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

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Headquartered at the
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Health Sciences • NIH-HHS

What's Inside:

Birnbaum elected to Institute of Medicine

Article by Eddy Ball reprinted from *eFACTOR*, November 2010

NIEHS/NTP Director Linda Birnbaum, Ph.D., became one of the newly elected members of the Institute of Medicine (IOM) of the National Academies Oct 1. She will join other new members of what is known as the IOM Class of 2011, during a formal welcome at the group's next annual meeting Oct. 16-17, 2011.

In his notification to Birnbaum, IOM President Harvey Fineberg, M.D., Ph.D., pointed to Birnbaum's "professional achievement and demonstrated interest, concern, and involvement with problems and critical issues that affect the health of the public."

IOM's more than 1,700 members and foreign associates are distinguished scientists chosen from the ranks of government at all levels, educational institutions and non-profit organizations, and the private sector. IOM selects as many as 65 new members and up to five new foreign associates each year.

The IOM is an independent, nonprofit organization that works outside of government, to provide unbiased and authoritative advice to decision makers and the public. According to the IOM, more than 2,000 individuals, members, and non-members volunteer their time, knowledge, and expertise each year to advance the nation's health through the work of the IOM.

IOM asks and answers the nation's most pressing questions about health and health care in reports authored by committees of leading national and international scientists. The 2010 IOM reports highlight such topics as "The Future of Nursing," "Antibiotic Resistance," and "Breast Cancer and the Environment." Currently underway at the request of the U.S. government is "The 1946-1948 Public Health Service STD Inoculation Study," investigating the scientific and ethical issues surrounding this controversial chapter in the history of American medical research.

Established in 1970, the IOM is the health arm of the National Academy of Sciences, which was chartered under President Abraham Lincoln in 1863. Nearly 150 years later, the National Academy of Sciences has expanded into what is collectively known as the National Academies, which comprises the National Academy of Sciences, National Academy of Engineering, National Research Council, and IOM.

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NTP board reviews Biomolecular Screening Branch and Tox21

Article by Ernie Hood reprinted from *eFACTOR*, January 2011

Predictive toxicology – the emerging science that uses high-throughput screening of chemicals in cells and cell lines to understand outcomes in human health and disease – was the focus of the NTP Board of Scientific Counselors (BSC) meeting Nov. 30 – Dec. 1 at NIEHS. Much of the meeting was taken up by the board's review of the Biomolecular Screening Branch (BSB), which is responsible for NIEHS/NTP participation in Tox21, the multi-agency, multidisciplinary collaboration designed to initiate a new era in toxicity testing for the 21st century.

Tice, shown at an earlier talk about Tox21 high-throughput screening, was the keynotes speaker during the review of BSB and Tox21

The first BSC review of the BSB and Tox21 comes at a propitious moment. "This is the first time that the BSC has had an opportunity to consider and comment on the breadth of our activities and our plans for the future," said Raymond Tice, Ph.D., chief of the BSB and the NTP point of contact for Tox21. "This was the most appropriate time to have this review as we move from our Phase I proof-of-principle efforts to Phase II, and from screening a library of approximately 2,800 compounds to one of more than 10,000 compounds, in addition to our other activities".

Tox21 was established in 2008 with a Memorandum of Understanding (MOU) that was expanded in July 2010 to include the FDA along with the original partners, NIEHS/NTP, EPA, and the National Institutes of Health Chemical Genomics Center (NCGC). Each partner has an agency point of contact as its lead representative, and is represented by a co-chair for each of the four Tox21 Working Groups: Chemical Selection, Assays and Pathways, Informatics, and Targeted Testing.

The BSC was briefed on progress by each of the Tox21 partners and Working Groups, and was updated on BSB activities directly related to Tox21, including the *C. elegans* "Worm Tox" Screening Facility, a collaboration with University of North Carolina at Chapel Hill that is probing mechanisms of inter-individual susceptibility to toxicants with population-based experimental approaches, a project exploring mining the NTP Tissue Archives for gene signatures, a program that is developing a bioinformatics-based approach to identify assays that query human health effects, and the mouse methylome project, which is being conducted by the Host Susceptibility Group within the BSB.

