



GAINING CONFIDENCE IN THE USE OF NEW APPROACH METHODS THROUGH INTEGRATED APPROACHES TO TESTING AND ASSESSMENT

Bob Diderich, OECD, September 2023

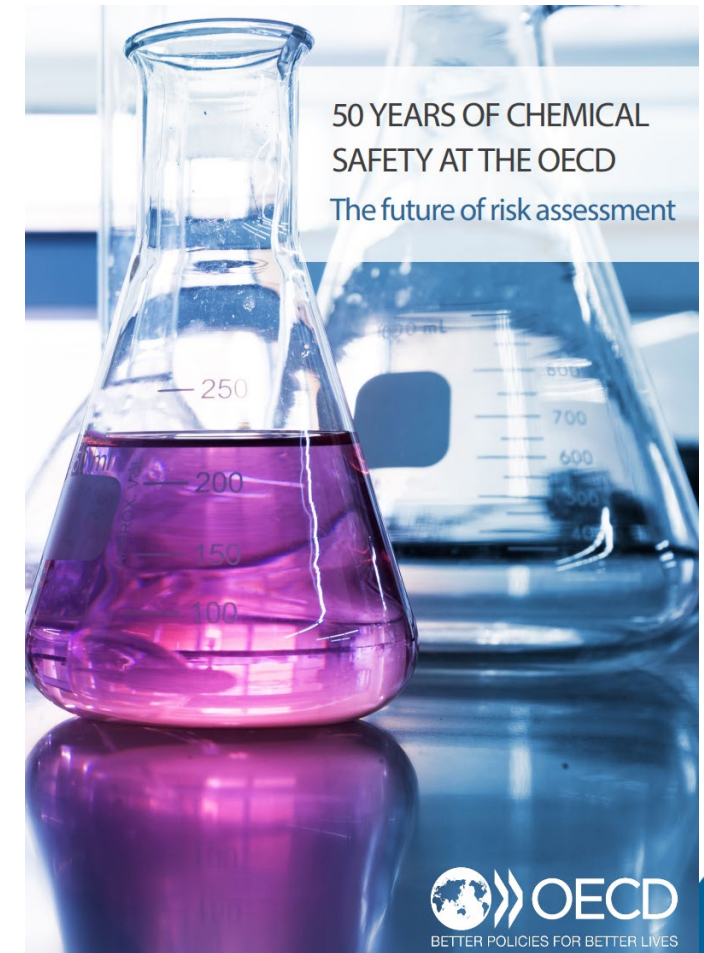


OECD Chemical Safety Programme

Is a forum for governments and other stakeholders to:

