ASPIS

ONTOX

PRECISION TOX

RISK HUNT3R

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)

This output reflects only the author's view and the Directorate-General for Research and Innovation (DG RTD) cannot be held responsible for any use that may be made of the information contained therein.

Open Symposium

2-3 July 2026

Maastricht
The Netherlands

ONTOX Probabilistic Risk Assessment (OPRA):

An AI-enabled framework

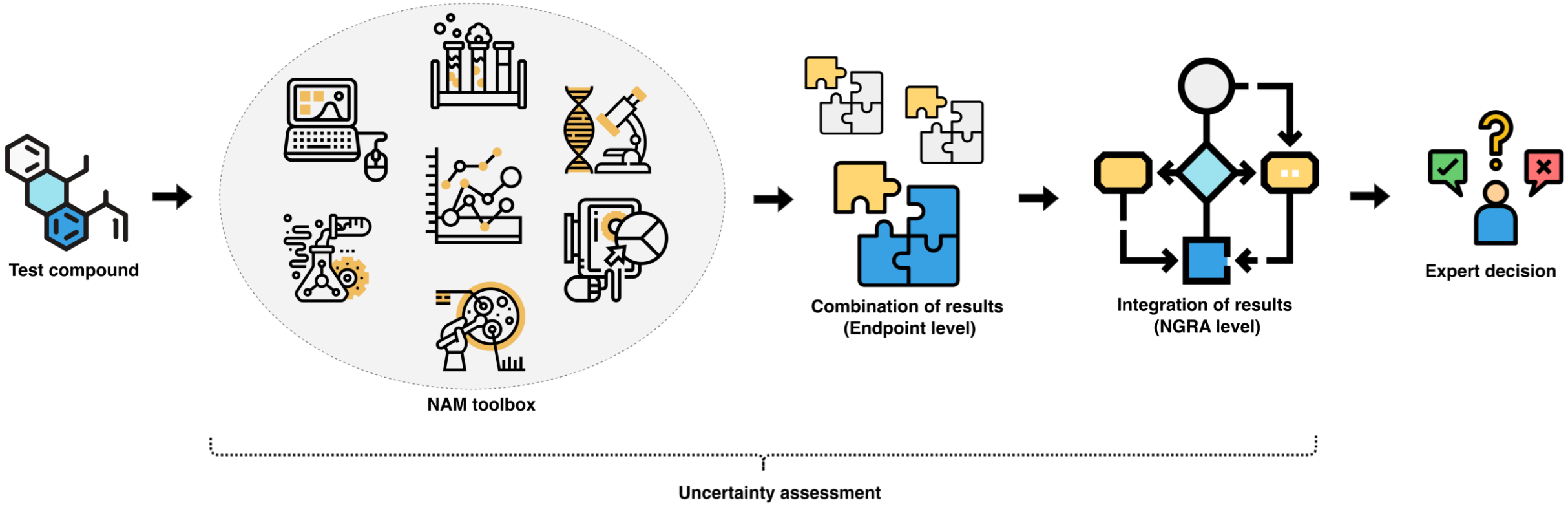
Karolina Kopańska, PhD

Johns Hopkins Center for Alternatives to Animal Testing (CAAT)

Project: ONTOX

Next Generation Risk Assessment (NGRA) …

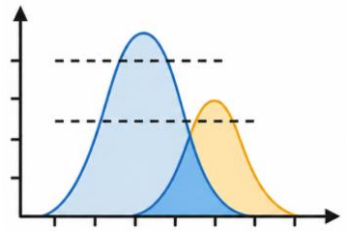
… is defined as a hypothesis-driven (and exposure-led) approach that integrates results derived from the New Approach Methodologies (NAMs)



Methods for uncertainty assessment and combination of evidence

Probabilistic methods

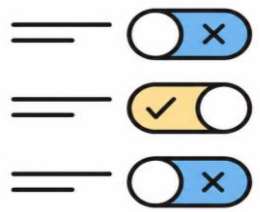
- Require data for calculations
- Assumes that uncertainty can be represented as distributions



