THE USE OF NEW APPROACH METHODS IN CHEMICAL RISK ASSESSMENTS

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Chemical Grouping

- GD 194: [GD on Grouping of Chemicals, Second Edition](#) (2014)
  - Recommendations on grouping strategies
  - Data needs to support groups
- In the process of updating the document to reflect learnings and use of additional methods
  - Lesson learned from case studies on grouping and read across approaches
  - Use of Omics to support chemical groups

	Chemical 1	Chemical 2	Chemical 3	Chemical 4	
Structure	xxxxxxxxx	xxxxxxxxx	xxxxxxxxx	xxxxxxxxx	
Property 1	● ⇒ ○		● ⇒ ○		SAR/Read-across
Property 2	● ⇒ ○		○ ⇐ ●		Interpolation
Property 3	○ ⇐ ●		● ⇒ ○		Extrapolation
Activity 1	● ⇒ ○		● ⇒ ○		SAR/Read-across
Activity 2	● ⇒ ○		○ ⇐ ●		Interpolation
Activity 3	○ ⇐ ●		● ⇒ ○		Extrapolation

● Existing data point   ○ Missing data point

- Free software application to predict the properties of chemicals (version 4.7 launched in 2024)

- Estimate missing experimental values by read-across and trend analysis (grouping of similar chemicals, chemical categories)

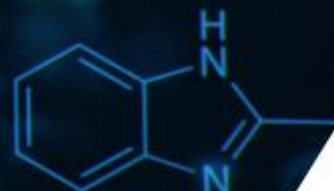www.qsartoolbox.org

(Quantitative) Structure-Activity Relationships

(Q)SAR Assessment Framework:
Guidance for the regulatory assessment of (Quantitative) Structure Activity Relationship models, predictions, and results based on multiple predictions

Series on Testing and Assessment No. 386

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WEBINAR ON THE NEW OECD (Q)SAR ASSESSMENT FRAMEWORK: GUIDANCE FOR ASSESSING (Q)SAR MODELS AND PREDICTIONS

The webinar provided an overview of the new OECD (Q)SAR Assessment Framework for evaluating the scientific validity of (Q)SAR models, predictions, and results from multiple predictions. The QAF provides assessment elements for existing principles for evaluating models as well as new principles for evaluating predictions and results. In addition to the principles, assessment elements, and guidance for evaluating each element, the QAF includes a checklist for reporting assessments.
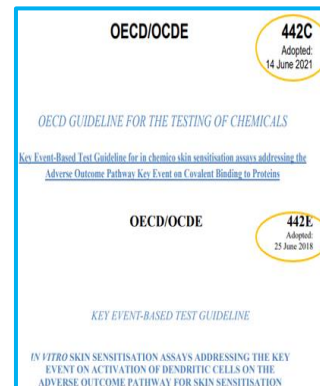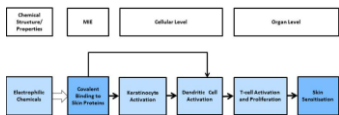
This new Framework provides regulators with a consistent and transparent approach for reviewing the use of (Q)SAR predictions in a regulatory context and increases the confidence to accept alternative methods for evaluating chemical hazards. The OECD worked closely together with the Istituto Superiore di Sanità (Italy) and the European Chemicals Agency (ECHA), supported by a variety of international experts to develop a checklist of criteria and guidance for evaluating each criterion. The aim of the QAF is to help establish confidence in the use of (Q)SARs in evaluating chemical safety, and was designed to be applicable irrespective of the modelling technique used to build the model, the predicted endpoint, and the intended regulatory purpose.

The webinar provided an overview of the project and presented the main aspects of the framework for assessing models and results based on individual or multiple predictions.*

OCED Test Guidelines

- 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 439

TG 431

TG 437
TG 438

TG 491   TG 492
TG 494   TG 496

Test Guideline No. 439
In Vitro Skin Irritation: Reconstructed Human Epidermis Test Methods

14 June 2021

OECD Guidelines for the Testing of Chemicals

Test Guideline No. 431
In Vitro Skin Corrosion: Reconstructed Human Epidermis (RhE)Test Method

18 June 2019

OECD Guidelines for the Testing of Chemicals

Test Guideline
Bovine Corneal Opacity And Permeability Test Method For Identifying i) Chemicals Inducing Serious Eye Damage And ii) Chemicals Not Requiring Classification For Eye Irritation Or Serious Eye Damage

