

NON-ANIMAL SAFETY ASSESSMENT: Frameworks and Tools for Safe Cosmetics

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Safety Assessment Seminar
CTFA South Africa
August 28th, 2025

ICCS
INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

IIVS
Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together



Seminar Outline

I. NAMs 101: Frameworks and Tools to Support Non-Animal Toxicology (45 mins)

II. Collaborative Efforts to Advance NAMs and NGRA for Cosmetics and their Ingredients (45 mins)

III. Interactive Discussion (30 mins)



NAMs 101: Frameworks and Tools to Support Non-Animal Toxicology

Kristie M. Sullivan, MPH

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About Us: Institute for In Vitro Sciences



We interact with dozens of companies and regulatory agencies to help them **integrate and validate non-animal methods**



GLP testing laboratory and validation experts for **thousands of products and ingredients**.



We collaborate with other scientists, teach workshops, hands-on training, and lecture courses for companies and organizations internationally

We are regarded as an independent **technical authority by industry, animal protection and governments around the world**

Science Education & Outreach



Talk Outline

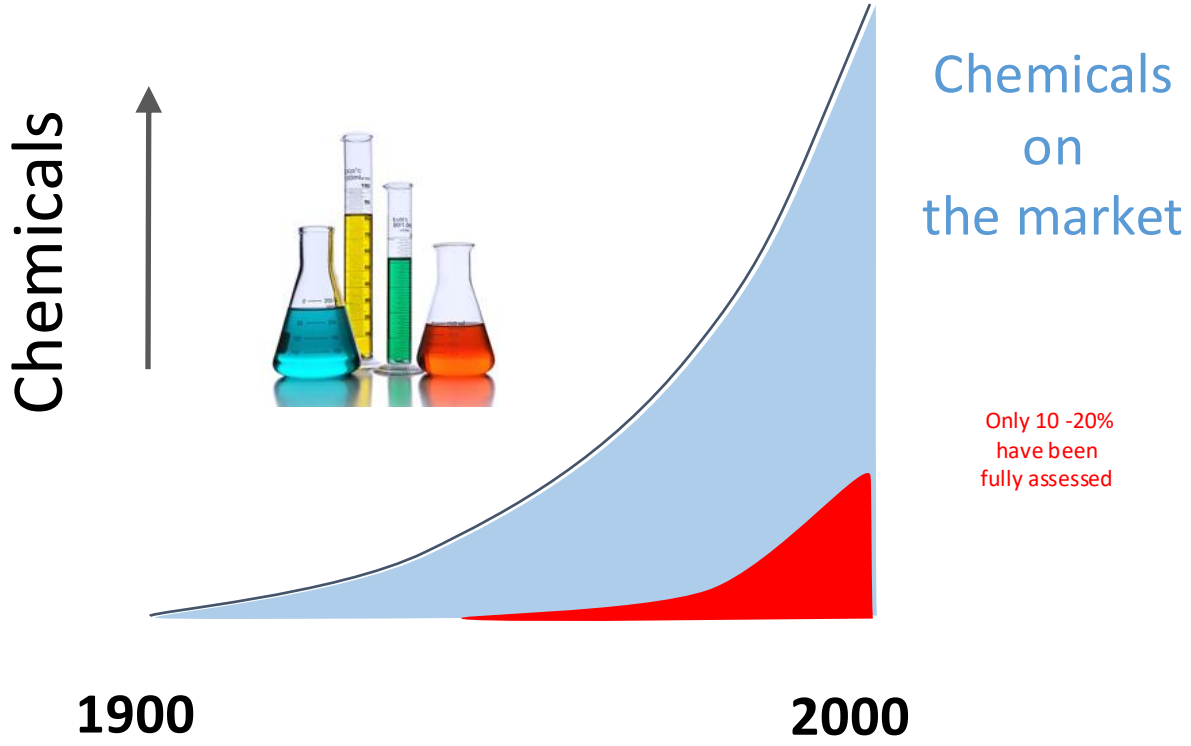
I. Scope of Available NAMs
   I. In vitro approaches
   II. In silico approaches
II. Key Concepts for Regulatory Application
   I. IATAs, DAs, AOPs
   II. NGRA
III. Guidance for Application and Standardization
IV. Resources

Scope of Available NAMS

Why are NAMs an Essential Part of Toxicology?

- *In vivo* tests are cost-, time-, and animal-intensive
- *In vivo* tests don't usually adequately capture population diversity, sensitivities, emerging concerns
- In vitro models can provide human-relevant information and take advantage of advanced technology
- Computational models can assess large numbers of chemicals efficiently, target experimental testing, manage and interpret data and information, and make predictions

Image: Bob Diderich, OECD



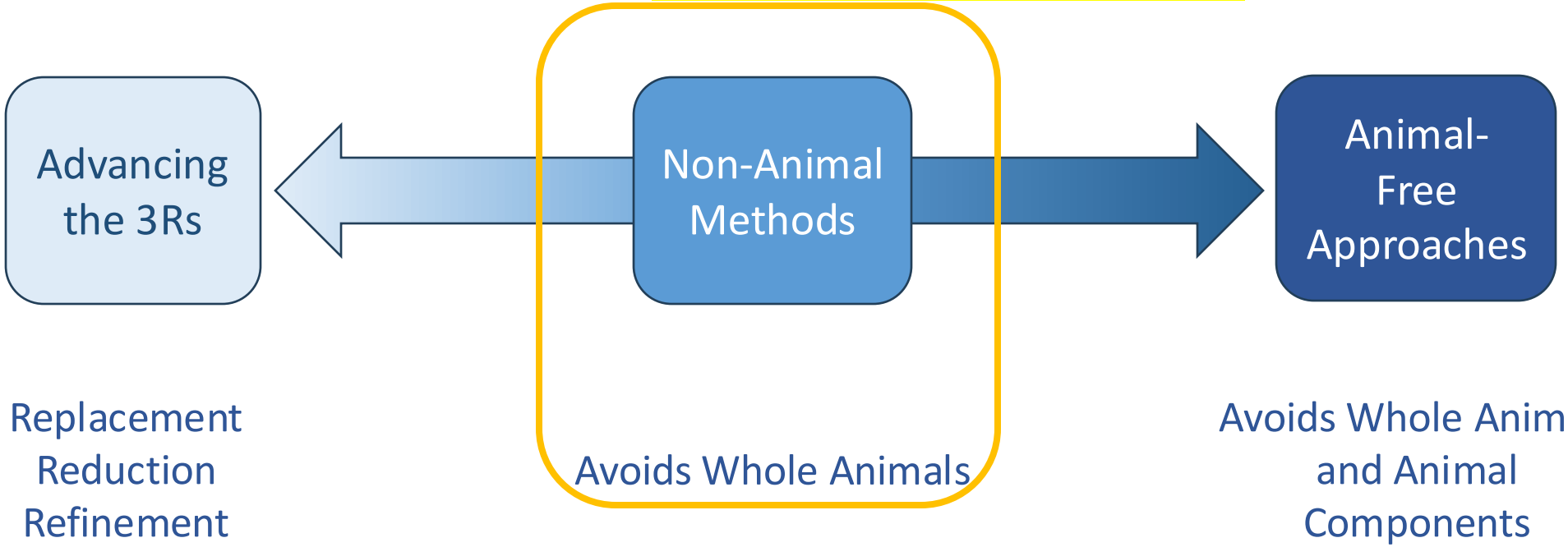


What is a NAM?

- Non-Animal Method (e.g., ecopa symposium 2019, https://doi.org/10.14573/altex.2003041)
- New Approach Method/Methodology (EPA, ECHA, others)
  - UK DEFRA: "New Approach Methodologies are essentially cruelty-free methods that can enhance the assessment and regulation of hazardous chemicals, by improving the performance and reliability of toxicological testing, based upon an understanding of the chemical MoAs, and providing appropriate protection levels for human health and/or the environment." (Recommendations for the Adoption of New Approach Methodologies (NAMs) in UK Chemical Regulation, Nov 2024)
  - SCCS: "…include in vitro, ex vivo, in chemico and in silico methods, grouping, RAx, as well as combinations thereof" and, e.g., "Due to the animal testing ban under the Cosmetics Regulation, it is now out of scope to test cosmetic ingredients in vivo for potential endocrine disruptive effects." (SCCS Notes of Guidance for the Testing of cosmetics Ingredients and their Safety Evaluation, 12th Revision, May 2023)
  - ECHA: "…alternatives to traditional toxicity methods that typically involve animal testing. These alternatives are useful for predicting and assessing chemical risks and hazards, by providing mechanistic information for biologically complex endpoints. They include, e.g. in vitro, in chemico methods and in silico computational models, which may be used alone or in combination with other methods and have the potential to be quicker, cheaper and use less animals." (ECHA Report on Alternatives to Animal Testing, 2023)

What is a NAM?

- UK NC3Rs: "…replacement (full and partial) technologies for use in assessing chemical or drug toxicity…" https://nc3rs.org.uk/3rs-resource-library/new-approach-methodologies-nams-toxicology
- FDA: "…methods that can reduce, refine, or replace animal testing." (FDA NAMs page)
- EPA: "…any technology, methodology, approach, or combination that can provide information on chemical hazard and risk assessment to avoid the use of animal testing." (EPA NAMs Work Plan, 2021)



In Vitro Approaches

2D, 3D cell-based assays

Multi-cell cultures

Fish hepatic cell lines

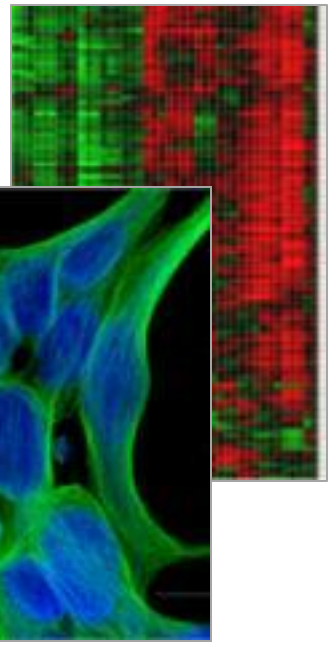
Organoids, spheroids

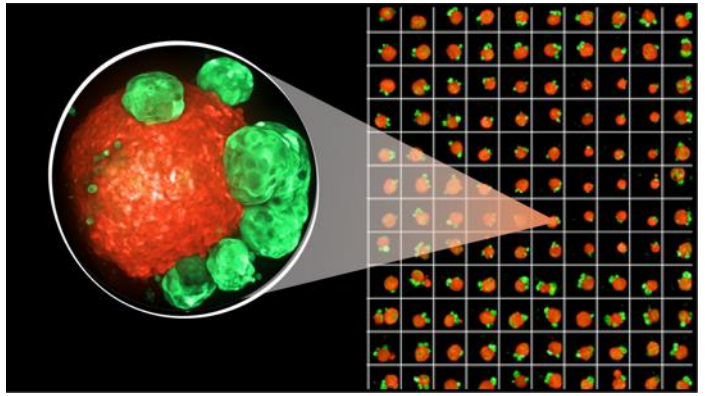
Organs-on-chips

Genomics

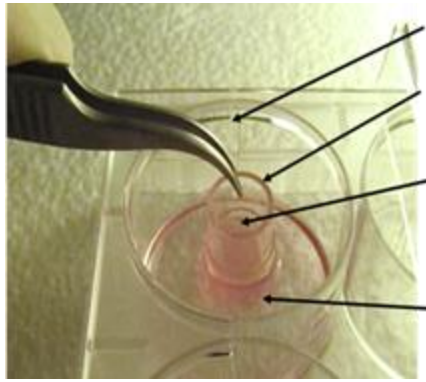
High-throughput and high-content assays

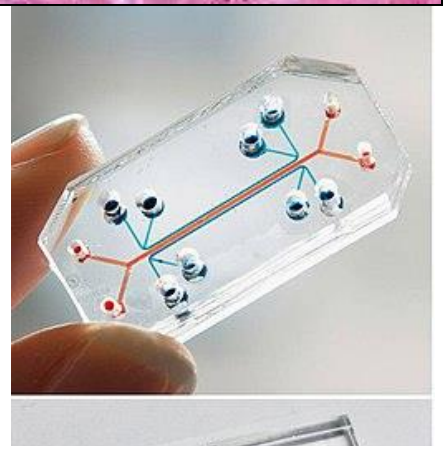
Cell stress panels

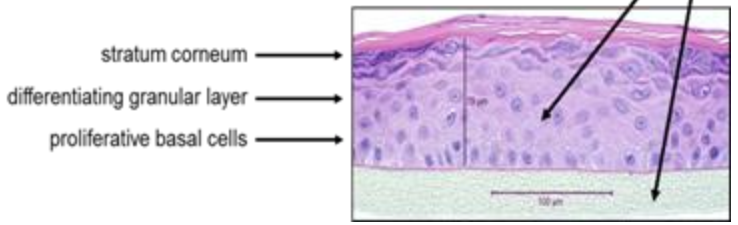




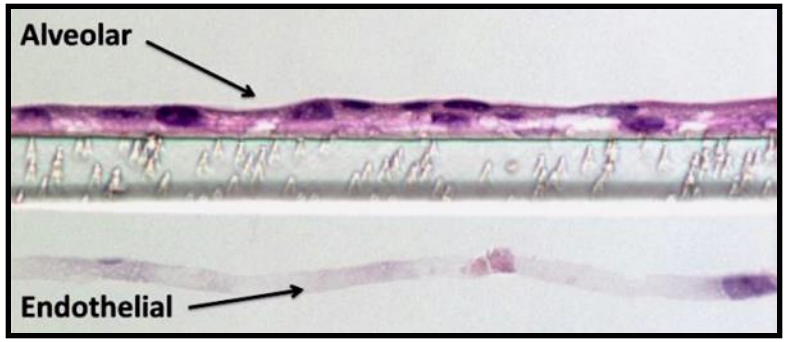








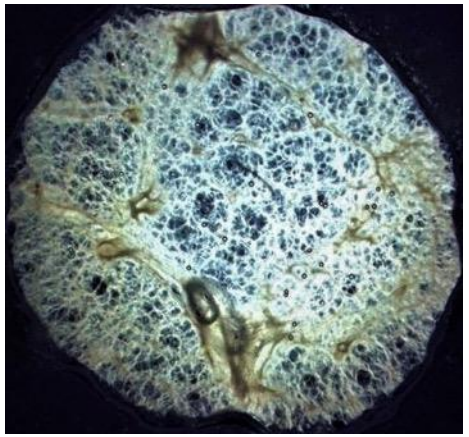




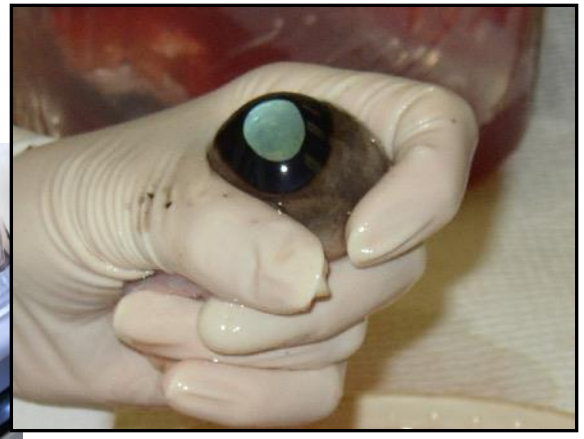
Images: Kbjung; ToxCast/EPA; InSphero, IIVS

