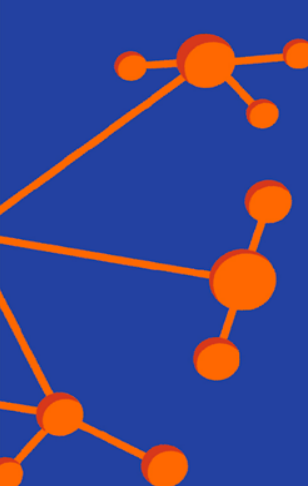




Data integration, ontology, & AI

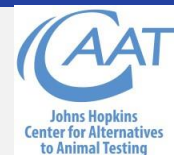
WP5

CAAT

WP Leader: Hartung
Presenter: Bozada



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ONTOX-ECETOX-VHP4Safety Workshop

28-October-2025



Task 5.1, 5.2, 5.3, & 5.4

1. Objectives

- Original: combined ontology-driven and AI-based approach for probabilistic hazard prediction
- Current: replicate OPRA framework with automated logic, tools, and queries

2. Progress since January, 2025

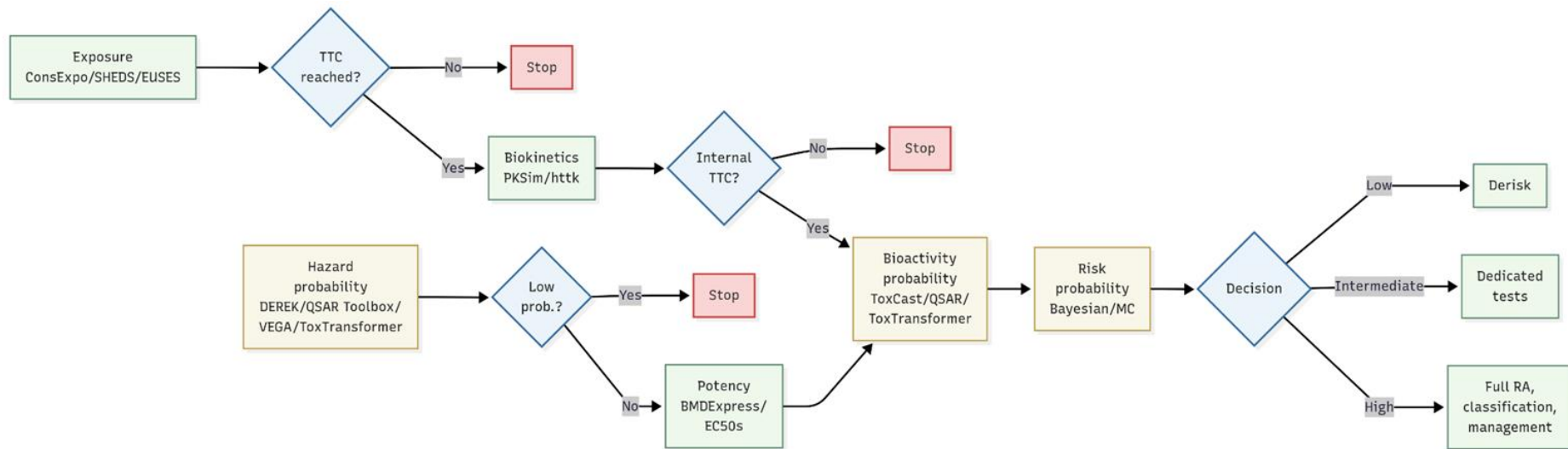
- OPRA framework defined and shared
- [ToxIndex.com](https://toxindex.com) live and publicly accessible
 - Current workflow is NOT OPRA (see later slides)