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Upcoming Events

January 11-13, 2011

NTP Workshop: Role of Environmental Chemicals in the Development of Diabetes and Obesity

Raleigh Marriott Crabtree Valley
4500 Marriott Drive
Raleigh, NC

[registration is closed]

ICCVAM Best Practices for Regulatory Safety Testing Workshops

January 19, 2011: Assessing the Potential for Chemically Induced Eye Injuries
January 20, 2011: Assessing the Potential for Chemically Induced Allergic Contact Dermatitis

NIH Natcher Conference Center
Bethesda, MD

January 26, 2011

Peer Review of Draft NTP Technical Reports

NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

March 29-30, 2011

ICCVAM Peer Review Panel Meeting: Evaluation of an *In Vitro* Stably-Transfected Estrogen Receptor Transcriptional Activation Assay for Identification of Potential Endocrine Disruptor Activity

NIH Natcher Conference Center
Bethesda, MD

April 5, 2011

Peer Review of Draft NTP Technical Reports

NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

April 12-13, 2011

NTP Board of Scientific Counselors

NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

http://ntp.niehs.nih.gov/go/calendar

Board members Ruthann Rudel, left, of the Silent Spring Institute, and Russell Cattley, V.M.D., Ph.D., of Amgen, paid close attention to the updates on Tox21 and the BSB.

BSC Chair Raymond Novak, Ph.D., who is corporate director of research at Shriners Hospitals for Children International, said the board's reaction to the BSB/Tox21 review was, overall, very enthusiastic. "They were excited about all of the different components that were brought together in a cohesive manner, the communication and the coordination that had occurred for that to take place, and the incredible opportunities that exist to achieve a final product that could be directed toward a rational approach to risk assessment in human populations," he said. As Novak explained, the bottom line is that "if the NTP and all of these other resources can't get predictive toxicology to work, then no one can."

The next BSC meeting is scheduled for April 12-13, 2011.

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison)

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In Other Business

During her update to the Board on Institute developments, NIEHS/NTP Director Linda Birnbaum, Ph.D., announced the appointments of Richard Woychik, Ph.D., as new deputy director of NIEHS and Gwen Collman, Ph.D., as director of the Divison of Extramural Research and Training. She also presented retiring board members Tracie Bunton, D.V.M., Ph.D., Edward Carney, Ph.D., Russell Cattley, Ph.D., William Janzen, Ph.D., and departing chair Novak with certificates of service, as she thanked them for their contributions to NTP.

Looking back on his tenure with the NTP BSC, Novak said, "it was a great experience. It offered an opportunity to provide inputs and make comments on various studies that were either being proposed or had been completed, for which a determination had to be made. It was also an opportunity to make a difference, and to make a difference from a long-term perspective.

In other business, the BSC voted to support a Contract Concept for a program to perform sperm count and vaginal cytology evaluations on tissues obtained from animals in the NTP's 90-day toxicity studies. The Board also reviewed NTP Testing Program Concepts regarding men working with bisphenol A, toxicological approaches to assessing complex mixtures, N-butylbenzenesulfonamide, and selected flame retartdants (see materials online).

Tice talks Tox21

Article by Ernie Hood reprinted from *eFACTOR*, January 2011

Ray Tice, Ph.D.

As a follow-up to the BSC review of the NTP Biomolecular Screening Branch (BSB), Chief Ray Tice, Ph.D., responded to several questions about Tox21 and its future directions.

One of the threads that emerged during the meeting was the need to communicate with the lay public about Tox21. Given the platform to do so, what would you most like to put forth?

