



# UPDATE

National Toxicology Program

U.S. Department of Health and Human Services

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## NIEHS employees honored with NIH Director's Awards

Article reprinted from *eFACTOR*, September 2011



Collins, left, joined representatives of the Gulf Long-term Followup (GuLF) STUDY team. Shown, left to right, Collins, Sandler, Birnbaum, and Miller. (Photo courtesy of NIH)

Twenty-five NIEHS employees were among the 378 individuals recognized for exemplary service at the 2011 NIH Director's Award ceremony August 2 in Bethesda, MD. The award, the highest given by NIH to its employees, recognizes superior performance or special efforts significantly beyond regular duty requirements, but directly related to fulfilling the NIH mission.

The [NIH Director's Award](#) honors leadership and superior performance for employees in four categories: scientific/medical, technical/clerical/support, administrative, and common fund leadership.

NIEHS and NTP employees were singled out for their contributions to the Deepwater Horizon Gulf Oil Spill Response, GuLF STUDY (Gulf Long-term Followup Study), and NIH PROMIS Working Group. NIEHS/NTP Director Linda Birnbaum, Ph.D., was one of the dignitaries on stage. She both represented the Institute and received an award as part of the Deepwater Horizon Gulf Oil Spill Response Team.

Emceed by Phil Lenowitz, NIH deputy director of Human Resources, the program opened with remarks by NIH Director Francis Collins, M.D., Ph.D. Referring to concern over raising the debt ceiling, Collins said, "It's perhaps particularly appropriate that we gather here this afternoon to celebrate the dedication of many giving themselves in such a thoughtful, creative way to try to serve the public."

As he pointed to specific efforts recognized by the awards, Collins added with pride, "This is NIH. This is who we are." He singled out for individual mention Randy Schools, who has served as president of the NIH Recreation and Welfare Association since 1977. Collins noted, "It's about time to say 'thank you' to Randy."

Continuing a tradition at ceremonies of this kind, Collins segued easily from talk to music, as he accompanied himself on guitar and sang a ballad he composed, "Dare to Dream." The audience joined him for the chorus, which included the song's title and the words, "Of the need to help the world/we all agree/This is NIH/ So let's make history."

### NIEHS scientists and staff honored for trans-NIH efforts

Deepwater Horizon Gulf Oil Spill Response Team: For the 2010 Gulf Oil Spill response, implementing public health protection programs for cleanup workers, developing the GuLF STUDY, and assembling a research consortium.

Kathy Ahlmark, Robin Arnette, Ph.D., Eddy Ball, Ph.D., Sharon Beard, Linda Birnbaum, Ph.D., John Bucher, Ph. D., Gwen Collman, Ph.D., Allen Dearry, Ph.D., Dorothy Duke, Christine Flowers, Chip Hughes, Paul Jung, M.D., Lora Kutkat, Richard Kwok, Ph.D., Robin Mackar, Scott Masten, Ph.D., Aubrey Miller, M.D., Ted Outwater, James Remington,



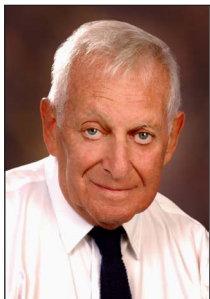
Dale Sandler, Ph.D., Anne Thompson, Cheryl Thompson, Claudia Thompson, Ph.D., and Leroy Worth, Ph.D.

Gulf Long-term Followup (GuLF) STUDY: For rapidly developing protocol for Gulf Long-term Followup (GuLF) STUDY, obtaining institutional review board clearance and Office of Management and Budget approval, completing administrative tasks associated with longitudinal federal research study.

