

International Regulatory Needs for Acute Toxicity Data

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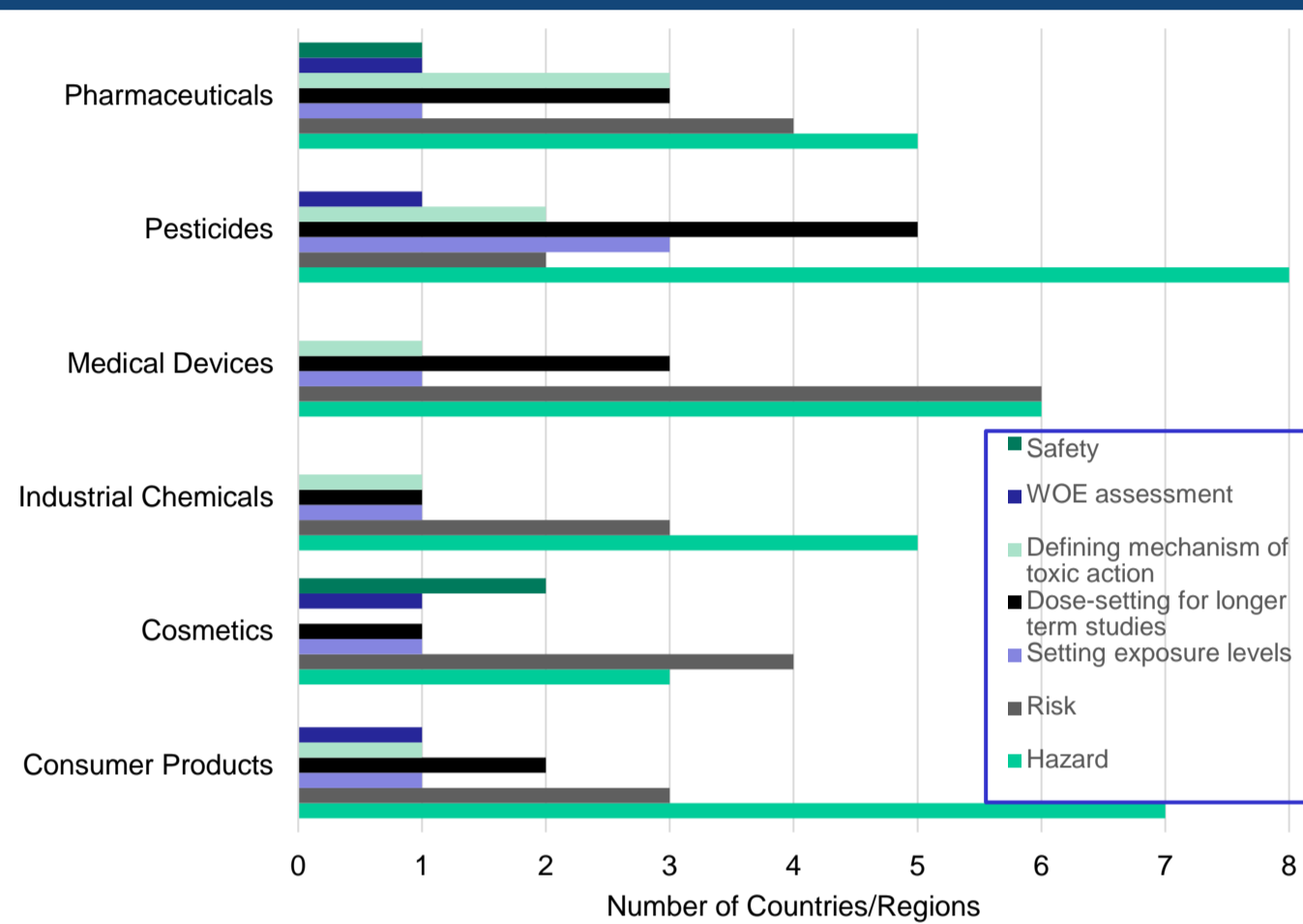
Introduction

- 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).

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.