Basically, we want the lay public to understand the purpose and goals of Tox21; to appreciate that, currently, we are conducting a research program since we do not yet have enough information to demonstrate the adequacy of using data from assays using cultured cells and lower organisms to identify compounds that are harmful to humans, other animals, and the environment; and to understand it will likely be several to many years before there are sufficient data for the kind of critical evaluation needed.

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How important is Tox21 to NTP and NIEHS?
What role does it play, and how do you think that will evolve?

The purpose of Tox21 is to support the evolution of toxicology from a predominantly observational science at the level of disease-specific models, to a predominantly predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations using cultured cells, 3D model tissues, and phylogenetically lower organisms. This can only be accomplished if we utilize the complementary expertise and capabilities of multiple organizations – no single organization could succeed in this endeavor by itself. The knowledge bases and informatics tools developed to support this effort will be used by the NIEHS/NTP to gain a much better understanding of the relationship between compounds, genes, pathways, and disease, in order to prioritize compounds for more comprehensive testing, to identify mechanisms of action, and to develop predictive models of human disease.

How has the interagency collaboration among the partners worked out?

Absolutely great. We are all committed to a common goal, and where our respective approaches differ, they differ in a way that is complementary rather than in conflict. It's difficult for me to imagine working with a better group of scientists.

It seems from the presentations at the BSC meeting that Tox21 has made remarkable progress in a very short period of time.

I agree. We have been working on Tox21-related efforts since late 2004, but it's only since the first MOU was signed in February 2008 that we established a formal infrastructure to integrate our respective Tox21 activities. Given that, I believe that our success to date has largely been due to, first, the 2007 release of the National Academy of Sciences report called "Toxicity Testing in the 21st Century: A Vision and a Strategy." Second, I would cite the very active support of senior management at the different federal agencies participating in Tox21, along with the commitment of the Tox21 staff to a common goal. Finally, there has been the recognition of the international scientific community that this is an effort worthy of support.

I do think we're making faster progress than I originally anticipated, but like all great endeavors, we might encounter a major obstacle tomorrow or the next day that will require brand new approaches for moving Tox21 forward.

What's next for Tox21?

We plan to expand our interactions with other individuals and organizations, whether government, academic, or private, in order to accelerate the acquisition of data and the development of new tools. We will keep focused on our overall Phase II strategy, while remaining flexible in the event that a major advance in basic biology, medicine, or toxicology might necessitate a shift in focus. We will continue to make sure that all of the data we collect are made openly accessible to the international scientific community as quickly as possible. And, of course, we will continue to try to make sense out of the data we have collected.

(Ernie Hood is a contract writer for the NIEHS Office of Communications and Public Liaison)

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NTP Technical Reports Peer Review

On January 26, 2011, the NTP will convene a Technical Reports Peer Review Panel to review six draft NTP Technical Reports. This meeting will be held at the NIEHS, 111 T. W. Alexander Drive, Research Triangle Park, NC, 27709 and is open to the public with time scheduled for oral public comment. The peer review panel will be charged to (1) peer review the scientific and technical elements of the study and their presentation and (2) determine whether the study's experimental design and conduct support the NTP's conclusions regarding the carcinogenic activity of the substance tested. The panel consists of experts in general pathology, carcinogenesis, dermal toxicology, gastrointestinal pathology, and environmental toxicology.

The tentative list of draft reports includes studies on kava kava extract, methyl *trans*-styryl ketone, retinyl palmitate/retinoic acid, senna, styrene-acrylonitrile trimer, and alpha/beta-thujone. The draft reports, agenda, and other meeting information will be posted on the meeting page (http://ntp.niehs.nih.gov/go/36051) as available. This meeting was announced in the Federal Register (75 FR 73085).

Contact Information: Dr. Lori White, Designated Federal Officer, NTP Office of Liaison, Policy and Review
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NTP scientists earn prestigious toxicology certification

Article by Eddy Ball reprinted from *eFACTOR*, December 2010

Four more National Toxicology Program (NTP) scientists made an important advance in toxicology's professional ranks by satisfying requirements for Diplomate of the American Board of Toxicology (D.A.B.T.) certification.