In chemico, ex vivo Approaches











- Barrier integrity
- Peptide reactivity
- Cell free assays
- Bovine cornea
- Human, porcine skin
- Tissue slices

Images: Wikimedia, IIVS

In silico Approaches



Read Across, Structural Profilers

Databases, Cheminformatics

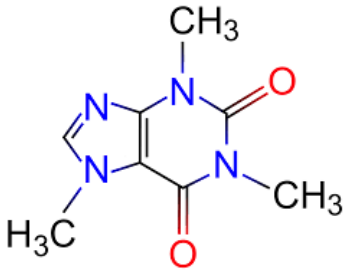
Machine Learning

Predictive and Process Modeling

Exposure, PBK Modeling

IVIVE

TTC



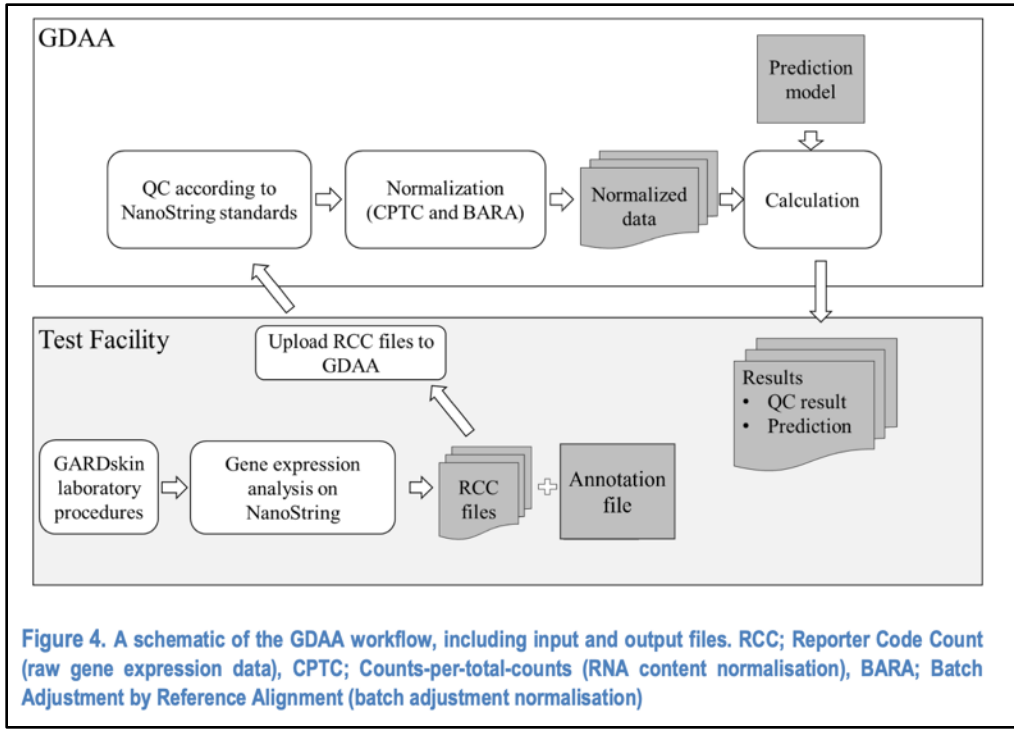
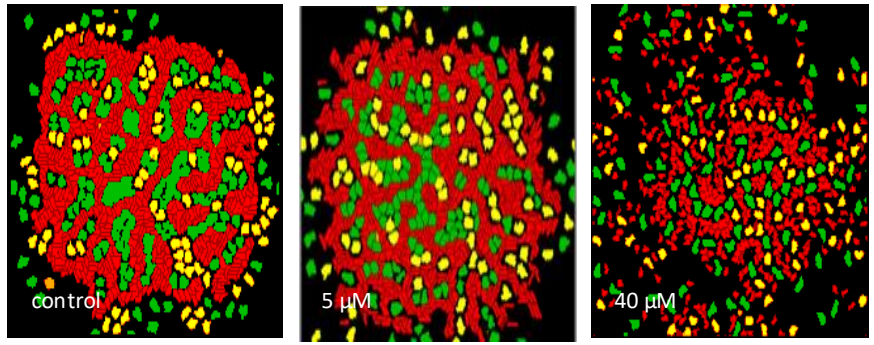
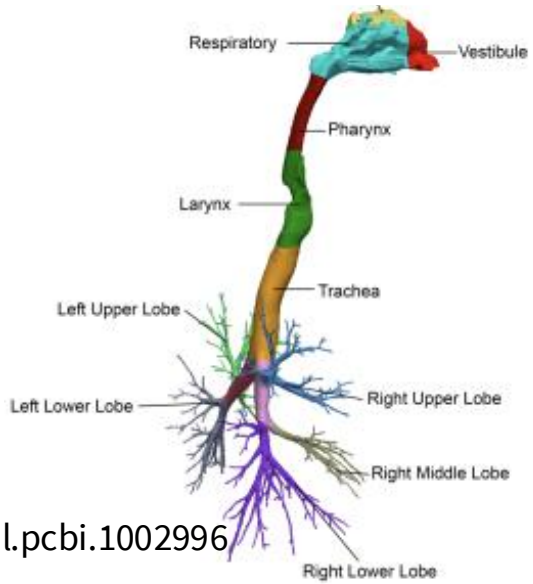


Figure 4. A schematic of the GDAA workflow, including input and output files. RCC; Reporter Code Count (raw gene expression data), CPTC; Counts-per-total-counts (RNA content normalisation), BARA; Batch Adjustment by Reference Alignment (batch adjustment normalisation)

OECD (2023), TG442E. https://doi.org/10.1787/9789264264359-en



Kleinstreuer et al (2013). *PLOS Computational Biology* doi: 10.1371/journal.pcbi.1002996



Corley et al(2021). *Tox Sci 182(2):243-259. doi: 10.1093/toxsci/kfab062*



Stages of Method Development and Standardization

Laboratory development

Initial use and pre-validation

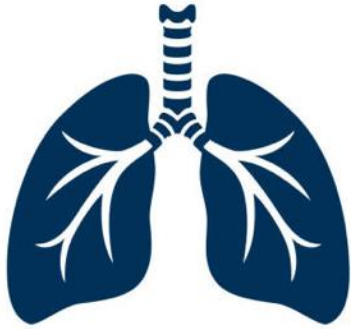
Testing and standardization, application case studies

Formal validation

Test Guideline development and broad use

Methods can be used at any stage, depending on the purpose

Array of *in vitro*, *in chemico*, and *ex vivo* assays to answer a variety of questions



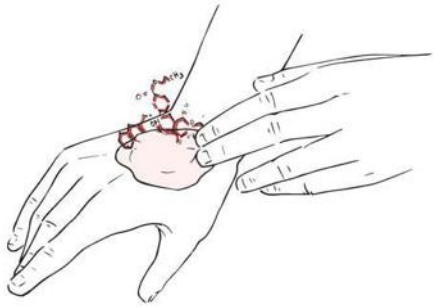
Respiratory Toxicology

Using 2D cell culture models, 3D tissue models, and precision-cut human lung slices



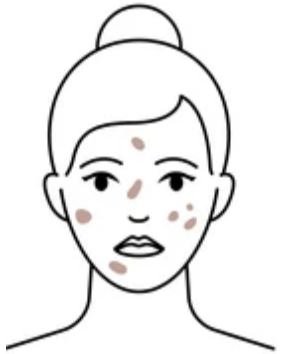
Skin Irritation and Corrosion

Corrositex (OECD 435),
Skin Corrosion Test (OECD 431),
Skin Irritation Test (OECD 439),
Dermal Irritation Time to Toxicity,
Inflammatory Cytokine Expression



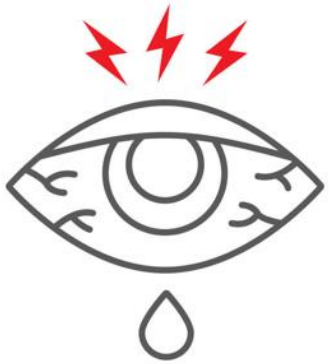
Skin Sensitization

DPRA (OECD 442C),
EpiSensA, Keratinosens™ (OECD 442D),
Human Cell Line Activation Test (OECD 442E),
Kinetic DPRA (OECD 442C)
Predicted EC3 Evaluation, Potency Assessment



Skin Pigmentation

Melanoderm
(Pigmentation and Melanogenesis)



Eye Irritation

Eye Sting Assay (NociOcular)
Eye Irritation Test (OECD 492)
Eye Irritation Time to Toxicity
BCOP (OECD 437) and Histopathology
Short Time Exposure (OECD 491)
Irritection (OECD 496)
CAMVA



Photosafety

UV-Vis Analysis
3T3 Phototoxicity (OECD 432)
rHE Phototox (OECD 498)
Photo-DPRA



Mucosal Irritation

Oral-Gingival Screening
Vaginal Irritation



Genetic Toxicology

Reconstructed Skin Micronucleus
Bhas 42 Cell Transformation Assay
ToxTracker

Reconstituted Human Airways (RHuA)



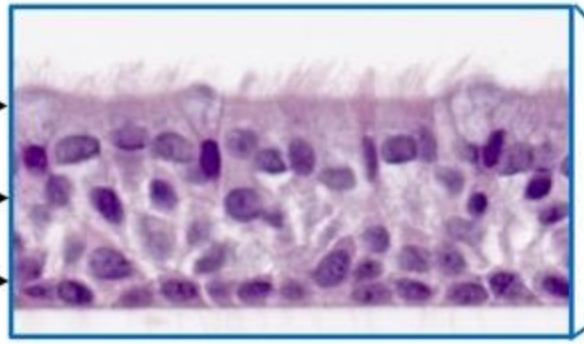


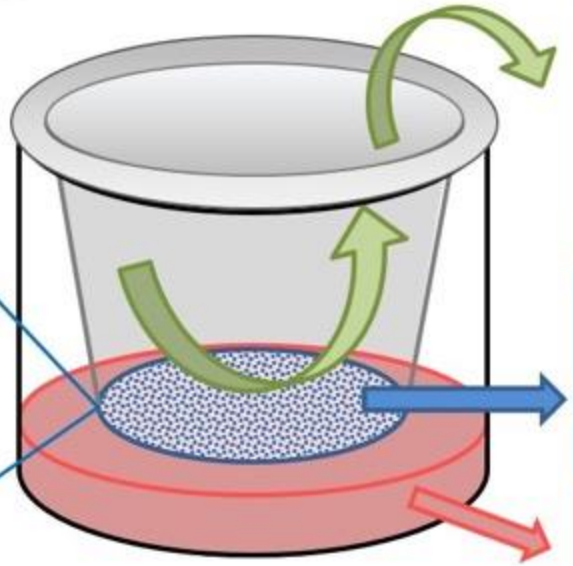
Tissue Culture Insert

Compartments offer Differential Analysis

Cells:

Pseudostratified Epithelium





- Fibroblast and endothelial layer options
- Macrophage addition possible

Apical Layer
- Ciliary beating
- Mucus/surfactant changes
- Leakage/signaling marker responses (LDH, cytokines, chemokines)

Airway Tissue
- Tissue responses (multicellular)
- -omics, biomarker regulation
- Histology –morphology changes

Medium
- "Systemic" exposures
- Leakage/signaling marker responses (LDH, cytokines, chemokines)

Pros: *3D epithelium & multiple cell types. RHuA offer airway "lumen", mucous layer, & beating cilia. Long term cultures possible.*
Cons*: Closed system and no recruitment/systemic response. RHuA offer fewer cell types. Expensive & multi-week creation.*

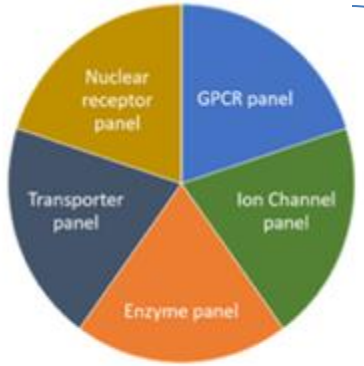
More complex tools becoming used more often

To investigate specific biological activity with 79 key targets involved in drug attrition (Pharma) and additional targets relevant to exposure to cosmetics

US EPA ToxCast Assays

Toxcast uses hundreds of high-throughput assays to understand perturbations from chemical exposures and doses at which they happen

