Testimony

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ICCVAAM Public Forum Thursday, May 27, 2021 (9:00 AM – 5:00 PM)

Good afternoon. I am Jessica Ryman-Rasmussen, Senior Policy Advisor at the American Petroleum Institute (API). API represents all segments of America's oil and natural gas industry. API is actively involved in both research and science policy for new approach methods (or NAMs) that are fit-for-purpose for risk assessment. My comments today describe API's research and science policy activities regarding NAMs with a view to realizing EPA's Directive to phase out animal testing and reliance by 2035.

Petroleum and petroleum substances are comprised of chemicals that can number in the hundreds. Additionally, composition can vary due to differences in natural sources and refining conditions. For this reason, petroleum and petroleum substances are types of Unknown or Variable Composition, Complex Reaction Products and Biological Materials, also known as UVCBs. To API's knowledge, very few (if any) NAMs have been validated for UVCBs. On the science-policy side, API reminds regulatory agencies of this limited validation for UVCBs and the need to be able to continue to use animal data until sufficient validation, including definition of the relevant applicability domain, for UVCBs is better understood. On the research side, API is contributing to this effort by funding our own validation research for skin and eye irritation NAMs. For example, we have funded research comparing the Draize test *in vivo* to reconstituted human skin and eye epithelium models *in vitro* for Ultra-Low Sulfur Diesel. API has also funded the generation of Simplified Molecular Input Line Entry System (or SMILES) libraries for Ultra-Low Sulfur Diesel that can be used in *in silico* models that are compatible with SMILES to identify skin and eye irritation. This work, conducted with collaborators, will be presented in a poster at QSAR 2021 next month.

Earlier this year, API submitted public comments on US EPA's IRIS Handbook. API stated that the Handbook that governs how assessments are done today can move the needle toward the animal-free assessments of tomorrow. As EPA transitions to the use of NAMs that are fit-for-purpose for risk assessment, including hazard identification and dose-response assessment, Mode of Action (MOA) and Adverse Outcome Pathway (AOP) frameworks will not be optional, but essential. API suggested that PBPK and MOA data be separately tagged and elevated to the same level as PECO instead of being relegated to Supplemental Information and stated that the IRIS Program should also encourage the use of MOAs and AOPs to support endpoint identification and dose response assessment.

On the research side for AOPs, API has funded research to develop a new AOP. API will soon submit this for publication in the peer-reviewed scientific literature.

On the research side for MOAs, API, via the Naphthalene Research Committee, has funded hypothesis-based, weight of the evidence studies to inform the MOA for naphthalene carcinogenesis. These studies are published in the peer-reviewed scientific literature. More recently, API funded a manuscript that used ToxCast data and a PBPK model for naphthalene to further inform the weight-of-the-evidence. This manuscript has also been published in the peer-reviewed scientific literature.

In conclusion, API has been an active stakeholder in both science policy and research related to NAMs. We are grateful for inter-agency forms, such as ICCVAAM, that share knowledge to advance non-animal testing. API is also grateful for the opportunity to provide public comment today.