Examples: Frequentist (MLE), Bayesian (inference, networks)…

Non probabilistic methods

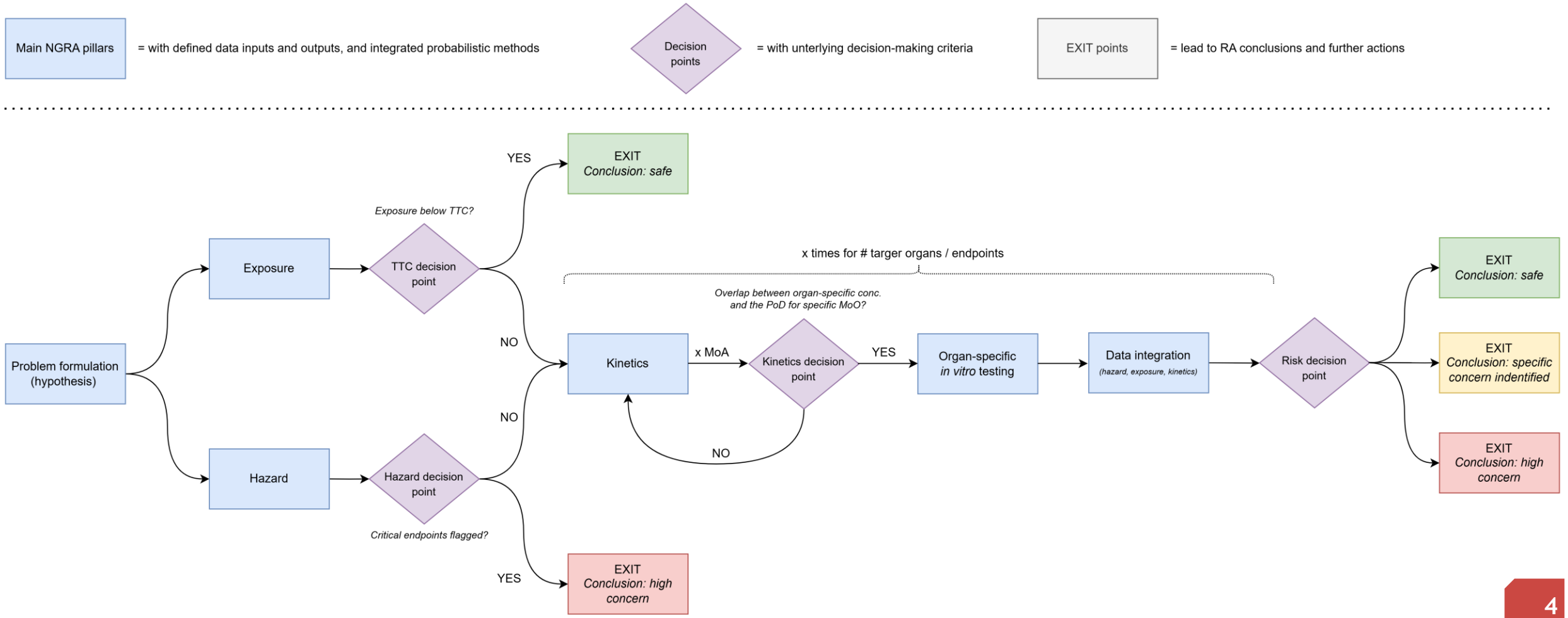
- When data is incomplete or low quality
- Output as range of possibilities, uncertainty represented as intervals, bounds, sets..



