
# Bridging Innovation and Regulation

## A Mapping Review of Strategies to Enable the Global Uptake of New Approach Methodologies (NAMs) in Chemical Toxicology

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parera
Plateforme d'Analyse des Risques et d'Excellence en Réglementation des Aliments

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# Outline

- Introduction, Objectives & Methodology
- Descriptive Observations
- Reported Challenges
- Reported Enablers

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# Implementation of NAMs in the Regulatory System

## Scientific & Regulatory Support

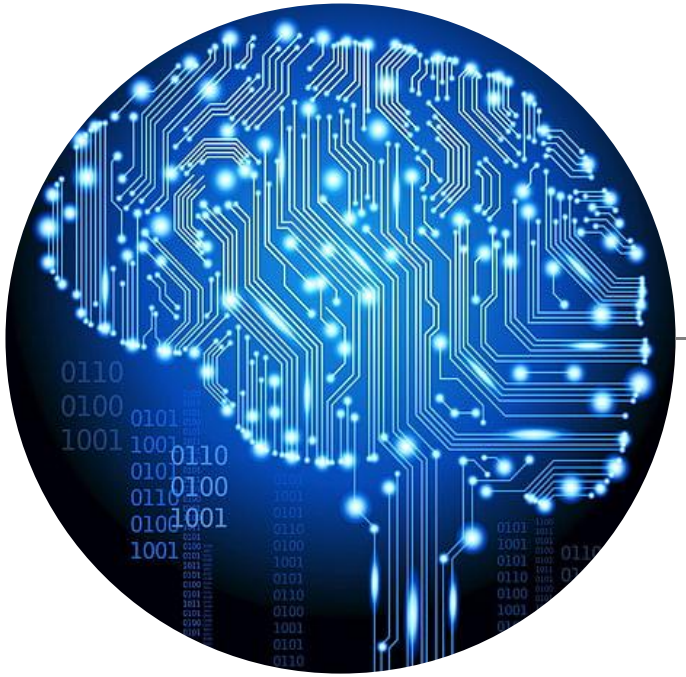
- ☑ Broad consensus: the use of NAMs in regulatory risk assessment ("Next Generation Risk Assessments - NGRA) offers a great opportunity to further advance the protection of human health.
- ☑ Better tools for new and complex toxicological challenges.
- ☑ Used to replace, reduce or refine animal toxicity testing.

## Implementation Gap

- ⚠ Despite advances, uptake in regulatory toxicology is still slow.
- ⚠ NAMs data alone often seen as insufficient for major regulatory decisions.

***Bridging innovation and policy: accelerating NAMs uptake !***

# Objectives of the Mapping Review



01 Identify, classify, and synthesize recent strategies enabling NAMs integration

02 Cover chemical safety in food and consumer safety contexts

03 Provide a structured analysis of national, regional and global efforts

04 Highlight recurrent barriers and enabling factors

05 Offer evidence-based recommendations for promoting harmonized NAMs adoption

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# Mapping Review Methodology

### Scope & Eligibility Definition

Define the review's purpose and target period (2013–2025).
Establish inclusion/exclusion criteria based on relevance to NAMs in regulatory toxicology.
Include peer-reviewed articles, official reports, grey literature, and project documentation

### Literature Collection

Search relevant databases (e.g., Scopus, PubMed) and institutional websites (e.g., OECD, EFSA, EPA).
Gather documents from ongoing projects/platforms (e.g., EU-ToxRisk, PARC, ASPIS).
Apply snowballing to identify additional references cited in key documents

### Screening & Selection

Conduct title and abstract screening followed by full-text review when necessary.
Apply eligibility criteria systematically to ensure consistency.
Exclude documents unrelated to regulatory NAM strategiesusiness

### Data Extraction

Extract key fields: author/year, jurisdiction, entity, NAM focus, strategy type, barriers/enablers, and outcomes.