3. Problems/solutions and next steps

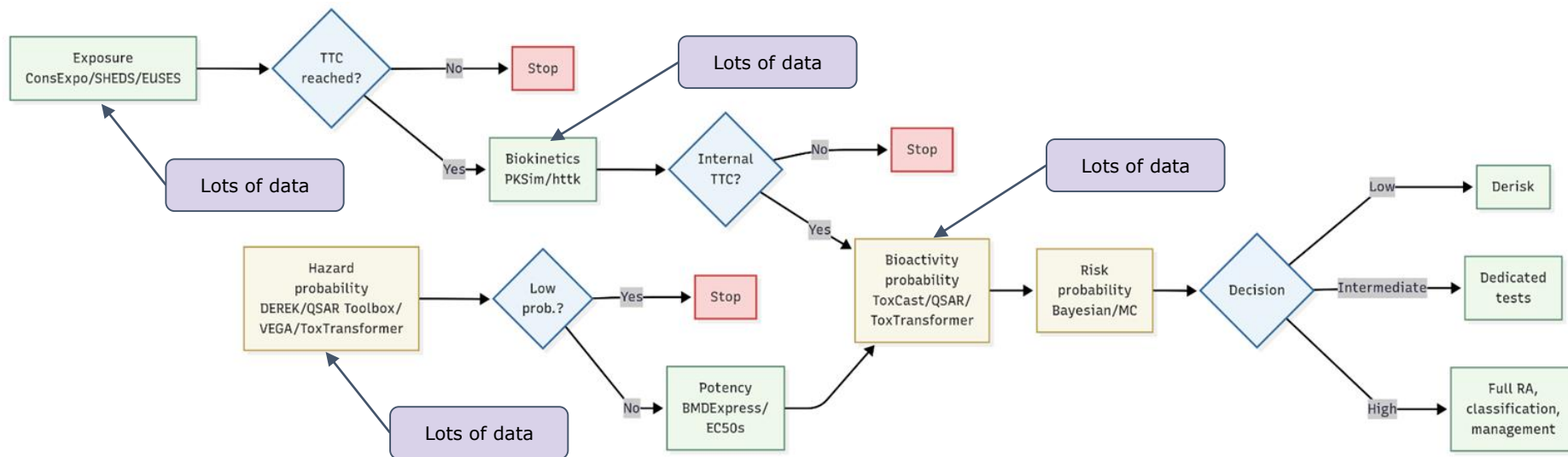
- Theoretical - how are outputs (e.g. probabilities) to be interpreted? How is exposure defined?
- Platform - which tools should be used for each step in OPRA?
- Pragmatism - which tools can be used for each step today?