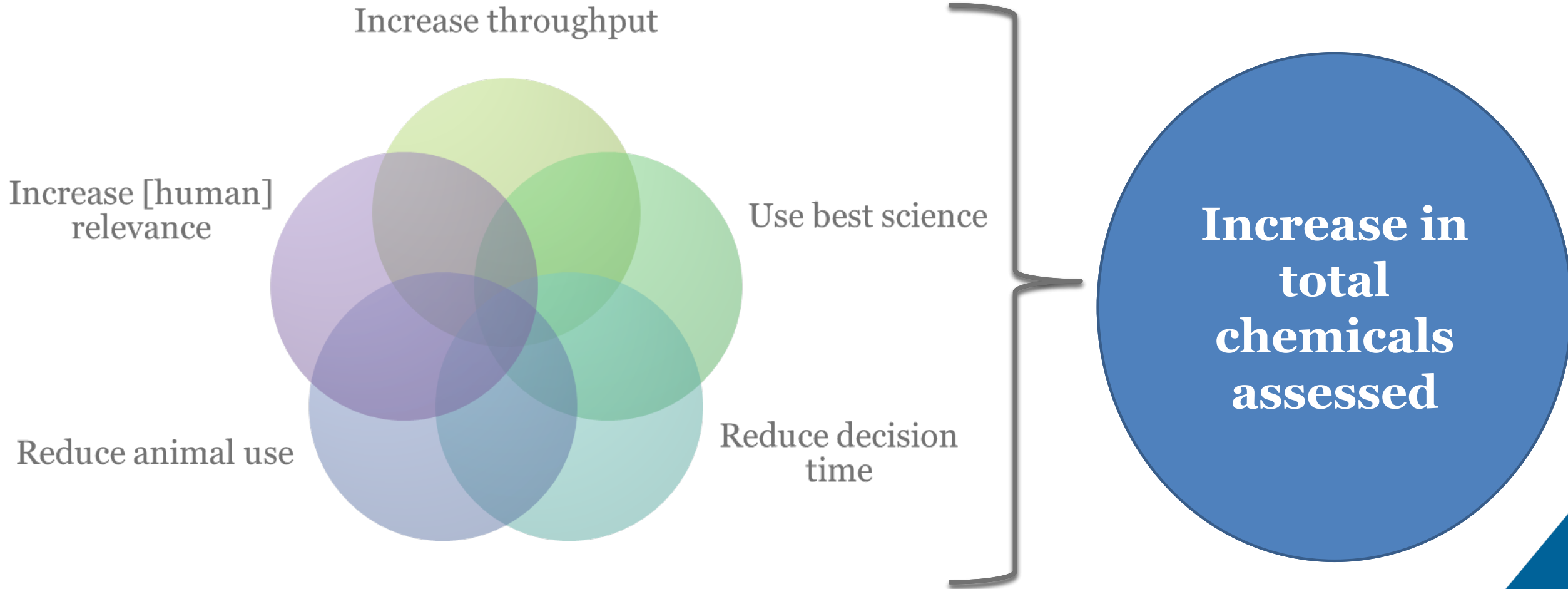
- Develop methods and approaches for evaluating the safety of chemicals
- Discuss and share their experiences on issues of mutual concern;
- Promote harmonized approaches and data sharing
- Increasing focus on the use of New Approach Methods

OECDiLibrary
www.oecd-ilibrary.org
OECD's global knowledge base





Global drivers to modernise chemical risk assessment





OECD Test Guidelines and Mutual Acceptance of Data -> Increased capacity for risk assessment globally

- Results of OECD internationally harmonised Test Guidelines conducted according to Principles of Good Laboratory Practice are covered by Mutual Acceptance of Data
 - Reduces costs of chemical testing for governments and industry
 - Monetary savings of 309 MEUR per year:
<https://www.oecd.org/environment/saving-costs-in-chemicals-management-9789264311718-en.htm>
 - Increases the number of chemicals that can be tested globally
 - If each industry/government/lab can only perform X tests per year, Mutual Acceptance of Data increases the total number of chemicals tested globally



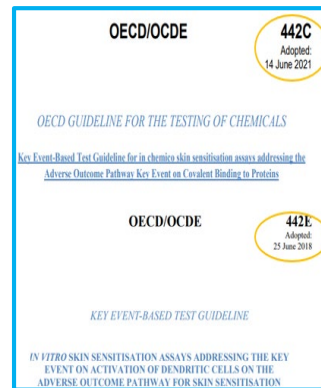
Test Guidelines Programme

• Most projects on OECD Test Guidelines Programme today are about harmonisation of non-animal methods

• Achievements include a number of **harmonised TGs** e.g.

- skin and eye irritation/corrosion
 - associated **Performance Standards**
 - related **Guidance Document** on IATA

- skin sensitisation
 - Underpinning **AOP**
 - IATA case studies
 - **Key event-based TGs**
 - **Defined Approaches TG**