### Classification & Mapping

Categorize initiatives by level (national, regional, international), strategy type (e.g., guidance, training, research), and regulatory focus.
Identify thematic clusters and cross-jurisdictional efforts.
Highlight recurring mechanisms and implementation patterns

### Synthesis & Visualization

Summarize findings in tables, typologies, and global maps.
Identify trends, gaps, and leading practices

# Geographical Coverage

**Canada**: National programs (CMP) supporting risk prioritization and NAMs-based policy reform

**EU**: Horizon Europe-funded consortia; regulatory integration under the Chemicals Strategy for Sustainability (CSS)

**USA**: Strategic plans: Toxic Substances Control Act (TSCA) and interagency collaborations

**China**: Food Toxicology Program promoting development of NAMs

**Brazil**: Emerging regulatory acceptance

**Australia**: National programs (AICIS) supporting risk prioritization and NAMs-based policy reform

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# Types of Documents Reviewed

## Documents published or active [2013-2025]

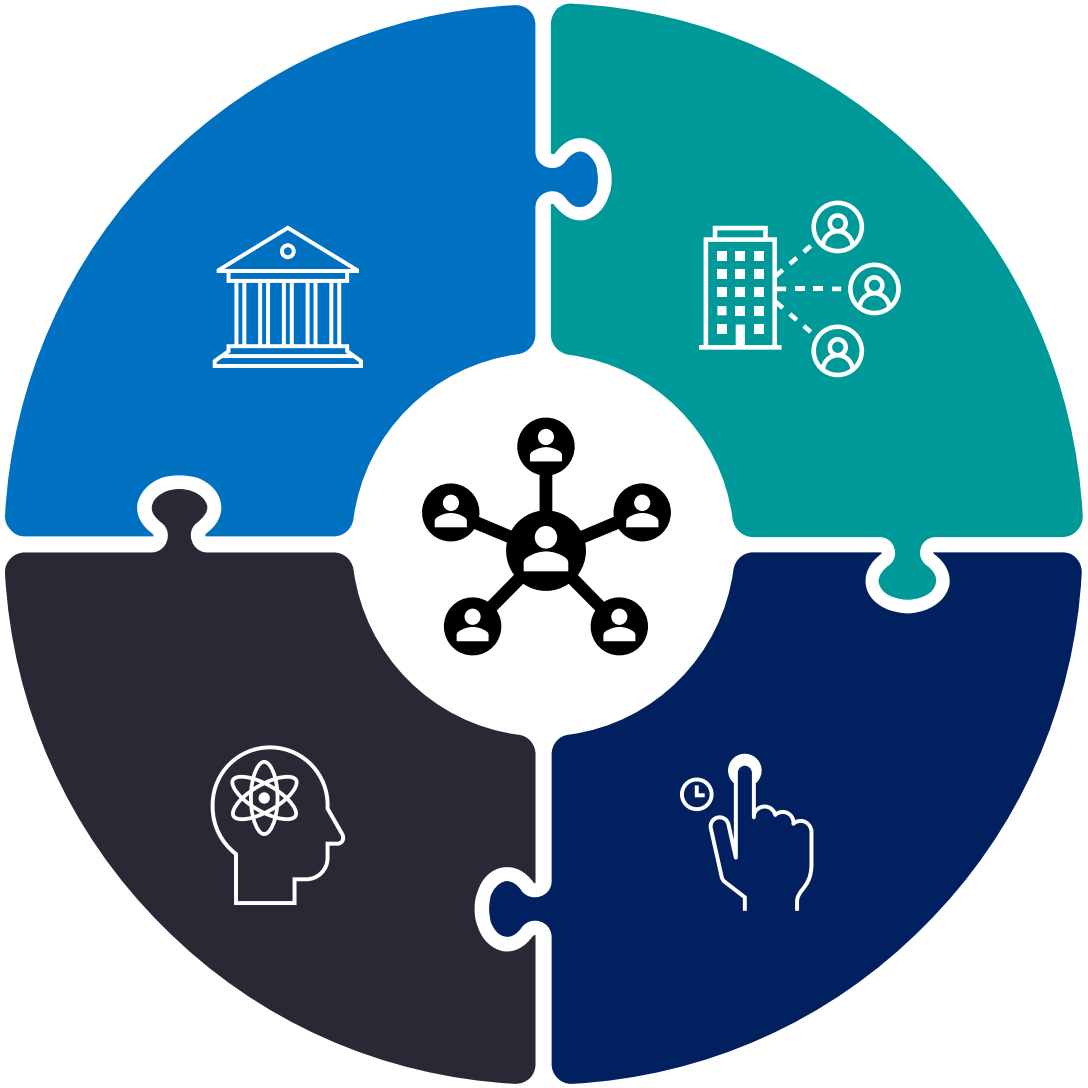
*(72 Documents in total)*