Examples: Dempster-Shafer Theory, Fuzzy theory, Interval analysis…

ONTOX Probabilistic Risk Assessment (OPRA)

$$NGRA + uncertainty\ assessment\ methods + AI = OPRA$$



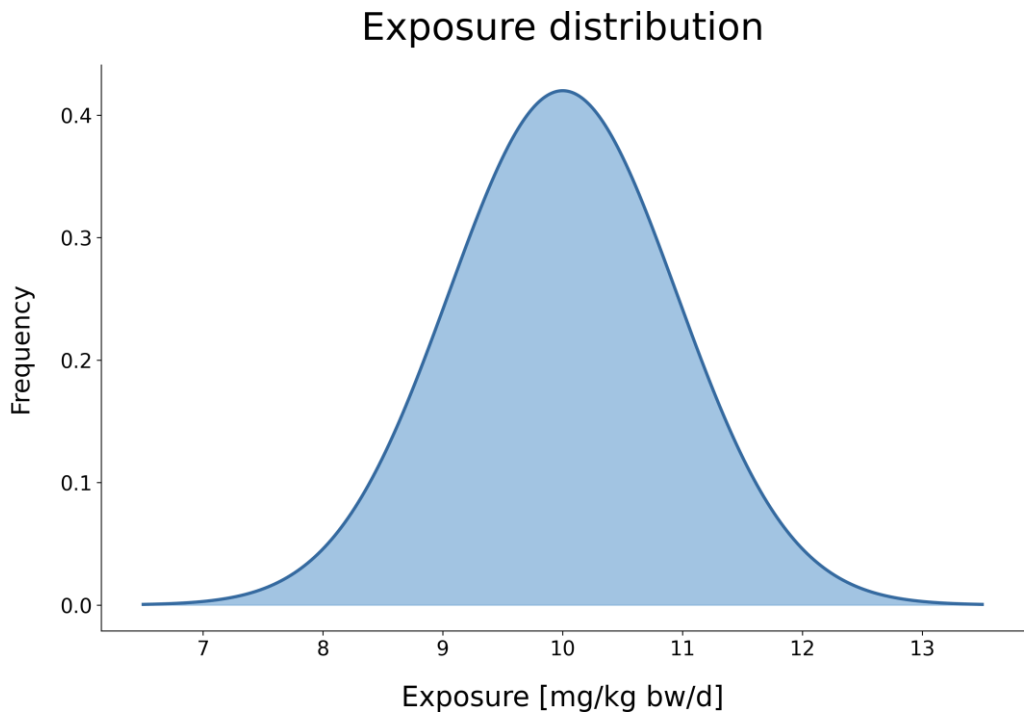
Example main risk assessment pilar

Clearly defined inputs and outputs are essential for effective AI implementation

Input:

- **Exposure scenario**
  - Exposure frequency, duration, route
  - Population of interest
- **Probabilistic framework**
  - Frequentist (MC)
- **Exposure simulation**
  - Mean
  - Data spread (e.g., standard deviation)
  - Data distribution (e.g., normal)

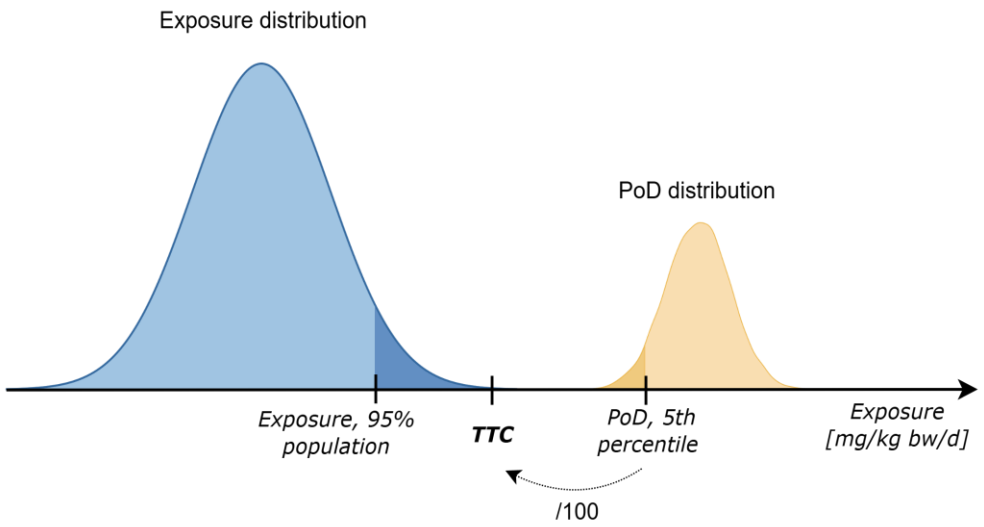
Output:



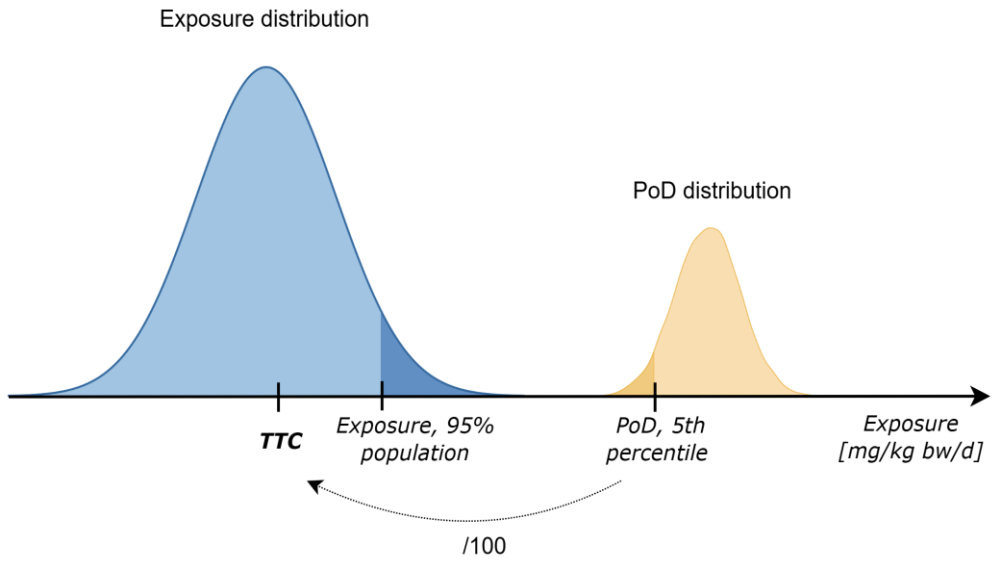
Example decision point

Modernized Threshold of Toxicological Concern (TTC)-based approach

- Scenario with no concern



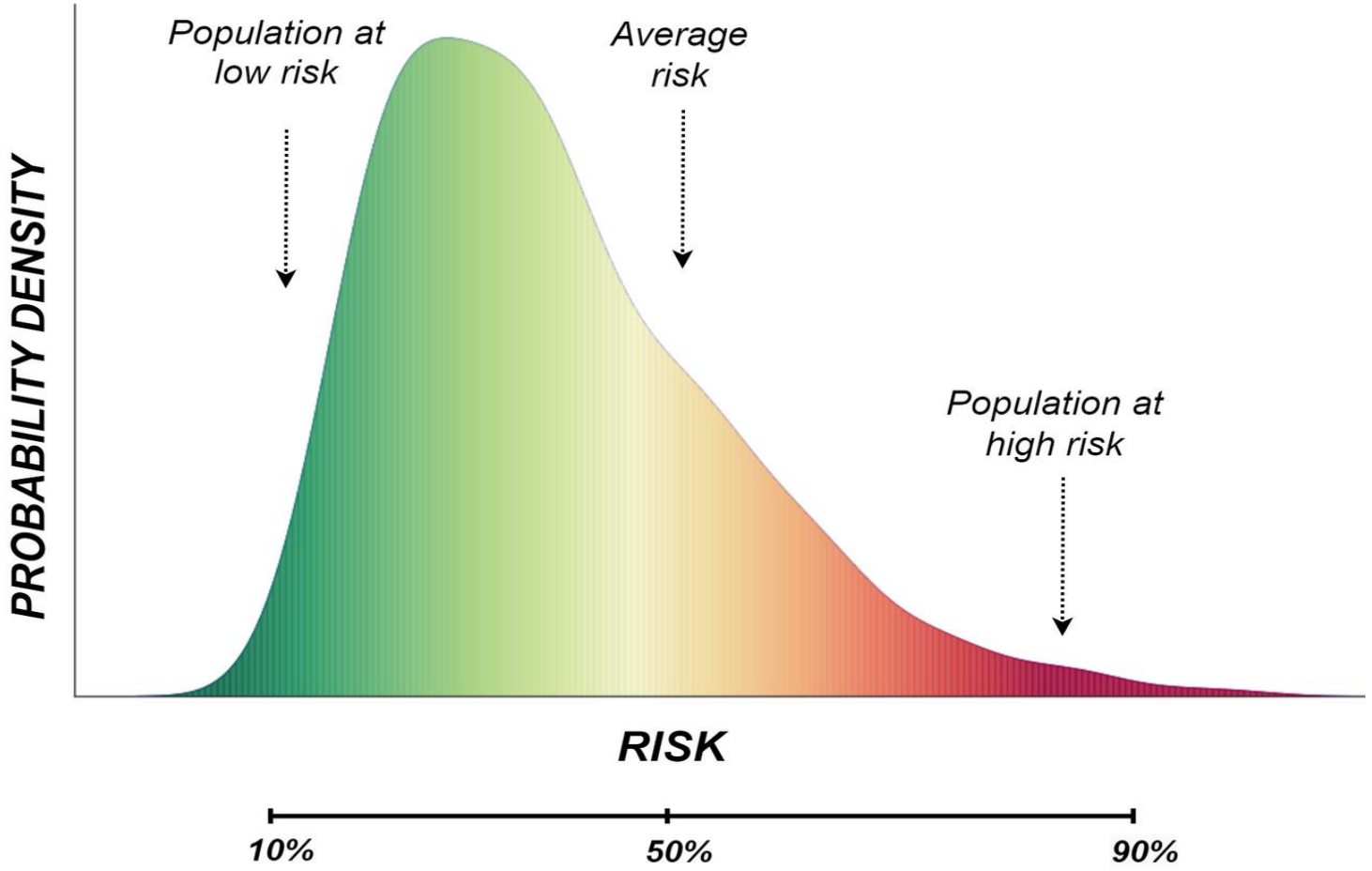
- Scenario with concern



From thresholds to odds: the role of thresholds of toxicological concern (TTC) in modern risk assessment

Karolina Kopańska[1,2,**], Costanza Rovida[2,3**], Eric Antignac[4], Tara Barton-Maclaren[5], Ian Corgreave[6], Sylvia E. Escher[7], Matthias Herzler[8], Heli M. Hollnagel[9], Eliška Kuchovská[10], Alexandra Maertens[11], Julia M. Malinowska[12], Grace Patlewicz[13], Tomasz Sobański[14], Thomas Hartung[1,2,11,15,16***]

The goal: informed and transparent assessment



Main NGRA-related challenges (I)

Open Symposium 2-3 July 2026 Maastricht The Netherlands

Substance

Cyproconazole — 2-(4-chlorophenyl)-3-cyclopropyl-1-(1,2,4-triazol-1-yl)butan-2-ol | **CAS 94361-06-5** | MW 291.77 Da | $C_{15}H_{18}ClN_3O$

A 1,2,4-triazole systemic fungicide. Not approved in the EU (Reg. 1107/2009) and withdrawn in GB.

Classified as a **Highly Hazardous Pesticide** (HHP Types I and II) by FAO/WHO and PAN criteria.