According to the organization, the certification is an international recognition of broad expertise in general toxicology for those with formal training in toxicology, as well as those trained in other related disciplines, often confers an advantage in the job market and career advancement, and is an objective demonstration of a toxicologist's breadth and currency of knowledge and supports scientific credibility.

The American Board of Toxicology officially certified the following NTP scientists as diplomates:

- Chad Blystone, Ph.D., of the NTP Toxicology Branch
- Susan Elmore, D.V.M., of the NTP Pathology Group
- Gloria Jahnke, D.V.M., of the NTP Report on Carcinogens Center
- Mike Sanders, Ph.D., of the NTP Program Operations Branch

In a message to the new diplomates, NIEHS/NTP Director Linda Birnbaum, Ph.D., who also holds D.A.B.T. certification, wrote, "Congratulations to all of you, and welcome to the team of outstanding diplomates at NTP." Speaking from experience, she added, "It's no mean feat to become a D.A.B.T., and your achievement is one more testament to the high caliber of science conducted by the NTP."

The American Board of Toxicology was established in 1979 to advance standards in the field of toxicology and to confer recognition upon those members of the profession who, measured against such standards, demonstrate competence. Certification requirements include a combination of education and experience, and a three-part examination.

Diplomates hold initial ABT certification for 5 years and must demonstrate that they actively practice toxicology, engage in continuing education, and maintain expert knowledge in their field prior to pursuing recertification.

DrugMatrix:™ A new NTP toxicogenomics reference database and informatics system

Contributed by Scott Auerbach, NTP Biomolecular Screening Branch

DrugMatrix is the scientific communities' largest molecular toxicology reference database and informatics system. The NTP acquired DrugMatrix along with the automated toxicogenomics report generation system, ToxFX, in September 2010. The ultimate goal of this acquisition is to facilitate the integration of toxicogenomics into hazard characterization. DrugMatrix is populated with the comprehensive results of thousands of highly controlled and standardized toxicological experiments in which rats or primary rat hepatocytes were systematically treated with therapeutic, industrial, and environmental chemicals at both non-toxic and toxic doses. Following administration of these compounds *in vivo*, comprehensive studies of the effects of these compounds were carried out at multiple time points and in multiple target organs. These studies included extensive pharmacology, clinical chemistry, hematology, histology, body and organ weights, and clinical observations. Additionally, a curation team extracted all relevant information on the compounds from the literature, the Physicians' Desk Reference, package inserts, and other relevant sources. The heart of the DrugMatrix database is large-scale gene expression data generated by extracting RNA from the toxicologically relevant organs and tissues and applying these RNAs to the GE Codelink™ 10,000 gene rat array and more recently the Affymetrix whole genome 230 2.0 rat GeneChip® array. DrugMatrix contains toxicogenomic profiles for 638 different compounds; these compounds include FDA approved drugs, drugs approved in Europe and Japan, withdrawn drugs, drugs in preclinical and clinical studies, biochemical standards, and industrial and environmental toxicants. NTP expects to make the database public in the first half of 2011.

Contact Information: Scott Auerbach, Ph.D., NTP Biomolecular Screening Branch, NIH/NIEHS, P.O. Box 12233, K2-08, Research Triangle Park, NC 27709; T: (919) 541-4505; FAX: (919) 541-4255; auerbachs@niehs.nih.gov

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NIEHS/NTP postdocs win at NC SOT meeting

Article by Eddy Ball reprinted from *eFACTOR*, November 2010

NIEHS and NTP postdoctoral fellows dominated the competition for the President's Award for Research Competition at the North Carolina Regional Chapter of the Society of Toxicology (NC SOT) Fall Meeting Oct. 7 at NIEHS. The first order of business at the annual event was presentation of awards before a near-capacity audience that included NIEHS/NTP Director Linda Birnbaum, Ph.D., and many members of the NTP, along with members from other organizations involved in toxicology.