- **Peer-reviewed scientific literature** (e.g., toxicology and regulatory science journals)
- Scientific and technical **strategy reports**
- **Project deliverables** from consortia (ONTOX, PARC, RISK-HUNT3R, and PrecisionTOX)
- **Regulatory guidance** (e.g., EPA, EFSA, ECHA, OECD reports)
- Grey literature, including institutional **white papers** and **workshop summaries**

# Stakeholder Categories

## Regulatory Bodies

EFSA, ECHA, EPA, ANSES, Health Canada, NICNAS/AICIS, NMPA/CFSA (China), ANVISA (Brazil)



## Multilateral Organizations

OECD, WHO, ISTNET

## Research Consortia

ASPIS cluster (ONTOX, RISK-HUNT3R, PrecisionTOX), EU-ToxRisk, PARC

## National/Regional Scientific Agencies

NIVA (Norway), JRC (EU), BfR (Germany), RIVM (Netherlands)

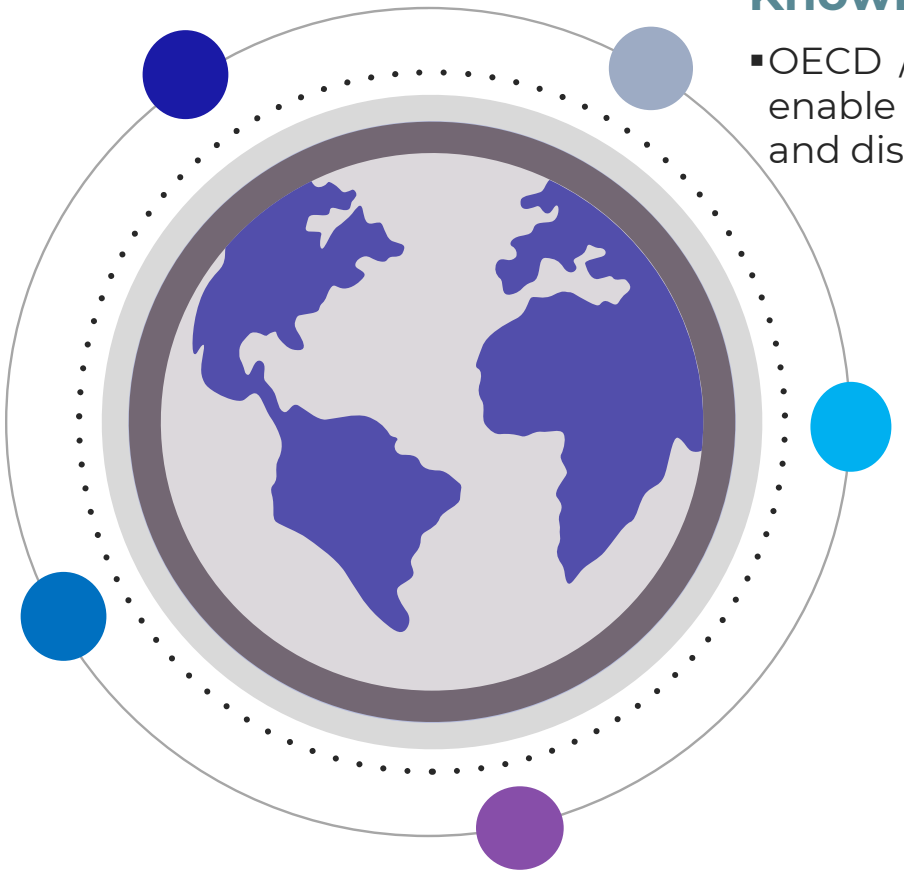
# Global Frameworks Driving NAMs Regulatory Readiness

## OECD Leadership

- Developed core guidance on IATA and AOP frameworks / Promotes regulatory convergence via the Mutual Acceptance of Data (MAD) system.
- Published standardized guidance for reporting non-animal methods
- Provides case studies on endpoints like bioaccumulation, carcinogenicity, and chronic toxicity.