Lawrence Engel, Ph.D., Christine Flowers, Richard Kwok, Ph.D., Aubrey Miller, M.D., Dale Sandler, Ph.D. ●

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## In memorial



Article adapted from *eFACTOR*, September 2011

NTP is sad to announce that Joe Wachsmann, Ph.D. passed away July 10, in Denver, following a brief illness. Dr. Wachsmann worked in several groups at NIEHS during his tenure as a special volunteer from the early 1990s to the mid 2000s. He joined the Institute following his retirement as a professor at the University of Illinois (UI) at Urbana-Champaign and an appointment at the University of North Carolina at Chapel Hill. Along with

his interest in oxidative stress, Wachsmann is remembered for an early paper on epigenetics. Published in 1997 in *Mutation Research*, the paper explored "DNA methylation and the association between genetic and epigenetic changes: Relation to carcinogenesis," a topic that has stirred widespread interest among the scientific community in the years that followed its publication. As noted by many, he had a broad range of interest and an insatiable curiosity, humor, and enthusiasm for science. He will be missed by his many friends at NIEHS. ●

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## Peer Review of the Draft NTP Monograph on the Health Effects of Low-level Lead

On November 17-18, 2011, an external scientific panel will meet to peer review the Draft Monograph on the Health Effects of Low-level Lead, which was prepared by the Office of Health Assessment and Translation (OHAT), formerly named the Center for the Evaluation of Risks to Human Reproduction (CERHR). Lead exposure is a significant health concern despite policies and practices that have resulted in continued progress in reducing exposures and lowering blood lead levels in the U.S. population. OHAT selected low-level lead for evaluation because of: (1) widespread human exposure, (2) published studies on health effects associated with low blood lead levels (<10µg/dL) in humans, and (3) public concern.

## Upcoming Events

October 11-13, 2011

NICEATM Workshop: International Workshop on Alternative Methods for Human and Veterinary Rabies Vaccine Testing: State of the Science and Planning the Way Forward

U.S. Department of Agriculture  
Center for Veterinary Biologics  
Ames, Iowa

CANCELLED

October 19-20, 2011

Peer Review of Draft NTP Monograph on Developmental Effects of Cancer Chemotherapy during Pregnancy

NIEHS  
111 TW Alexander Drive  
Research Triangle Park, NC

November 17-18, 2011

Peer Review of Draft NTP Monograph on the Health Effects of Low-Level Lead

NIEHS  
111 TW Alexander Drive  
Research Triangle Park, NC

December 15-16, 2011

NTP Board of Scientific Counselors

NIEHS  
111 TW Alexander Drive  
Research Triangle Park, NC

February 8-9, 2012

NTP Technical Reports  
Peer Review Panel

NIEHS  
111 TW Alexander Drive  
Research Triangle Park, NC

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



The peer review will be held at NIEHS, 111 T. W. Alexander Drive, Research Triangle Park, NC. The meeting is open to the public and public comment both written and oral is welcomed on the draft monograph. Written comments should be received by November 3, 2011. The draft monograph, meeting registration, [Federal Register](#) notice, and other meeting-related information will be posted on the NTP website (<http://ntp.niehs.nih.gov/go/36639>) as available. ●

**Contact Information:** Danica Andrews, Designated Federal Officer, NTP Office of Liaison, Policy and Review, NIH/NIEHS, P.O. Box 12233, MD K2-03, Research Triangle Park, NC 27709; T: (919) 541-2595; FAX: (919) 541-0295; [andrewsda@niehs.nih.gov](mailto:andrewsda@niehs.nih.gov)

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## NTP postdocs pass laboratory animal medicine boards

by Eddy Ball reprinted from eFACTOR, August 2011



Jacquelyn Tubbs,  
D.V.M., DACLAM



Coralie Zegre-Cannon,  
D.V.M., DACLAM

NTP postdoctoral fellows Jacquelyn (Jai) Tubbs, D.V.M., and Coralie Zegre-Cannon, D.V.M., learned in July that they've taken an important step in their careers by satisfying requirements for certification as Diplomates of the [American College of Laboratory Animal Medicine \(ACLAM\)](#). Tubbs is currently a member of the [NTP Laboratory Animal Management Group](#) headed by Angela King-Herbert, D.V.M., who oversees the fellowship in Laboratory Animal Medicine training program within the NTP Cellular and Molecular Pathology Branch (CMPB). Zegre-Cannon was also part of the group until December 2010.