As first place winner, visiting fellow Yuanyuan Xu, M.D., Ph.D., received a cash award of $500 and the opportunity to give a 20-minute presentation of her research at the meeting. Xu is a member of the National Toxicology Program Cellular and Molecular Pathology Branch, headed by research pharmacologist Michael Waalkes, Ph.D.

The NC SOT president congratulated the NIEHS/NTP postdocs on their exceptional research this year. From left to right are Foster, Yin (third place), Sun (second place), and Xu (first place). (Photo courtesy of Mike Hughes, EPA)

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She was first author on a study titled "Epithelia Malignantly Transformed by Arsenic or Cadmium Drives Nearby Normal Stem Cells Towards a Malignant Phenotype," with co-authors Erik Tokar, Ph.D., and Waalkes.

With her second-place win, visiting fellow Yang Sun, Ph.D., received a cash award of $250 and recognition by NC SOT. Sun is also a member of the Waalkes group. She is first author on a study titled "Overabundance of Putative Cancer Stem Cells in Human Skin Keratinocyte Cells Malignantly Transformed by Arsenic."

The third place winner is Visiting Fellow Zhengyu Yin, Ph.D., a member of the NIEHS Cell Biology Group headed by Principal Investigator Anton Jetten, Ph.D. Yin received a cash of award of $100 for his paper titled "RAP80 Plays a Critical Role in Maintaining Genomic Stability." Jetten was a co-author.

The NC SOT meeting was organized around the theme of "Bioengineered Cellular and Animal Models for Toxicology." With 322 members, NC SOT is one of the largest regional chapters of SOT. It is preparing a regional chapter poster and time capsule as part of the 50th anniversary celebration of SOT this March in Washington, D.C.

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New NTP data downloads

Contributed by Laura Hall and Beth Bowden, NTP Program Operations Branch

Are you an informaticist or a biostatistician interested in toxicology? You may want to investigate using the NTP data downloads. With the new NTP Data Downloads web page (http://ntp.niehs.nih.gov/go/downloads), you can access NTP data by downloading a few files.

Summary data on all NTP chemicals can be downloaded in a single file. If you would like more detailed data, you can also download data for an individual study type. *Currently, cancer bioassay, CHO Cell Cytogenesis, Drosophila, Micronucleus, Mouse Lymphoma, Rodent Cytogenetics, and* Salmonella *study types are available for detailed data downloads.*

NTP plans to add files for the developmental and immunology study types. Be the first to learn when new study types and updated data are available by joining the NTP ListServ (http://ntp.niehs.nih.gov/go/getnews). NTP will update the data on a quarterly basis.

Format of NTP data downloads

The NTP used Extensible Markup Language (XML) to create the data files for downloading. XML is a free, open standard computer language with a set of rules that encodes documents in "machine readable" format. The XML files contain the data. The NTP also provides schema files that show how the data in the files are organized and formatted. That information can be used to create custom programs to download the NTP data into specific applications or databases that fit a user's specific needs.

Online searching remains available!

If you have used the NTP Database Search, it is still available at http://ntp-apps.niehs.nih.gov/ntp_tox/. This search allows you to view NTP data on a particular test article or a particular study online.

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NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

U.S. federal agencies accept ICCVAM recommendations for new test methods to identify allergic contact dermatitis hazards

NIEHS and other U.S. Federal agencies have accepted or endorsed recommendations on new test methods to identify chemicals and products that could cause allergic contact dermatitis (ACD). The recommendations were made by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), an interagency committee supported and administered by NICEATM, following its comprehensive evaluation of the scientific validity of the proposed test methods. Regulatory agencies' acceptance of these recommendations is expected to result in fewer animals being used to identify potential allergic contact dermatitis hazards, and in the elimination of pain or discomfort for those animals that are used for such testing.