In vitro pharmacological profiling

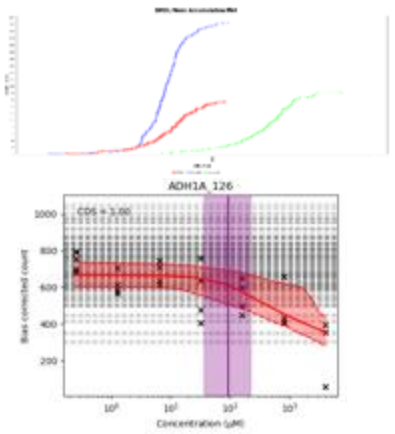




Bowes et al. 2012. Nat Rev Drug Discov 11(12): 909-22

High-Throughput transcriptomics (HTTr)

- TempO-seek technology – full gene panel
- 24hr exposure
- 7 concentrations
- Various cell models (e.g. HepG2, MCF7, HepaRG)
- Dose-response analysis using BMDExpress2 and BIFROST model



Reynolds et al. 2020. Comp Tox 16: 100138
Baltazar et al. 2020. Toxicol Sci 176(1): 236–252

Cell stress panel (CSP)

- Characterize non-specific biological activity
- 36 biomarkers covering 10 cell stress pathways
- HepG2
- 24hr exposure
- 8 concentrations
- Dose-response analysi
  BIFROST model

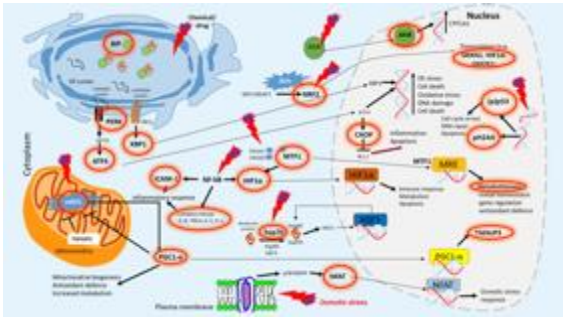


Image kindly provided by Paul Walker (Cyprotex)

Hatherell et al. 2020. Toxicol Sci 176(1): 11-33

Wide Variety of Computational Tool Functions

- Grouping and read across
- Endpoint profiling or prediction
- Data analysis (manual or ML)
- Molecular docking, compound screening
- Exposure/ADME/PBK modeling
- Process modeling
- Population modeling, sensitivity analysis
- Literature compilation, sorting, data extraction

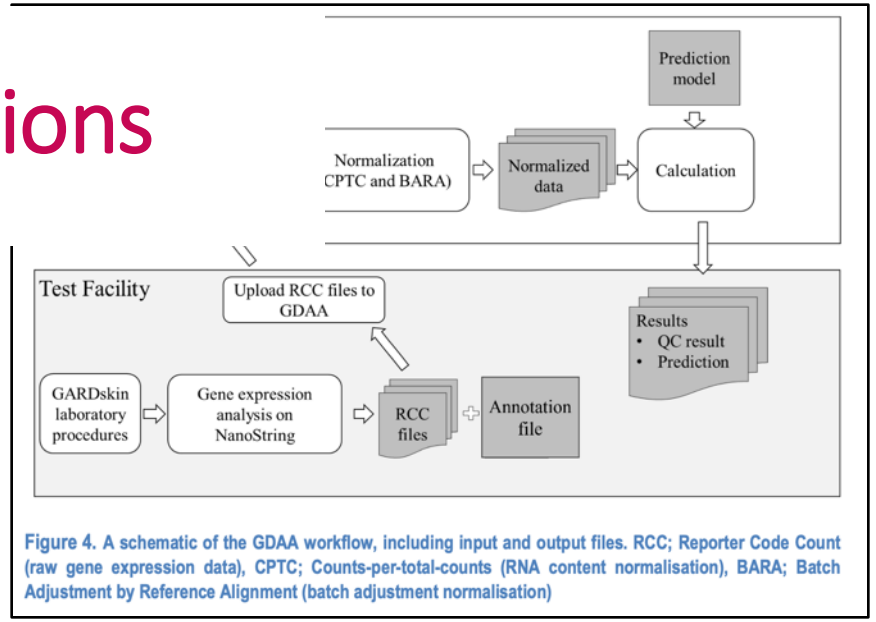
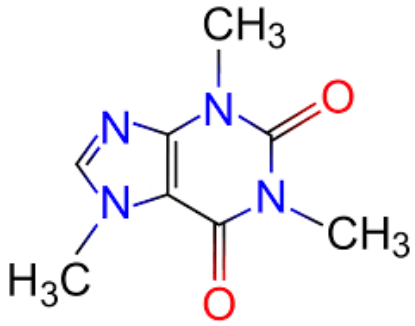
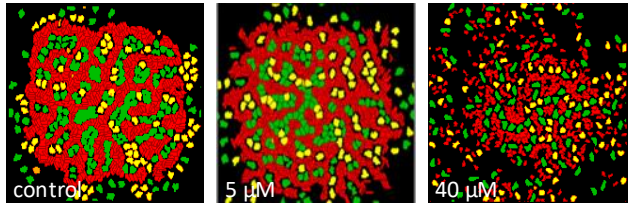


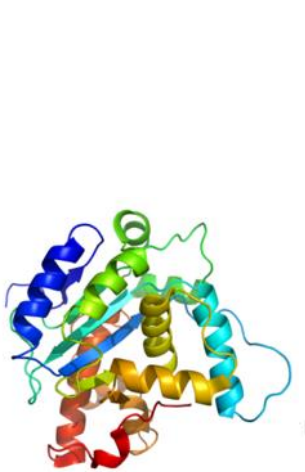
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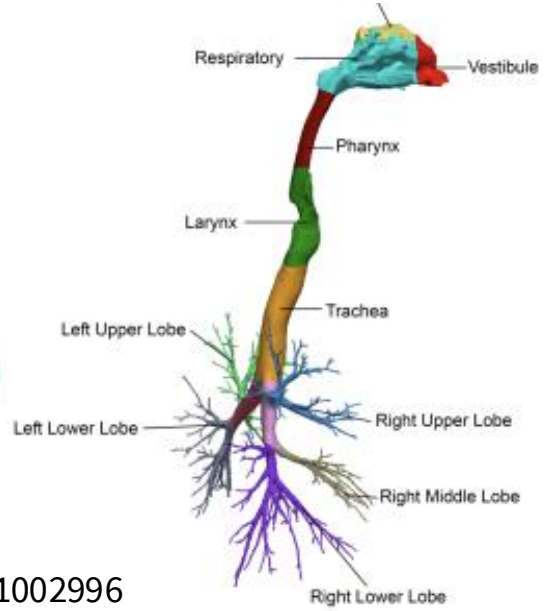
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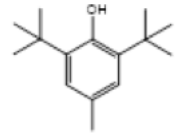
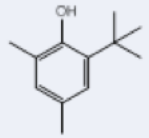
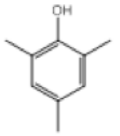
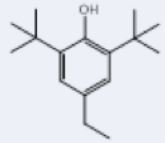
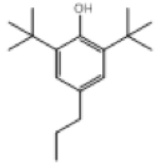
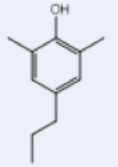
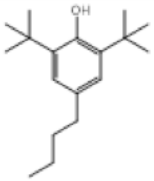
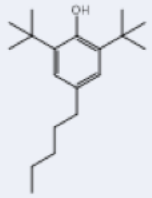
Structure Activity Relationships

Figure 1. Graphical representation of a chemical category and some approaches for filling data gaps

	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

[OECD No 194, Guidance on Grouping, 2nd EdItion. https://one.oecd.org/document/env/jm/mono(2014)4/en/pdf](https://one.oecd.org/document/env/jm/mono(2014)4/en/pdf)

CAS No.	Chemical structure
128-37-0	
1879-09-0	
527-60-6	
4130-42-1	
4973-24-4	
13037-82-6	
5530-30-3	
4973-26-6	

[OECD No 323, case study on alkyphenyl grouping. https://one.oecd.org/document/ENV/JM/MONO(2020)19/en/pdf](https://one.oecd.org/document/ENV/JM/MONO(2020)19/en/pdf)



Structure ACTIVITY Relationships

- Three-dimensional structure
- Hazard data
- Mechanistic data
- Bioactivity data
- Property characteristics
- Metabolic pathways
- Structure-activity fingerprints
- Chemotypes

Many models freely or easily available

- **General databases and models**

- OECD (Q)SAR Toolbox
- NICEATM Integrated Chemical Environment (ICE)
- EPA CompTox Chemicals Dashboard
- COSMOS
- ChemTunes·ToxGPS

Specific endpoint models

- CATMOS—acute tox
- SkinSensPred
- Universal Immune System Simulator
- Genotoxicity
- Fish acute toxicity
- Respiratory Sensitization

OECD QSAR Toolbox—www.qsartoolbox.org

- Find data - 62 Databases, 100,000 chemicals, 3 million data points
  - Phys-Chem properties
  - Environmental fate and transport
  - (Eco)toxicological information
- Group and assess chemicals - 70 Profilers
  - Fate, Toxicity, Mechanistic
- Understand/predict metabolism
  - 5 Databases and 11 Simulators
- Fill data gaps - 254 QSAR Models
- Inventories

Endpoint tree
Acute toxicity
Carcinogenicity
Developmental toxicity/Teratogenicity
Genetic toxicity
Irritation/ Corrosion
Photoinduced toxicity
Repeated dose toxicity
Sensitization
Toxicity to reproduction

US EPA CompTox Chemicals Dashboard

https://comptox.epa.gov/dashboard/

- Predictions on chemical properties and effects
  - Fish toxicity
  - Oral rat LD50
  - ER binding, etc.
- In vitro ToxCast data
- Use and exposure data and predictions
- Toxicokinetics tools
- Easy to use read across tool (GenRA)

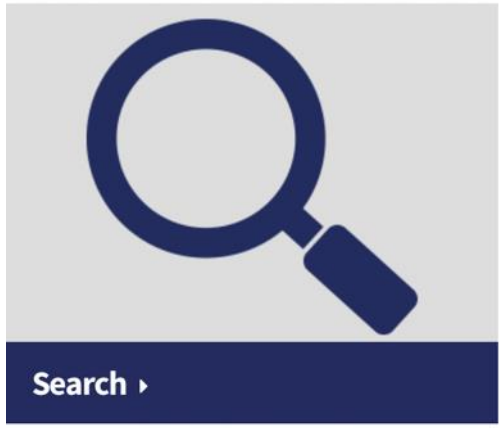
Collaborative Acute Toxicity Modeling Suite (CATMoS)

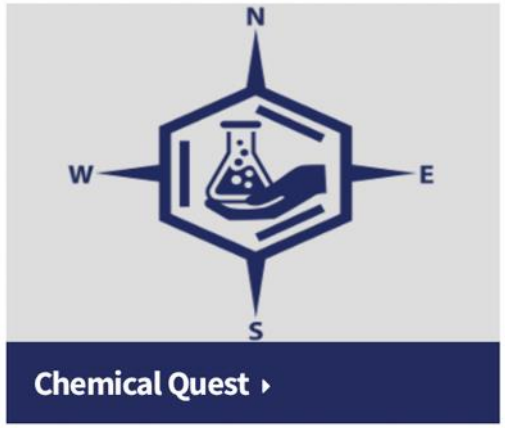
- Consensus model built from large dataset of LD50 data and 139 individual models
- Binary (toxic/non-toxic), Continuous (LD50), and Categorical (GHS & EPA) predictions
- Performance:
- Availability:
  - Within NICEATM ICE
  - Within EPA Dashboard

Github:
https://github.com/NIEHS/OPERA
Reference:
https://doi.org/10.1186/s13321-018-0263-1

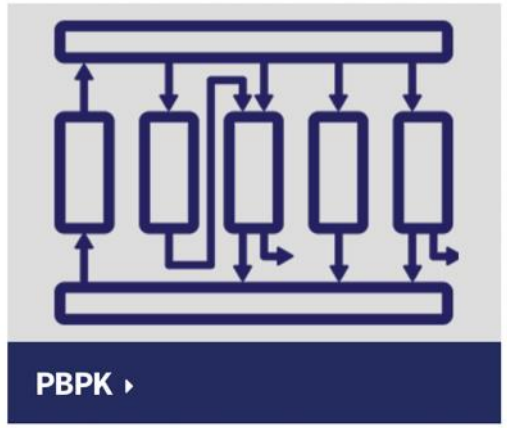
	Very Toxic		Non-Toxic		EPA		GHS	
	Train	Eval	Train	Eval	Train	Eval	Train	Eval
Sensitivity	0.87	0.70	0.88	0.67	0.81	0.62	0.80	0.58
Specificity	0.99	0.97	0.97	0.90	0.92	0.86	0.95	0.90
Balanced Accuracy	0.93	0.84	0.92	0.78	0.87	0.74	0.88	0.74
***In vivo* Balanced Accuracy**	0.81		0.89		0.82		0.79	