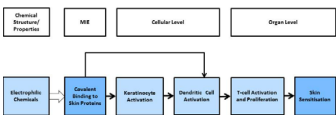
TG 442C



TG 442E

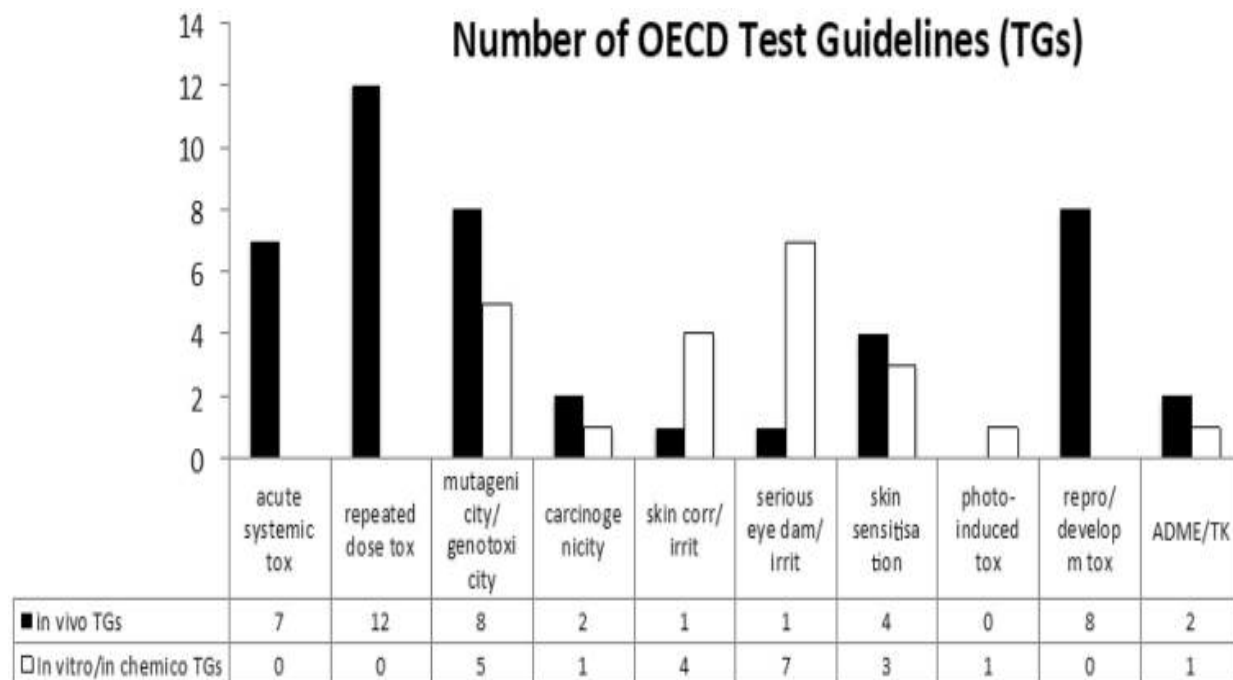


TG 497





Current number of Test Guidelines based on New Approach Methods



- ~35 NAM TGs
- 2 Defined Approaches
- Almost all focused on human health
- Most on simple endpoints and acute toxicity

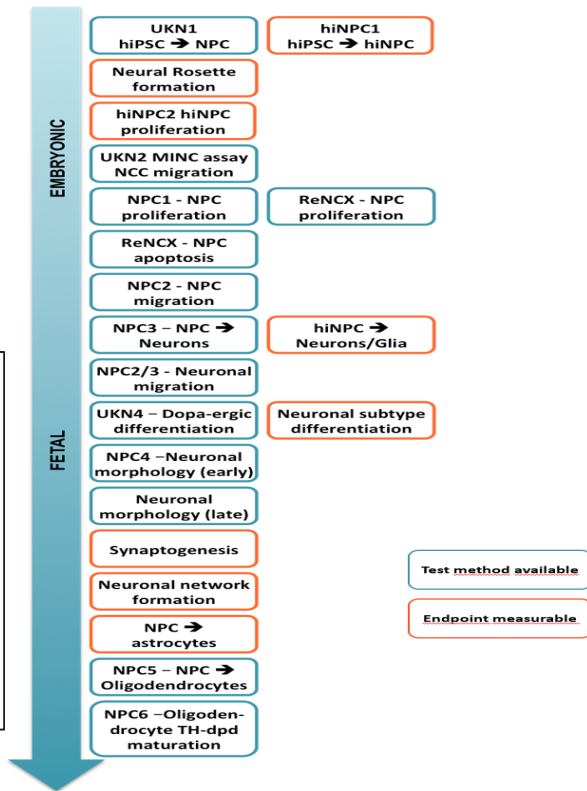
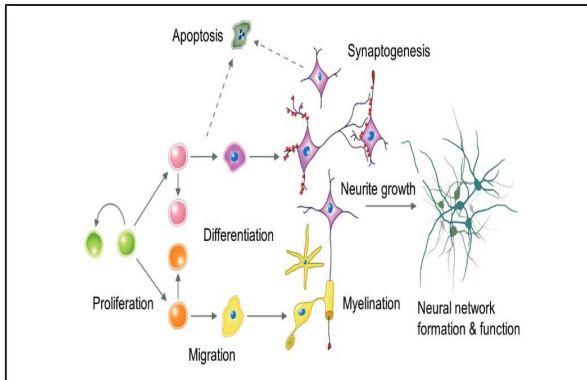
From Pistollato et al., 2021



