and Permeability and Isolated Chicken Eye Test Methods: Collection of Tissues for Histopathological Evaluation and Collection of Data on Nonsevere Irritants” was formally adopted by the OECD in 2011 after international review. The document includes general procedures to guide the routine collection of tissues for histopathology evaluation. An expanded histopathology database will support future evaluations to determine if histopathology can increase the accuracy of the in vitro methods and potentially support broader applications of the BCOP and ICE test methods.
NICEATM Workshop Report on Vaccine Testing now available

A workshop organized last year by NICEATM and ICCVAM is the subject of the current issue of the journal Procedia in Vaccinology. The “International Workshop on Alternative Methods to Reduce, Refine, and Replace the Use of Animals in Vaccine Potency and Safety Testing: State of the Science and Future Directions” was convened to review the state of the science of available alternative methods for human and veterinary vaccine potency and safety testing. Workshop participants also identified specific activities that will be needed to advance test methods with the potential to reduce, refine and replace animal use for vaccine testing. Compared to toxicity testing, vaccine testing uses significantly more animals and a larger proportion of animals experience unrelieved pain and distress.

Nearly 200 scientists from 13 countries attended the workshop, which was held on September 14-16, 2010, at the National Institutes of Health in Bethesda, Maryland. Over 30 invited participants included scientists from U.S. government research and regulatory agencies as well as representatives from the governments of Japan, Canada, the United Kingdom, the Netherlands, and the European Union. National and multinational corporations and research institutions were also represented. The workshop report is comprised of 27 manuscripts and summarizes the plenary session presentations as well as the conclusions and recommendations developed by the workshop participants.

One of the key accomplishments of this workshop was the identification of the highest priority vaccines for future reduction, refinement, and replacement efforts. In addition to priorities for future efforts, numerous recommendations from the September 2010 workshop are included in the workshop reports. Some examples include:

- Specific non-animal antigen quantification approaches that have successfully replaced animals for potency testing for some vaccines should be expanded for use with other vaccines through identification, purification and characterization of vaccine protective antigens.
- Procedures should be implemented now to reduce both the numbers of animals used and the pain and distress experienced by animals while and where animal testing is still needed.
- International harmonization and cooperation efforts as well as closer collaborations between human and veterinary vaccine researchers should be enhanced in order to support more rapid progress towards reduction, refinement, and replacement of animal use.

The workshop was organized by NICEATM and ICCVAM in partnership with the European Centre for the Validation of Alternative Methods (ECVAM), the Japanese Center for the Validation of Alternative Methods (JaCVAM), and Health Canada. The workshop was cosponsored by the Society of Toxicology.

The report of the September 2010 workshop is available online at the Procedia in Vaccinology website.1 Materials from the workshop, including the agenda, presentations from the workshop, and abstracts of posters presented at the workshop poster session, are available on the NICEATM-ICCVAM website.2

NICEATM and ICCVAM convene Workshop on Rabies Vaccine Testing

NICEATM and ICCVAM convened 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. Over 70 scientists from around the world gathered at the workshop to review testing methods that are expected to reduce, refine, and

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1 http://www.elsevier.com/wps/find/journaldescription.cws_home/720522/description
2 http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm
eventually replace the use of animals for potency testing of rabies vaccines, and to
develop recommendations for their validation and implementation.

The workshop was organized in response to recommendations from the 2010 NICEATM-ICCVAM Workshop, where rabies vaccine potency testing was identified as one of the top three priorities for alternative methods to reduce, refine, and replace the use of animals for both human and veterinary vaccine testing (see story above). The workshop was organized by NICEATM and ICCVAM in partnership with ECVAM, JaCVAM, and Health Canada, and was co-sponsored by the International Alliance for Biological Standardization.

Recent scientific and technological advances may allow several alternative approaches for rabies vaccine potency testing to be implemented immediately or in the near future. The goals of this workshop were to review the current state of the science of these methods and to define efforts necessary to achieve global acceptance and implementation.

Workshop participants reviewed a recent international study on a method that measures protective antibodies from vaccinated animals to assess rabies vaccine potency. This method eliminates the need for challenge testing with live virus, thereby avoiding severe pain and distress to the test animals and providing for improved worker safety. An action plan was formulated to achieve global implementation of this alternative method.