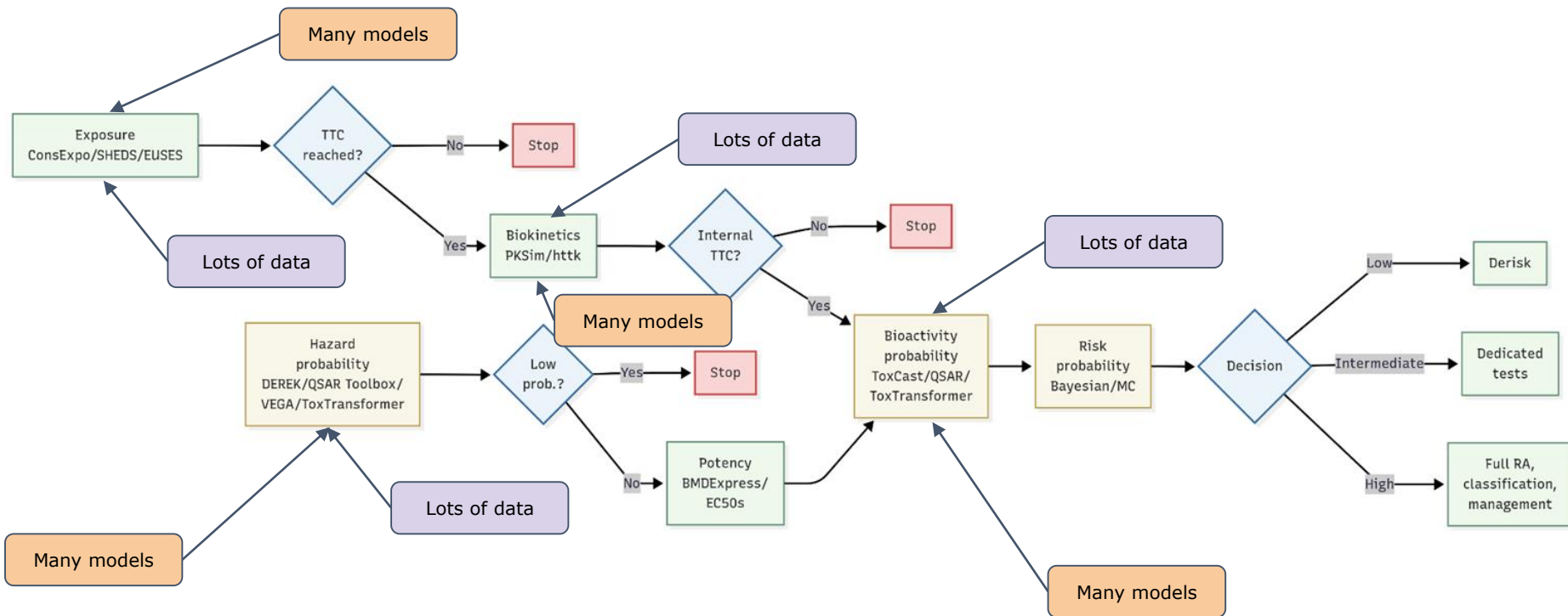
OPRA framework



OPRA framework - realized



OPRA framework - realized



There are many (automated/AI) tools

<https://www.atsdr.cdc.gov/toxprofiles/tp9-c3.pdf>

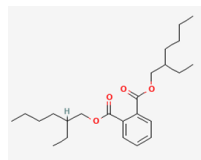
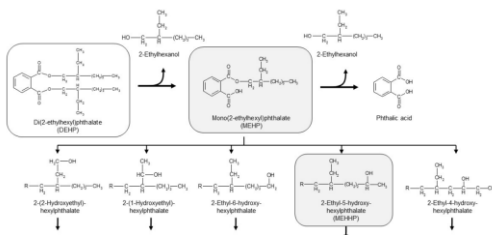


Figure 3-1. Metabolic Pathway of DEHP*

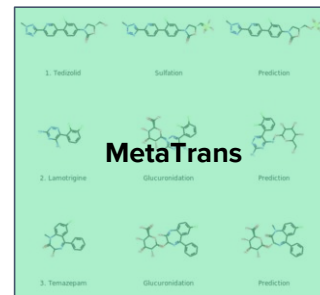


Structure + prompt →
Synthesis
Structure + prompt →
Classification
Structure + prompt →
Candidate generation

A REVIEW OF LARGE LANGUAGE
MODELS AND AUTONOMOUS
AGENTS IN CHEMISTRY. Ramos,
Collison, White

	BBBP1	Tox21	ClinTox2	HIV1	BACE1	SIDER
RF	71.4	70.9	71.3	78.1	86.7	68.4
SVM	72.9	81.8	66.9	79.2	86.2	68.2
MOGCM	85.0	85.0	73.8	73.4	55.2	—
D-MPNN	71.2	69.0	80.9	75.0	85.3	63.2
DimNet	—	—	—	—	—	61.5
Large-scale chemical language representation capture molecular structure and properties	71.4	70.9	71.3	78.1	86.7	68.4
10+ models referenced	72.4	78.1	90.1	80.6	85.6	67.2
ChEMBL	72.4	78.1	90.1	80.6	85.6	67.2
MOLFORMER-XL	93.7	84.7	94.8	82.2	88.21	69.0

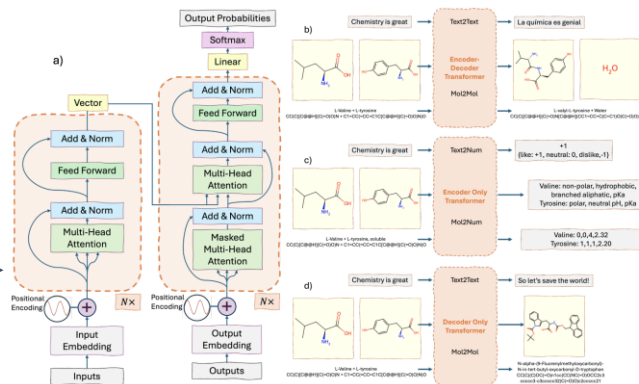
bold indicates the top-performing model. All models were evaluated using the area under the receiver operating characteristic curve on scaffold splits. Baseline performances are adopted from ref. 25, 26, 27. "—" signifies that the values were not reported for the corresponding task.



