



Open **2-3 July 2026** Symposium

Maastricht
The Netherlands

ASPIS Risk Assessment Task Force:
Advancing NGRA through collaboration

Projects: ONTOX/RISK-HUNT3R/PrecisionTox



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aspis-cluster.eu



... was created to ensure scientific alignment and promote convergence towards practical NGRA solutions.

ASPIS RATF serves as a cross-project platform for:

- comparing and sharing methodologies
- exchanging knowledge and ideas
- developing joint activities and case studies
- identifying strengths and limitations of individual approaches



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RISK HUNT3R:

- Alternative Safety Profiling Algorithm (ASPA) & ASPA-assist
- *In silico models* and *in vitro* data

ONTOX:

- AI platforms and models (Toxindex, Toxtransformer, protoQSAR models, ESQlabs models, VEGA models, physiological maps)

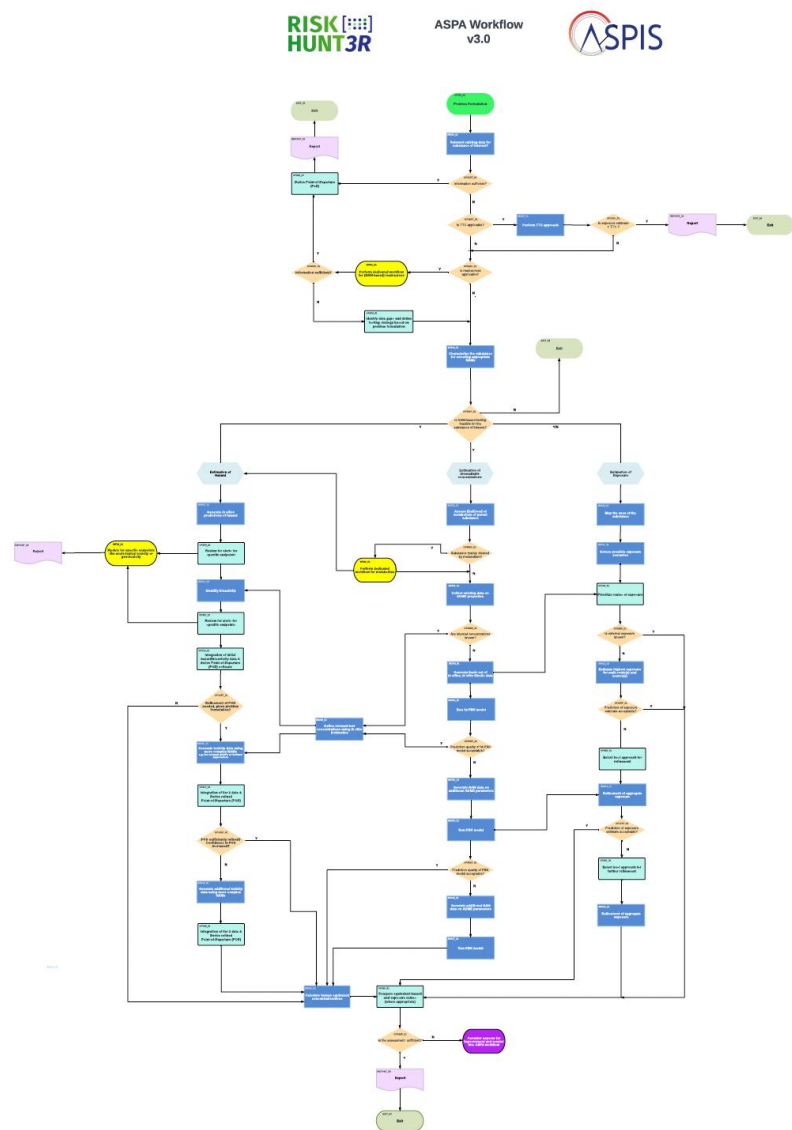
PrecisionTox:

- Non-sentient data (Zebrafish, other model animals)