## WHO, ECETOC, and ISTNET Contributions

- WHO and ISTNET support training, knowledge sharing, and technical alignment.
- ECETOC advances omics integration (e.g., transcriptomics, metabolomics) to support mechanistic risk.



## Knowledge Platforms

- OECD / AOP Knowledge Base and ISTNET enable harmonized method development and dissemination of best practices.

## Academic & Research Institutions

- SCAHT (Switzerland) and Vrije Universiteit Brussel are key contributors to test readiness criteria and omics-based AOP integration.

## Intergovernmental Collaboration

- The EU, USA, Canada, and Japan collaborate on IATA case studies and mutual recognition of regulatory assessments

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# Regional Initiatives – European Union

## EUTOXRISK

**2016-2021**

- Led by Leiden University
- Systemic toxicity via IATA, AOPs, and in vitro/in silico methods
  Involved 30+ partners from 13 EU countries

## PARC

Partnership for the Assessment of Risks from Chemicals

**2022-2029**

- Led by ANSES in partnership with EFSA & ECHA
- 200+ organizations from 28 countries
- Building an EU-wide framework for chemical risk assessment

## ASPIS

ONTOX · PRECISION TOX · RISK HUNT3R

## ONTOX

**2021-2026**

- Led by Vrije Universiteit Brussel
- AI-enabled NAMs for repeated dose toxicity
- Partners from Italy, Germany, Spain, Netherlands
- **Part of ASPIS cluster**

## RISK HUNT3R

**2021-2026**

- Led by Leiden University
- NGRA-focused, pathway-based safety assessments
  Partners include ETH Zurich (CH), BfR (DE), FIOH (FI)
- **Part of ASPIS cluster**

## PRECISION TOX

**2021-2026**

- Led by University of Birmingham
- Population genomics & cross-species comparisons for predictive toxicology
- Partners from France, Norway, Italy, Greece, and Sweden
- **Part of ASPIS cluster**

# National Initiatives – United States of America (USA)


## Tox21 (2008)

- Agencies: EPA, FDA, NIEHS, NCATS
- Focus: High-throughput, mechanism-based toxicity testing

## HTTK

- Agencies: EPA, NIEHS
- Focus: Predict internal dose & simulate chemical behavior

## ToxCast (2007)

- Agency: EPA
- Focus: Bioactivity data generation via 900+ in vitro assays

## NICEATM

- Agency: NIEHS
- Function: Supports ICCVAM through modeling, IVIVE tools (ICE platform)

## CompTox

- Agency: EPA
- Function: Public platform for NAMs data (Tox21, ToxCast, HTTK).

## ICCVAM

- Support: Operates via NIEHS/NICEATM
- Role: Policy alignment, international collaboration (e.g., OECD)

# National Initiatives – Others

## Canada

Chemicals Management Plan (CMP)
Contributor to OECD Test Guidelines Program

## Australia

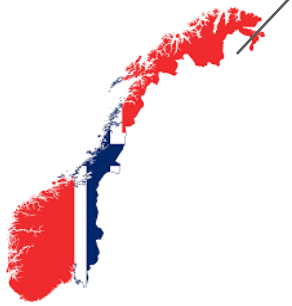
Australian Industrial Chemicals Introduction Scheme (AICIS)

## Brazil

ANVISA and IBAMA have begun accepting OECD-validated in vitro tests and are promoting their use in pesticide and industrial chemical evaluations

## China

MEE Order No. 12 formalized new chemical registration procedures that accept non-animal testing data



## Norway

Active role in European regulatory science project

## Switzerland

SCAHT's efforts towards reducing reliance on animal testing

# Strategies for NAMs Integration

## Regulatory Frameworks and Policy Instruments

### EU Chemicals Strategy for Sustainability (CSS)

- Promotes the Safe-and-Sustainable-by-Design (SSbD) concept.
- Supports systematic integration of NAMs into chemical regulation.