2024 Meta Predictor: in silico prediction of drug metabolites based on deep language models with prompt engineering

2020 Bio Transformer: a comprehensive computational tool for small molecule metabolism prediction and metabolite identification

2019 MetaTrans - Litsa Prediction of drug metabolites using neural machine translation



Each has a time and place

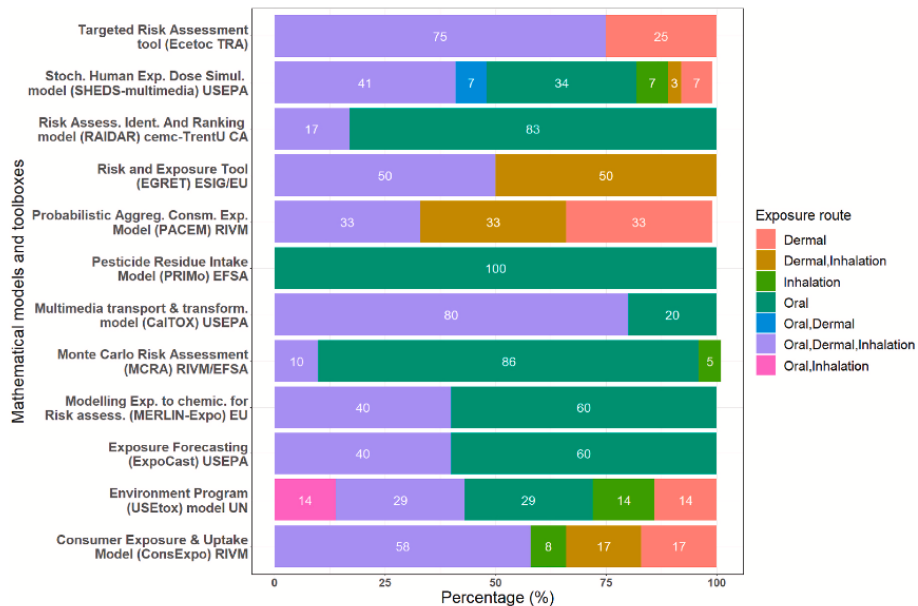


Fig. 5. Mathematical models and toolboxes most frequently used to estimate exposure in the included 299 papers versus exposure route.

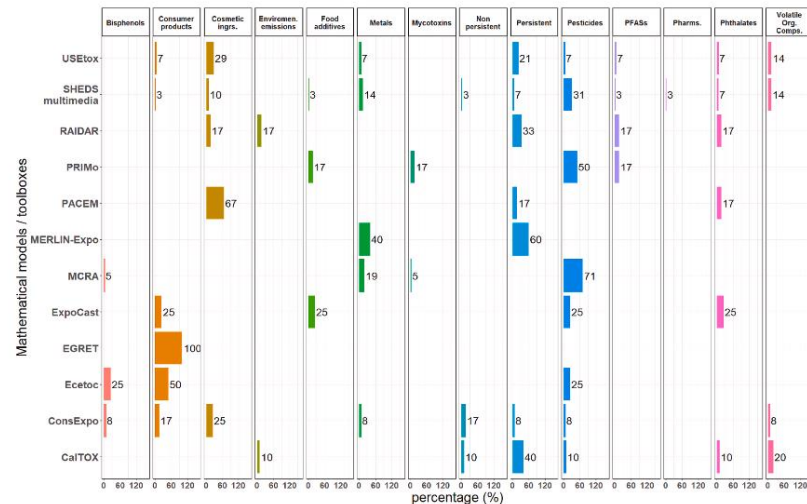


Fig. 6. Mathematical models and toolboxes most frequently used to estimate exposure in the included 299 papers versus chemical classes.

Exposure Route and Chemical type per evaluated exposure model(Klavya, 2014)



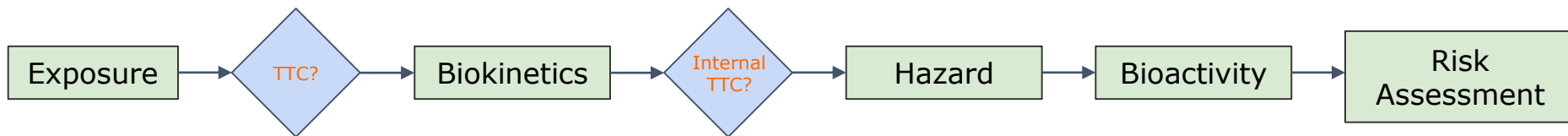
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Including within OPRA

Which exposure model(s)
should be used?

