Adverse outcome pathway workshop generates enthusiasm and collaboration

By Catherine Sprankle

A workshop Sept. 3-5 at the National Institutes of Health (NIH) in Bethesda, Maryland, brought together scientists from 21 countries, representing industry, academia, regulatory agencies, and special interest groups. The workshop, Adverse Outcome Pathways: From Research to Regulation, considered how the adverse outcome pathway concept could improve regulatory assessments of chemical toxicity. The National Toxicology Program Interagency Center for the Evaluation of Alternative Methods (NICEATM *(http://ntp.niehs.nih.gov/?objectid=6288C486-CFF1-8A95-D6F2CCED6B6CC819)*) co-sponsored the workshop with the nonprofit Physicians Committee for Responsible Medicine.

At the opening session, Austin related the adverse outcome pathways concept to research translation, which is the process of turning laboratory observations into interventions that improve the health of individuals and the public. (Photo courtesy of Catherine Sprankle)

An adverse outcome pathway organizes existing knowledge on chemical mode of action, for example, from an initiating event such as receptor binding, through key processes, and ending with an adverse outcome such as disease or toxicity.

The workshop featured plenary presentations, as well as breakout sessions to consider adverse outcome pathway applications, development of new pathways, and challenges to their adoption. Participants appreciated the collaborations and enthusiasm that the workshop generated, and the closing session emphasized the need to maintain that momentum.

Better understanding and practical applications

In his opening remarks, Christopher Austin, M.D., head of the NIH National Center for Advancing Translational Sciences, characterized the process of predicting toxicity as a grand challenge. “Traditionally we have exposed animals or humans and waited for the outcome at the other end, without understanding what goes on in between,” he said. “This limits our understanding of mechanisms by which these things happen.”

In addition to supporting a better understanding of how disease develops after chemical exposure, adverse outcome pathways help identify where more research is needed to understand underlying mechanisms, aid in chemical classification and prioritization for future testing, and guide the development of new testing approaches that use fewer or no animals.

Nicole Kleinstreuer, Ph.D., left, a contractor for NICEATM, and Kristie Sullivan, director of regulatory testing issues for the Physicians Committee for Responsible Medicine, co-chaired the workshop steering committee. (Photo courtesy of Catherine Sprankle)

Two well-received presentations demonstrated online tools for developing and sharing pathways. Stephen Edwards, Ph.D., of the U.S. Environmental Protection Agency, previewed a new wiki launched *(http://www.oecd.org/chemicalsafety/launch-adverse-outcome-pathways-knowledge-base.htm)* in September by the Organisation for Economic Co-operation and Development. Hristo Aladjov, Ph.D., a consultant at the Organisation, demonstrated Effectopedia *(http://www.effectopedia.org/)* , an online data collection and collaboration tool for delineating pathways. “I really appreciated the Effectopedia demonstration,” commented one attendee. “I want to download it as soon as I get home!”

Participants look forward

“I don’t think I’ve ever seen this much energy associated with a workshop,” noted Warren Casey *(http://www.niehs.nih.gov/research/atniehs/dntp/assoc/niceatm/staff/casey/index.cfm)* , director of NICEATM, which committed to establishing and managing an email list to keep attendees informed of related activities.

Presentations and links to webcasts from the workshop will be posted *(http://ntp.niehs.nih.gov/pubhealth/evalatm/3rs-meetings/past-meetings/aop-wksp-2014/index.html)* , and a workshop report will be published early next year.

(Catherine Sprankle is a communications specialist for ILS, the contractor supporting NICEATM.)

During the poster session, Zhoumeng Lin, Ph.D., of Kansas State University, discussed his study on the effects of short-term atrazine exposure with Jessica Helm, Ph.D., of the Silent Spring Institute. (Photo courtesy of Catherine Sprankle)

Aladjov answered questions during the closing session. (Photo courtesy of Catherine Sprankle)

Finding alternatives to animal testing

The term alternative methods *(http://www.niehs.nih.gov/health/topics/science/sya-iccvam/index.cfm)* refers to methods of research and testing that use fewer or no animals, or that reduce animal pain and distress. The National Toxicology Program (NTP) is involved in three committees that ensure the involvement of all stakeholders in the advancement of alternative testing methods.

• The **Interagency Coordinating Committee on the Validation of Alternative Methods** (ICCVAM *(http://ntp.niehs.nih.gov/pubhealth/evalatm/iccvam/index.html)*) is composed of representatives of federal agencies. The committee coordinates their activities to replace, reduce, or refine animal use.

• The **NTP Interagency Center for the Evaluation of Alternative Methods** (NICEATM *(http://ntp.niehs.nih.gov/pubhealth/evalatm/index.html)*) supports ICCVAM activities and NTP high-throughput screening projects, and conducts other projects relevant to test method development, maintaining and promoting scientific quality and the protection of human and animal health and the environment.

• The **Scientific Advisory Committee on Alternative Toxicological Methods** (SACATM *(http://ntp.niehs.nih.gov/about/org/sacatm/index.html)*) advises NICEATM, ICCVAM, and the NIEHS director. Representatives are drawn from industries regulated by ICCVAM member agencies, animal welfare organizations, academia, test method developers, and regulatory agencies outside of the federal government.

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