Regulatory Classifications *(Revision 2 — Gaps Closed)*

Authority	Classification	Source
CLP (2013)	**H301 + H373** (STOT RE 2, liver) + **H360D** (Repr. 1B) + **H400 + H410**	PPDB (A5)
US EPA (1992)	**Group B2** — Probable human carcinogen	OEHHA CIC 2011
WHO	**Class II** — Moderately hazardous	PPDB
HHP Type I (FAO/WHO)	**Yes** — Criterion C4 (Reproductive tox 1A/1B ≈ H360)	PPDB (Doc 02)
HHP Type II (PAN)	**Yes** — R04 (Reproductive tox 1A/1B), **R05** (Confirmed ED per WHO)	PPDB (Doc 02)

Regulatory Reference Doses *(Revision 2 — Gap Closed)*

Parameter	Value (mg/kg bwd)	Quality	Source
ADI (Acceptable Daily Intake)	0.02	A5	PPDB
ARfD (Acute Reference Dose)	0.02	A5	PPDB
AOEL (Acceptable Operator Exposure Level)	0.02	A5	PPDB
AAOEL (Acute AOEL)	—	—	PPDB

1. Key Physicochemical Properties

Property	Value	Unit	Source
Molecular weight	291.77	g/mol	Doc 01
Log K_{ow} (exp.)	2.90	(—)	Doc 01, Ref 3
Water solubility (20 °C)	126 (± 140)	mg/L	Doc 01, Ref 3/23
Vapor pressure (25 °C)	2.59×10^{-7}	mmHg	Doc 01
Melting point	107.5	°C	Doc 01
Boiling point (pred.)	>250 (exp.)	°C	Doc 02
Henry's Law constant	7.1×10^{-10}	atm·m³/mol	Doc 02
pK_a (triazole N)	2.9	(—)	PPDB A5
Dissociation constant (pH 7)	No dissociation	(—)	Doc 02
Density (20 °C)	1.26 (g/mL)	g/mL	Doc 02
Octanol/water K_d (pred.)	125	L/kg	EPI Suite 4.11
UV-Vis λ_{max} (MeOH)	295–297	nm	PPDB A5

2. Environmental Fate (Modelled/Experimental)

Endpoint	Value	Unit	Source
DT_{50} soil (aerobic)	110	days	Doc 02
DT_{50} soil (anaerobic)	422	days	Doc 02
DT_{50} water (hydrolysis)	Stable	(—)	Doc 02
DT_{50} sediment	> 365	days	PPDB
K_{oc} (exp.)	364	mL/g	PPDB A5
BCF (fish)	15–59X	(—)	EPA EFED
BAF (exp.)	11–13	L/kg	Doc 02
K_{froc}	3.04	(—)	Doc 02
GUS leach. index	3.04	(—)	Doc 02
Level III fugacity (air)	Low	(—)	PPDB

3. Toxicokinetics (Summary)

Parameter	Value	Unit	Source
Oral absorption	≥ 70	%	Doc 03/04
Dermal absorption	5–20	%	Doc 03/04
Oral bioavailability	80–90	%	Doc 03/04
Plasma protein binding	80–90	%	Doc 03/04
BBB penetration	Probable	(—)	Doc 03
Metabolism (rat)	Extensive	(—)	Doc 04
Elimination $t_{½}$ (rat)	1.21 (n=36)	h	Doc 03
Primary route	Feces (65–80%)	(—)	Doc 03
Renal excretion	16–33	%	Doc 03

4. Toxicity Data (Experimental)

4.1 Acute Toxicity

Endpoint (Species)	Value	Unit	Source
LD_{50} Oral (Rat)	1095	mg/kg	Doc 09, 10
LD_{50} Dermal (Rat)	>2000	mg/kg	Doc 12
LD_{50} Inhalation (Rat, 4 h)	>5.85	mg/L	Doc 10
LD_{50} Oral (Mouse)	942	mg/kg	Doc 09
LD_{50} Dermal (Mouse)	>2000	mg/kg	Doc 09
LD_{50} Inhalation (Mouse, 4 h)	>5.85	mg/L	Doc 09
LC_{50} Fish (96 h)	0.23	mg/L	Doc 10
EC_{50} Daphnia magna (48 h)	0.026	mg/L	Doc 10
EC_{50} Algae (72 h)	0.028	mg/L	Doc 10
LD_{50} Honeybee (contact 48 h)	>100	µg/bee	PPDB A5

