ASPIS

ONTOX

PRECISION TOX

RISK HUNT3R

Open Symposium

2-3 July 2026

Maastricht
The Netherlands

ASPIS Risk Assessment Task Force: Advancing NGRA through collaboration

Projects: ONTOX/RISK-HUNT3R/PrecisionTox

These projects have received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement
No. 963845 (ONTOX),
No. 965406 (PrecisionTox),
No. 964537 (RISK-HUNT3R)

aspis-cluster.eu

ASPIS Risk Assessment Task Force (ASPIS RA TF)

… 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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Comparing and sharing methodologies

RISK HUNT3R:

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

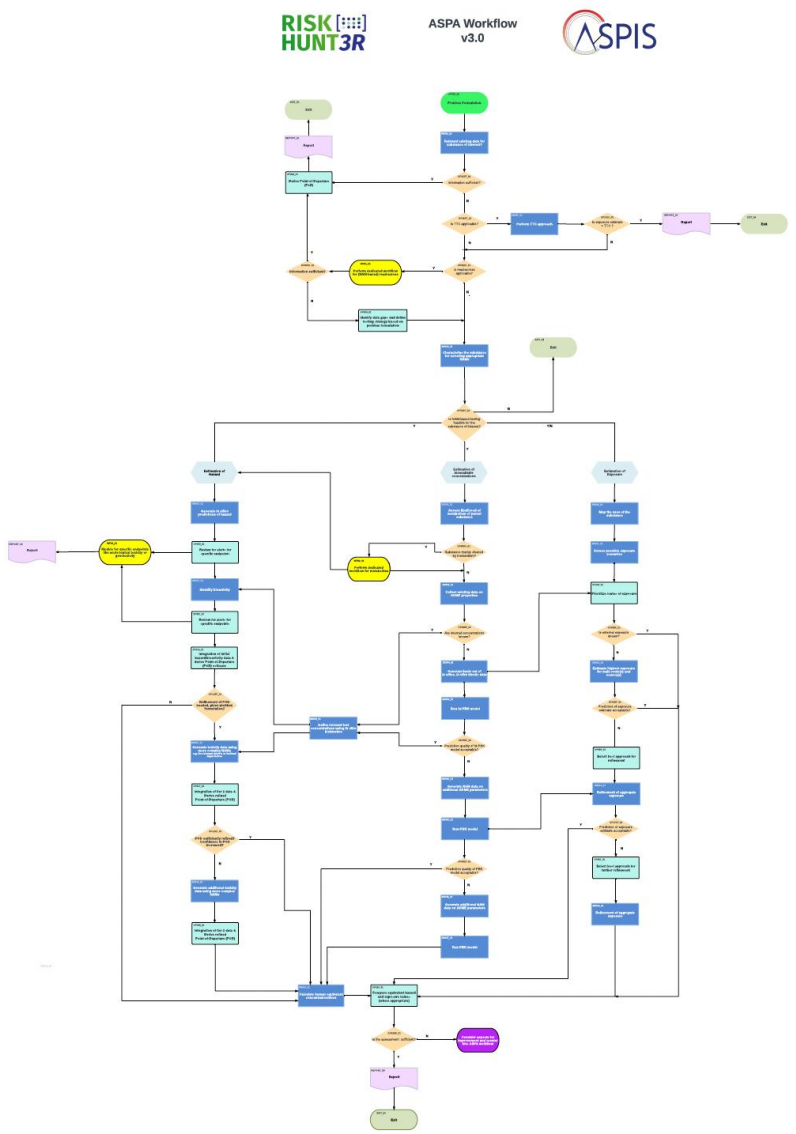
ONTOX:

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

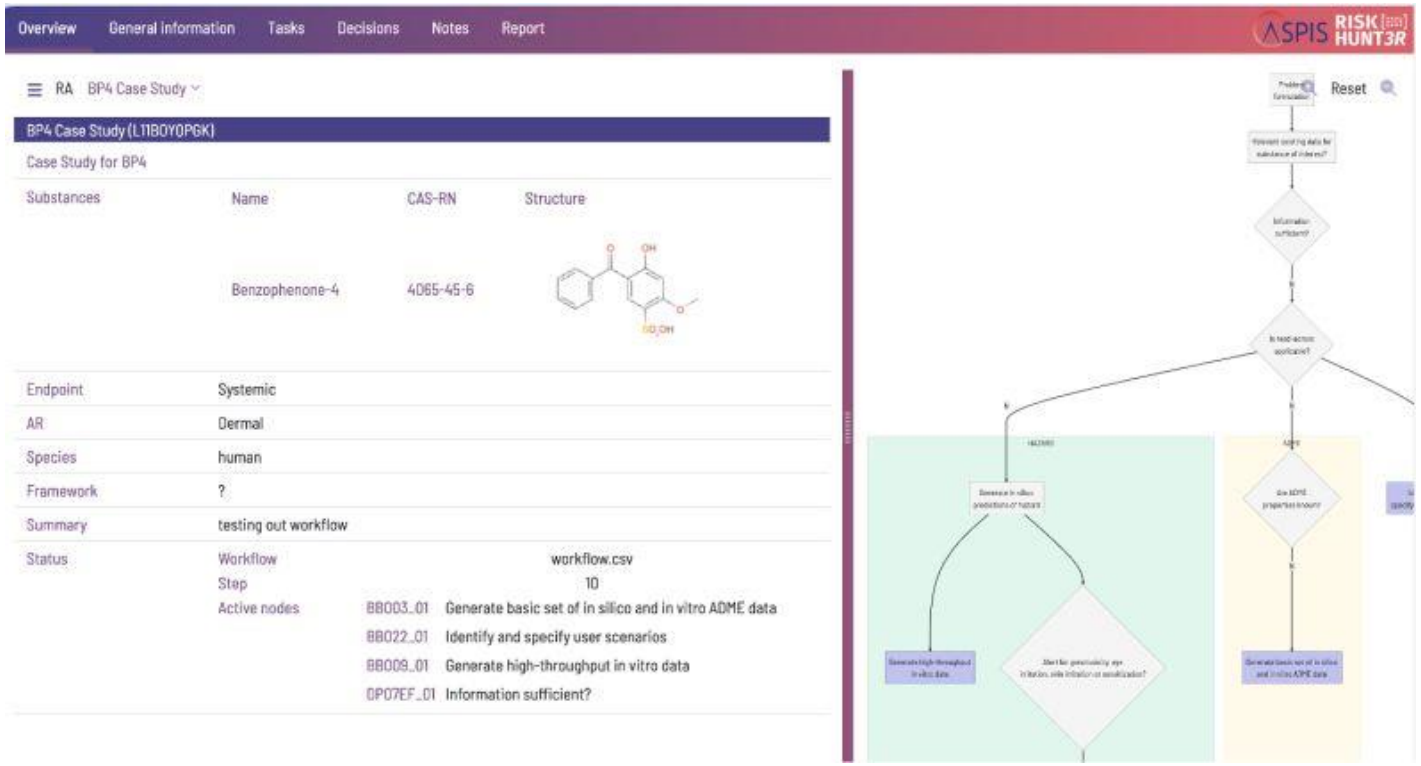
PrecisionTox:

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

RISK HUNT3R: ASPA & ASPA assist



ASPA 3.0



ASPA assist

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

ToxIndex

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

PrecisionTox: non-sentient data

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

Exchanging knowledge and ideas

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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Case study: Cyproconazole (I)

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.*

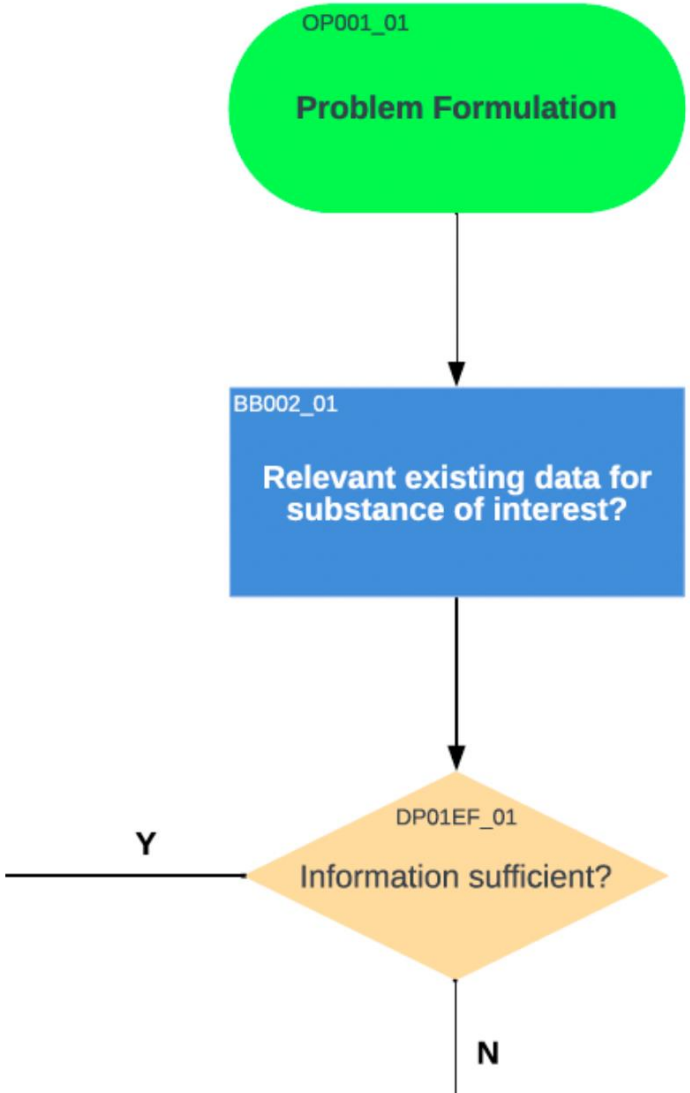
1) Use ASPA, integrated into ASPA-assist, as a baseline framework