The ICCVAM recommendations addressed the usefulness and limitations of the first two nonradioactive versions of the murine local lymph node assay (LLNA) and expanded applications of the LLNA for assessing the allergic contact dermatitis hazard potential of chemicals and products. The nonradioisotopic methods are the LLNA: 5-bromo-2-deoxyuridine-ELISA (LLNA: BrdU-ELISA) and the LLNA: Daicel Adenosine Triphosphate (LLNA: DA) test methods. Their expanded applications are for pesticide formulations, metals, aqueous solutions, and other products.

ICCVAM-recommended LLNA: BrdU-ELISA and LLNA: DA test method protocols formed the basis for two new test guidelines adopted by the Organisation for Economic Co-operation and Development (OECD) in July 2010. These test guidelines will allow use of these methods by the 33 member countries of OECD. Regulatory acceptance of these recommendations is expected to support further reduction and refinement (decrease or elimination of pain and distress) of animal use for required allergic contact dermatitis hazard testing. The nonradioisotopic versions of the LLNA also are safer for laboratory personnel and provide an environmental advantage by avoiding the generation of radioactive laboratory waste.

Protocols for the recommended LLNA methods and other ICCVAM-recommended test methods are available on the test method protocols page of the NICEATM-ICCVAM Website at: http://iccvam.niehs.nih.gov/methods/protocols.htm. Information about the ICCVAM recommendations on new versions and applications of the LLNA is available at: http://iccvam.niehs.nih.gov/methods/immunotox/llna.htm.

NICEATM Director Dr. William Stokes (second from left) and Acting ICCVAM Chair Dr. Jodie-Kulpa Eddy (second from right) are pictured here at the Langen meeting with: (from left) Dr. Robin Levis, FDA/CBER; Dr. Donna Gatewood, Center for Veterinary Biologics, USDA/APHIS; Dr. Juan Arciniega, FDA/CBER; Dr. Jean-Marc Spieser, European Directorate for the Quality of Medicines, and Dr. Carmen Jungback, Paul Ehrlich Institute.

ICCVAM agencies and NICEATM director present at international meeting on alternative methods for vaccine potency testing

Dr. William Stokes, Director of NICEATM, presented conclusions and recommendations from the September 2010 NICEATM-ICCVAM workshop on vaccine safety and potency testing at the recent international meeting, Potency Testing of Veterinary Vaccines: The Way From *In Vivo* to *In Vitro*. The meeting took place on December 1-3, 2010, at the Paul Ehrlich Institute in Langen, Germany and was co-sponsored by the German government, the European Directorate for the Quality of Medicines, and the International Association of Biologicals. Dr. Stokes also served on the scientific committee and as a session chair.

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Dr. Stokes spoke on "Recent Progress and Future Directions for the 3Rs in Vaccine Potency and Safety Testing: Conclusions and Recommendations from the 2010 U.S. International Workshop."

At that workshop nearly 200 scientists from 13 countries gathered to discuss the state of the science of alternative methods development for both human and veterinary vaccine potency and safety testing.

In his presentation, Dr. Stokes summarized the priorities recommended for future research and development efforts needed to advance new methods and approaches for vaccine potency and safety testing. By applying new technology and scientific knowledge, improved methods that also reduce, refine, and replace animal methods are anticipated. Examples include *in vitro* protective antigen quantification assays, serological assays combined with *in vitro* antibody quantification, incorporation of earlier more humane endpoints when challenge testing is still necessary, and identification and avoidance of experimental variables that can further reduce animal use.

ICCVAM workshop recommendations to accelerate global progress in development and implementation of alternatives for human and veterinary vaccine testing include: (1) improved accessibility of information on new initiatives, documents, and guidances; (2) increased international harmonization of validation principles for new vaccine safety and potency test methods; (3) harmonized tests for protective antigens; (4) accelerated product-specific validation of available alternative methods by vaccine manufacturers; and (5) increased support for research and development into new alternative methods.