Do we have enough information?
What is the **confidence** in our prediction?



What data is known?
What can be predicted?
By **which model(s)**?

Can we make a **decision**?
Do we need **more tests**?
Which ones?



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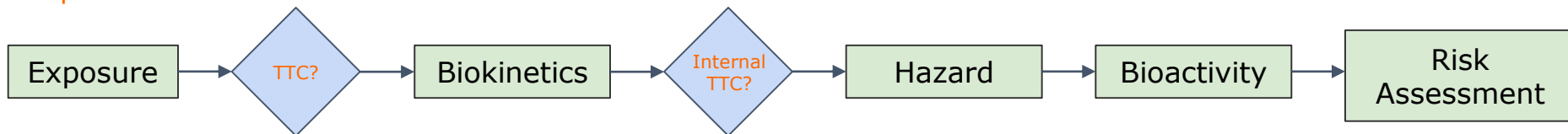
Agentic orchestrators can help

Which exposure model(s)
should be used?

Depends on chemical &
exposure

Do we have enough information?
What is the **confidence** in our prediction?

Benchmarking informs applicability



What data is known?
What can be predicted?
By **which model(s)**?

Aggregate databases
Run available and relevant models

Can we make a **decision**?
Do we need **more tests**?
Which ones?

Hazard ranking, testing
prioritization, new data ingestion



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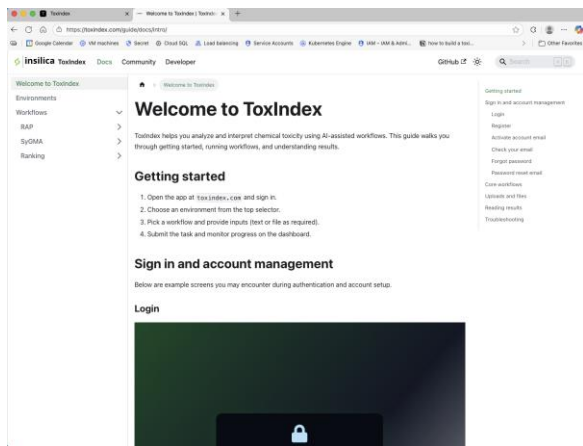


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Enter ToxIndex (<https://github.com/insilica/toxindex>)

Interdependent Agents

- aggregate all known information
- integrate multiple tools
- query / execute only when required



Start a Task

☒ Tasks ☐ Archive

Create a Dose Response Analysis Report

Crnute Risk Assessment IN PROGRESS

Review Genotoxicity Data

IN PROGRESS IN PROGRESS

Prepare Exposure Assessment

IN PROGRESS IN PROGRESS

Conduct a Risk Assessment

IN PROGRESS IN PROGRESS

MMCS Sample Data Review

IN PROGRESS IN PROGRESS

Does PFOA cause cholestasis?



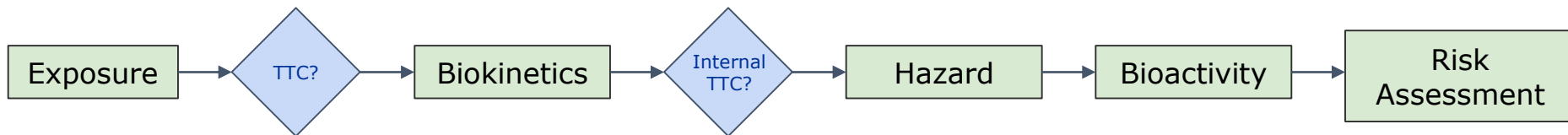
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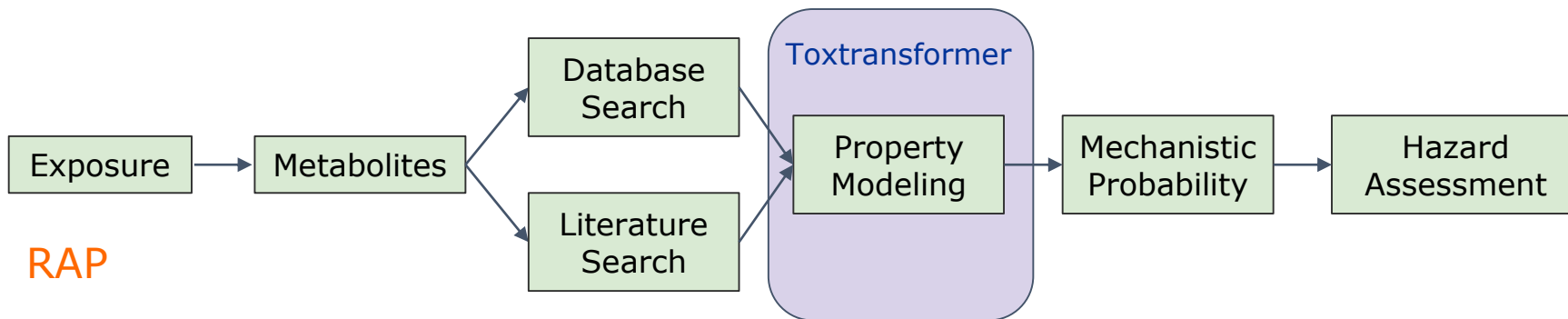
ECETOC/VHP4Safety/ONTOX WS 28 – 29 October 2025

