

J Strickland¹, A Daniel¹, DG Allen¹, N Kleinstreuer², E Haugabrooks³

¹ILS, RTP, NC, USA; ²NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA; ³Physicians Committee for Responsible Medicine (PCRM), Washington, DC, USA

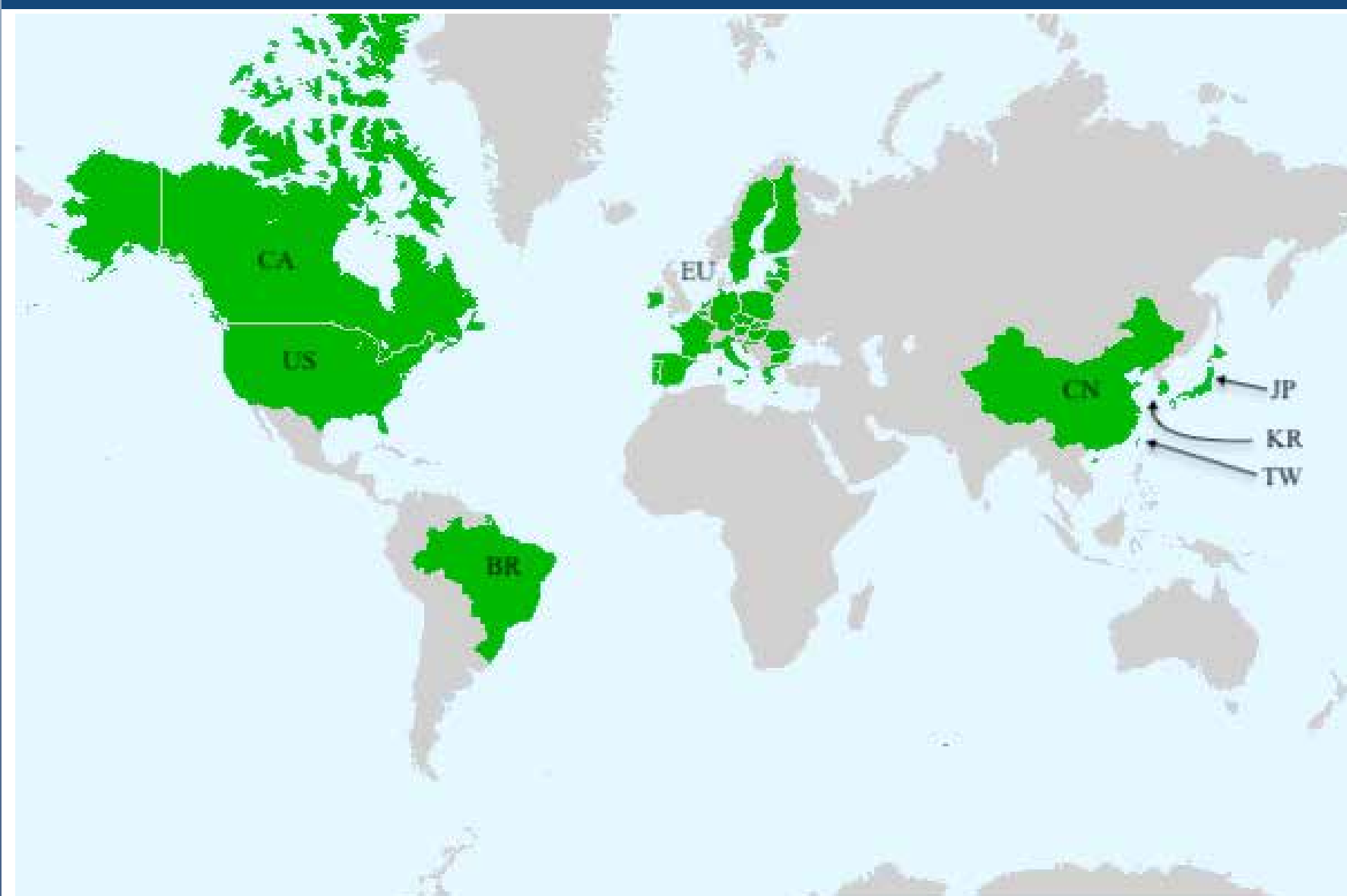
Highlights

- We reviewed regulatory requirements for acute systemic toxicity testing, by chemical sector, of eight countries or regions.
- This review summarizes data uses for acute systemic toxicity testing and currently accepted animal tests and non-animal alternatives.
- This effort will inform international strategies for implementing non-animal approaches for acute systemic toxicity testing.

Introduction

- Acute systemic toxicity data for oral, dermal, and inhalation exposure routes are often used to support the safe use and management of chemicals and products.
- Data are typically obtained from rodent experiments with lethality as an endpoint.
- To identify opportunities for regulatory uses of non-animal approaches for this endpoint, we reviewed acute systemic toxicity testing requirements for eight countries or regions that participate in the International Cooperation on Alternative Test Methods (ICATM).