In a message to the new diplomates, Molecular Pathology Group Leader and CMPB Chief [Robert Sills, D.V.M., Ph.D.](#) congratulated Tubbs and Zegre-Cannon.

"This is a major achievement and a significant success for yourself and the NTP Training Program."

Sills also praised King-Herbert for her leadership. "This is also a tremendous honor for yourself as the head of the training program and to all your lab animal medicine colleagues at NIEHS and in the RTP [Research Triangle Park, N.C.] who partnered with you in making the training program a success," he wrote. "Having 100 percent success for the first trainees in the NTP Laboratory Animal Medicine Training Program is outstanding."

### ACLAM Diplomates

ACLAM Diplomates are involved in a wide variety of activities, including management and direction of animal resource facilities and programs; clinical medicine, surgery, and programs of disease prevention; consultation on the care and use of laboratory animals; assisting institutions in achieving compliance with animal care and use regulations; collaborative and independent research; and instruction and training, including informing the public about the humane use of animals in biomedical research.

ACLAM recertification is required at eight-year intervals, commencing with the first calendar year following initial certification. The recertification periods are staggered so that only about one-eighth of the ACLAM membership comes up for recertification each year. A total of 400 recertification credits must be attained during each recertification period. ●

### NTP training in laboratory animal medicine

As part of the NTP Laboratory Animal Management Group, Tubbs and Zegre-Cannon are part of the oversight effort for the laboratory animal-related matters for the NTP, including:

- Assisting in the selection and provision of disease-free genetically defined rodent models, as well as monitoring animal care and use in NTP studies.
- Aiding in the preparation of NTP Technical Reports.
- Advising the NTP on animal care and animal welfare issues.



The fellowship in Laboratory Animal Medicine is designed for individuals to participate in NTP and NIEHS laboratory animal veterinary care. The training program includes clinical and surgical responsibilities, animal care facility management, participation in research projects, and laboratory animal pathology. In addition to trainees being involved in a variety of laboratory animal science settings, they also have the opportunity to attend outside training activities and scientific meetings, as well as to engage in collaborative research with NTP and NIEHS scientists. Trainees also have clinical responsibilities and participate in training at the nearby University of North Carolina at Chapel Hill Division of Laboratory Animal Medicine. ●

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## NTP researcher wins poster award at conference in Germany

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By Ian Thomas reprinted from *eFACTOR*, September 2011



NTP scientist Scott Auerbach, Ph.D., took home top poster honors at the [OpenTox 2011 InterAction Meeting](#) for his work on bioinformatics and disease-informing assays. Hosted by the OpenTox community of collaborators and funded by the European Union Seventh Framework Programme, this year's gathering was held August 9-12 at the Technical University of Munich in Germany.

"Most of the work presented at the meeting was focused on computational methods for predicting toxicity," recalled Auerbach, a molecular toxicologist for the NTP Host Susceptibility Group in the Biomolecular Screening Branch.

Auerbach's work used bioinformatics to link *in vitro* assays to chronic disease processes, such as type 2 diabetes. It then leveraged the assay-disease relationships to identify chemicals with the potential to influence disease processes.

"It's clear that the existing assay data covers certain areas of disease reasonably well," Auerbach explained. "Other areas, such as neurological disease for instance, aren't as well accounted for, in large part due to our limited understanding of certain disease processes and the inherent complexities surrounding them."

Still, Auerbach is happy for the chance to share his work and broaden his research horizons, something he sees as key to the future.