Workflow Similarities

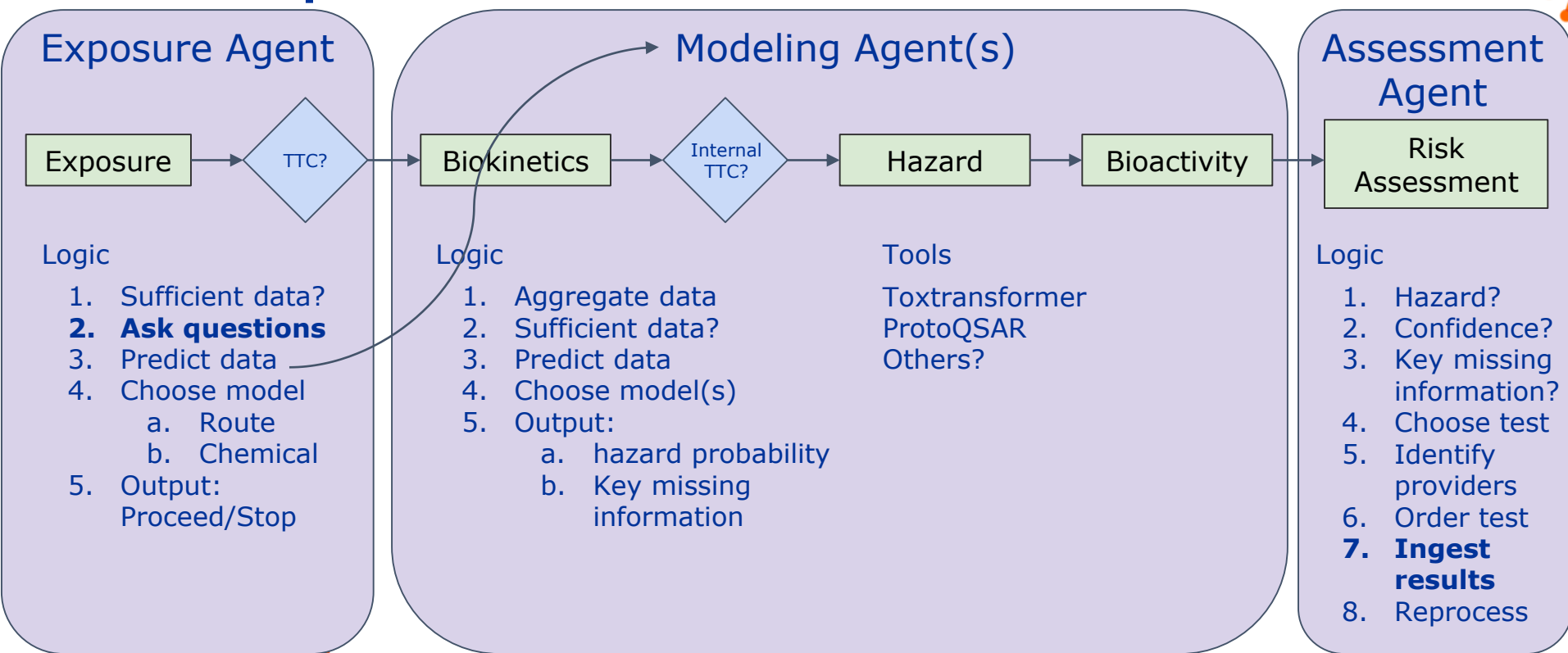
OPRA



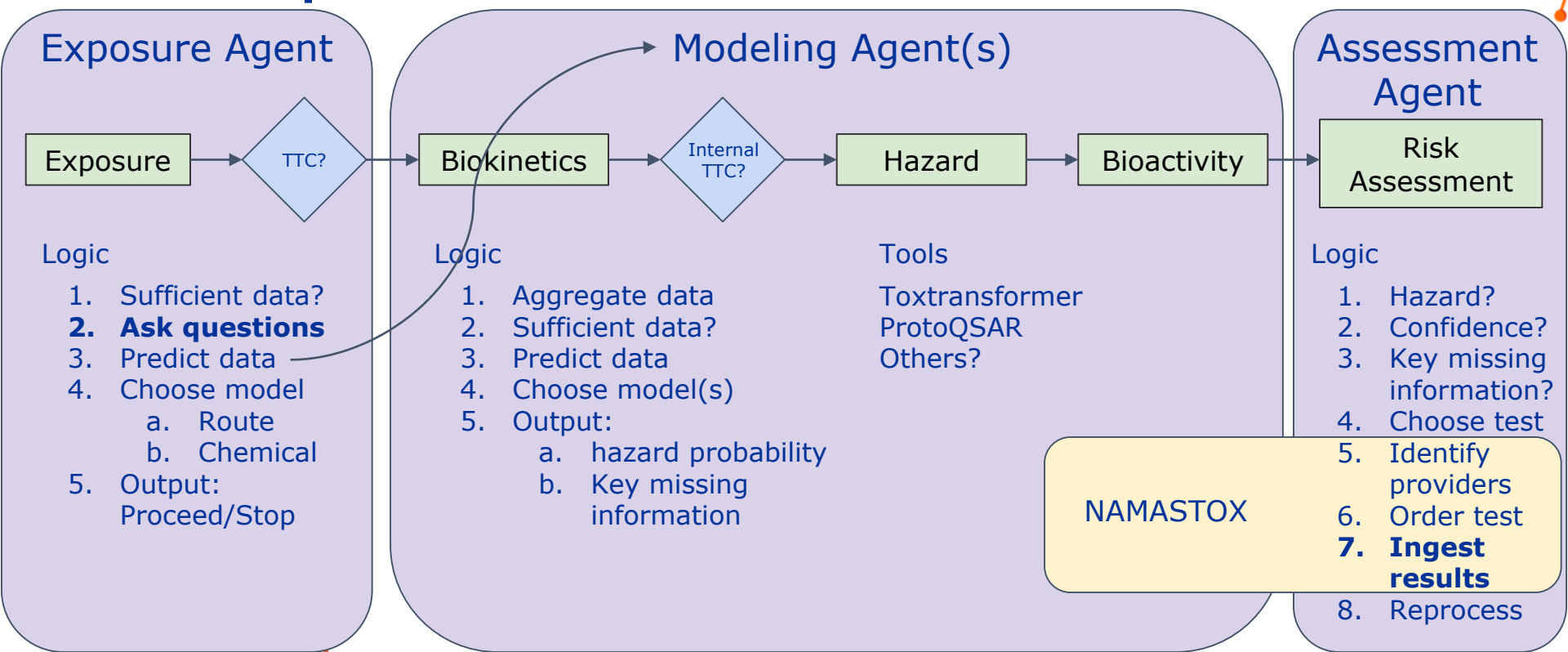
RAP



Next step: OPRA in Toxindex



Next step: OPRA in Toxindex



Toxtransformer: abbreviated

1. Multi-property model

- a. Diverse data
 - i. Trained on 12 databases
 - ii. Predicts for > 4000 properties
- b. Transfer learning
 - i. Allow for conditional predictions (ITS)

2. Easily extended

- a. More data, more power
 - i. New-experimental
 - ii. Existing-literature/database

3. Further testing

- a. Can identify important data gaps

Performance

The Chemprop-Transformer model is trained on a diverse set of 12 chemical property databases, with performance metrics shown below. A separate holdout dataset is maintained for independent evaluation and is excluded from all training procedures.