Participating Countries and Regions

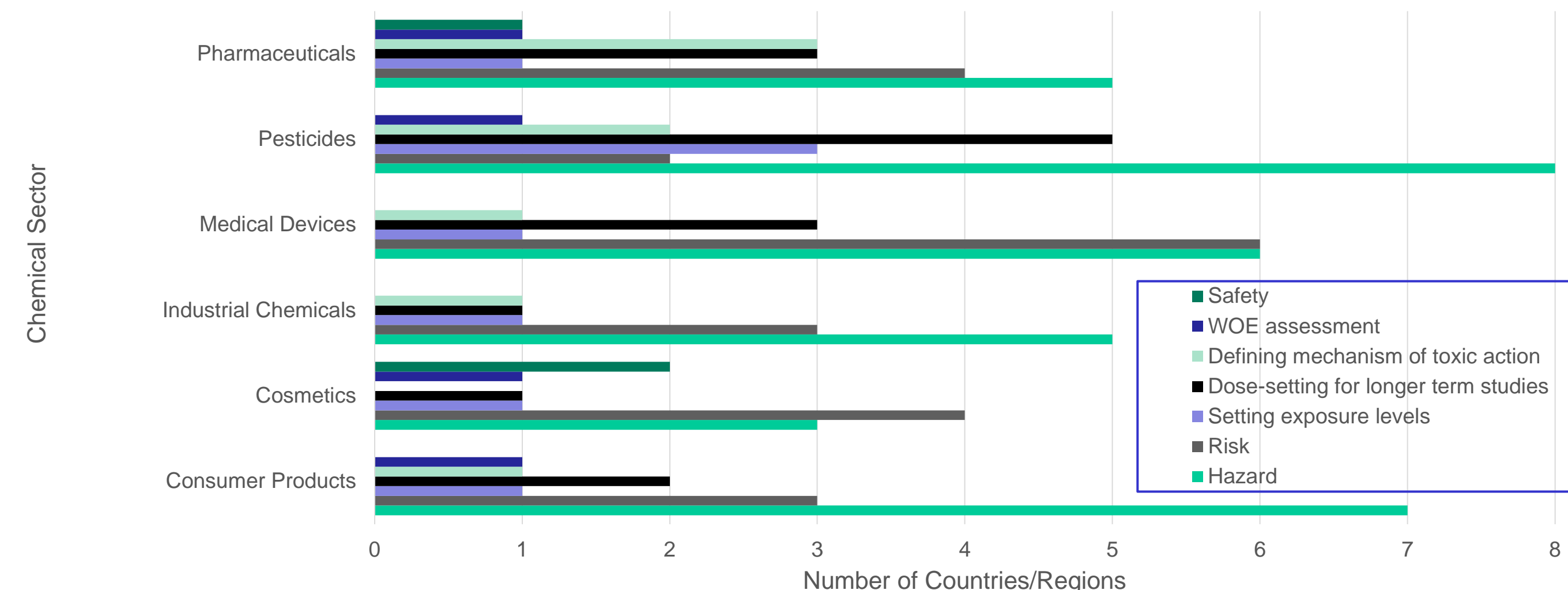


OECD Members

BR	Brazil	
CA	Canada	✓
CN	China	
EU	European Union	✓
JP	Japan	✓
KR	South Korea	✓
TW	Taiwan	
US	United States	✓