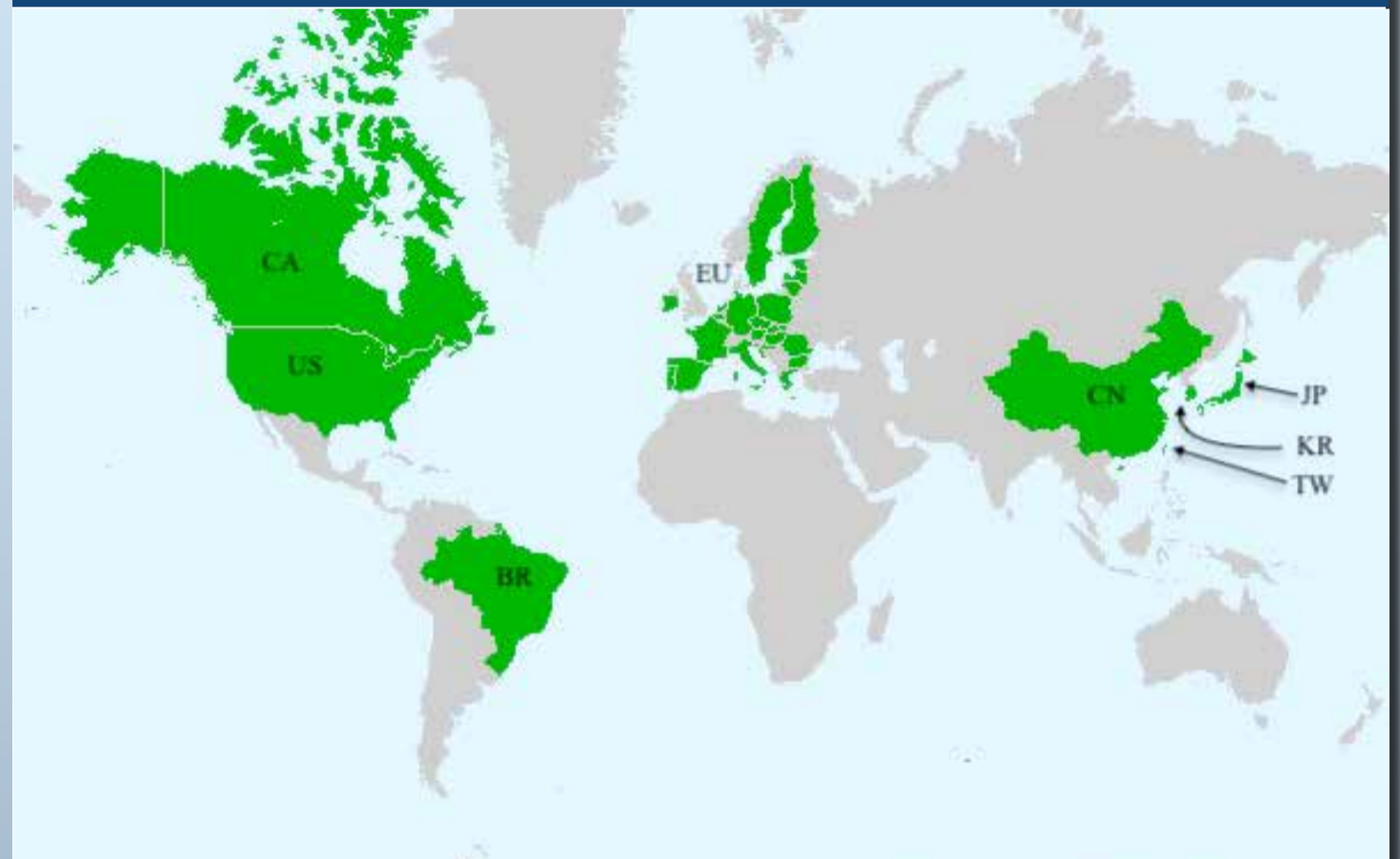
Rationale for Acute Systemic Toxicity Data Needs by Sector



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.