Developmental Neurotoxicity

Guidance on use of an in vitro battery (IVB) of assays for DNT (EFSA-EC/DK/US)

EFSA/OECD
WS (2017)



Readiness/ Test method	Phase I	Phase II	Phase III	Overall readiness
UKN1	A	B	B	B+
NPC1	A	A	A	A
NPC2	A	A	A	A
NPC3	A	A	B	A-
NPC4	A	B	C	B
NPC5	A	A	B	A-
NPC6	A	B	B	B+
UKN2 (cMINC)	A	B	A	A-
MESn	C	D	D	D+
UKN4 (NeuriTox)	A	A	A	A
NSR	C	D	D	D+
SYN	B	B	B	B
Nnff	B	A	B	B+
3Dh	B	C	C	C+

Bal-Price et al, 2018

Mapping of key biological targets for DNT

Identifying test methods for DNT targets

Evaluating assays readiness level

Testing chemical libraries and analysing data

Identifying gaps and finding new assays

Evaluating reproducibility of assays between labs

Dev. of tiered-testing strategy

Proposing a Guidance Doc.

Encouraging case study applications under IATA case study project (Hazard Assessment Programme)

Determining IVB performance (sens 82%, spec. 88%)



National initiatives for NAMs

A non-animal technologies roadmap for the UK

Advancing predictive biology

EXTERNAL SCIENTIFIC REPORT



APPROVED: 2 May 2022

doi:10.2903/sp.efsa.2022.EN-7341

Development of a Roadmap for Action on New Approach Methodologies in Risk Assessment

Sylvia E. Escher¹, Falko Partosch¹, Sebastian Konzok¹, Paul Jennings², Mirjam Luijten³, Anne Kienhuis³, Victoria de Leeuw³, Rosmarie Reuss⁴, Katrina-Magdalena Lindemann⁴, Susanne Hougaard Bennekou⁵

¹ Fraunhofer ITEM, ² Vrije Universiteit Amsterdam, ³ National Institute for Public Health and the Environment, ⁴ Eura AG, ⁵ The National Food Institute Denmark

A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States



EPA 600/X-21/209 | December 2021 | www.epa.gov/research

New Approach Methods Work Plan

U.S. Environmental Protection Agency
Office of Research and Development
Office of Chemical Safety and Pollution Prevention

December 2021



New Approach Methodologies in Regulatory Science

Proceedings of a scientific workshop

Helsinki, 19–20 April 2016

동물대체시험법 활성화 실행계획 토론회

“ 잠시 후 14시부터 '동물대체시험법 활성화
실행계획 토론회' 가 시작됩니다.
많은 시청 부탁드립니다 ”





New approach methods for modern risk assessment

“OECD supports use of **NAMs** when suitability can be demonstrated...”

- **What counts as a “New Approach Method”?**

- The OECD working assumption is **everything** that is **not an “old approach”**

- *in chemico*, *in vitro*, computational, *in vivo* methods
- stand-alone or (more often) integrated approaches to testing and assessment (IATAs)
- data science/machine learning/AI (i.e. based on existing data)

- Not “non-animal methods”, but aligned with the 3Rs

- Faster time to safety decisions
- Less resources intensive



What is required for OECD adoption of NAM-based Test Guidelines

*“...when suitability can be demonstrated (to be **as good or better** than existing approaches)”*

- **What counts as “as good or better”?**
 - Results must be **reproducible**
 - The test system must be **relevant**, e.g.:
 - Sensitive to chemical-changes
 - Has a demonstrated relationship to the toxicological endpoint
 - Is **biologically relevant** to the target species
 - Should include a consideration of **approaches** that are **currently in use**
 - e.g. >80% do not have full suite of chemical safety data