Workshop participants also reviewed the state of the science for methods that measure the specific protective protein in vaccines as a way to assess potency without animal testing. Finally, workshop participants recommended steps that can be taken immediately to relieve animal pain and distress, including routine use of anesthetics and analgesics, and to reduce the number of animals required in the current potency test.

More information about the workshop, including presentations and a summary of the workshop conclusions, is available on the NICEATM-ICCVAM website3. Proceedings from the workshop will be published in 2012 in the journal Biologicals.

NICEATM Director presents at International Conference on Animal Models and Drug Testing


This conference was convened to provide participants an opportunity to examine the traditional role of animal models in drug discovery, the strengths and weaknesses of these animal models, and ways in which to reduce, refine, and replace animal models in biomedical research. The conference was organized by The Global Medical Excellence Cluster and The New York Academy of Sciences in collaboration with Imperial College London and King’s College London. NIEHS, the National Center for Research Resources, and the National Institute of Diabetes and Digestive and Kidney Diseases provided support for the conference.

Stokes’ presentation focused on advances in science and technology that have been applied to develop new testing methods and strategies that can reduce, refine, and in some cases replace animal use in drug safety assessments. The continued development and appropriate use of scientifically sound testing methods is expected to further improve animal welfare, reduce and replace animal use, and support improved health for people, animals, and the environment.

A comprehensive open access multimedia conference report is available on the NYAS website4.

NICEATM seeks comments relevant to updating of NICEATM-ICCVAM Five-Year Plan

In 2008, NICEATM and ICCVAM published a five-year plan that identified priorities to be addressed and outlined goals and objectives for the years 2008-2012. NIEHS and NICEATM are now requesting public input to be considered as the current plan is updated for the years 2013-2017.

The existing Five-Year Plan addresses: (1) research, development, translation, and validation of new and revised non-animal and other alternative test methods for integration into Federal agency testing programs and (2) identification of areas of high priority for new and revised non-animal and alternative assays to reduce, refine, and replace animal tests.

With regards to reducing, refining, and replacing animal use, ICCVAM identified and ranked the types of regulatory safety tests that it considers to be the highest priority for the development and validation of alternative test meth-

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4 www.nyas.org
ods. These include: acute eye irritation and corrosion, acute skin toxicity (corrosion, irritation, sensitization, and absorption), acute systemic toxicity (oral, dermal, and inhalation), and biologics/vaccines as the four highest priority testing areas; immunotoxicity, endocrine disruptors, pyrogenicity, reproductive/developmental toxicity, and chronic toxicity/carcinogenicity as other priority testing areas; and neurotoxicity as an area of interest. NIEHS and NICEATM seek public input on the following questions:

– Are the priority areas listed above appropriate with regards to NICEATM and ICCVAM activities over the next five years?
– Considering available science and technology, what development, translation, and validation activities are most likely to have the greatest impacts within the next five years on reducing, refining, or replacing animal use in the priority areas?
– What research and development activities hold the greatest promise in the long-term for reducing, refining, or replacing animal use in the priority areas?
– What are appropriate measures for evaluating progress in enhancing the development and use of alternative test methods in the priority areas? Please submit comments via the NICEATM-ICCVAM website5. Individuals submitting comments are asked to include appropriate contact information (name, mailing address, phone, fax, email, and affiliation or sponsoring organization, if applicable). All comments received will be posted on the NICEATM-ICCVAM website and identified by the individual’s name and affiliation or sponsoring organization. Comments received before January 15, 2012, will be considered in development of the draft 2013-2017 Five-Year Plan, which will be made available for public comment later in 2012.

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 are typically addressed with international validation studies, workshops, conferences, or test method independent scientific peer review meetings.
– When validation studies for a test method have been completed that adequately characterize its 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 are also available on the NICEATM-ICCVAM website6.

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 website7.

5 http://iccvam.niehs.nih.gov/contact/FR_pubcomment.htm
6 http://iccvam.niehs.nih.gov/SuppDocs/submission.htm
7 http://iccvam.niehs.nih.gov/contact/ni_list.htm