"I'm incredibly grateful for the support I've received here at NIEHS," Auerbach said. "I'm a firm believer that the future advancements of the toxicology field will begin with insights spawned from cross-disciplinary collaborations like this. Therefore, I'm thrilled to have been a part of it." ●

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

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### Committee Recommends Alternative Method to Identify Chemicals and Products with Significant Potential to Cause Allergic Contact Dermatitis

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), which NICEATM administers, recently forwarded recommendations to Federal agencies [[announced in the Federal Register on July 28](#)] for using the murine local lymph node assay, or LLNA, to categorize the potency of some chemicals that cause allergic contact dermatitis in humans as strong sensitizers. Strong sensitizers are those substances considered to have a significant potential for causing skin hypersensitivity resulting in allergic contact dermatitis.

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The recommendations are based on a comprehensive test method evaluation by ICCVAM and NICEATM. ICCVAM concluded that the LLNA could correctly categorize some substances as strong sensitizers using a criterion published in the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). However, nearly half of the known human strong sensitizers evaluated by ICCVAM were not identified using GHS criterion. ICCVAM concluded that additional information would need to be considered to confirm whether substances that do not meet this criterion are or are not strong sensitizers.

Substances with the potential to cause allergic contact dermatitis (ACD) can also be categorized with traditional test methods using guinea pigs. However, the LLNA uses fewer animals than guinea pig test methods, requires less time to perform, provides dose-response information, and, in most cases, eliminates the potential for pain and distress in the test animal. In accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, the LLNA should be routinely considered when planning animal studies to evaluate whether chemicals and products are strong sensitizers in order to minimize animal use and to avoid pain and distress.

The ICCVAM evaluation is detailed in a report entitled *ICCVAM Test Method Evaluation Report: Usefulness and Limitations of the Murine Local Lymph Node Assay for Potency Categorization of Chemicals Causing Allergic Contact Dermatitis in Humans* (NIH Publication No. 11-7709). The ICCVAM report and recommendations have been transmitted to Federal agencies for their review and response; responses from all agencies will be available by early 2012. The report can be found on the NICEATM-ICCVAM website at <http://iccvam.niehs.nih.gov/methods/immunotox/LLNA-pot/TMER.htm>.

NICEATM and ICCVAM are also currently evaluating several *in vitro* and *in chemico* methods for their potential to further reduce and eventually replace animal use for ACD safety testing. Information on NICEATM and ICCVAM evaluations of methods for ACD safety testing can be found at <http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm>.

### ICCVAM Proposes Procedures to Reduce Animal Use for Eye Safety Testing

ICCVAM is proposing eye hazard classification criteria that will provide the same or greater level of eye hazard classification as current U.S. Federal Hazardous Substances Act regulations, while using 50% to 83% fewer animals.

The draft recommendations are based on an analysis conducted in collaboration with NICEATM. A manuscript describing the NICEATM analysis was recently published (Haseaman et al. *Regulatory Toxicology and Pharmacology* 61(1):98-104).

NICEATM announced availability of the draft recommendations and requested public comment via a [Federal Register notice published August 12](#). ICCVAM will consider all public comments and comments made by the Scientific Advisory Committee on Alternative Toxicological Methods when finalizing its recommendations. Final ICCVAM recommendations will be made available on the NICEATM-ICCVAM website and forwarded to relevant Federal agencies for their consideration.

Links to the [Federal Register](#) notice, the ICCVAM draft recommendations, the *Regulatory Toxicology and Pharmacology* article, and other information about the NICEATM analysis may be found on the NICEATM-ICCVAM website at:

<http://iccvam.niehs.nih.gov/methods/ocutox/reduccenum.htm>.

### NICEATM Staff Showcase Alternative Test Method Progress at International Meeting

NICEATM staff delivered presentations on recent progress at the Eighth World Congress on Alternatives and Animal Use in the Life Sciences, which took place in Montreal, Canada, on August 21-25. The World Congress is a biennial meeting that supports progress in the life sciences and application of the ethical principles of animal use embodied in the "three Rs" (reduction, refinement, and replacement of animal use).