The use of NAMs changes testing paradigms

- Regulations **vary** in:
 - Specific data requirements defined in regulations
 - Flexibility to fulfil requirements
 - Explicit national/organisational mandates to use NAMs
- **Creates potential divergence among countries & regulatory authorities**
 - A variety of NAM roadmaps
 - Use of NAMs is not harmonised
 - Potential threat to Mutual Acceptance of Data



OECD Integrated Approaches to Testing and Assessment (IATA) Case Studies Project

- Forum to share experiences with the use of novel non-standardised methods for chemical assessment in a regulatory context
 - Best practices and approaches
 - Identify aspects that can be harmonised
 - Standardised reporting formats
 - Structured data
- How to bring together new and existing information
 - How to use and **build confidence** in New Approach Methods (NAMs)
- **Not bound by MAD**, thus flexible, innovative approaches
 - Some of which **may become TGs**, e.g. TG 497 on Defined Approaches for Skin Sensitisation started as IATAs



How do you build confidence in NAMs?

Documentation

- Clear problem formulation/context of use
- Rationale for selection of method

Reproducibility

- Description/Standardisation of method
- Demonstration of consistency over time/between users

Relevance

- Performance against robust set of reference chemicals
- Consideration of relevance to target species (biology)

Uncertainty

- Transparent description of domain of applicability
- Limitations (technical + lack of information)

Reviews

- Method and data documentation
- Use of reporting standards for evaluation



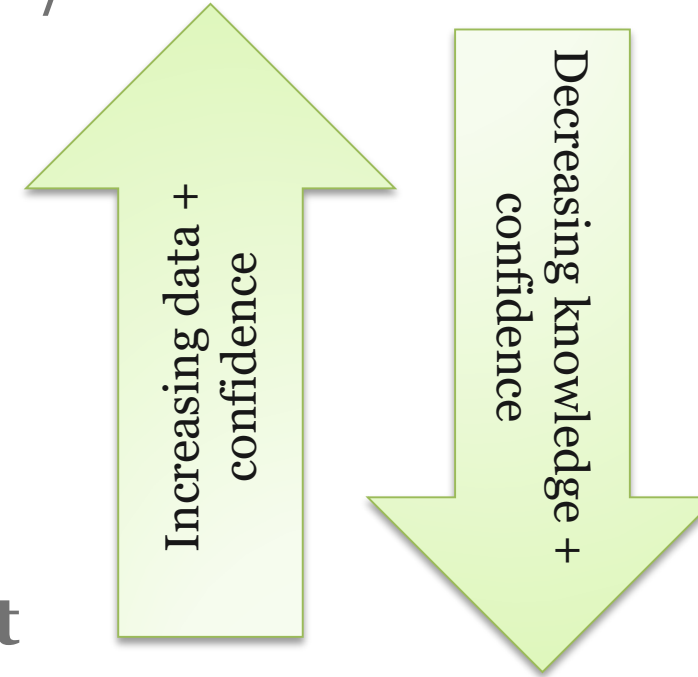
Identify aspects that can be standardised

- Experience reviewing case studies has led to development/refinement of a system of **reporting standards** that support:
 - Documentation
 - Initial problem formulation/ defining context of use
 - Peer review
 - Transparent reporting of
 - Technical limitations
 - Biological limitations
 - Limitations due to lack of information
 - Communication of the strengths/limitations of the approach



Internationally applicable solutions

- IATAs must have a clear regulatory application/ problem formulation; e.g.:
 - Risk assessment
 - Hazard characterisation (e.g. GHS)
 - Hazard identification
 - Prioritisation
- Suited to different types of chemicals, e.g.: cosmetics, agrochemicals, industrial chemicals
- **IATA acceptance does not mean countries must use the approach, but they can chose to do so**
- Likely to be a continuum
 - progress towards regulatory application that require more data/less uncertainty as more experience/knowledge is acquired