Dataset	Chemprop	MOLFORMER
BBBP	98.31%	93.7%
Tox21	93.93%	84.7%
ClinTox	95.53%	94.8%
BACE	95.21%	88.2%
SIDER	92.03%	69.0%
ICE	84.69%	
Toxcast	88.37%	
BindingDB	82.44%	
Pubchem	86.94%	
ChEMBL	87.03%	

Table AUC Performance:

AUC performance of chemprop when allowed to see 5 known properties for chemicals across different datasets. Performance is compared to Molformer, a state of the art QSAR only model. [10.1038/s42256-022-00580-7](https://doi.org/10.1038/s42256-022-00580-7)



Predict.toxindex.com

Find & Rank Adverse Outcomes for a Chemical & Prompt

Enter a *toxname* pairs

DEHP:bis(2-ethylhexyl) phthalate
DUP:disinoddecyl phthalate
DTP:disinoddecyl phthalate
DIP:disinoddecyl phthalate
DNP:disinoddecyl phthalate

Enter a prompt (e.g., 'endocrine disruption')

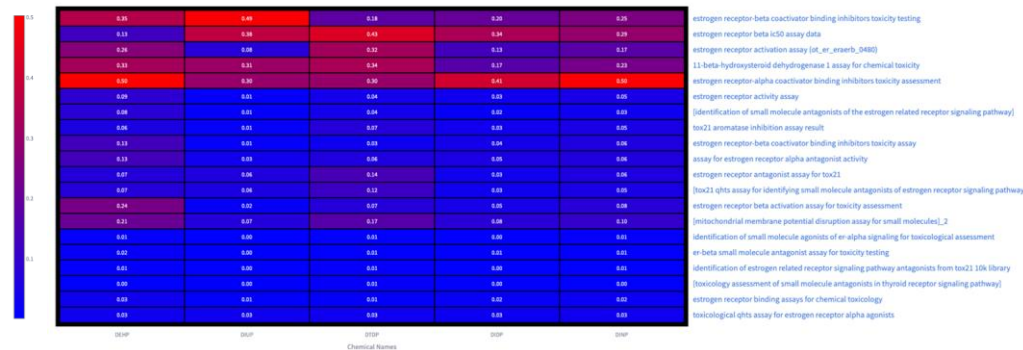
endocrine disruption

Workflow steps

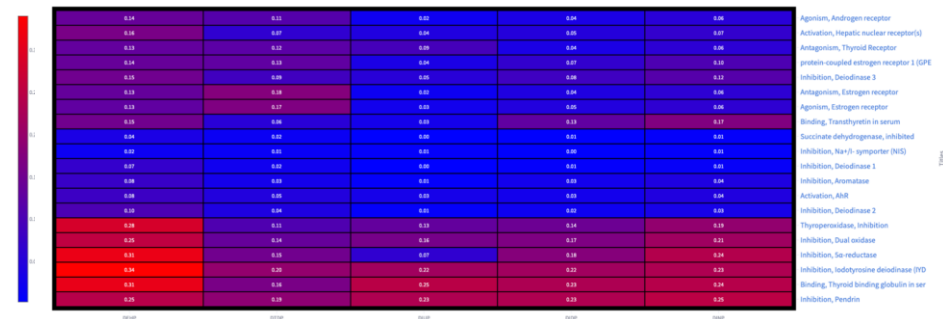
- Aggregate data
- Predict for attributes (Toxtransformer)
 - Includes OECD assays
- Cluster attributes into MIEs/KEs
- Predict for overall hazard based on mechanistic pathways

Property Heatmap

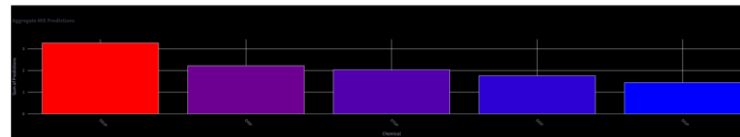
Property Predictions Heatmap



Property Predictions Heatmap



Aggregate Predictions



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Workshop time



1. Explore

a. toxindex.com

- Ask any question

b. predict.toxindex.com

- Choose an existing chemical(s)-hazard pair or create your own

2. Imagine

- What tools should OPRA include?
- What decision trees are necessary to decide when and where to use a tool?
- Which audiences may find value in the output?
- And in what form should that output be delivered?





tj@insilica.co