4.2 Repeated Dose / Chronic Toxicity

Study	Species	Dur.	NOAEL	LOAEL	Unit	Source
90-day	Rat	90 d	2.2	6.4	mg/kg/d	Doc 12
90-day	Mouse	90 d	1.4	4.2	mg/kg/d	Doc 12
90-day (dermal)	Rat	90 d	>50	—	mg/kg/d	Doc 13
1-year	Dog	1 y	0.5	1.5	mg/kg/d	Doc 14
2-year	Rat	2 y	0.25	1.0	mg/kg/d	Doc 14
18-month (onc)	Mouse	18 m	0.1	0.3	mg/kg/d	Doc 15
Carcinogenicity (rat)		2 y	Negative	—	—	Doc 15
Reproductive tox (2-gen)	Rat	2 gen	0.22	0.7	mg/kg/d	Doc 16
Developmental tox (rat)	Rat	GD 6-15	0.2	0.6	mg/kg/d	Doc 17
Neurotoxicity (DNT)		90 d	—	—	—	Doc 18

5. Mechanistic / Mode of Action (Key Endpoints)

Endpoint	Finding	Evidence
Aromatase (CYP19) inhibition	Yes — decreased estrogen production	In vitro, rat
ER binding	Antagonist	In vitro
AR binding	Antagonist	In vitro
Oxidative stress	Increased ROS in vitro	Cell-based
Genotoxicity (Ames)	Negative	Bacterial reverse mutation
Chromosomal aberration	Positive (EPA)	In vitro (CHO)
Micronucleus	Negative	In vivo (rat BM)

6. Key Gaps / Uncertainties

Area	Description	Impact
Acute inhalation LC_{50}	Only limit test available	Moderate
Aquatic chronic NOEC	Limited species coverage	Moderate
ED (endocrine disruption)	MOA data supportive but not conclusive	High
Immunotoxicity	No data	Moderate
Mixture effects	Not evaluated	Low

7. Summary Benchmarks (Regulatory Context)

Benchmark	Value	Unit	Basis	Source
ADI	0.02	mg/kg bw/day	NOAEL 2.2 mg/kg/dy / 100 (rat, 90-d)	PPDB
ARfD	0.02	mg/kg bw	NOAEL 2.2 mg/kg / 100	PPDB
AOEL	0.02	mg/kg bw/day	Same as ADI	PPDB
DRfA (oral, cancer slope factor)	0.012	$(mg/kg/day)^{-1}$	Q1*TR = 2.4 (upper bound)	EPA (Rereg)
Margin of Exposure (MOE)	250	(—)	BMDL10 (liver) 5 mg/kg/day / ADI 0.02	Internal calc

8. Consolidated Hazard Profile (Top Findings)

Endpoint	Classification / Outcome	Confidence
Acute oral toxicity	GHS Cat. 3 (H301)	Very High
Genotoxicity	Negative (in vitro caveat)	Very High
Carcinogenicity	EPA Group B2 (probable) / CLP Cat. 2	Very High
Reproductive toxicity	Repr. 2 (H361f)	High
Endocrine disruption	Confirmed ED (per WHO/PPDB)	Very High
Aquatic toxicity (acute)	Cat. 1 (H400)	Very High
Aquatic toxicity (chronic)	Cat. 1 (H410)	Very High
Persistence	Very Persistent	Very High
Bioaccumulation	Low (BCF 15–59X)	High
Neurotoxicity	Possible class concern	Medium

ONTOX Probabilistic Risk Assessment (OPRA): An AI-enabled framework

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

Automated Assessments

REACH dossiers, chemical risk assessments, OEL/HBEL reports, ingredient safety reviews. Provide a substance and get an assessment with an audit trail you can hand to a regulator.

Conversational AI

Ask a question in plain language, get a cited answer. The AI has access to the full dataset and model library, so you can explore data, run predictions, or kick off assessments without leaving the chat.