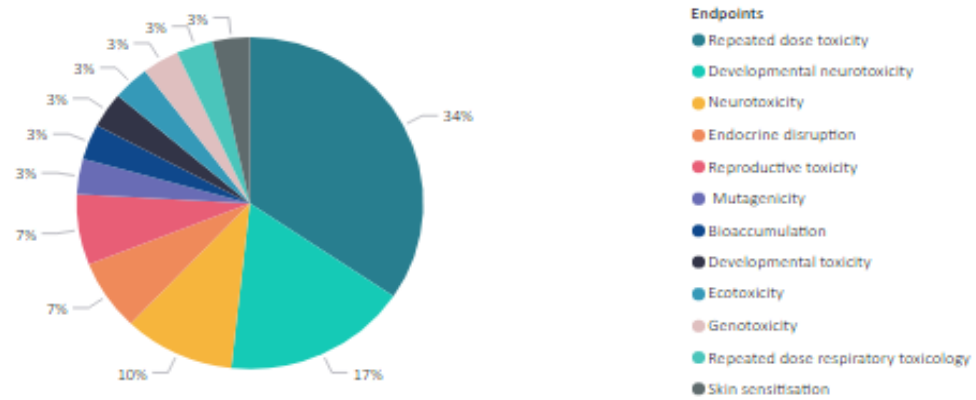
Case Studies on IATA

The OECD IATA Case Studies Project allows countries to share and explore the use of novel methodologies in IATA for chemical hazard characterisation within a regulatory context. In the interactive reports below, you will find:

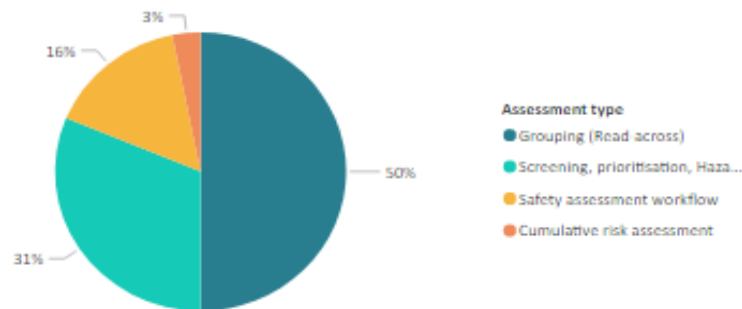
- › The total number of case studies by endpoints, assessment type and IATA topics
- › The full list and links to the case studies
- › The consideration documents captures learnings and lessons from the review experience.

This report shows the number of case studies published by the OECD by **endpoints, assessment types and IATA topics**.

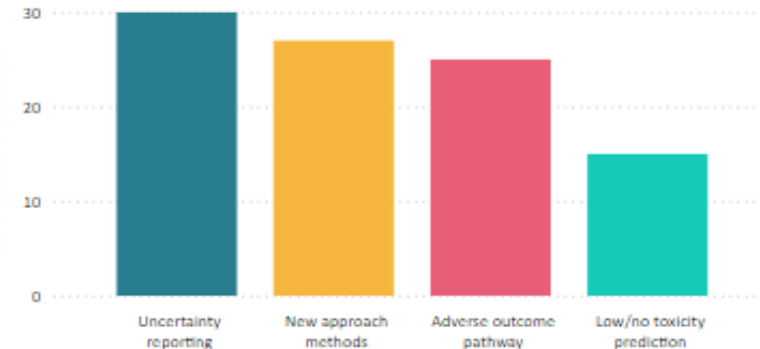
Number of case studies by endpoints



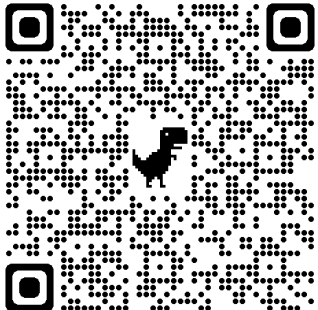
Number of case studies by assessment types