Other scientists affiliated with ICCVAM or ICCVAM-member agencies who presented at the Langen meeting include:

- Dr. Jodie Kulpa-Eddy, Senior Staff Veterinarian with the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) and Acting Chair of ICCVAM. Dr. Kulpa-Eddy's presentation was titled "Successful Development and Validation of *In Vitro* Replacement Assays for Veterinary Vaccine Potency Tests – Lessons Learned: An Authority's Point of View."
- Dr. Donna Gatewood, Section Leader of the Virology Section of the USDA/APHIS Center for Veterinary Biologics. Dr. Gatewood presented the talk, "Testing of Vaccines Against Rabies: Replacement of Challenge by *In Vitro* Tests – Considerations for Development of the Test," and also served as a session chair.
- Dr. Juan Arciniega, Research Microbiologist at the Center for Biologics Evaluation and Research (CBER) of the U.S. Food and Drug Administration (FDA), and member of the ICCVAM Interagency Biologics Working Group. Dr. Arciniega's presentation was titled "Potential Application of the Consistency Approach for Vaccine Potency Testing."
- Dr. Karen Brown, President of Pair O'docs Enterprises, presented the talk, "Approach to *In Vitro* Potency Testing When Developing a New Vaccine; Is a Parallel *In Vivo* Potency Test Necessary? (Important Issue in R&D)." Dr. Brown is a member of ICCVAM's Scientific Advisory Committee on Alternative Toxicological Methods.

The proceedings of the ICCVAM workshop will be published in 2011 as a dedicated issue of *Procedia in Vaccinology*. The ICCVAM Interagency Biologics Working Group is currently addressing implementation of the workshop's recommendations. Presentation slides and more information about the ICCVAM workshop are available on the NICEATM-ICCVAM Website at: http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm.

Two ICCVAM workshops on best practices for regulatory safety testing to be held in January 2011

NICEATM and ICCVAM will convene two one-day workshops, "Assessing the Potential for Chemically Induced Eye Injuries" and "Assessing the Potential for Chemically Induced Allergic Contact Dermatitis," on January 19 and 20, 2011, respectively. The workshops are co-sponsored by the Society of Toxicology and the Society for Risk Analysis. They are open to the public and will be held at the William H. Natcher Conference Center on the main campus of the National Institutes of Health (NIH) in Bethesda, Maryland.

These workshops will help participants gain a practical understanding of the theory and application of available validated and accepted methods that can be used to evaluate the hazard potential of chemicals and products while minimizing animal use and avoiding pain and distress. Participants will learn the strengths and weaknesses of available alternative test methods, become familiar with the types of data they provide, and learn how to use these data for regulatory safety assessment decisions.

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The program will include summaries of U.S. requirements for consideration of available alternatives, current regulatory requirements for ocular and allergic contact dermatitis safety testing, and acceptance status of applicable alternative methods. Background information on the scientific basis of the test methods and discussion of the current validation status of the test methods will then be provided. Discussions of case studies in breakout groups will provide practical instruction on applying the test methods including the selection of appropriate methods and data interpretation. Each day's program will conclude with presentations on new models currently being evaluated or ongoing validation studies. A poster session will highlight new methods and technologies applicable to ocular or allergic contact dermatitis safety assessment.

Topics discussed during these workshops will be of particular interest to those involved in conducting safety tests for chemically induced eye injuries and/or chemically induced allergic contact dermatitis, those responsible for reviewing study protocols prior to testing, and regulators who will review data generated by the tests.

The workshops are free of charge and attendance is limited only by the space available. Those interested in attending may register for one or both workshops; preregistration on the NICEATM-ICCVAM Website is requested. More information on each workshop, a draft agenda, information on planned webcasts, and a link to online registration are available on the NICEATM–ICCVAM Website at: http://iccvam.niehs.nih.gov/meetings/Implement-2011/ImplmtnWksp.htm.

