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Submitted via email: ICCVAMquestions@niehs.nih.gov

RE: Interagency Coordinating Committee on the Validation of Alternative Methods; Notice of Public Meeting; Request for Public Input

Dear Dr. Kleinstreuer,

Cruelty Free International appreciates the opportunity to submit written comments in advance of the 2023 Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Public Forum. Our comments are focused on suggestions for future ICCVAM workgroups to help progress activity in some key areas where animal tests are ripe for full replacement. We presented these suggestions at previous meetings held by ICCVAM and the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM).

One of the goals described in the January 2018 publication, *A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medicinal Products in the United States*, is to "encourage the adoption and use of new methods and approaches by federal agencies and regulated industries". This refers to the adoption of existing non-animal methods that have already been validated and accepted. With this goal in mind, we compiled a list of ten animal tests that should be prioritized for phase-out due to the availability of internationally accepted non-animal methods. This list includes the rabbit pyrogen, skin and eye irritation and skin sensitization tests as well as antibody production and various batch safety tests. We have presented this list at several international meetings and conferences, including the 11th World Congress (WC11) on Alternatives and Animal Use in the Life Sciences.

Coincidentally, a few of these tests have also been identified by SACATM members (at the September 2020 meeting) as some of the "easiest" areas where animal replacement and/or reduction could be achieved. Batch testing for biologicals was recognized by SACATM members as an area of regulatory toxicology that is responsible for the largest use of animals and it was stated that, while there were no current planned activities or an agenda for batch testing, ICCVAM was open to suggestions. The ongoing use of animals for antibody production, marine biotoxin testing and pyrogenicity testing were also identified by members as other key areas where the technology already exists to replace animals but is not being applied consistently.

We therefore encourage ICCVAM to establish workgroups focused on these four areas to further encourage the adoption of non-animal approaches.

1. Batch testing for biologicals – workgroup activities could include seeking deletion of the laboratory animal safety batch test (LABST) and target animal safety batch test (TABST) from all legal requirements in the United States (US), setting a deadline for companies to remove the abnormal toxicity test (ATT) from their product licences, and preparing a strategy to phase out all routine batch tests for biologicals, including the identification of priority areas where significant progress has already been made (e.g. leptospirosis, rabies, clostridial vaccines) as well as possible targets (e.g. GSK has set a target of 75% reduction in the use of animals for routine batch testing by 2025[1]).

2. Antibody production – workgroup activities could include publishing a formal written recommendation on the use of non-animal derived antibodies (similar to the 2020 ECVAM recommendation in the EU[2]), organizing a workshop and/or training webinars to tackle the misconceptions and identify the benefits of using non-animal derived antibodies, and creating a national resource that lists all key manufactures and suppliers of non-animal antibodies.

3. Pyrogenicity testing – workgroup activities could include seeking deletion of the rabbit pyrogen test (RPT) from all legal requirements in the US (e.g. RPT to be deleted from all EU. Ph. monographs within the next five years[3]), conducting a nationwide survey to scope the use of the RPT in the US (e.g. the results of an EU-wide survey were presented at WC11[4]), and organizing a workshop and/or training webinars to encourage the use of the available non-animal methods.

4. Marine biotoxin testing – workgroup activities could focus on conducting a nationwide survey to scope the use of the mouse bioassay and organizing a workshop to discuss the perceived limitations of the non-animal methods, including concerns about cost, and to identify where improvements could be made to encourage implementation.

Additionally, in light of recent developments, we encourage ICCVAM to reactivate its skin sensitization workgroup to work towards the widespread adoption of defined approaches using non-animal methods for testing chemicals (approved by the OECD in 2021[5]) and to encourage the replacement of guinea pig tests across all sectors.

Cruelty Free International would welcome the opportunity to discuss any of these suggestions with ICCVAM and its member agencies to help progress the adoption of existing non-animal approaches in the US and around the globe.

[1] Cecchi, R. 2021. Meningococcal group B vaccine: a journey towards a complete animal test free release process. 11th World Congress on Alternatives and Animal Use in the Life Sciences, 23 Aug – 2 Sep 2021, Maastricht, The Netherlands.
[2] EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM). 2020, May 12. Recommendation on Non-Animal-Derived Antibodies. Available at: https://publications.jrc.ec.europa.eu/repository/handle/JRC120199
[3] European Directorate for the Quality of Medicines & HealthCare (EDQM). 2021, June 26. European Pharmacopeia to put an end to the rabbit pyrogen test. Available at: https://www.edqm.eu/en/-/european-pharmacopoeia-to-put-an-end-to-the-rabbit-pyrogen-test
[4] Schutte, K. 2021. Harmonization of the 3Rs in biologicals. 11th World Congress on Alternatives and Animal Use in the Life Sciences, 23 Aug – 2 Sep 2021, Maastricht, The Netherlands.
[5] Organisation for Economic Cooperation and Development (OECD). 2021, June 22. OECD test guideline no. 497: defined approaches on skin sensitisation. Available at: https://www.oecd-ilibrary.org/environment/guideline-no-497-defined-approaches-on-skin-sensitisation_b92879a4-en

Thank you for the consideration of our comments. We look forward to your response.

Sincerely,

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