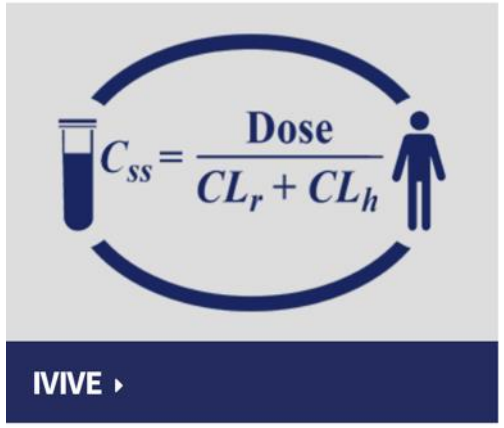
US NIH Integrated Chemical Environment

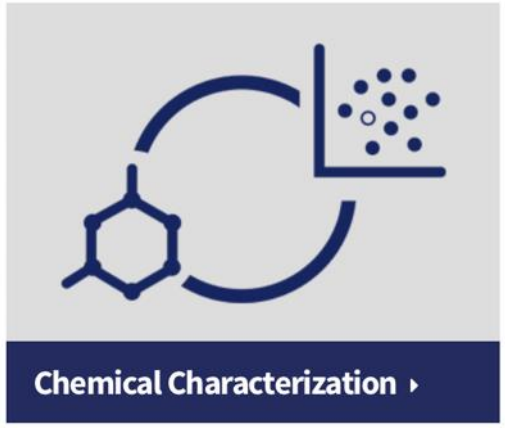
















https://ntp.niehs.nih.gov/whatwestudy/niceatm/comptox/ct-ice/ice

Key Concepts for Smoother Regulatory Application of NAMs

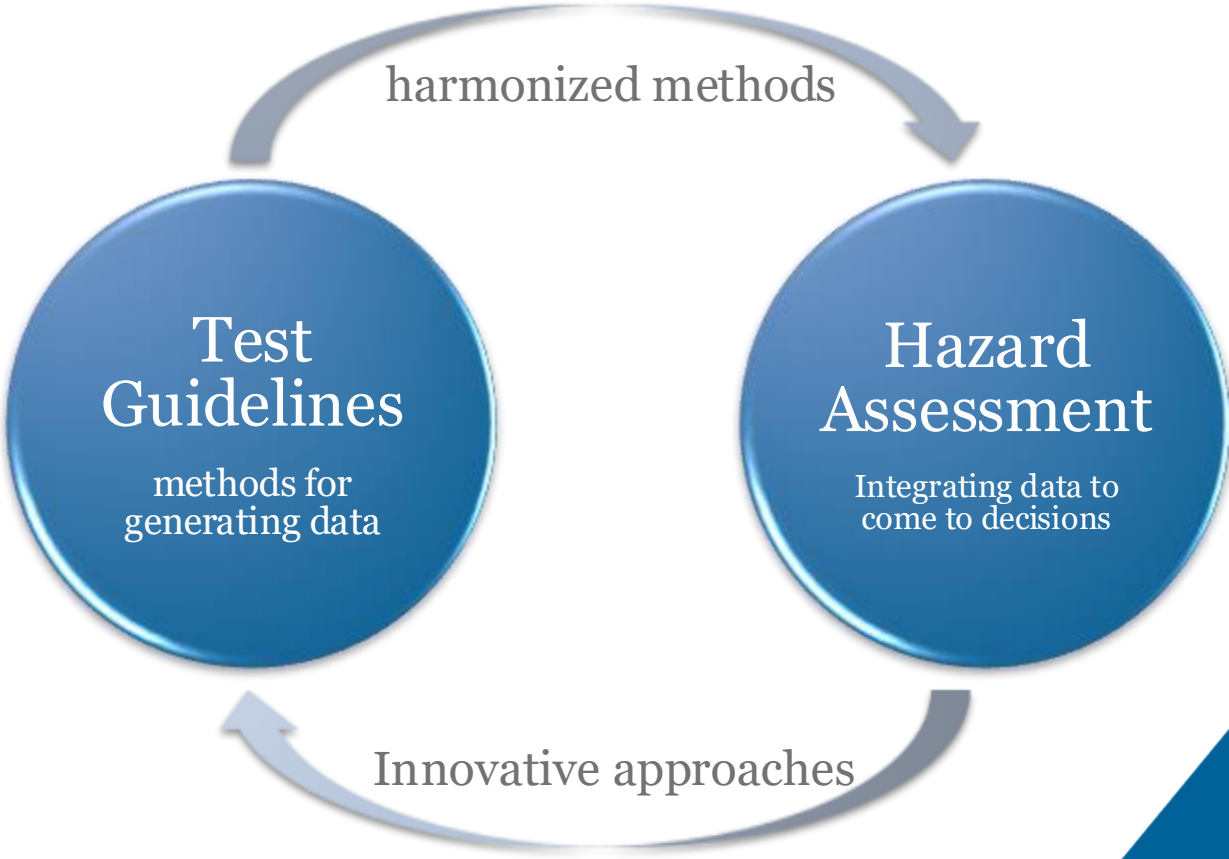
OECD Chemical Safety Program

- Provides multiple efforts and a collaborative forum for governments and stakeholders to share their experiences and needs
- Develops methods and approaches for evaluating the safety of chemicals
- Promotes harmonized approaches and data sharing



Test Guidelines and Hazard Assessment

- **Test Guidelines** Programme
  - Methods
  - Guidance on data interpretation, testing needs, state of the science for specific methods/endpoints, etc.
- **Hazard Assessment** Programme
  - Conclusions
  - Guidance on how to integrate data, fill data gaps, extrapolate, etc.
  - Innovative tools and alternative methods



Slide: Patience Browne



Integrated Approaches for Testing and Assessment (IATA)

Problem Formulation

AOP

Defined Approaches

In vivo / in vitro Test Guidelines

Validated in vivo / in vitro Assays

Non-validated Assays or Studies

In Silico Models

Grouping & Read-Across

Chemical-specific information

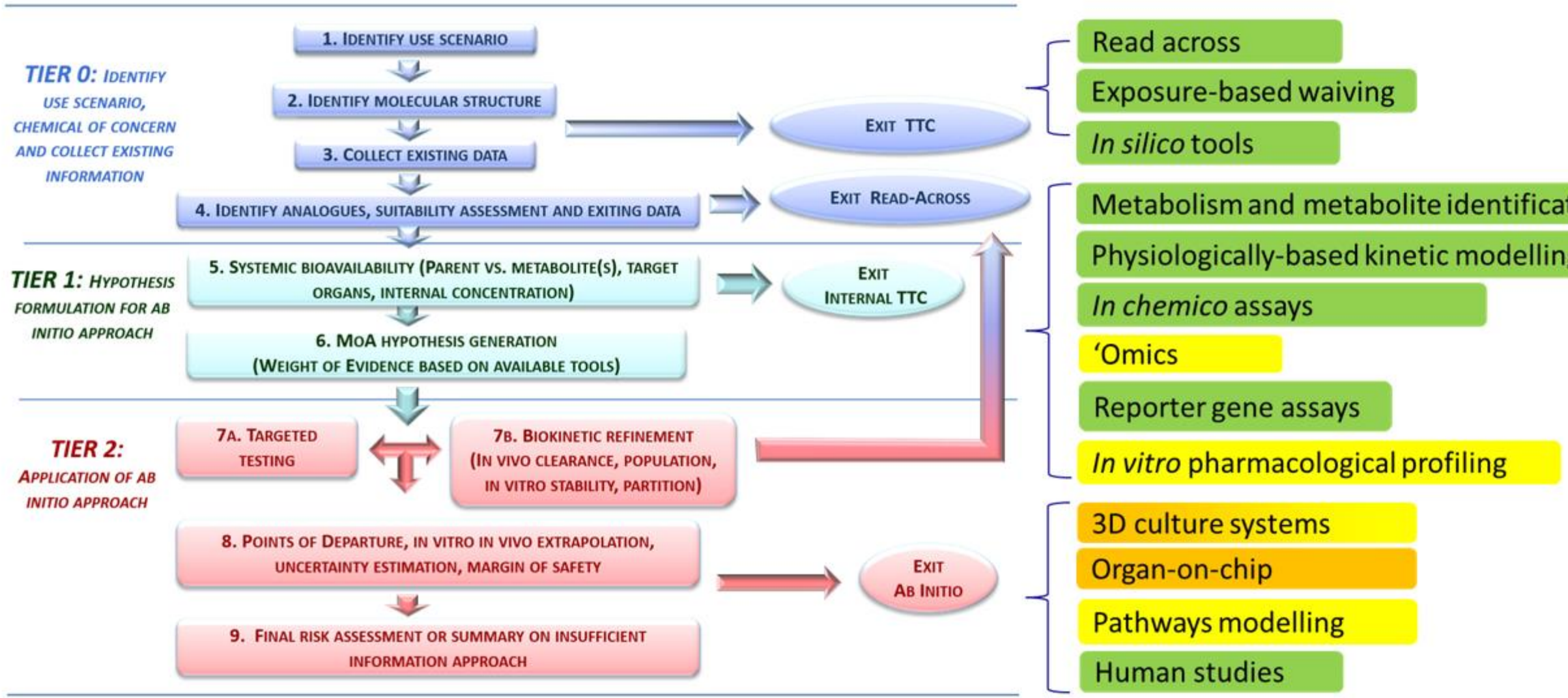
PK/ ADME

Exposure Information

Weight of Evidence

Adapted from: OECD (2020), Overview of Concepts and Available Guidance related to Integrated Approaches to Testing and Assessment (IATA), OECD Series on Testing and Assessment, No. 329, Environment, Health and Safety, Environment Directorate, OECD.

Tiered IATA – Hypothesis-driven testing



Berggren et al 2017. Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods. Comput Toxicol. doi: 10.1016/j.comtox.2017.10.001.

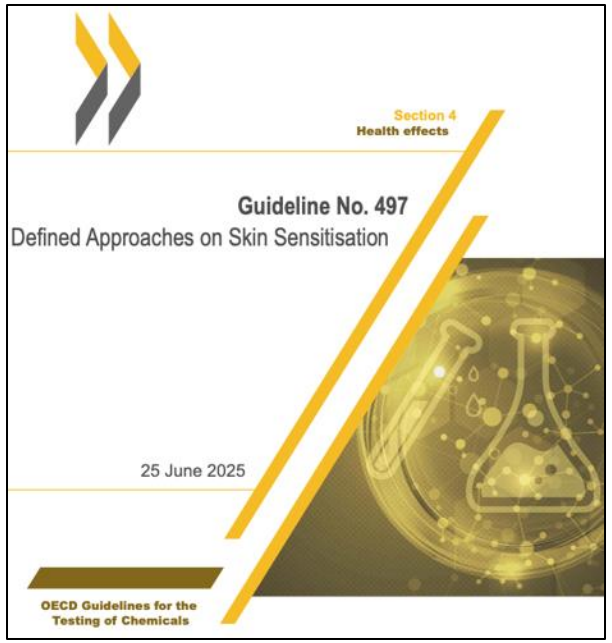
OECD-Published IATAs

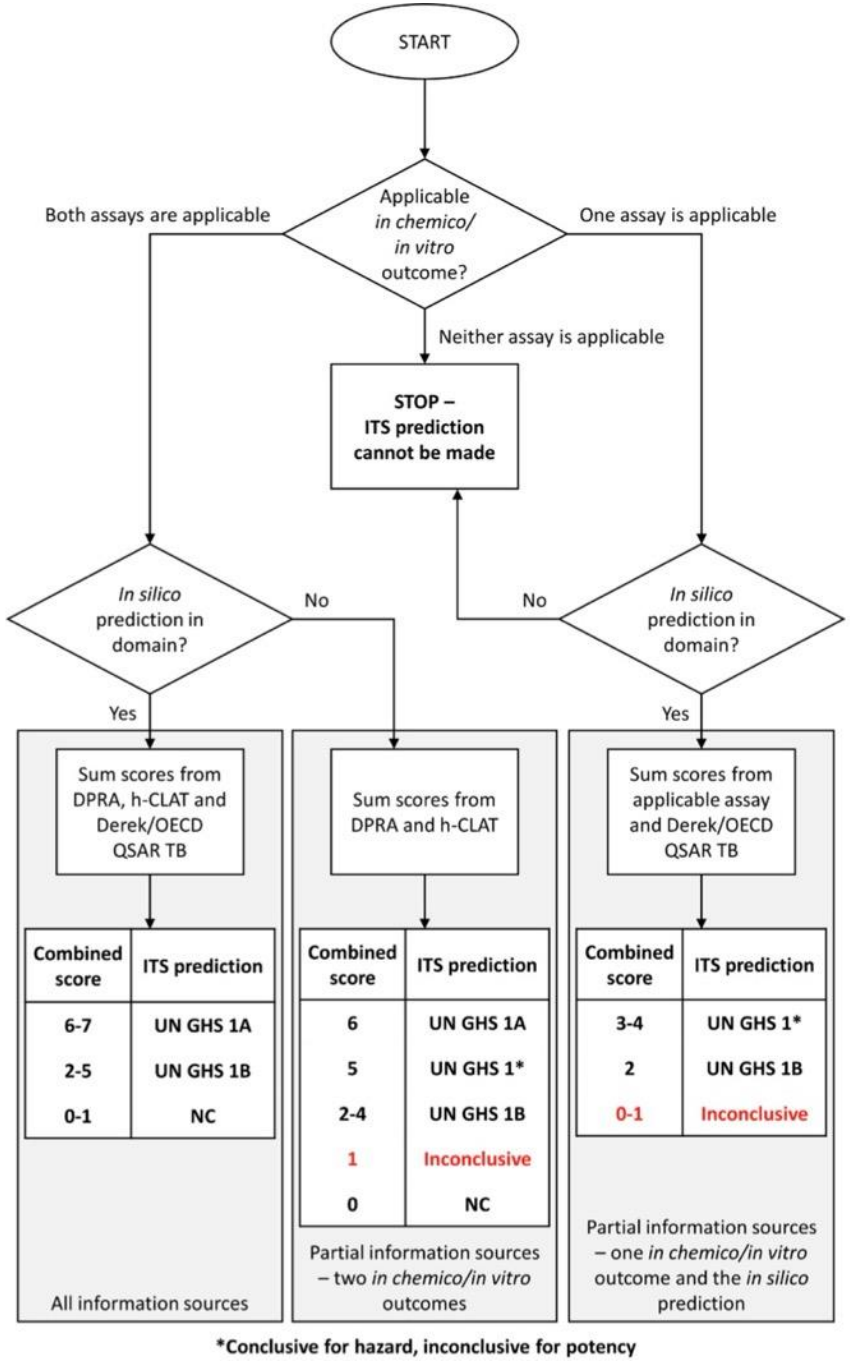
- Phototoxicity Testing (No. 397) (2024)
- Skin Corrosion and Irritation (No. 203) (2017)
- Serious Eye Damage and Eye Irritation (No. 263) (2019)
- Skin Sensitisation Information Sources (No. 256) (2017)

Documents that provide the latest guidance on methods, approaches, and information that can be used in combination to understand the potential for the particular endpoint (and how to use them).