RISK HUNT3R: ASPA & ASPA assist

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ASPA 3.0

Overview General information Tasks Decisions Notes Report

RA BP4 Case Study

BP4 Case Study (LT180Y0PGK)

Case Study for BP4

Substances	Name	CAS-RN	Structure
	Benzophenone-4	4065-45-6	<chem>COc1cc(O)c(cc1C(=O)c2ccccc2)C(=O)O</chem>

Endpoint	Systemic
AR	Dermal
Species	human
Framework	?
Summary	testing out workflow
Status	Workflow
Step	10
Active nodes	BB003_01 Generate basic set of in silico and in vitro ADME data BB022_01 Identify and specify user scenarios BB009_01 Generate high-throughput in vitro data OP07EF_01 Information sufficient?

workflow.csv

The ASPA assist workflow diagram is a simplified version of the ASPA 3.0 workflow. It starts with 'Problem Formulation' and 'Reset'. A decision point 'Is the problem well-defined?' leads to 'Information Sufficient?'. If 'No', it leads to 'Generate high-throughput in vitro data'. If 'Yes', it leads to 'Generate basic set of in silico and in vitro ADME data'. The workflow then branches into 'Systemic' and 'Dermal' paths. The 'Systemic' path involves 'Generate high-throughput in vitro data' and 'Generate basic set of in silico and in vitro ADME data'. The 'Dermal' path involves 'Generate high-throughput in vitro data' and 'Generate basic set of in silico and in vitro ADME data'. The final outcome is a 'Report'.

ASPA assist



Propylparaben (CAS 94-13-3): Toxicological Risk Assessment



CONTENTS

- ✓ 1. Substance ID
- ✓ 2. Metabolites
- ✓ 3. Chemical Transform...
- ✓ 4. Toxicokinetics (AD...
- 5. Environmental Fate
- 6. Acute Toxicity
- 7. Repeat-Dose Tox
- 8. Genotoxicity
- 9. Carcinogenicity
- 10. Reproductive Tox
- 11. Developmental Tox

1. Substance Identification

Propylparaben (CAS 94-13-3) is a propyl ester of p-hydroxybenzoic acid widely used as a preservative in cosmetics, pharmaceuticals, and food products. **Y12**

KG3

Molecular Weight	180.20 g/mol
LogP	2.98
Water Solubility	500 mg/L at 25°C
Melting Point	96°C

2. Metabolites & Biotransformation

Primary metabolite is p-hydroxybenzoic acid (PHBA) via esterase-mediated hydrolysis, subsequently conjugated as glucuronide and sulfate metabolites.

KG45 **L8**

2000 Databases
100 bln Data Points
90 mln Reg. Documents
127 Computational Tools



Phylotoxicology

Replace traditional animal testing with an evolutionarily diverse suite of biomedical model organisms from multiple branches of the tree of life.



Variation in Susceptibility

Determine safe levels of exposure to chemicals based on genetic variation.



Embedded Translation

Collaborate with regulators and other key stakeholders in project planning, selection of chemicals for investigation, and case studies for applying Precision Toxicology in policy and law.



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The RATF helps establish common principles across the ASPIS projects, focussing on different topics:

- scientific (e.g., integration of data for different endpoints, assessment of uncertainty in individual and combined results, alignment ASPA-OPRA)
- practical (e.g., looking at different tables at the same time when making decisions, using different platforms for risk assessment)
- regulatory (e.g., definition of universal rules for risk assessment vs. making decisions on a case-by-base basis)



