August 2024 ICCVAM Method Developers Forum: New Approaches for Carcinogenicity Testing

Questions for Developers

Method Description

Provide a brief overview of your method and its relevance to carcinogenicity testing.

a. Be sure to include enough technical detail and data for regulatory and industry stakeholders to understand how your method may meet their needs. Consider that your audience will potentially include both people who will be running the assay in the lab and people who will only be interacting with and interpreting the assay data and outcomes.
b. Describe any limitations of the applicability domain (e.g., types of chemicals that cannot be tested using the method, types of chemicals for which the results produced by that method are considered unacceptable).

Context of Use

Context of use refers to a clearly articulated description delineating the manner and purpose of use for a particular method, approach, or application. Establishing context of use includes crafting a statement that fully and clearly describes the way a method is intended to be used and its regulatory purpose (if applicable). Using the following questions as a guide, describe your method's specific context of use and the regulatory testing need(s) it addresses.

a. How is your method intended to be used (e.g., chemical screening, hazard identification, potency evaluation, developing adverse outcome pathways (AOPs), point of departure, identification for qualitative or quantitative risk assessment)?
b. What regulatory testing need does your method address (e.g., replacing an animal assay, investigating mode of action or therapeutic target, or targeted endpoint of evaluation)?
c. What regulatory space does your method address (e.g., agrochemicals, pharmaceuticals, medical devices, cosmetics, food/food additives, industrial chemicals)?
d. Has data generated by your method been used for regulatory submissions?

Biological Relevance

Biological relevance refers to a measure of appropriateness for assessing the effects of a chemical within the taxa of interest. Using the following questions as a guide, describe the relationship between your method and the carcinogenesis process.

a. Mechanistic understanding: How does the information provided by your method support known mechanistic knowledge of the carcinogenesis process (e.g., an AOP or toxicologically relevant biological process)?
b. Reference compounds: What are well-characterized and understood compounds that can be used or were used to assess the scientific validity or transferability of your method?
c. Comparison to existing laboratory animal methods: How does your method provide information that is equivalent or better than that from existing methods used for regulatory purposes? How

does your method contribute to the reduction, refinement, or replacement of animal assays, and what complementary method development might be needed to comprehensively address carcinogenesis?

Technical Characterization

Technical characterization is a key aspect to demonstrating the quality and scientific validity of a method. Using the following questions as a guide, describe how your method has been characterized.

a. How have the sources of variability (e.g., interference, culture conditions, technique, contaminants) been evaluated?
b. How has robustness (i.e., the ability of the method to be reproduced under different conditions or circumstances, without the occurrence of unexpected differences in the obtained results) been evaluated?
c. How has intra-laboratory reproducibility (i.e., the consistency of individual test results obtained within a laboratory using the same test protocol and test samples) been evaluated?
d. How has transferability (i.e., the ability of the method to be accurately and reliably performed in different, competent laboratories) been evaluated (if relevant)?