Defined Approach: A Type of IATA

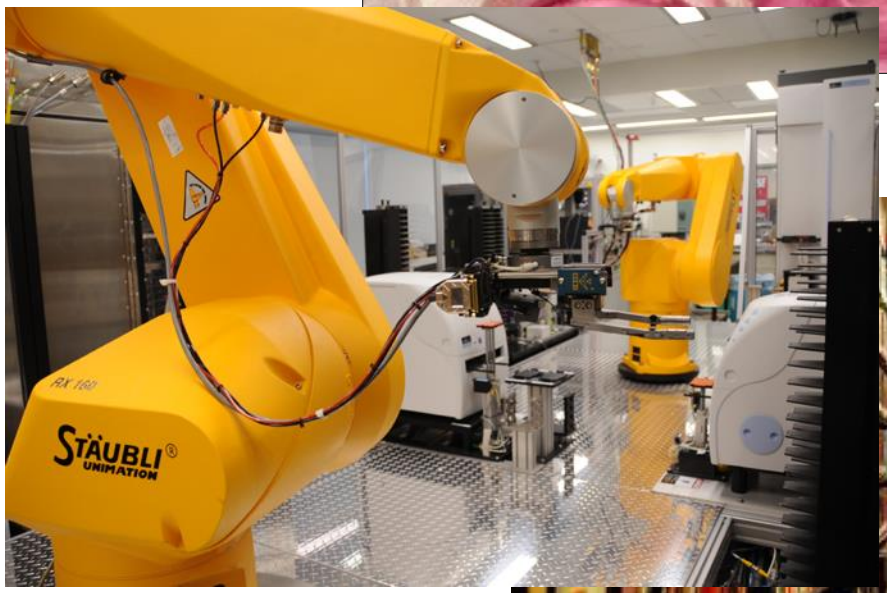
- Defined information sources
  - Experimental methods
  - Characteristics
  - Predictions
- Fixed data interpretation procedure
  - Algorithm for interpreting data
  - Manual or automated
- Offers potential for mutual acceptance of in silico predictions via DA GL
- Increases harmonization and certainty of acceptance in certain contexts





Adverse Outcome Pathways









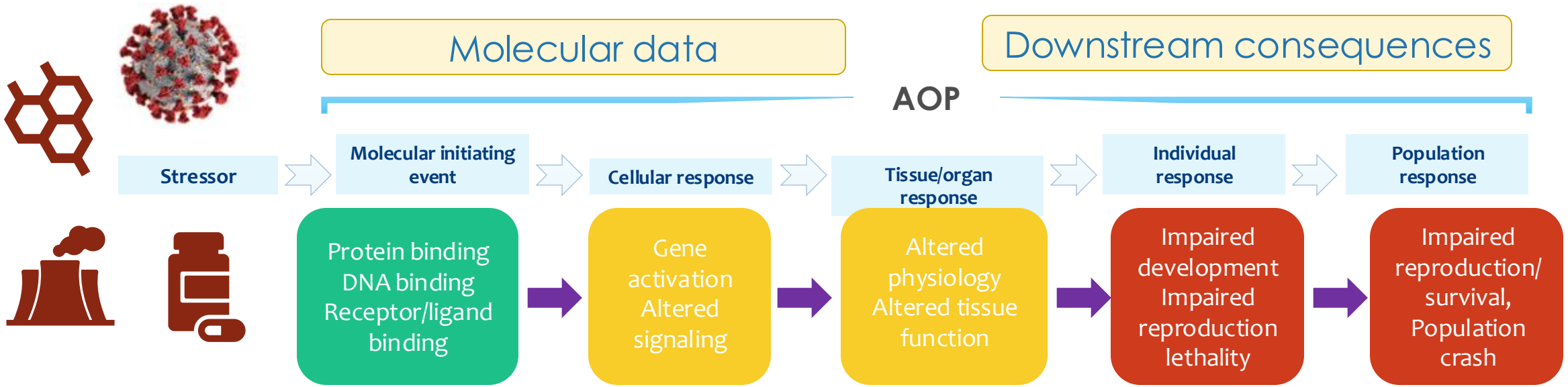
Regulatory Toxicology

A-O-P-Wiki

www.aopwiki.org

Images: IIVS, Inc., NIH/NTP, Wikimedia

AOPS: Link Molecular Information to Adverse Outcomes; Demonstrate Relevance of an Approach



SAR, QSAR

Experimental or Modeling

In Vitro studies

In vivo Studies

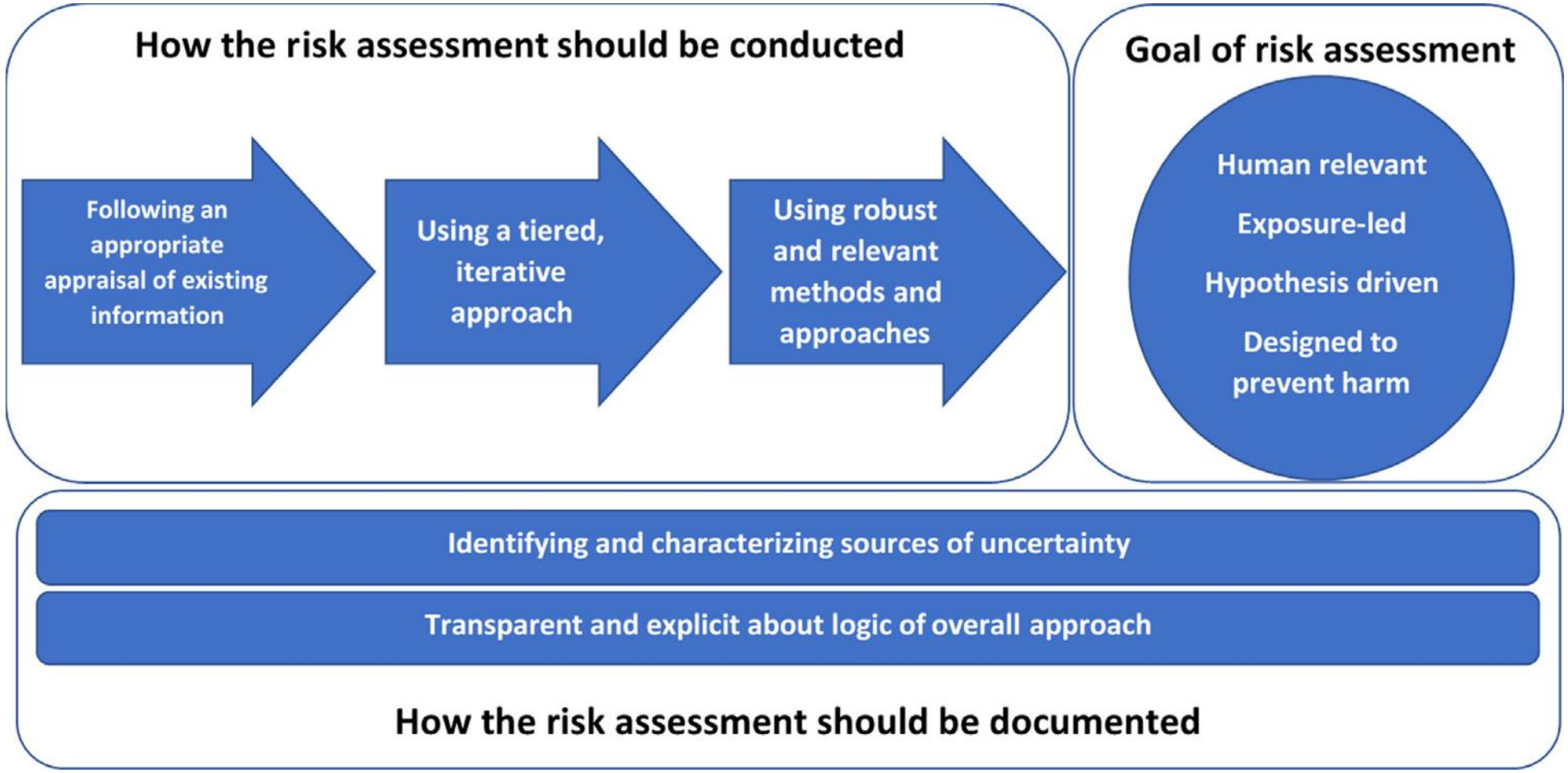
Mechanistic Data ('omics, biomarkers)

Clinical, Epidemiology, Field Studies

Slide adapted from C. Willett

Next Generation Risk Assessment: Underlying Principles

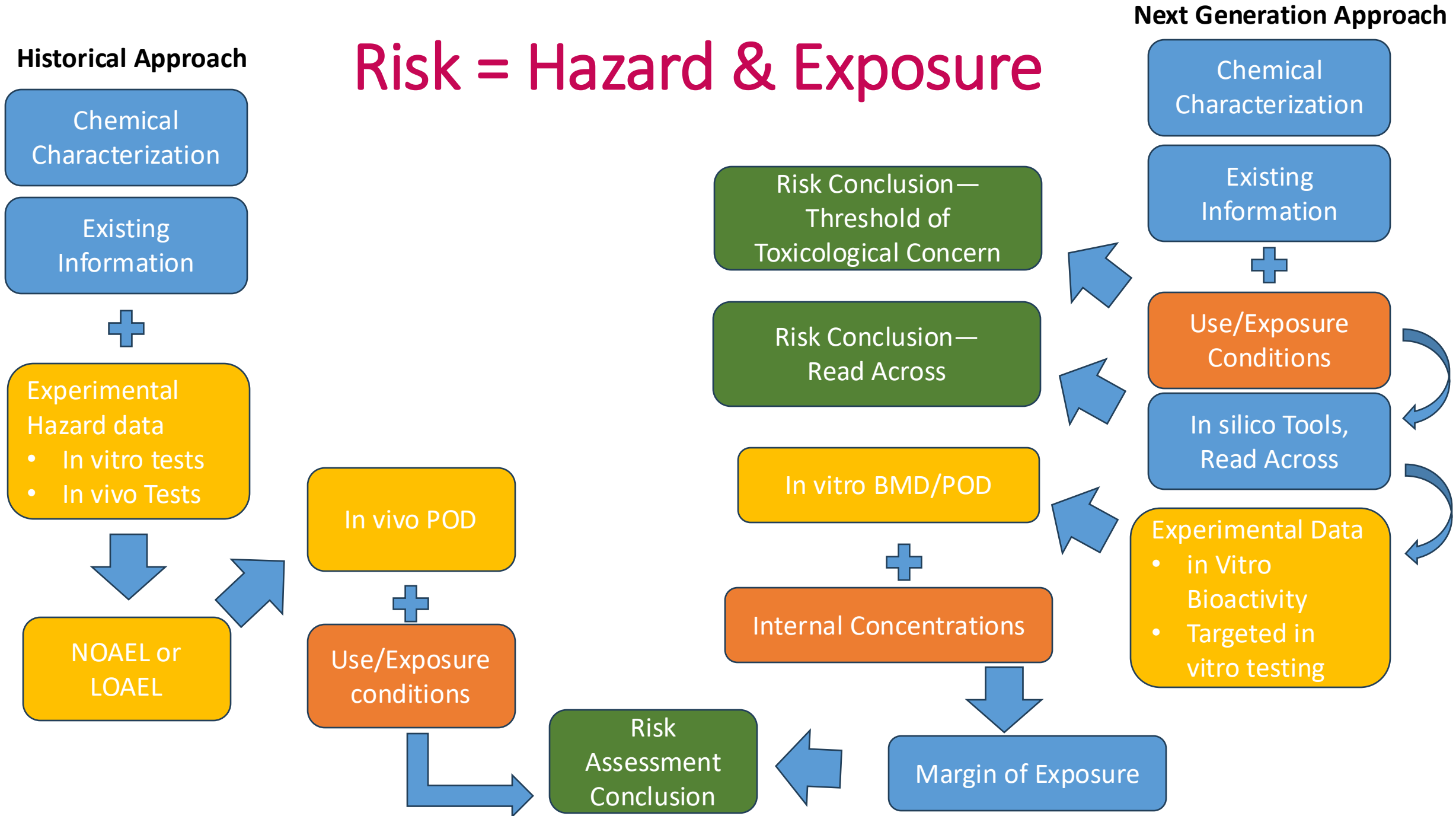
NGRA is defined as ***an exposure-led, hypothesis-driven*** *risk assessment approach that* ***integrates New Approach Methodologies (NAMs)*** *to assure* ***safety without the use of animal testing***



Dent et al. 2018. Computational Toxicology. doi: 10.1016/j.comtox.2018.06.001

ICCR International Cooperation on Cosmetics Regulation

Risk = Hazard & Exposure



Components of an NGRA

External and Internal Exposure Modeling & Assessment

Use scenarios

External dose/exposure

Metabolite Identification

Internal Exposure (PBK)

ADME parameters

Chemical Characterization

Molecular structure

In silico predictions

Read Across

Phys/chem properties

Existing Literature



Pharmacological Profiling

Cell painting

Single Assays

3D cell models

High-throughput transcriptomics

Receptor-Binding Assays

Hazard, Bioactivity, & Mechanistic Evaluation

Higher-tier tools (e.g., MPS)