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

Case study: Cyproconazole (II)

ASPA 3.0



Toxindex: Collect data from available sources

Collected data - Toxindex

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

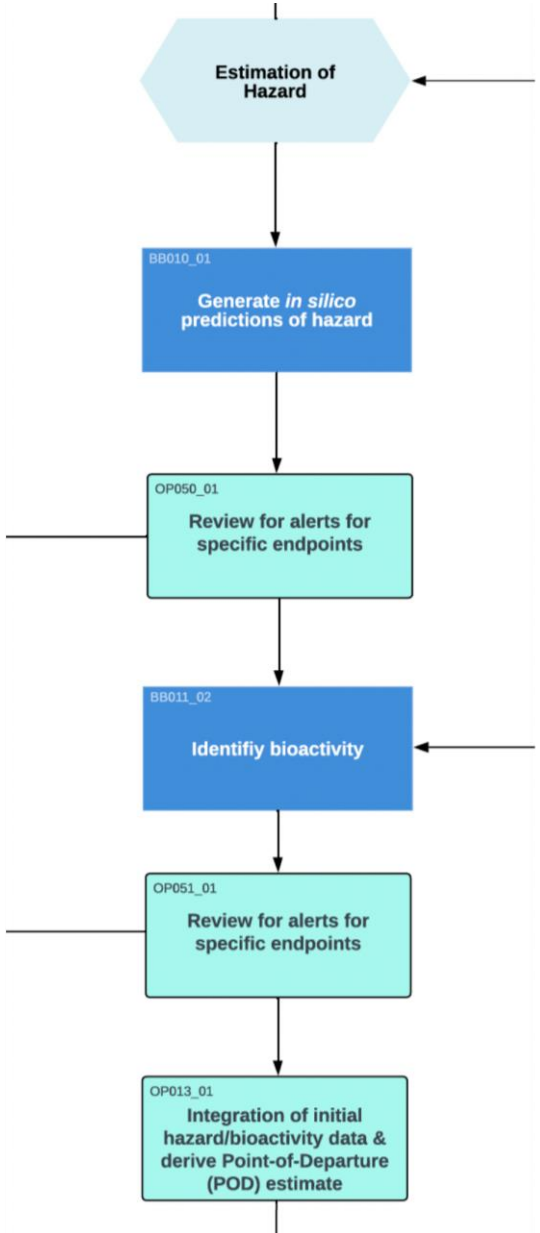
09-Hazard - No Re... | 01-Physchem - No ... | +

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	`CC(C1CC1)C(CN2C=NC=N2)(C3=CC=C(C=C3)Cl)O`	[1]
CAS	94361-07-6 (QSAR Toolbox) / 113096-99-4 (alternate)	[1][2]
Formula	$C_{15}H_{18}ClN_3O$	[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]