Number of case studies by IATA topics



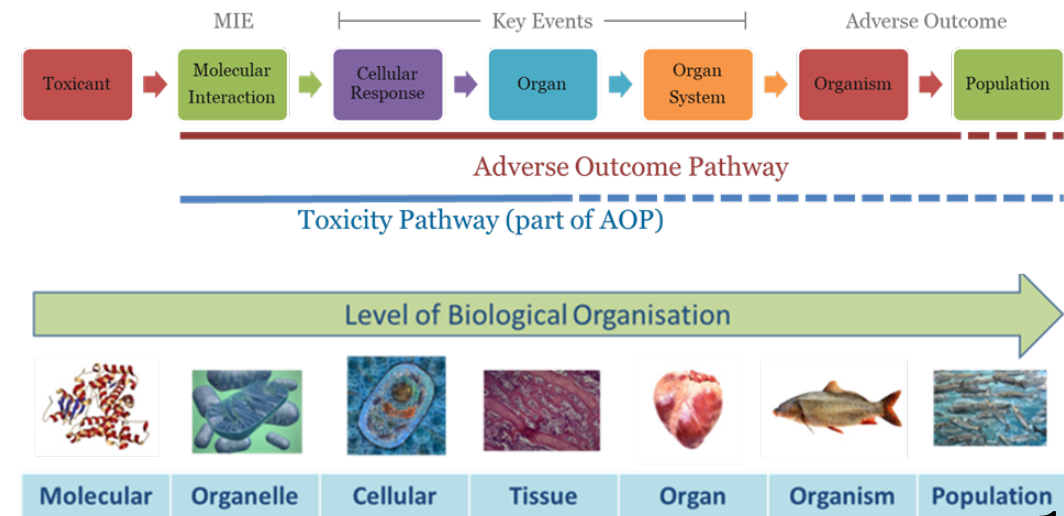
[Series on Testing and Assessment: publications by number - OECD](#)





The first wave of NAMs: Mechanistic understanding and AOPs

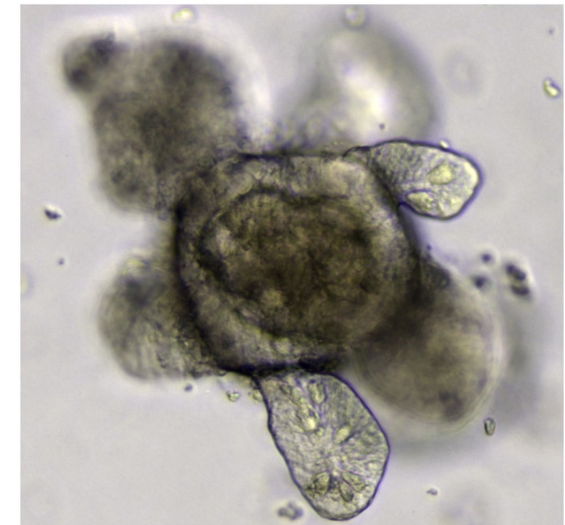
- Pathway defined NAMs (i.e. AOP-amenable):
 - good understanding of mechanisms and key events
 - Establish plausible links between mechanistic and apical responses using existing test data and biological knowledge
 - approaches **predict** an **apical outcome(s)**





The next wave of NAMs: Physiological understanding

- Pathway undefined NAMs:
 - test systems that mimic [human] biology;
 - perturbation of signalling *could* lead to a variety of outcomes
 - changes are assumed to be undesirable
 - approaches **protective** against **potentially adverse effects**





Evolution of IATA Case Study Project

- Increasing “usability” of case studies
 - Reduce resources requirements by “reusing” same IATA
 - Identify endpoints with regulatory data requirements that **do not have** NAM solutions
- Provide guidance for regulators via lessons learned in reviews
 - *Considerations* based on IATA Case Study Project reviews
 - Clusters of case studies addressing same endpoint
 - Identify knowledge gaps and priorities where additional guidance is needed
- Need more experience with IATAs addressing ecotoxicology endpoints
 - Most examples have focused on human health endpoints



What we need to get there



- Available data for review
 - Examples of hazard assessments comparing IATAs to traditional animal test data
- Continued engagement
 - IATA Case Study authors and reviewers
 - Communities of practice
 - Case Study authors and expert reviewers willing to contribute to guidance for use
- Engagement of regulators and data submitters to provide feedback
 - Retrospective engagement
 - NAMs that are submitted/reviewed
 - challenges/road blocks
 - possible solutions



Interested in learning more about IATAs? Visit the new interactive OECD IATA Website