Test Guideline No. 492
Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage

18 June 2019

OECD Guidelines for the Testing of Chemicals

EpiOcular Tissue Model

Opacity

OECD/OCDE   442C
Adopted: 14 June 2021

OECD GUIDELINE FOR THE TESTING OF CHEMICALS

Key Event-Based Test Guideline for in chemico skin sensitisation assays addressing the Adverse Outcome Pathway Key Event on Covalent Binding to Proteins

OECD/OCDE   442E
Adopted: 23 June 2018

KEY EVENT-BASED TEST GUIDELINE

IN VITRO SKIN SENSITISATION ASSAYS ADDRESSING THE KEY EVENT ON ACTIVATION OF DENDRITIC CELLS ON THE ADVERSE OUTCOME PATHWAY FOR SKIN SENSITISATION

TG 442C

TG 442E

Guideline No. 497
Guideline on Defined Approaches for Skin Sensitisation

14 June 2021

TG 497

Integrated Approaches to Testing and Assessment

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. Find all the published case studies in the interactive table below.

Year

All

Type of Assessment
- [ ] Select all
- [ ] Defined Approach
- [ ] IATA workflow
- [ ] In vitro battery

Endpoint
- [ ] Select all
- [ ] Bioaccumulation
- [ ] Developmental neurotoxicity
- [ ] Developmental toxicity
- [ ] Ecotoxicity
- [ ] Endocrine disruption
- [ ] Eye damage/irritation
- [ ] Genotoxicity
- [ ] Mutagenicity
- [ ] Neurotoxicity

Chemical sctor
- [ ] Select all
- [ ] Cosmetic
- [ ] Industrial chemical
- [ ] Industrial chemical, Pesticide
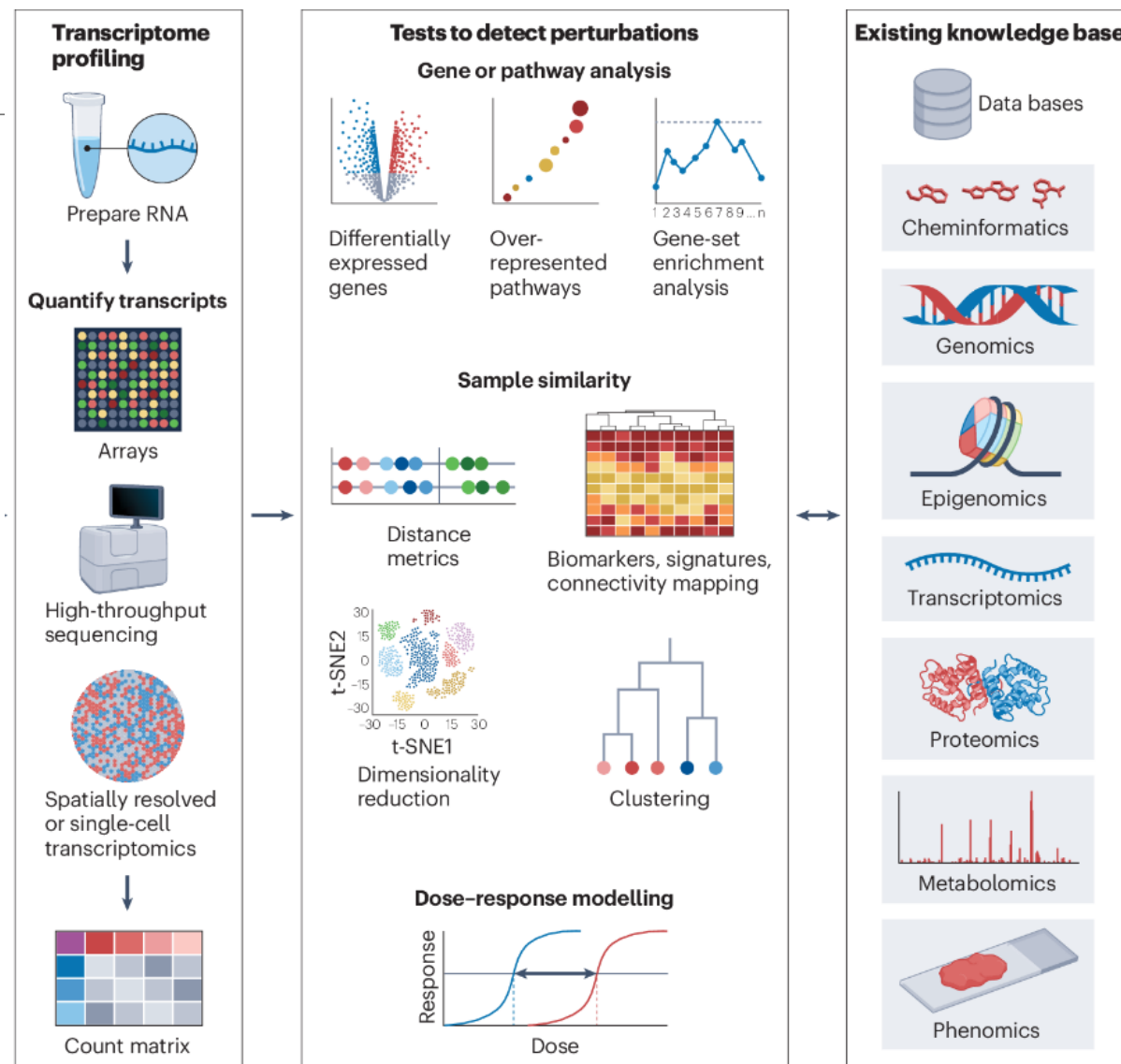- [ ] Pesticide