OECD = Organization for Economic Cooperation and Development

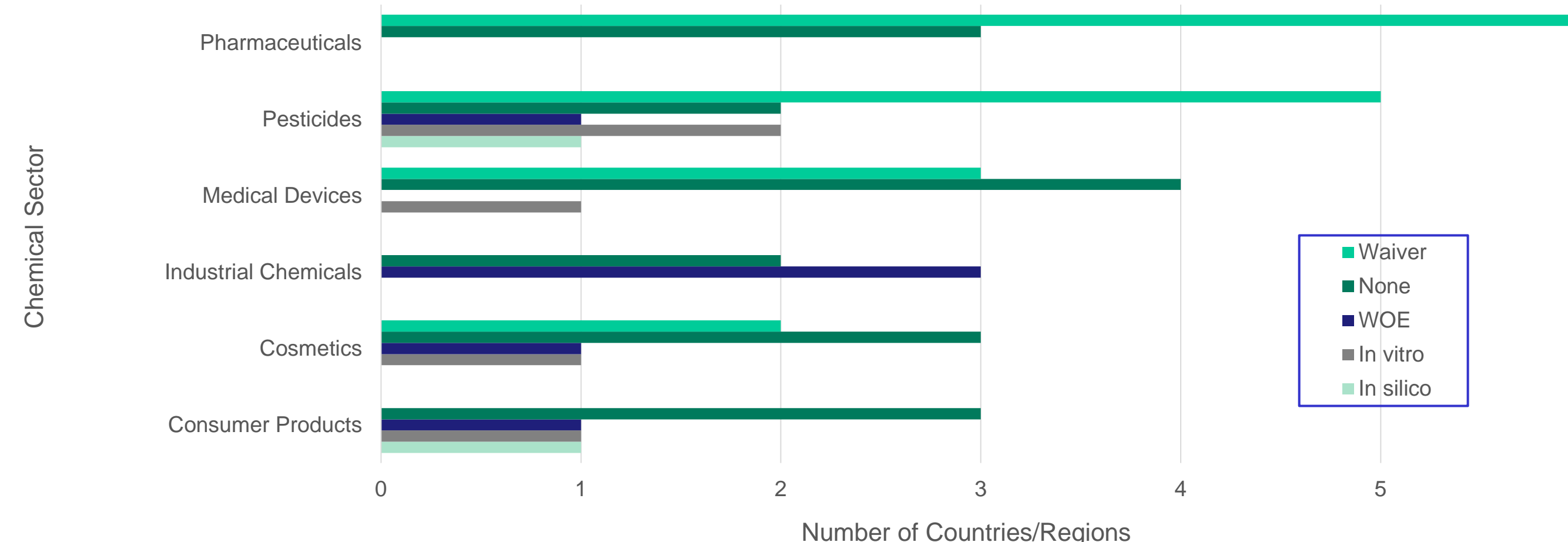
Rationale for Acute Systemic Toxicity Data Needs by Sector



WOE = weight-of-evidence assessment for which acute systemic toxicity is one component of a complete chemical toxicity profile. Some sectors use acute systemic toxicity data for more than one purpose.

- ICATM participants identified acute systemic toxicity data needs for the chemical sectors shown.
- Data were most frequently needed for the purposes of hazard assessment, risk assessment, and dose-setting for longer term studies.

Use of Non-animal Alternatives by Sector



WOE = weight-of-evidence assessment using multiple non-animal methods. Some sectors accept more than one alternative approach.

- For each sector, at least two countries did not accept non-animal approaches ("None").
- The most frequently accepted non-animal alternative was test waivers.
- In vitro or in silico assessments were acceptable for some data needs, but specific methods were not defined.
- Pharmaceutical authorities in CA, EU, and BR use acute systemic toxicity data, but discourage lethality testing.
- BR and KR generally accept non-animal OECD test guidelines, but there are currently no non-animal OECD test guidelines for acute systemic toxicity.
- CA and US consider non-animal alternatives on a case-by-case basis for some sectors.

Preferred In Vivo Methods

- OECD test guidelines were preferred methods in at least one chemical sector for 7/8 countries/regions.
- All countries/regions preferred International Organization for Standardization (ISO) guidelines, or similar methods, for testing medical devices. Most countries/regions preferred International Conference on Harmonization (ICH) guidelines for pharmaceuticals.
- In some countries/regions, no testing is required for the following sectors: cosmetics (4/8), industrial chemicals (3/8), consumer products (1/8).

Conclusions

- No single non-animal test method or prescribed test battery is accepted, for any exposure route, to replace the required mammalian acute toxicity tests.
- Regulatory authorities for some countries/regions accept waivers and weight-of-evidence approaches; however, there is no accepted standardized approach.
- Generally, within many regulatory jurisdictions, guidance documents for the accepted non-animal approaches are either not easily accessible or not available at all.
- The cosmetic sector has the most legislative bans on animal testing, although acute toxicity testing is not always prioritized or characterized as a required toxicity test.
- More communication from regulatory authorities about the specific non-animal alternatives that are acceptable would encourage the use of alternatives.

More Information

The views expressed within this poster presentation do not necessarily represent the official positions of any federal agency. Since the poster was written as part of the official duties of the authors, it can be freely copied.

This project was funded by PCRM and with federal funds from the National Institute of Environmental Health Sciences, NIH, under Contract No. HHSN273201500010C.

Subscribe to the NICEATM News email list:
<https://list.nih.gov/cgi-bin/wa.exe?SUBED1=niceatm-I&A=1>

Visit [PCRM.org/TSCA](https://www.epa.gov/sites/production/files/2019-12/documents/alternative_testing_nams_list_first_update_final.pdf) for a list of regulatory New Approach Methodologies
See EPA's list of alternative methods and strategies at
https://www.epa.gov/sites/production/files/2019-12/documents/alternative_testing_nams_list_first_update_final.pdf

Visit [ICAPO.org](https://www.icapo.org) to learn more about non-animal approaches within the OECD.

Learn more about ICATM at <https://ntp.niehs.nih.gov/go/icatm>.