OECD Home

About

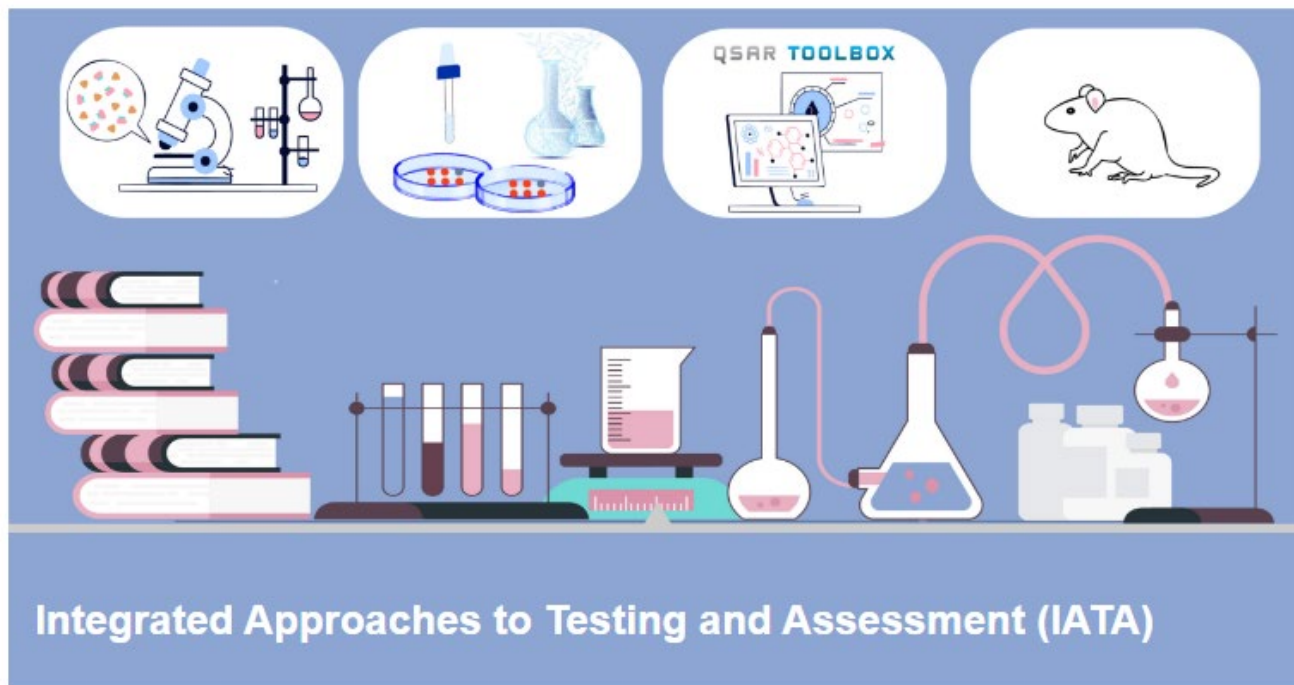
Countries ▾

Topics ▾

COVID-19

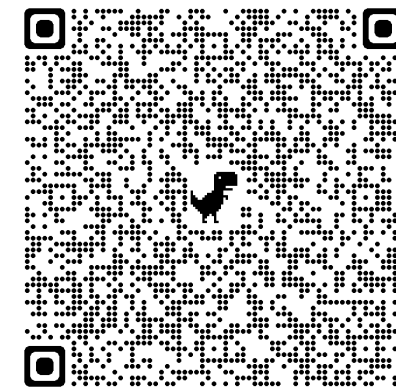
[OECD Home](#) > [Chemical safety and biosafety](#) > [Assessment of chemicals](#) > [Integrated Approaches to Testing and Assessment \(IATA\)](#)

Integrated Approaches to Testing and Assessment (IATA)



Includes information on:

- What an IATA is and how they support chemical safety
- Resources and Guidance for authors on how to develop an IATA
 - Templates
 - Guidance
- >30 IATA Case Studies searchable by key words





Recorded IATA Webinar



Webinar on Integrated Approaches to Testing and Assessment: concepts and OECD case studies

WHEN: 16 December 2022
14:00 - 16:00 CET
08:00 - 10:00 EST

 **OECD**
BETTER POLICIES FOR BETTER LIVES





Find out more

Thank You For Listening



Bob.diderich@oecd.org



<https://www.oecd.org/env/ehs/>

Twitter: https://twitter.com/OECD_ENV

YouTube: <http://bit.ly/youtube-chemical-safety>

Subscribe to our newsletter: <http://bit.ly/newsletter-chemical-safety>