ENDOCRINE SOCIETY
Hormone Science to Health

The Endocrine Society appreciates the opportunity to provide input on the forthcoming Commission Roadmap to phase out animal testing. As the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology our membership consists of over 18,000 scientists, physicians, educators, nurses, and students in more than 100 countries, including the world's leading experts on the health effects of endocrine-disrupting chemicals (EDCs). Our Society welcomes the development of new approach methodologies (NAMs) defined as "technologies and approaches (including computational modeling, in vitro assays, and testing using alternative animal species)" to reduce the use of vertebrate animals in regulatory assessments and ensure a high level of human health protection . However, we caution that NAMs have not been sufficiently developed to comprehensively assess biological complexity. Moreover, certain biological processes, including many developmental pathways that, if perturbed, result in later-life effects, may never be sufficiently replicated via NAMs to achieve the high level of protection required.

To be clear, the Endocrine Society supports the adoption of new or non-animal test methods when they demonstrably reflect human biological understanding as well as or better than traditional methods. Currently, most non-animal methods do not achieve this standard for important endocrine endpoints. For example, non-animal methods do not adequately address the critical role of thyroid hormone in neurodevelopment. At present, NAMs are suitable for screening to identify hazards currently uncharacterized by animal studies. However, due to their limitations NAMs should not be used to invalidate positive results from human or animal studies, nor should they be used in isolation to determine that a chemical is safe. This position is consistent with the assessments of multidisciplinary scientific bodies, such as the United States' National Academies of Science, Engineering and Medicine.

To achieve the stated goals of the Roadmap, we argue that regulatory agencies should make more efficient use of data that currently exists by:

1. Adopting group-based approaches to chemical assessments that utilize read-across to apply positive hazard data from one chemical to others in the same group.
2. Systematically incorporating data from academic labs.
3. Harmonizing assessments across agencies for chemicals that often have multiple exposure scenarios e.g., bisphenols, phthalates, PFAS.
4. Supporting observational research in humans (e.g. cohort studies) is a way to provide relevant information for issues related to the impact of environmental factors on health.

Finally, we note that policies to adopt NAMs to the exclusion of traditional methods may be inconsistent with legal text requiring that EDCs be identified based on an adverse effect in an intact organism. We therefore urge regulatory agencies to clearly describe how hazard data from NAMs will be accepted and used as a basis for restrictions and other controls before policies mandating their use are adopted.

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Thank you for considering these comments; our members look forward to working with the Commission as the Roadmap takes shape to ensure that assessments for endocrine disruption are science-based and health protective, while minimizing the use of animals in testing.