ICCVAM peer panel to review *in vitro* test method for identification of potential endocrine disruptor activity

NICEATM and ICCVAM will convene an international, independent panel on March 29-30, 2011, to peer review data from a NICEATM-sponsored validation study. The study is assessing the accuracy and reliability of BG1Luc4E2 ER TA, an *in vitro* estrogen receptor (ER) transcriptional activation (TA) test method for the qualitative detection of substances with *in vitro* ER agonist or antagonist activity. The panel will also consider draft ICCVAM test method recommendations on the usefulness and limitations of this test method for identifying potential ER agonists or antagonists.

Endocrine disruptors (EDs) are substances that may interfere with the normal function of hormones in the endocrine system and lead to abnormal effects on growth, development, or reproduction. A number of studies have been published indicating that animal populations exposed to high levels of these substances have an increased incidence of reproductive and developmental abnormalities. Exposure of humans to EDs has been linked to adverse health outcomes.

NICEATM coordinated an international, interlaboratory, validation study of the BG1Luc4E2 ER TA test method following development and standardization of the assay (LUMI-CELL) by XDS, Inc. as part of a Small Business Innovative Research grant from NIEHS. This international study included participating laboratories located in Italy, United States, and Japan and was the first validation study sponsored jointly by NICEATM-ICCVAM, the European Centre for the Validation of Alternative Methods, and the Japanese Center for the Validation of Alternative Methods.

A panel of expert scientists from seven countries will review the draft background review document (BRD) detailing the study's results. The panel will also consider the extent to which the BRD supports draft ICCVAM test method recommendations on the usefulness and limitations of the BG1Luc4E2 ER TA test method, a recommended protocol, future studies to further characterize the test method, and performance standards. These draft documents will be available for public review and comment prior to the meeting on the NICEATM-ICCVAM Website at: http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm.

The panel will meet at the Natcher Conference Center on the main NIH campus in Bethesda, Maryland. The peer review meeting is open to the public with no registration charge. More information on the meeting, draft agenda, and a link to online registration will be available in February on the NICEATM–ICCVAM Website at: http://iccvam.niehs.nih.gov/methods/endocrine/PeerPanel11.htm.

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In memorial

NTP is sad to announce that Nancy Stegman passed away December 19 following a courageous battle with cancer. Nancy was part of the NIEHS and NTP for more than two decades and made a number of major contributions. Those of you associated with the NTP from the mid 1980s to the mid 1990s will remember Nancy for her contribution to the NTP's Toxicity and Carcinogenicity Testing Program as the Discipline Leader for Data Management where she was involved in the overall assessment of the NTP contract testing laboratories' expansive data management efforts. She will be best remembered for her involvement in modifications to improve the NTP computer Toxicology Data Management System and for her integral role in the creation and implementation of the NTP Laboratory Data Acquisition System, which continues to be used today by NTP testing laboratories to collect animal room and pathology data. At her retirement from NIEHS in 2008, Nancy held the position of Chief of the Computer Technology Branch and Chief Information Officer. (http://www.legacy.com/obituaries/newsobserver/obituary.aspx?n=nancy-w-stegman&pid=147330159#ixzz18li7hOex)

The NTP is sad to announce that Janet Guthrie passed away on December 16 following a long and courageous battle with cancer. In the 1980s she was involved with NTP toxicity and carcinogenicity protocol design activities as a member of the Toxicology Design and Review Committee and was responsible for preparing records of the committees discussions and maintaining all final study protocols. After several years, Janet moved to the Office of Policy, Planning, and Evaluation, Office of the Director where she was a program analyst. Janet retired from the NIEHS in 2008 after a successful stint of more than 30 years. (http://www.newsobserver.com/2010/12/21/874310/janet-guthrie.html - storylink=misearch)

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The NTP website offers electronic files of the Report on Carcinogens and the library of NTP Technical Reports and NTP Toxicity Reports. The PDF files of these reports are available free-of-charge through the NTP website at http://ntp.niehs.nih.gov (see Resources).

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