### U.S. EPA NAM Strategic Plan (2018–2021)

- Aims for gradual reduction of animal testing.
- Emphasizes development, evaluation, and implementation of NAMs.

### Canada 's Chemicals Management Plan (CMP)

- Encourages use of NAMs for chemical prioritization and hazard identification.

### China's MEE Order No. 12 (Ministry of Ecology and Environment)

- Accepts non-animal test data for chemical registration.
- Aligns with OECD test guidelines

### Australia's Industrial Chemicals Introduction Scheme (AICIS)

- Limits new animal testing.
- Favors use of validated alternatives, including read-across and in silico tools.

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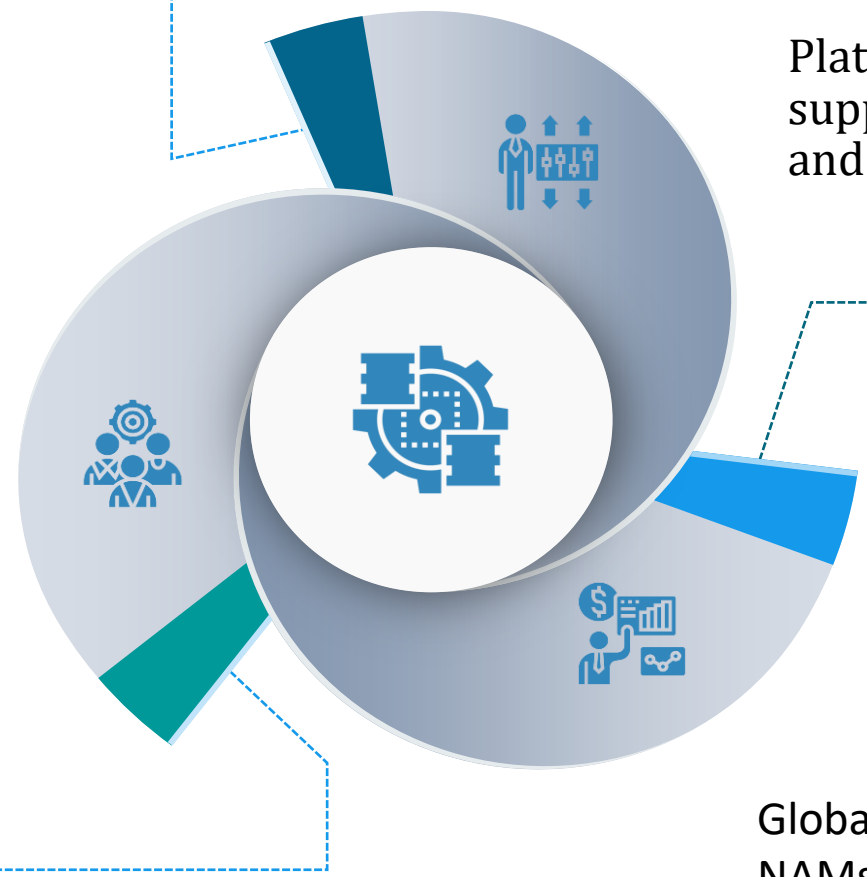
# Strategies for NAMs Integration: Cont.

## Scientific and Technical Infrastructure

Platforms, databases, and decision-support tools that manage, integrate, and interpret NAM-derived data.



## Research Consortia and Funding Programs

Global funding ecosystem ensuring that NAMs development is science-driven, context-specific, and responsive to regulatory priorities.

## Capacity-Building, Stakeholder Engagement, and Networks

Capacity-building efforts include training modules, support for academic-industry partnerships, and public communication strategies.