IVIVE

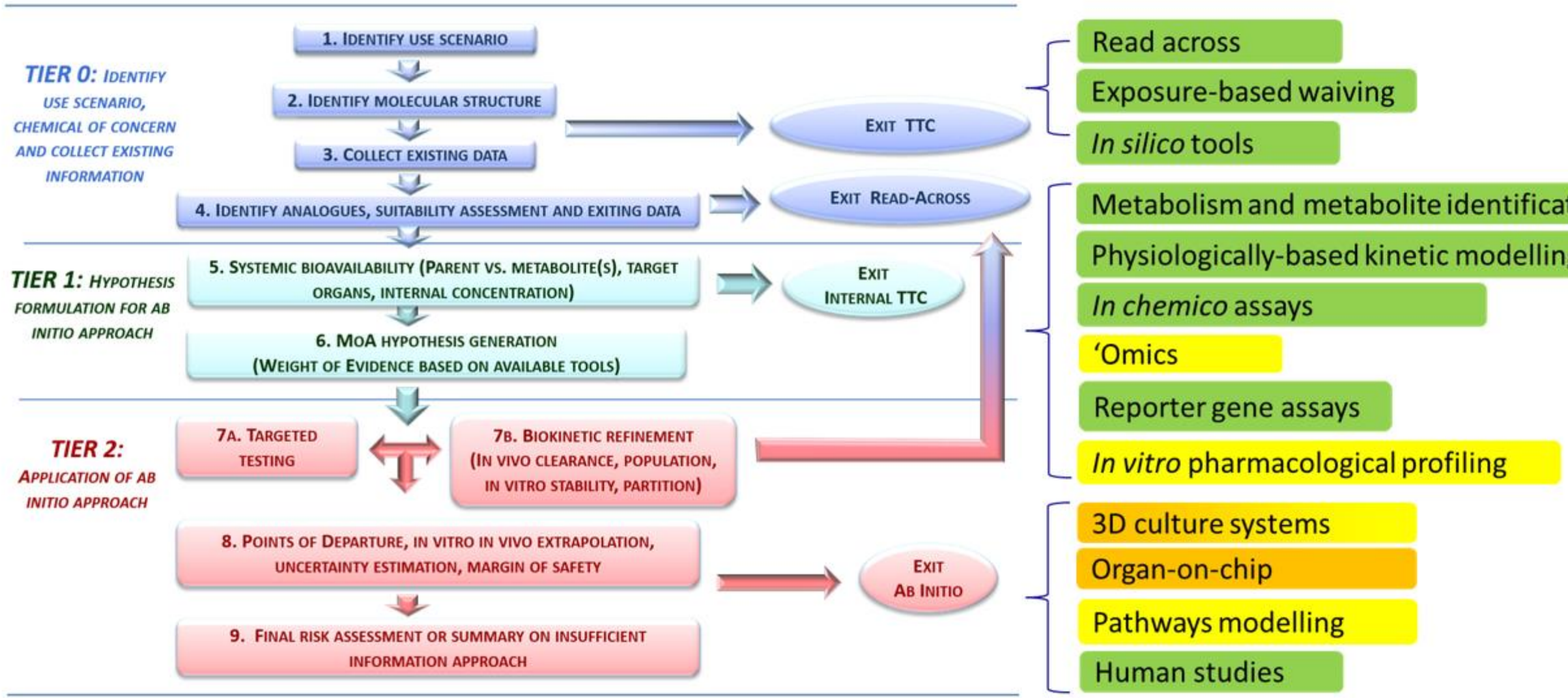
Population metabolism tools

Derive BMD and POD

Repeat Dose dynamics

MOE/BER Calculation & Additional Investigations

Tiered IATA – Hypothesis-driven testing



Berggren et al 2017. Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods. Comput Toxicol. doi: 10.1016/j.comtox.2017.10.001.

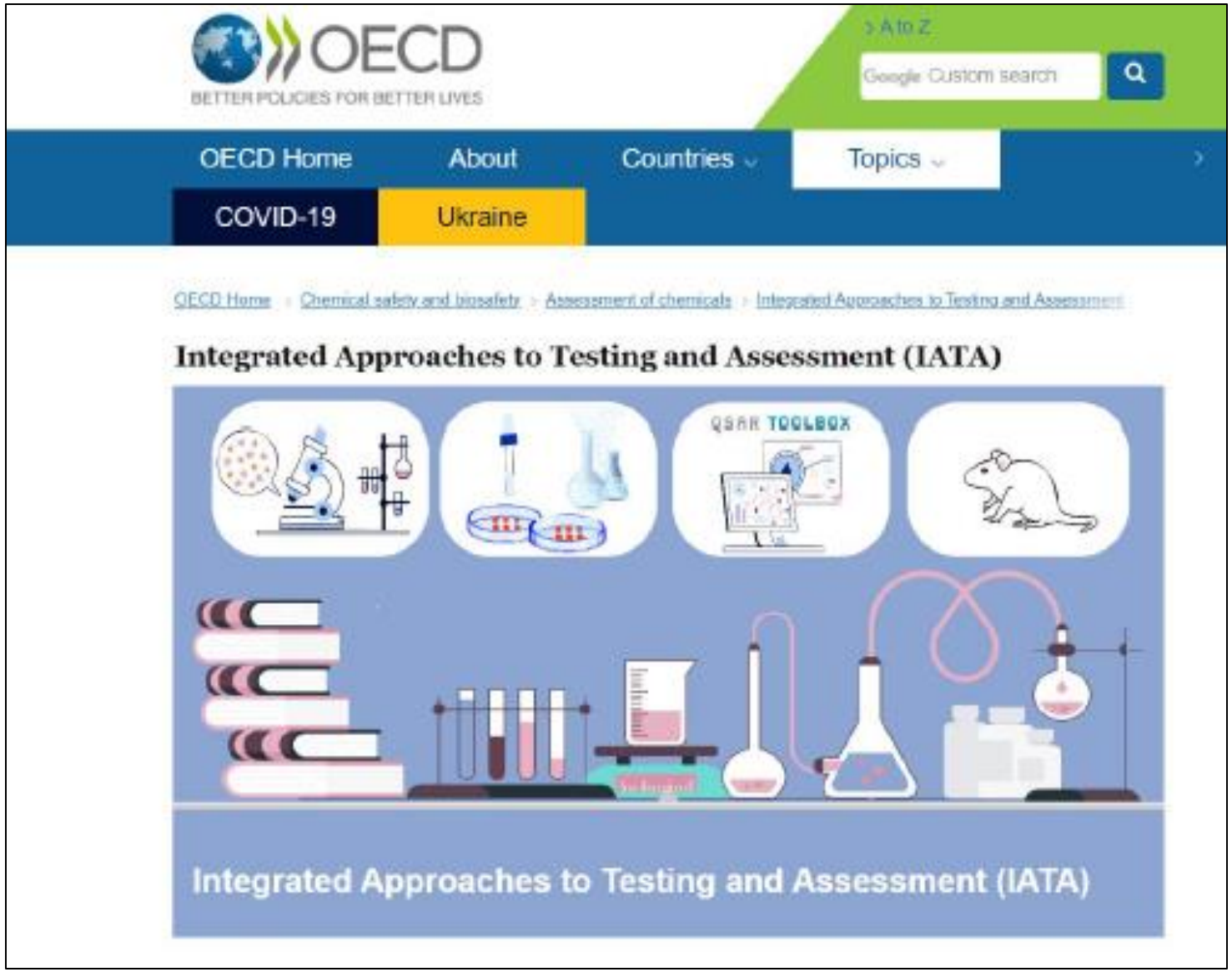
Guidance for Application and Standardization

OECD Frameworks for Chemical Safety

- OECD Harmonised Templates (OHTs) for chemical safety data
  - ~130 standard reporting formats for information used in risk assessment
  - GL and non-GL studies
  - Chemically agnostic
- QSARs (#386)
  - QSAR Model Reporting Formats
  - QSAR Prediction Reporting Formats
  - Expanding to be generalizable to in silico models
- Omics
  - Transcriptomics Reporting Framework
  - Metabolomics Reporting Framework
- PBK Models (#331)
- IATAs
  - General template
  - Read across template
  - Guidance for building blocks in IATA
  - IATA Case Studies Project
- Defined Approaches
  - to be used in IATA
  - New TG includes elements to stand-alone DA use
- AOPs
- GIVIMP
- GD#211—non-guideline methods

The goal is to make chemical safety data standardized, sharable, and interoperable

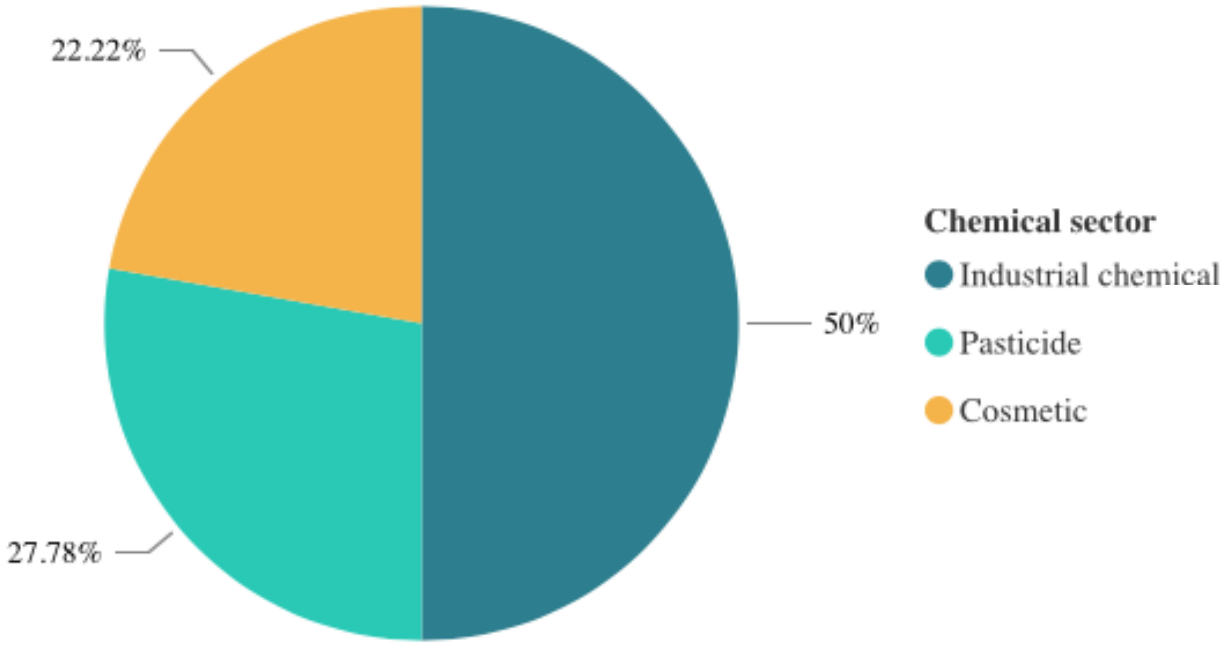
OECD IATA Case Studies project: Learning by Doing

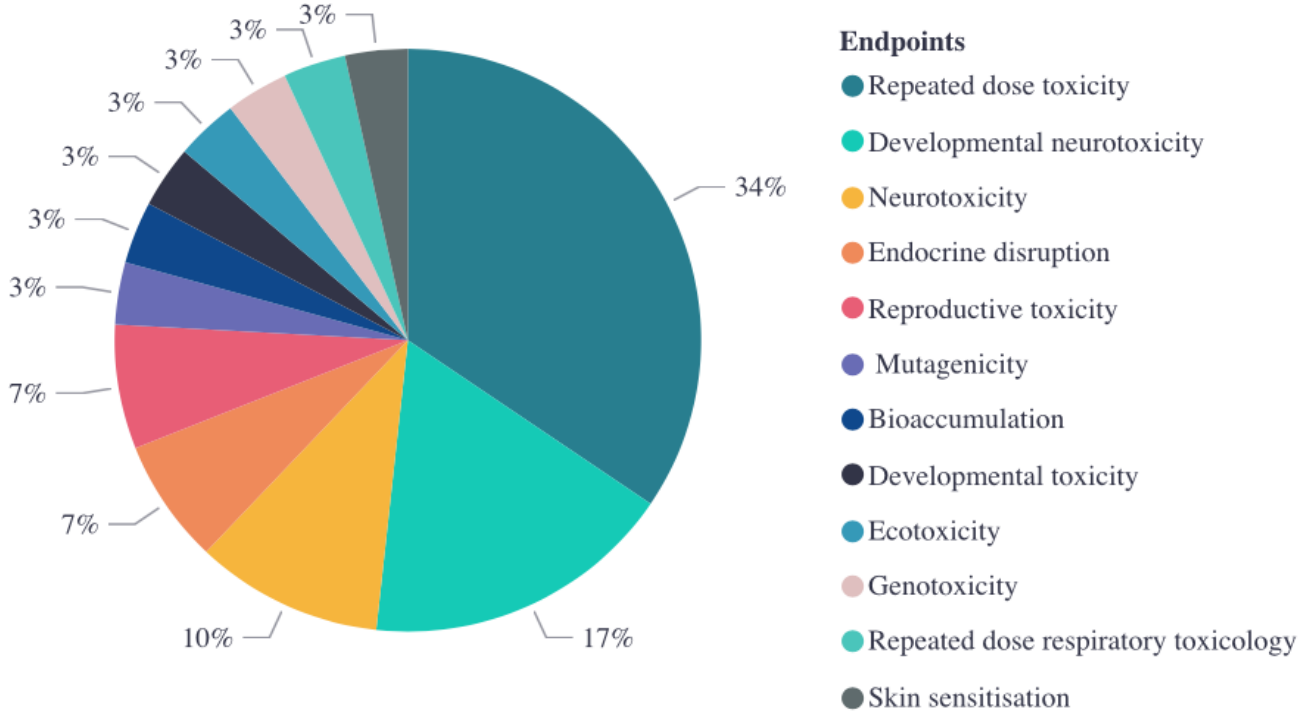




https://www.oecd.org/chemicalsafety/risk-assessment/iata/

~40 Case Studies Address Diverse Landscape





Assessment Types

- Grouping/read-across
- IATA workflow
- In vitro battery
- Defined approach

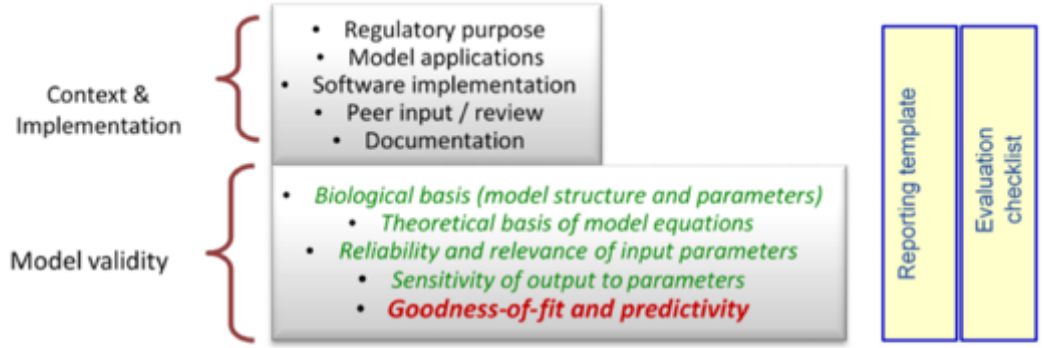
https://www.oecd.org/chemicalsafety/risk-assessment/iata/

