Attention NTP Interagency Center for the Evaluation of Alternative
Toxicological Methods Federal Register Notice: (78FR45253 -45254)
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Comments Submitted on Behalf of a Sponsoring Organization?: yes
Organization Name: The Humane Society of the United States Joined the NTP Listserv? yes
Comments: GENERAL COMMENTS

ICCVAM's new vision, validation strategies, and project pipeline are a welcome revision that, if successful, will not only bring ICCVAM in line with current scientific advances, but will reinstate ICCVAM's role as a facilitator in the development and regulatory use of alternative methods.

SPECIFIC COMMENTS

Priority Setting

The new plan represents a refocused and strategic emphasis on prioritization of projects to align with regulatory needs and describes an appropriate partnership with member agencies.
Sponsorship by an agency will certainly enhance the likelihood of regulatory acceptance for each project. In addition to sponsorship by a federal agency, successful application of the end result would be further ensured by a strong partnership with the agency or agencies for which the methods is applicable throughout the validation process (e.g. in study designs, choice of standard and reference chemicals, etc.). This could be facilitated by a Validation Oversight Committee composed of members from each agency to which the method is applicable.

In terms of prioritization of ICCVAM projects, it may also be helpful, in the context of limited resources, to categorize projects as (1) those in which ICCVAM will take the lead, (2) will serve as an active partner, or (3) will function in a support role in collaborative projects. For example, of the three projects listed, the Leptospira vaccine potency project (to be sponsored by USDA) and the Acute oral and dermal toxicity project (to be sponsored by EPA), may fall into category 1 with commensurate resources allocated to these projects (in addition, these are ongoing projects whose conclusions should be relatively short-term).
The sensitization project is being heavily pursued by other groups, including Cosmetics Europe and the European Centre for the Validation of Alternative Methods (ECVAM); therefore it would be appropriate for ICCVAM to function as an active partner or provide support to these ongoing projects, rather than initiate and independent activity.

The described improved international coordination and move toward integrated strategies (in contrast to the previous 1:1 replacement strategy) are also movements in a direction toward success. Design and implementation of integrated strategies would be greatly enhanced by adopting and developing related pathway-based informational design, such as the Adverse Outcome Pathway that has been adopted by the Test Guidelines Programme of the Organization for Economic Cooperation and Development (OECD)(1), for each project.

Improving communications with stakeholders and the public

Improving agency-specific 3Rs content on the ICCVAM website will bring greater visibility to agency activities in this area. In addition, ICCVAM could provide a coordinating and facilitating role within and between various agencies with related projects. For example, EPA and FDA have described initiatives to coordinate between divisions within their respective agencies, and the Tox12 project represents and interagency collaboration where ICCVAM could provide support for logistical coordination and translational preparation to make sure the methods are as broadly applicable as possible and to facilitate regulatory acceptance. This would complement the proposed inclusion of the US OECD national coordinator as an ad hoc member of ICCVAM.

In addition to the proposed ICCVAM-led workshops, webinars, etc., broader engagement of ICCVAM with the scientific community and stakeholders would be facilitated by members of ICCVAM becoming more regular participants in ongoing workshops and scientific meetings held by others (for example increased engagement in priority topic workshops, in relevant ILSI-HESI projects, etc.).

New paradigms for regulatory acceptance and utilization of alternative methods

The proposal to reconsider the concept of validation is urgently needed.
In addition to consideration of statistical approaches and consideration of different evaluation processes for different applications (e.g. prioritization vs. hazard assessment), it is also critical to tie assays and integrated strategies to pathway-based knowledge. As mentioned above, development, use, and evaluation of integrated testing strategies (as well as predictive models) would be greatly enhanced by linking each project to pathway development and coordination with international efforts in this area (2).

1. OECD Guidance on Document on Developing and Assessing Adverse
Outcome
Pathways:
http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2013)6&doclanguage=en
2. AOP Wiki collaboration between the European Commission Joint
Research Centre, the EPA Office of Research and Development, the Organization of Economic Cooperation and Development (OECD) and the international scientific community at large.
http://epa.gov/ncct/Tox21/

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