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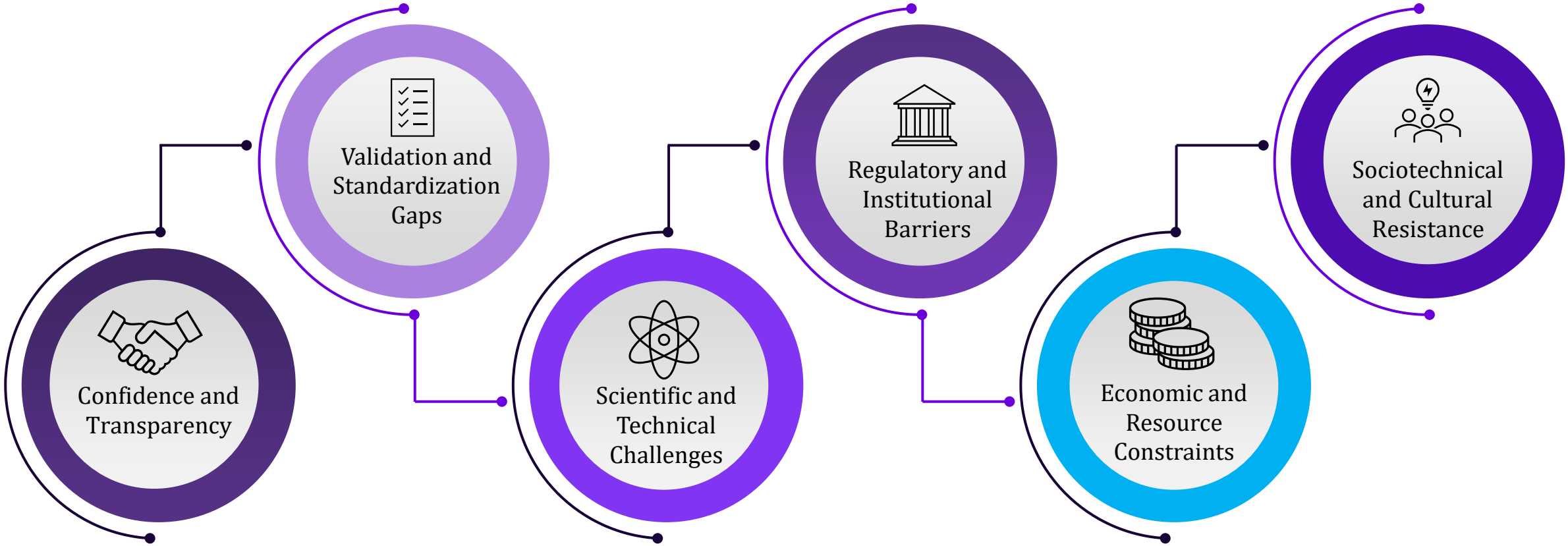
# Summary of Reported Barriers to NAMs Implementation