Model Documentation and Evaluation

[OECD GD 331: Guidance Document on the Characterisation, Validation and Reporting of PBK Models for regulatory purposes]

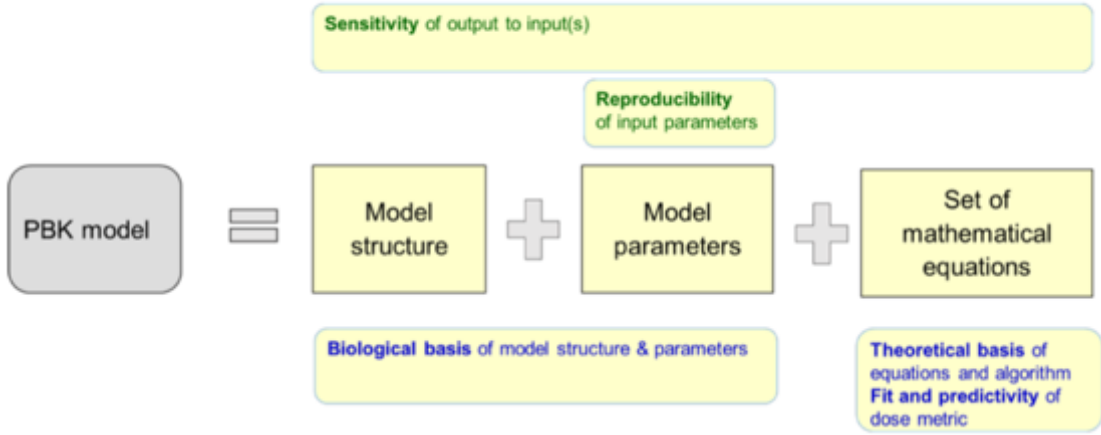
- Guidance for development and application
- Reporting template
- Checklists for model evaluation

Figure 3.1. Characteristics of an Assessment Framework for PBK Models. Key information and supporting references are addressed in the model reporting template (by the model developer/proponent), while key questions to facilitate confidence assessment in the purpose-specific application of a model are outlined in the evaluation checklist (for use by the assessor/regulator). Considerations in green text do not require *in vivo* data; those in red require *in vivo* data.



Consistent with the OECD definition of validation (OECD 2005), the scientific validity of a PBK model can also be thought of in terms its relevance and reliability, as illustrated in Figure 3.2.

Figure 3.2. The scientific validity (reliability and relevance) of a PBK model. Reliability considerations in green (above), relevance consideration in blue (below).



Documentation and Evaluation: QSAR Assessment Framework

Based on

- GD 49: Principles for the validation of QSARs (2004)
- GD 69: Guidance for Validation of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models (2007)

Sections on

- Principles for assessing models
- Principles for assessing predictions
- Principles for assessing results from multiple predictions

For each, development of assessment elements and a checklist of criteria

- Guidance on how to determine if criteria are met
- Examples illustrating how to evaluate criteria

QSAR Assessment Framework

QSAR Model Reporting Format
QSAR Prediction Reporting Format
Model checklists

Webinar recording

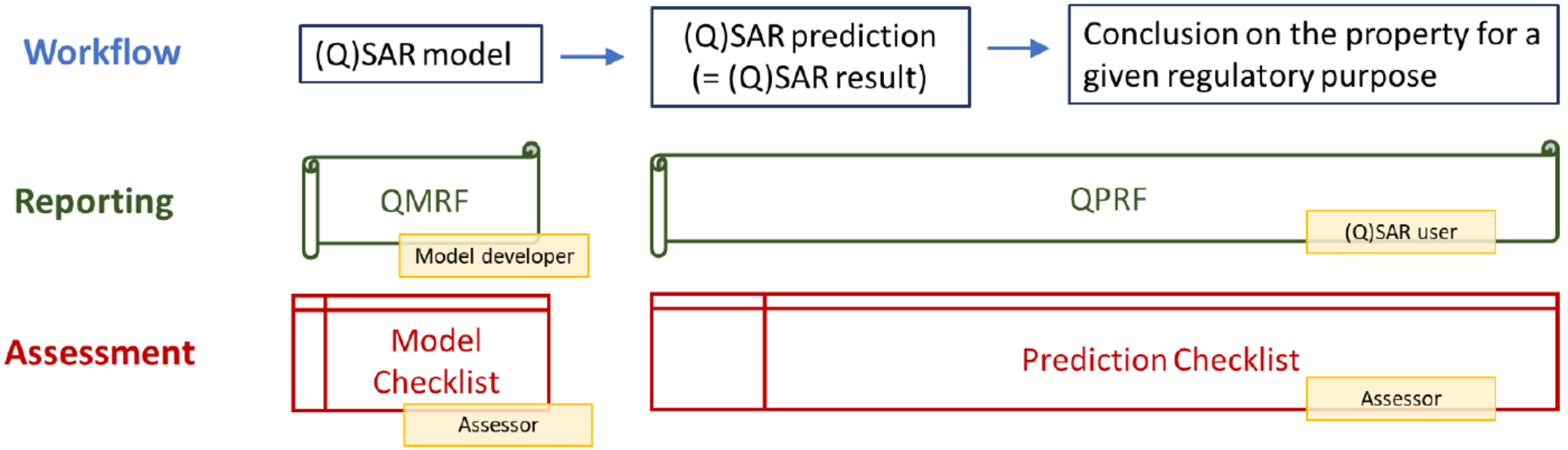
Short, readable document providing practical guidance through assessment elements & checklists to support regulatory use.

QSAR Assessment Framework – Validation Principles

1. Defined endpoint
2. Unambiguous algorithm
3. Defined domain of applicability
4. Appropriate measures of goodness-of-fit, robustness and predictivity
5. Mechanistic interpretation, if possible

QSAR Assessment Framework

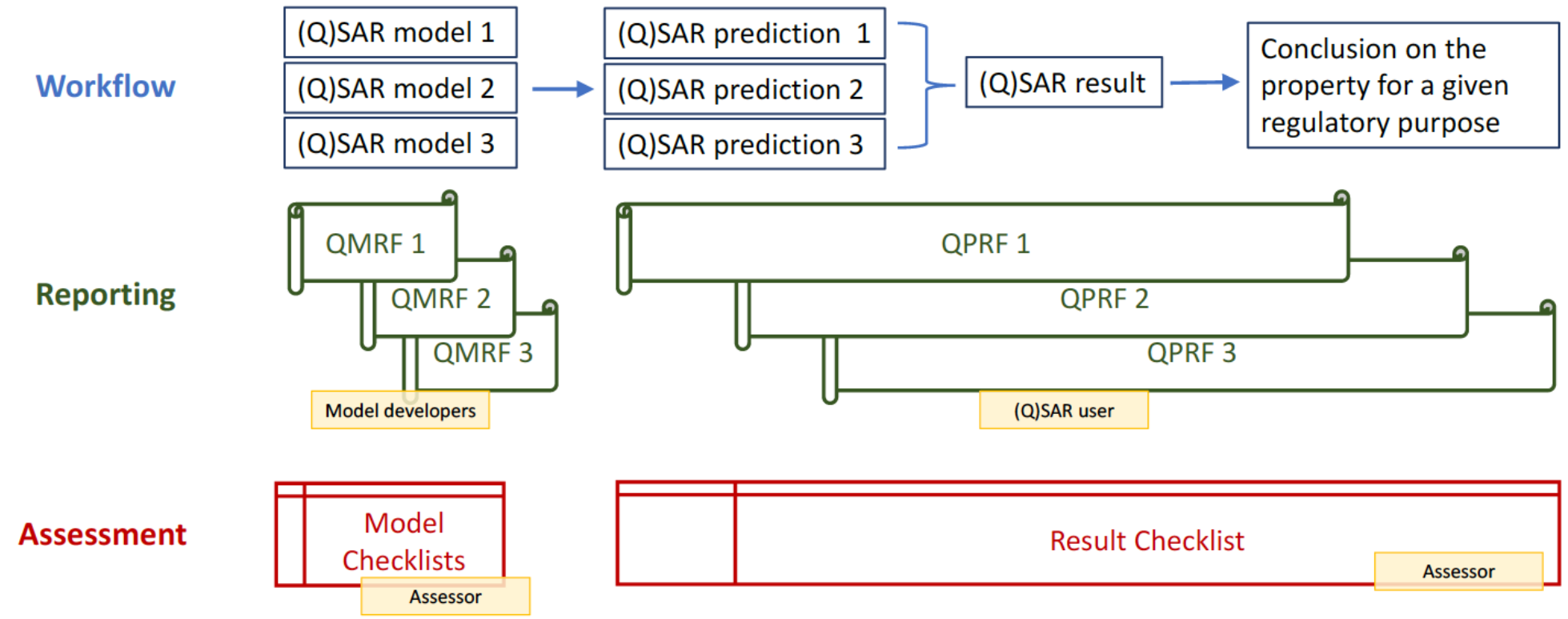
Figure 1. (Q)SAR Assessment Framework (QAF) Result based on an individual prediction



Note: Workflow of (Q)SAR information for a result based on an individual prediction according to the OECD (Q)SAR assessment framework (QAF). The information about the model is reported in the (Q)SAR Model Reporting Format (QMRF) document prepared by the model developer and assessed by regulators using the QAF Model Checklist. The information about the (Q)SAR prediction is reported in the (Q)SAR Prediction Reporting Format (QPRF) document by the (Q)SAR user and assessed by regulators using the QAF Prediction Checklist. Checklists could also be pre-compiled by the (Q)SAR user to facilitate the work of the assessor.

QSAR Assessment Framework

Figure 2. (Q)SAR Assessment Framework (QAF) Result based on multiple predictions

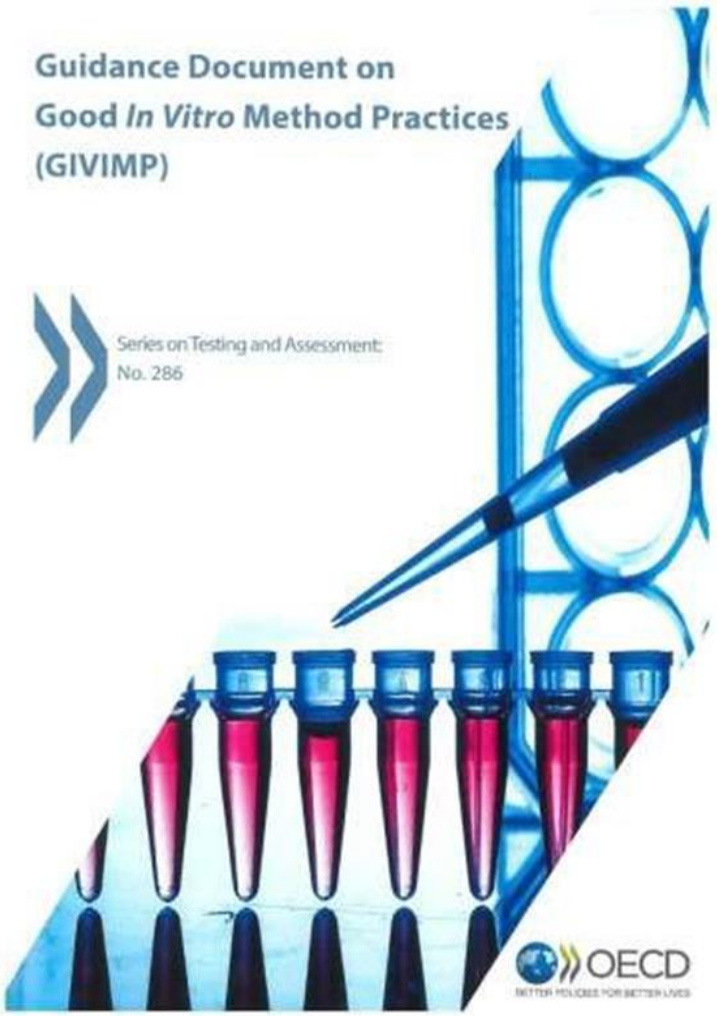


Note: Workflow of (Q)SAR information for a result based on multiple predictions according to the OECD (Q)SAR assessment framework (QAF). The information about the models is reported in the (Q)SAR Model Reporting Format (QMRF) documents prepared by the model developers and assessed by regulators using the QAF Model Checklist. The information about the (Q)SAR predictions and result is reported in the (Q)SAR Prediction Reporting Format (QPRF) document by the (Q)SAR user, and assessed by regulators using the QAF Result Checklist.