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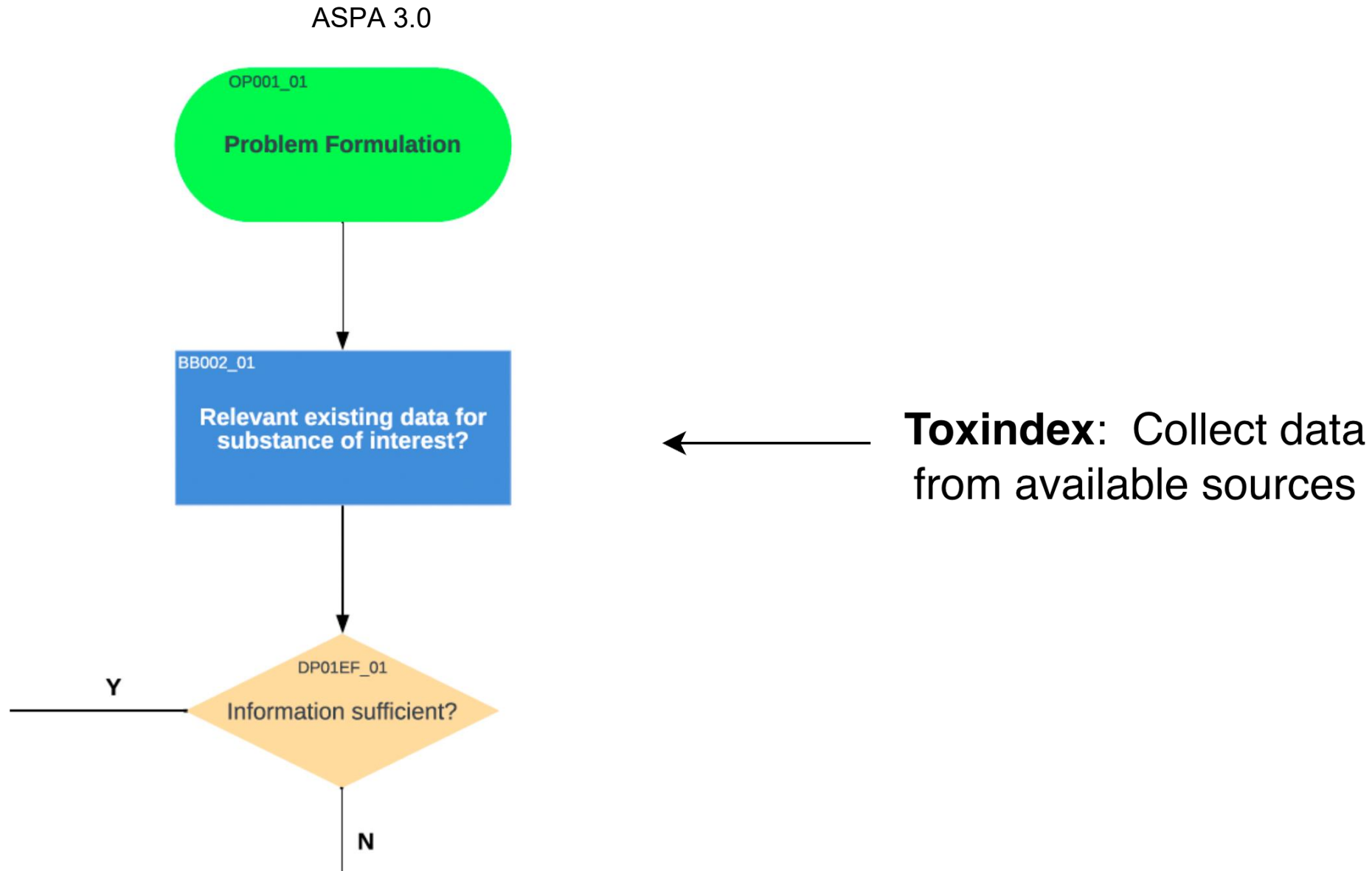


Problem formulation:

*“To assess health risks for Cyproconazole resulting from chronic oral exposure via food and drinking water for the European adult healthy population, with focus on systemic health effects.”**

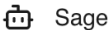
**Exceptions: Arbitrarily, ignore any information specifically about cyproconazole that originates from a regulatory report or regulatory database. e.g. EFSA, ECHA, JMPR, ATSDR, US EPA, IARC. For clarity, non-regulatory sources of information about cyproconazole may be used. Regulatory sources of information about chemicals-not-cyproconazole may be used.*

- 1) Use ASPA, integrated into ASPA-assist, as a baseline framework
- 2) Use AI-tools at different stages to collect/predict data, integrate available data
- 3) Use non-sentient data data to complement risk assessment and recalibrate, or validate AI models and tools





ToxIndex



Sage



Flow



Workspace

WORKSPACE

ASPIS / Cyproconazole

> flow-results

01-Physchem - No Reg.md

02-Physchem - Yes Reg.md

03-Toxicokinetic - No Reg.md

04-Toxicokinetic - Yes Reg...

