Opportunities for Encouraging the Consideration of Alternative Methods

S. Marko[1], D.G. Allen[2], H. Hogberg[3], O.B. Oyetade[2], N.C. Kleinstreuer[3], J. Carder[4]

OUSD(R&E), Alexandria, VA, United States[1]; Inotiv, RTP, NC, United States[2]; NIH/NIEHS/DTT/NICEATM, RTP, NC, United States[3]; USDA/AWIC, Beltsville, MD, United States[4]

Background and Purpose

In the United States, the Animal Welfare Act regulations require investigators to consider alternative methods prior to using animals for research, teaching, or testing whenever proposed procedures involve more than slight or momentary pain or distress [9 C.F.R. § 2.31 (d)(ii)(2022)]. However, there is little incentive for investigators that have long used specific in vivo models and well-established protocols to replace those models with new approach methodologies (NAMs). The Interagency Coordinating Committee on the Validation of Alternative Methods established the Consideration of Alternative Methods Work Group (CAMWG) to explore opportunities for encouraging investigators using animal-based models to not only consider, but actively pursue, potential NAMs that could contribute to replacing, reducing, or refining the use of laboratory animals (3Rs). This presentation summarizes targeted stakeholder discussions facilitated by the CAMWG on various aspects of using NAMs to explore how to increase the consideration and implementation of NAMs.

Methods

Virtual stakeholder meetings were held between May 2022 and May 2023 with CAMWG members and stakeholder group representatives from agrochemical, industrial chemical, consumer products, pharmaceutical companies; academic researchers; and academic Institutional Animal Care and Use Committee members. A common set of discussion questions was formulated and used to collect stakeholders' perspectives on how alternatives to traditional animal tests are considered when developing their respective organization's toxicology testing programs.

Results

Many stakeholders already use NAMs for mechanistic research, justification in animal protocols, internal company decision making, and various regulatory processes. Private sector stakeholders indicated specifically using NAMs for internal decisions in drug development, screening, safety and risk assessment and hazard characterization of products, and to meet regulatory needs for waivers, bridging, and weight of evidence. Barriers to using NAMs centered on limited funding available for NAM development, scientific and technical challenges, regulatory acceptance and harmonization issues, as well as limited knowledge and training on NAMs. Recommendations for overcoming these barriers included ensuring fit-for-purpose use of NAMs, developing national and global harmonized acceptance criteria, identifying funding sources, and increasing awareness about the strengths and limitations of NAMs.

Conclusions

Clearly NAMs are available and used by various stakeholders, but there are areas and application domains where NAMs are not yet suitable. Regulators, NAMs developers, and end-users need to increase dialogue on priorities and opportunities for NAMs. To foster increased consideration of

NAMs, targeted funding opportunities are needed to develop and incorporate NAMs in research and regulatory applications. This project was funded in whole or in part with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.

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