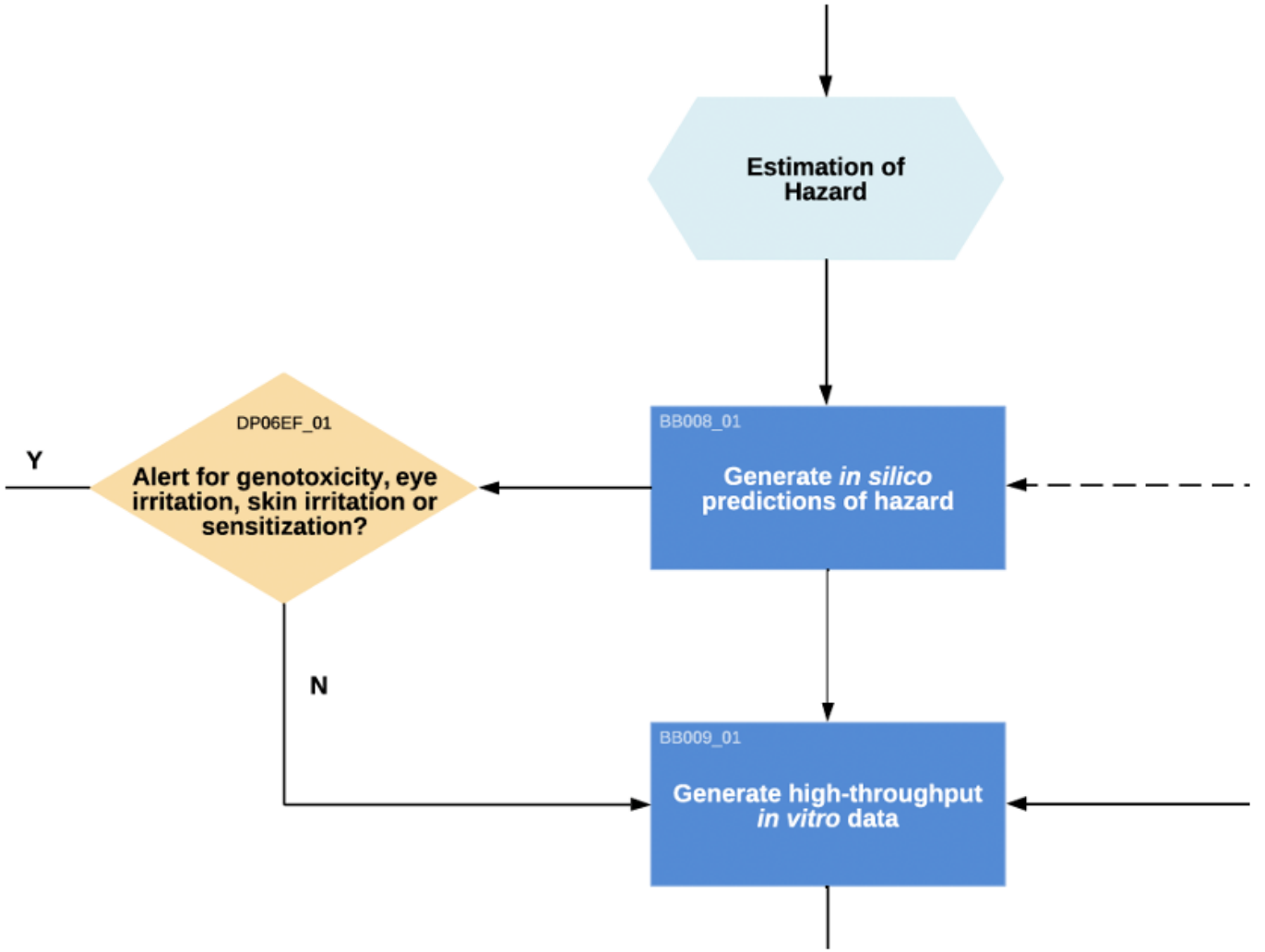
Case study: Cyproconazole (III)



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

ASPA 3.0

Initial ideas ASPA 2.0 (I)