Year	No.	Title	Key words provided by the authors	AOPs (When a case study includes a AOP that has a AOP-Wiki No., the AOP-Wiki No. is listed.)	Other AOP wiki number	Uncertainty reporting	NAMs	Low/no toxicity
2022	1	Case Study on the Use of Integrated Approaches for Testing and Assessment for skin sensitisation of Diethanolamine: Application of a Next Generation Risk Assessment Framework	• NGRA framework with inconsistent NAMs • Six DAs resulted in inconsistent predictions • PoD using WoE • MoE calculated by PoD • Refined NGRA framework.	X				
2022	2	Case Study on the use of Integrated Approaches for Testing and Assessment for "Eye hazard identification" of "non-surfactant neat liquids"	• Two rule-based DAs for eye hazard identification (TG467) • Four non-surfactant liquids with the different UN GHS • DAL-1: physchem and in vitro test • DAL-2 : in vitro only • Same conclusion with little uncertainty. • Feasibility and reliability of the TG 467\	X				
2021	1	Case study for the integration of in vitro data in the developmental neurotoxicity hazard identification and characterisation using deltamethrin as a prototype chemical	• In vitro developmental neurotoxicity testing battery (DNT-IVB) • Pyrethroids • In vivo developmental neurotoxicity study	X		X	X	
2021	2	Case study for the integration of in vitro data in the developmental neurotoxicity hazard identification and characterisation using flufenacet	• In vitro developmental neurotoxicity testing battery (DNT-IVB) • Flufenacet • In vivo developmental neurotoxicity study	X		X	X	X
2021	3	Case study on the use of Integrated Approaches for Testing and Assessment for DNT to prioritize a class of Organophosphorus flame retardants	• DNT – developmental neurotoxicity • Prioritisation • Flame retardants • Zebrafish	X		X	X	
2021	4	Case Study on the use of Integrated Approaches for Testing and Assessment for developmental neurotoxicity hazard characterisation of acetamiprid		X		X	X	
2021	5	Case Study on the use of Integrated Approaches for Testing and Assessment for developmental neurotoxicity hazard characterisation of imidacloprid and the metabolite desnitro-imidacloprid		X		X	X	
2021	6	Case Study on the use of Integrated Approaches to Testing and Assessment for potential Systemic Toxicity and Estrogen	• Hazard characterization of BPA and alternatives • Transcriptomic points of departure	X		X	X	

[Integrated Approaches to Testing and Assessment (IATA) | OECD](#)

The promise of omics for human health and environmental protection

- Molecular alterations occur before changes in apical endpoints

- Omics provides significant advantages over traditional toxicology tests
  - Rapid & cost-effective data generation
  - Reduction in animal use

Slide credit: M. Meier

Meier, M.J., Harrill, J., Johnson, K., Thomas, R.S., Tong, W., Rager, J.E., Yauk, C.L. *Nat Rev Genet* (2024).

Paving the Path to Confidence and Acceptance of Omics for Regulatory Applications

Transparency and Reproducibility

Interpretation

Relevance Application

Confidence

Validation Acceptance

OECD Omics Reporting Frameworks
- Transcriptomics
- Metabolomics
- Proteomics (under development)

Data Interpretation Procedures
- Work pending
  - Omics Based Biomarkers
  - Linking genes, proteins and metabolites to AOPs

OECD IATA Case Studies Project
- 4 IATA Case Studies
- Application Reporting Module for Chemical Grouping and Read-Across

Guidance Documents
- Special Omics section in the OECD Chemical Grouping Guidance
- OECD Guidance on Sampling for Omics

Test Guidelines
- GARDskin: OECD TG 442E
- Optional sample preservation in OECD test guidelines