05-Mechanistic - No Reg.md

06-Mechanistic - Yes Reg.md

07-Metabolism - No Reg.md

08-Metabolism - Yes Reg.md

09-Hazard - No Reg.md

10-Hazard - Yes Reg.md

11-Exec Summary - No Re...

12-Exec Summary - Yes R...

13-Comparative Matrix.md

09-Hazard - No Re...

01-Physchem - No ...

01-Physchem - No Reg.md 70 KB

Preview

Edit

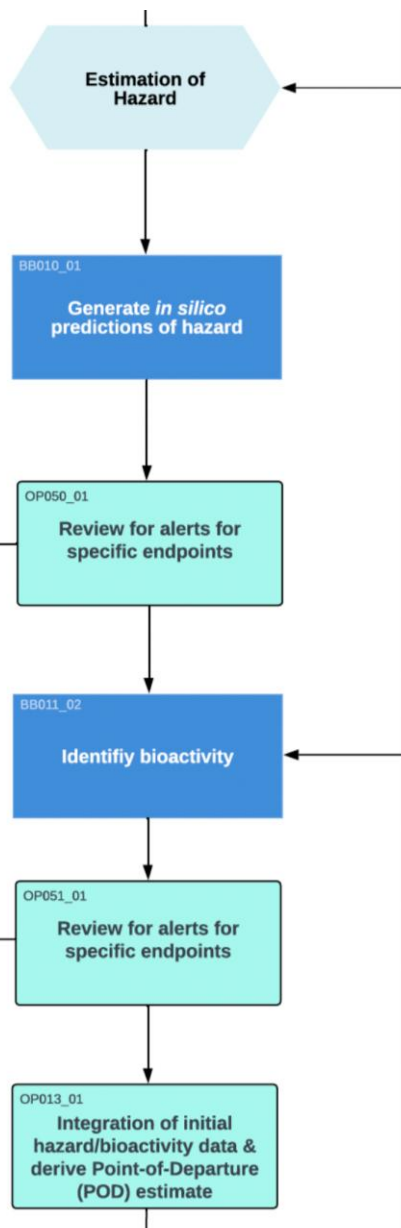
Copy

Property	Value	Source
Name	Cyproconazole	[1]
IUPAC	2-(4-chlorophenyl)-3-cyclopropyl-1-(1,2,4-triazol-1-yl)butan-2-ol	[1]
SMILES	<chem>CC(C1CC1)C(CN2C=NC=N2)(C3=CC=C(C=C3)C1)O</chem>	[1]
CAS	94361-07-6 (QSAR Toolbox) / 113096-99-4 (alternate)	[1][2]
Formula	C ₁₅ H ₁₈ ClN ₃ O	[1]
Molecular Weight	291.77 Da	[1]
InChIKey	UFNOUKDBUJZYDE-UHFFFAOYSA-N	[1]
ChEBI	CHEBI:83748	[1]
ChEMBL	CHEMBL2131954	[1]
PubChem CID	86132	[1]
HMDB	HMDB0250696	[1]
FDA SRS (UNII)	622B9C3E6T	[1]