NICEATM Director William Stokes, D.V.M., center, appears with two members of the panel at their meeting at CPSC headquarters. Pictured with Stokes are Dagmar Jírová, M.D., Ph.D., left, toxicologist at the National Institute of Public Health, Czech Republic, and Nathalie Alépée, Ph.D., right, research manager at L'Oréal Research and Development in France. (Photo courtesy of NICEATM)



NICEATM staff delivered platform presentations on topics relevant to the Center's ongoing activities. These included presentations on validation of 21st century predictive toxicology methods and validation of test methods to identify potential endocrine-active substances. NICEATM staff and ICCVAM members also delivered poster presentations to highlight current activities and test method evaluations. Five of these presentations highlighted recent ICCVAM recommendations and international regulatory acceptance for new versions and applications of the murine local lymph node assay to identify substances with the potential to cause allergic contact dermatitis. Others highlighted ICCVAM recommendations and regulatory acceptance of alternative methods for ocular safety testing as well as conclusions and recommendations from a NICEATM-sponsored 2010 workshop on alternative methods for vaccine potency and safety testing.

NICEATM staff also co-chaired four sessions at the meeting. NICEATM Director Dr. William Stokes co-chaired sessions summarizing the conclusions and recommendations from the NICEATM-sponsored workshop on vaccine potency and safety testing and a session providing updates from organizations participating in the International Cooperation on Alternative Test Methods (ICATM). NICEATM and ICCVAM participate in the ICATM agreement. NICEATM Deputy Director Dr. Warren Casey co-chaired sessions on validation of methods to identify potential endocrine-active substances and on *in vitro* models for detection and potency assessment of botulinum neurotoxin.

NICEATM also participated in satellite meetings that were convened in conjunction with the World Congress. One of these focused on developing alternatives to the *in vivo* test commonly used for safety testing of pertussis vaccines. Participants in this meeting will reconvene to continue discussions on this issue in the coming years. NICEATM will host a follow-up meeting in September 2012 at the William H. Natcher Conference Center at the National Institutes of Health in Bethesda, Maryland.

ICCVAM representatives and NICEATM staff also participated in a satellite meeting that brought together representatives of each ICATM organization. This enabled the five ICATM organizations to meet in person to discuss activities in the three major areas of cooperation: test method validation studies, international peer review, and harmonized test method recommendations.

A summary of all NICEATM-ICCVAM activities, including abstracts of poster and platform presentations and copies of all posters, can be found on the NICEATM-ICCVAM website at <http://iccvam.niehs.nih.gov/meetings/8WC/8WCablst.htm>.

Proceedings of the Eighth World Congress will be published as a special issue of the journal ALTEX in 2012. The Ninth World Congress will be held in Prague, Czech Republic, in August 2014.

### **NICEATM and ICCVAM Workshop on Rabies Vaccine Testing to be Held in October**

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. 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), or replace animals used in human and veterinary rabies vaccine potency testing. Participants will then develop an implementation strategy to achieve global acceptance and use of these alternatives.

Along with NICEATM and ICCVAM, the workshop will be co-sponsored by the European Centre for the Validation of Alternative Methods, the Japanese Center for the Validation of Alternative Methods, and Health Canada. The workshop will feature 17 speakers from nine countries and three breakout sessions that will allow participants to discuss the key issues to be addressed at the workshop. A poster session planned for the workshop will feature presentations on current work on alternative methods that may reduce, refine, or replace the use of animals in rabies vaccine potency testing.

Rabies vaccines serve a vital role in preventing deaths from this fatal disease and controlling rabies in certain animal populations. 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. Recent scientific and technological advances may allow several alternative approaches for rabies vaccine potency testing to be implemented immediately or in the near future.



More information about the workshop is available on the NICEATM-ICCVAM website at

<http://iccvam.niehs.nih.gov/meetings/RabiesVaccWksp-2011/RabiesVaccWksp.htm>.

Presentations from the workshop and a summary of the workshop conclusions will be posted in late October. Proceedings from the workshop will be published next year in the journal *Biologicals*. ●

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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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