# Summary of Reported Enablers

## Open Science and Data Sharing

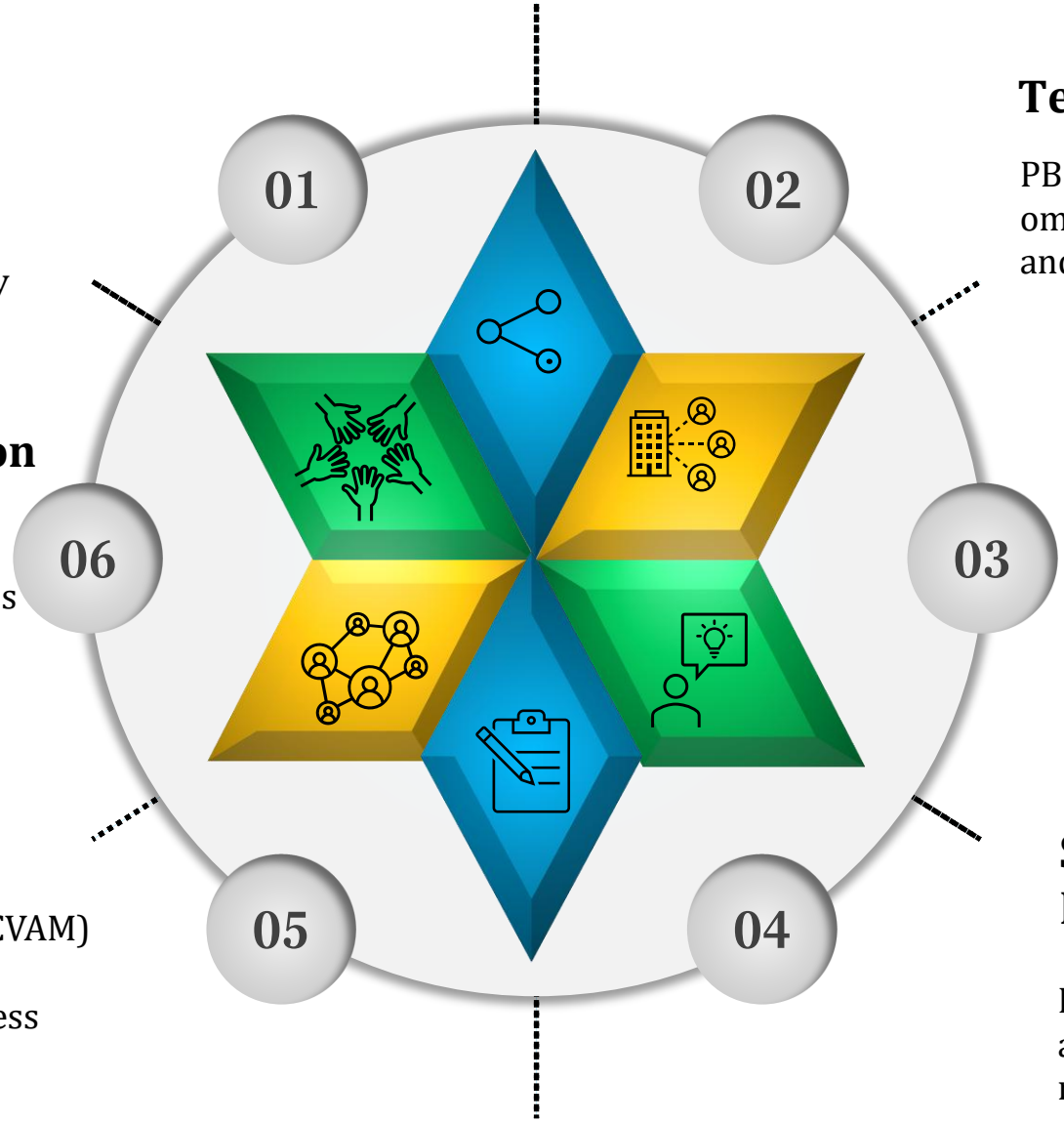
Platforms like ICE and RE-Place, combined with FAIR-compliant databases, promote transparency and interoperability especially for resource-limited stakeholders.

## Harmonization and Collaboration

OECD guidance, EESA alignment, and NIH supported programs build consistency across jurisdictions and reduce fragmentation.

## Stakeholder Engagement and Cultural Shift

Multi-sectoral collaboration (e.g., ASPIS, ICCVAM) enables consensus-building and promotes mutual understanding of scientific robustness and regulatory relevance.




## Technical Tools and Infrastructure

PBK modeling, validated in vitro guidelines, and omics interpretation tools improve data quality and reduce uncertainties.

## Training and Capacity-Building

Educational programs, early-career researcher support, and ongoing assessor training address workforce readiness gaps

## Strategic Frameworks and Regulatory Support

Initiatives such as the EU Green Deal, PARC, and EPRS TSCA Plan help counter inertia and reduce validation bottlenecks.

# Conclusion & Perspectives

Acknowledge the gradual integration of NAMs in regulatory chemical risk assessments across food, environmental, and consumer product sectors.

Take stock of current guidance developed by international bodies (e.g. OECD) or specific initiatives, and assess its:

- Impact on the conservativeness of assessment results.
- Role in regulatory alignment and consistency.
- Influence on decision-making outcomes.

Encourage the development of detailed and operational guidance on the use of NAMs:

- Embedded within risk assessment policies.
- Informed by practical experiences.
- Tailored to specific chemical classes or health endpoints.

Support harmonized and systematic incorporation of NAMs to improve consistency, reliability, and effectiveness of chemical risk assessments.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