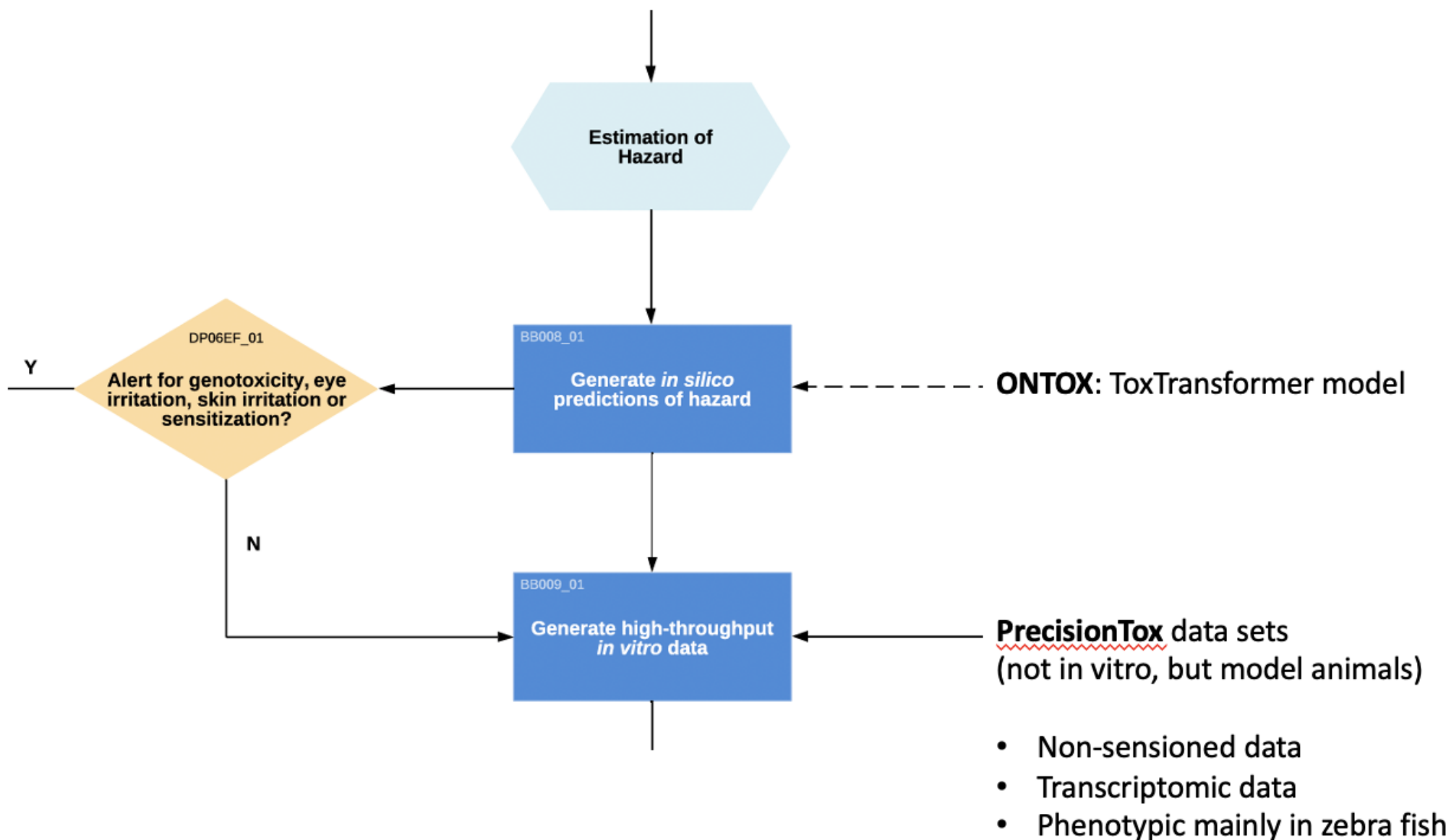
Case study: Cyproconazole (III)