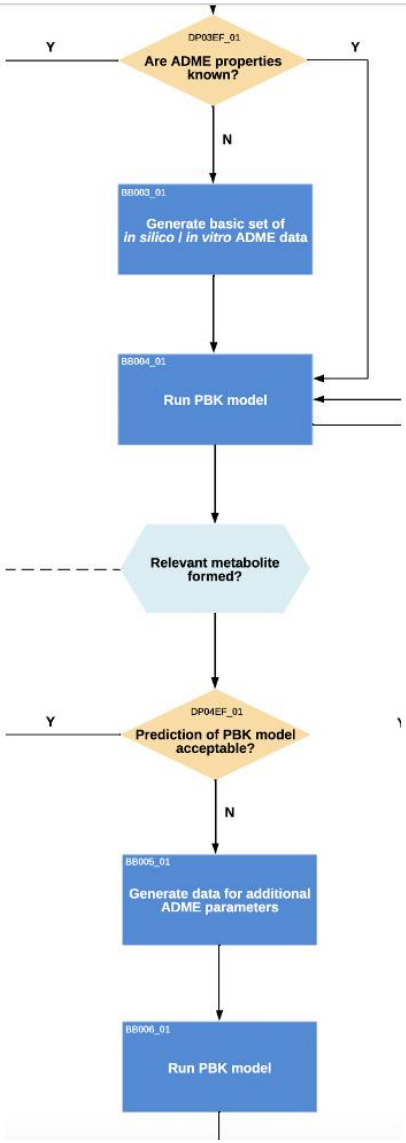


ONTOX: ToxTransformer model

PrecisionTox data sets
(not in vitro, but model animals)

- Non-sensioned data
- Transcriptomic data
- Phenotypic mainly in zebra fish

Initial ideas ASPA 2.0 (II)



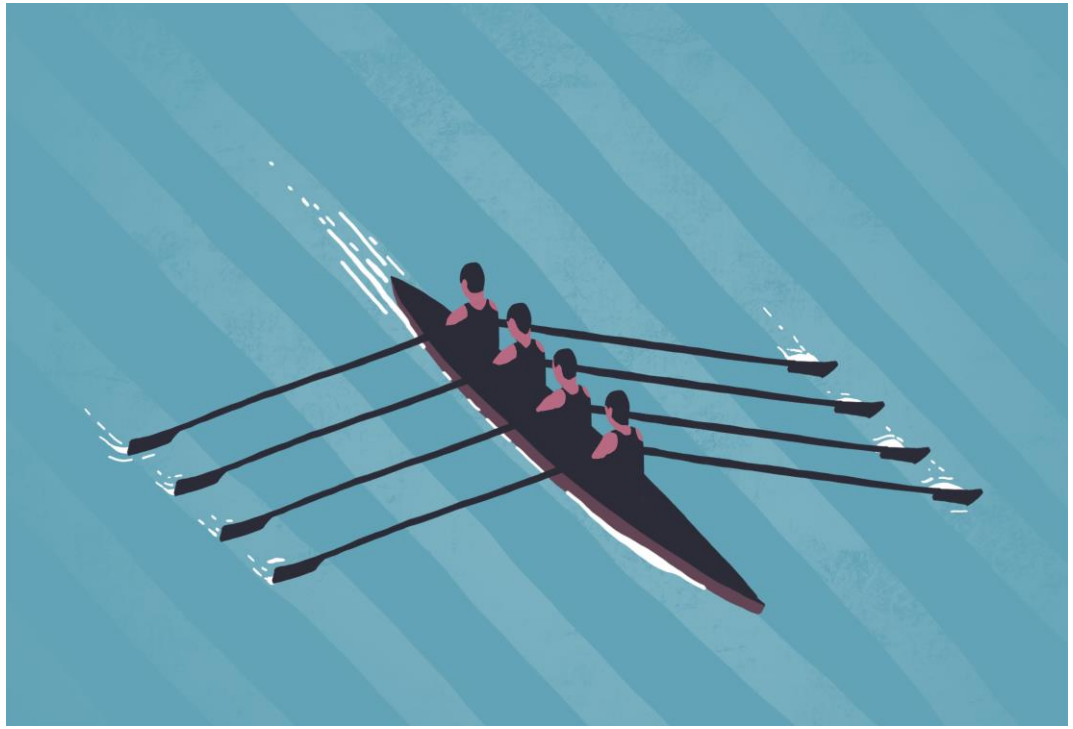
ONTOX: PBK models
RISK HUNT3R: PBK models from UKON, ITEM

PrecisionTox: data input on bioavailability and metabolism
→ these data can complement PBK models since we have both: external and internal concentrations

Members:

TJ Bozada (Insilica – ONTOX)
Hubert Dirven (FHI – ONTOX)
Matthias Herzler (BfR – RISK HUNT3R)
Hennicke Kamp (BfR – RISK HUNT3R)
Helena Kandarova (CEM – ONTOX)
Karolina Kopańska (CAAT – ONTOX)
Cyrille Krul (HU – ONTOX)
Mirjam Luijten (RIVM – RISK HUNT3R)
Stefan Scholz (UFZ – PrecisionTox)

We're all on the same boat…



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