QSAR Assessment Framework – Model Checklist

Unambiguous algorithm			
2.1	Description of the algorithm and/or software	Ensure that it is clear how the prediction is obtained and that it can be reproduced by others	- Check if a sufficient description of all descriptors and of approach used for their selection and calculation is provided; - Check the availability of a transparent description of the algorithm and/or software, explaining how the predictions were produced. - For fragment/alert based models, the list of the fragments (active, inactive, masks, etc. as relevant) together with information of all substructures and identification of its substituents should be provided. - For equation based models, a description of the equation and all data/descriptors and approach used for their selection should be provided.
2.2	Inputs and other options	Allowed input formats, pre-processing procedure for the input structures and customisable options/settings are explained.	- Availability of instructions to prepare the input. - Availability of information on the editable options/settings (if any).
2.3	Model accessibility	Assess if the model or computer program is or can be available to the assessor.	- Availability of the same model and version described in the documentation

Good In Vitro Method Practices (GIVIMP)



1) A detailed update on good practices for state-of-the-art *in vitro* methods applied to regulatory human safety assessment of a variety of compounds

2) Guidance to users and implementers of *in vitro* methods to help to ensure that methods are well-designed, robust, well-defined and well-described

3) Description of the key aspects that may impact the reliability and relevance of *in vitro* data

4) Description of the importance of reporting criteria, including establishing acceptance criteria and performance standards from *in vitro* data sets

Available on OECD e-Library
https://doi.org/10.1787/20777876

Also available on the
OECD Series for Testing and Assessment No. 286



Thank You

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www.iivs.org

www.ascctox.org/webinars

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Practical Methods
TRAINING IN NEW APPROACHES FOR RIGHT NOW

Acknowledgements

Unilever

Matt Dent

Gavin Maxwell

Maria Balthazar

IIVS

Hans Raabe

Emilia Costin

Argel Islas-Robles

Catherine Willett, HSI

Nicole Kleinstreuer, NICEATM

Patience Browne, OECD

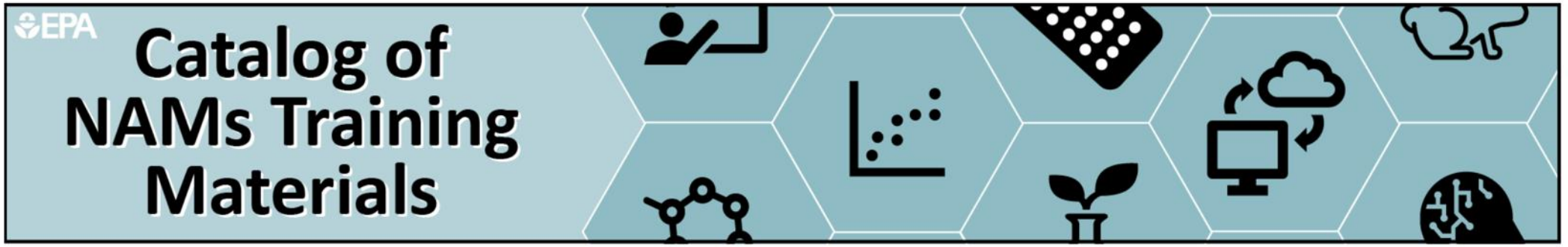
Resource slides

Additional Training Resources

- PCRM NURA: https://www.pcrm.org/nura
- ASCCT: https://www.ascctox.org/webinars
- EPIC Webinars: https://www.thepsci.eu/epicwebinars/

- OECD webinars
  - Webinar Series on Emerging Science to Improve Chemical Safety
  - Webinar Series on Testing and Assessment Methodologies
  - Integrated Approaches to Testing and Assessment (IATA)

New Approach Methods (NAMs) Training



NAMs Training Resources

- **New to NAMs?** Read background information on NAMs training resources.
- **Have questions?** Contact us.
- Join EPA NAMs email list for training updates.

Upcoming Training Events

- CompTox and Exposure Communities of Practice
- NAMs Tools Training In-Person Workshop: April 24-25
- EPA Office of Research and Development Events

Related Resources

- EPA New Approach Methods
- EPA Chemical Research
- EPA Computational Toxicology and Exposure Online Resources

Showing 109 resources

Search:

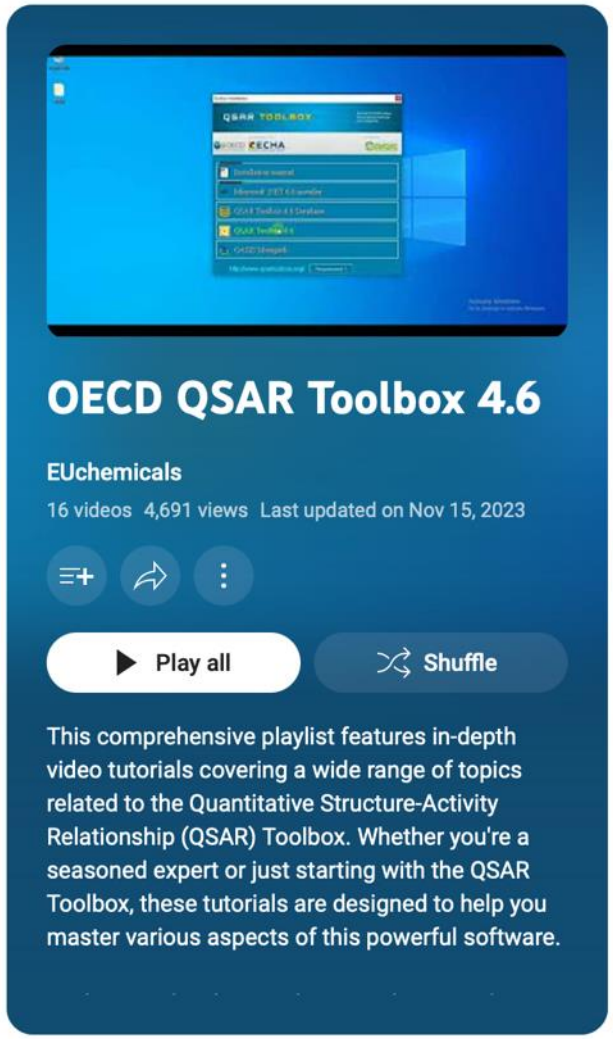
Year	Topic	Subtopic	Type	Title	Description
	ALL	ALL	ALL		
2024	Ecotoxicology	ECOTOX	Tool Tips	ECOTOX Knowledgebase Tool Tips	Series of short videos to inform new users about the basic functionality of the ECOTOX Knowledgebase
2024	Databases Relevant to Toxicity and Bioactivity	invitroDB	Slide deck	Software and Database Enhancements to ToxCast for Accessible Bioactivity Data for Toxicology (pdf) (3.1 MB)	Presenters: Madison Feshuk, Jason Brown, Sarah Davidson-Fritz , and Katie Paul Friedman for CompTox Communities of Practice webinar
2024	Databases Relevant to Toxicity and Bioactivity	invitroDB	Video	Software and Database Enhancements to ToxCast for Accessible Bioactivity Data for Toxicology	Presenters: Madison Feshuk, Jason Brown, Sarah Davidson-Fritz , and Katie Paul Friedman presenting on new updates to invitroDB and the ToxCast data pipeline (Length 47 minutes)

https://www.epa.gov/chemical-research/new-approach-methods-nams-training

OECD QSAR Toolbox

http://www.youtube.com/@ECHA

Playlist: OECD QSAR Toolbox



1 1. Installation process - OECD QSAR Toolbox 4.6
EUchemicals • 1.7K views • 5 months ago

2 2. User interface - OECD QSAR Toolbox 4.6
EUchemicals • 750 views • 5 months ago

3 3. Input Enter target chemical - OECD QSAR Toolbox 4.6
EUchemicals • 949 views • 5 months ago

4 4. Define target endpoint - OECD QSAR Toolbox 4.6
EUchemicals • 834 views • 5 months ago

5 5. Profiling - OECD QSAR Toolbox 4.6
EUchemicals • 768 views • 5 months ago

6 6. Data gathering - OECD QSAR Toolbox 4.6
EUchemicals • 657 views • 5 months ago

NGRA Training Resources

AFSA Master Class: https://www.afsacollaboration.org/masterclass/

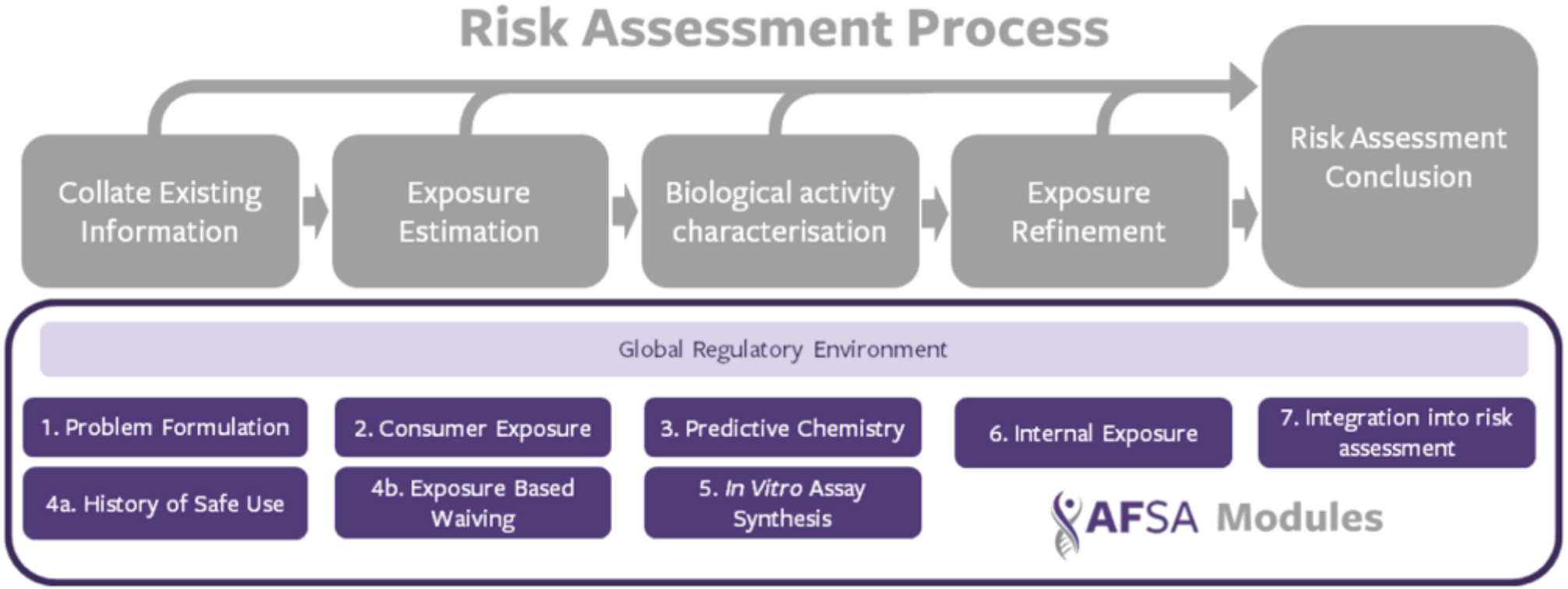


Image: Humane Society International

NGRA Resources—Databases & Tools

- Adverse Outcome Pathway Wiki: Mechanistic Information: https://www.aopwiki.org
- OECD eChemPortal: https://www.echemportal.org
- OECD QSAR Toolbox: http://qsartoolbox.org
- Interactive models available from NICEATM ICE: https://ice.ntp.niehs.nih.gov/
- US EPA CompTox Chemicals Dashboard data and models: https://comptox.epa.gov/dashboard/
- R package "httk" allows in *vitro-in vivo* extrapolation (IVIVE) and physiologically based toxicokinetics (PBTK): https://CRAN.R-project.org/package=httk

NGRA Resources—Computational Tools

Exposure modeling	Dose-response analysis	Bayesian statistics	Coding languages
Gastroplus	BMDExpress	MC-Stan	R & Rstudio
Simcyp	TCPL2.0	WinBUGS	Python
HTTK	BBMD	PyMC3	MATLAB
PK-Sim	PyHillfit	Turing	

NGRA Resources: Key Risk Assessment Publications

- A Next-Generation Risk Assessment Case Study for Coumarin in Cosmetic Products, (Balthazar et al., 2020; doi: 10.1093/toxsci/kfaa048).
- APCRA Case Study: “Utility of *In Vitro* Bioactivity as a Lower Bound Estimate of *In Vivo* Adverse Effect Levels and in Risk-Based Prioritization” demonstrated that HTTK, with appropriately propagated uncertainty, enhances new approach methodology (NAM)-based prediction of *in vivo* points of departure to inform regulatory decision-making (Paul Friedman et al., 2020; doi: 10.1093/toxsci/kfz201).
- Are Non-animal Systemic Safety Assessments Protective? A Toolbox and Workflow (Middleton et al., 2022; doi: 10.1093/toxsci/kfac068)
- Advancing systemic toxicity risk assessment: Evaluation of a NAM-based toolbox approach (Cable et al., 2024; doi: 10.1093/toxsci/kfae159)
- Adverse Effects in traditional and alternative toxicity tests (Browne et al., 2024); doi: 10.1016/j.yrtph.2024.105579)

NGRA Resource Documents

- Weitekamp et al. Quantitative and qualitative concordance between clinical and nonclinical toxicity data. Toxicol Sci. 2025 May 16:kfaf071. doi: 10.1093/toxsci/kfaf071.
- Paul-Friedman et al. Integration of new approach methods for the assessment of data-poor chemicals. Toxicological Sciences, 205:1, May 2025, https://doi.org/10.1093/toxsci/kfaf019.
- Paving the way for application of next-generation risk assessment to safety decision-making for cosmetic ingredients, [Dent et al., workshop report, 2019], doi: https://pubmed.ncbi.nlm.nih.gov/34389358/
- Bioactivity exposure ratio: Application in priority setting and risk assessment [Health Canada Science Approach Document, March 2021], https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/science-approach-document-bioactivity-exposure-ratio-application-priority-setting-risk-assessment.html

Next-Generation Risk Assessment: More Resources

ICCR "Integrated Strategies for Safety Assessment"

- Workshop Report
- Listing of available approaches
- Guidance for safety assessors

SCCS 12th Notes of Guidance

- Comprehensive description of NGRA principles
- Discussion of approaches available by endpoint