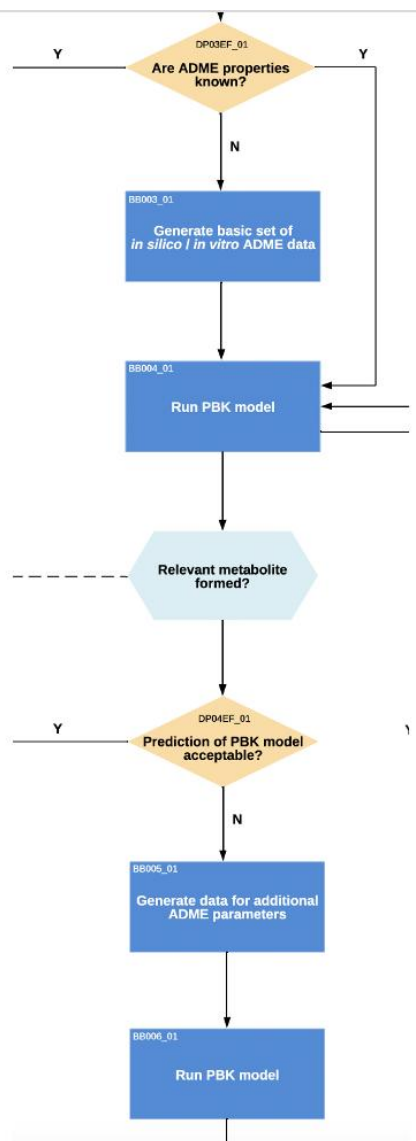
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← Toxtransformer, protoQSAR, UPF, LJMU, DTU, etc.. models

ASPA 3.0





ONTOX: PBK models

RISK HUNT3R: PBK models from UKON, ITEM

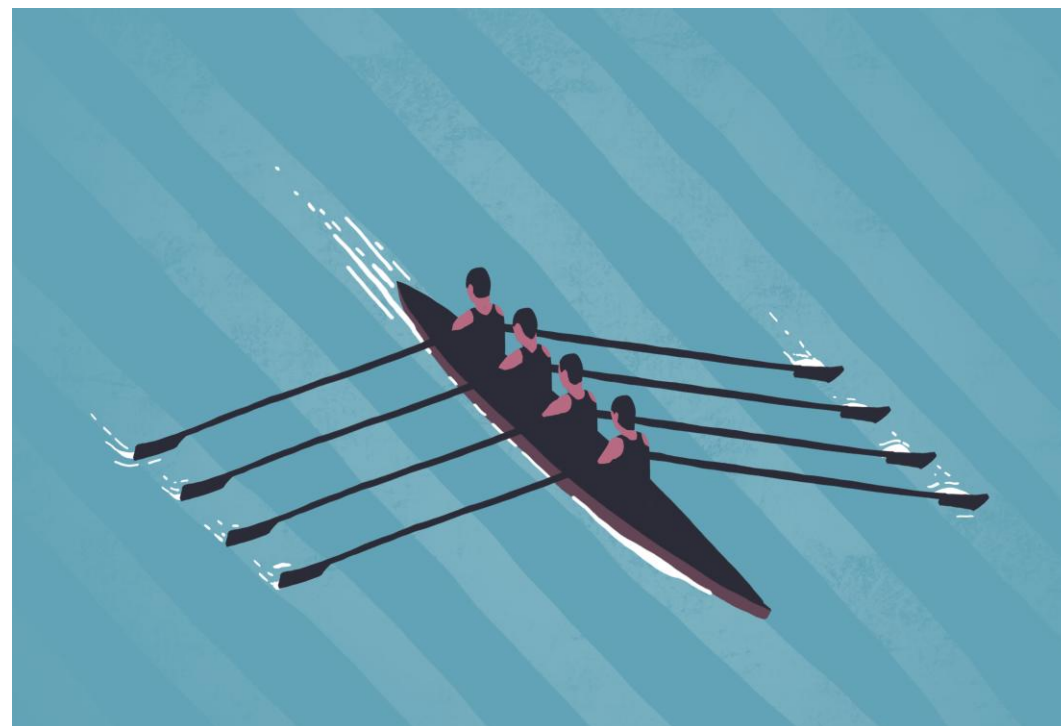
PrecisionTox: data input on bioavailability and metabolism

→ these data can complement PBK models since we have both:
external and internal concentrations



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Mirjam Luijten (RIVM - RISK HUNT3R)
Stefan Scholz (UFZ - PrecisionTox)

We're all on the same boat...





The best ideas often come from the most unexpected places...