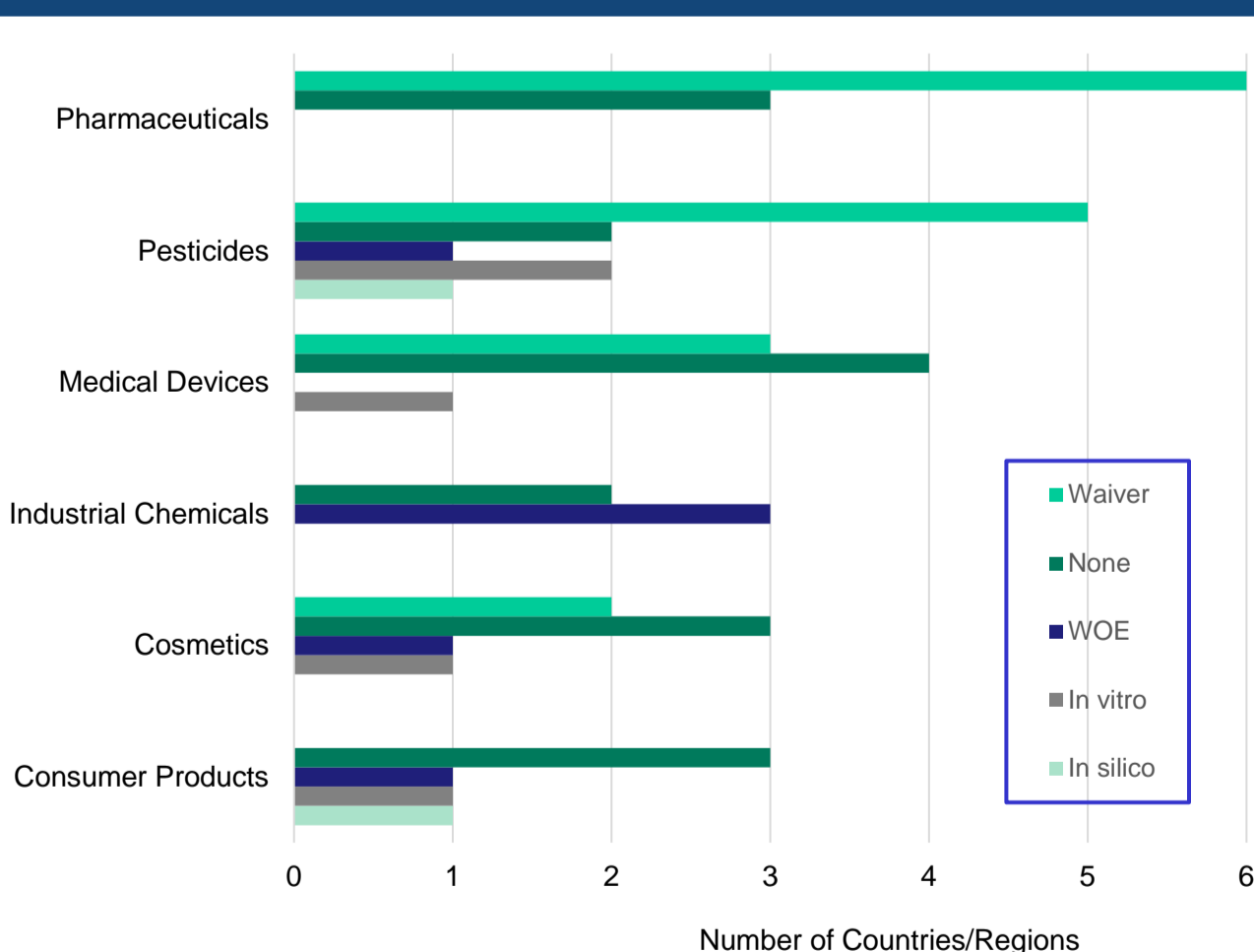
- ICATM participants identified acute systemic toxicity data needs for six chemical sectors.
- Data were most frequently needed for the purposes of hazard assessment, risk assessment, and dose-setting for longer term studies.

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	✓

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 test guidelines issued by the Organisation for Economic Cooperation and Development (OECD), 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 seven of the participating 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).

More Information

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Visit [PCRM.org/TSCA](https://www.pcrm.org/TSCA) for a list of regulatory New Approach Methodologies.

See the U.S. Environmental Protection Agency'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.oecd.org/icafo/) to learn more about non-animal approaches within the OECD.

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