Knowledge Graph

Hundreds of curated datasets linking chemicals to their hazards, classifications, and study results

Literature

Full-text search across 4M+ regulatory documents from EPA, ECHA, WHO, and 50+ other sources

Predictive Models

ToxTransformer, QSAR Toolbox, and hundreds of other models covering 4,000+ endpoints

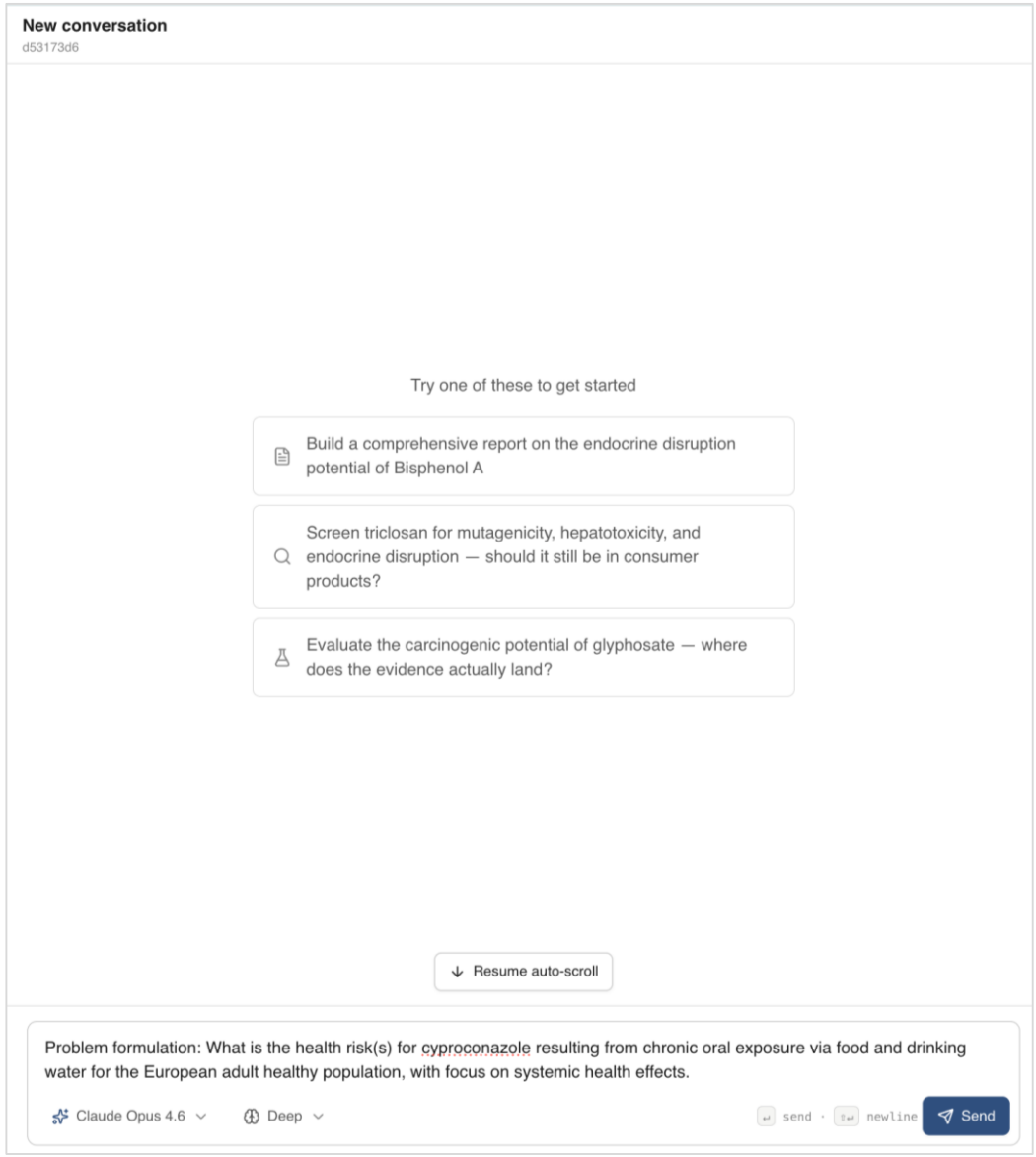
2000 Databases

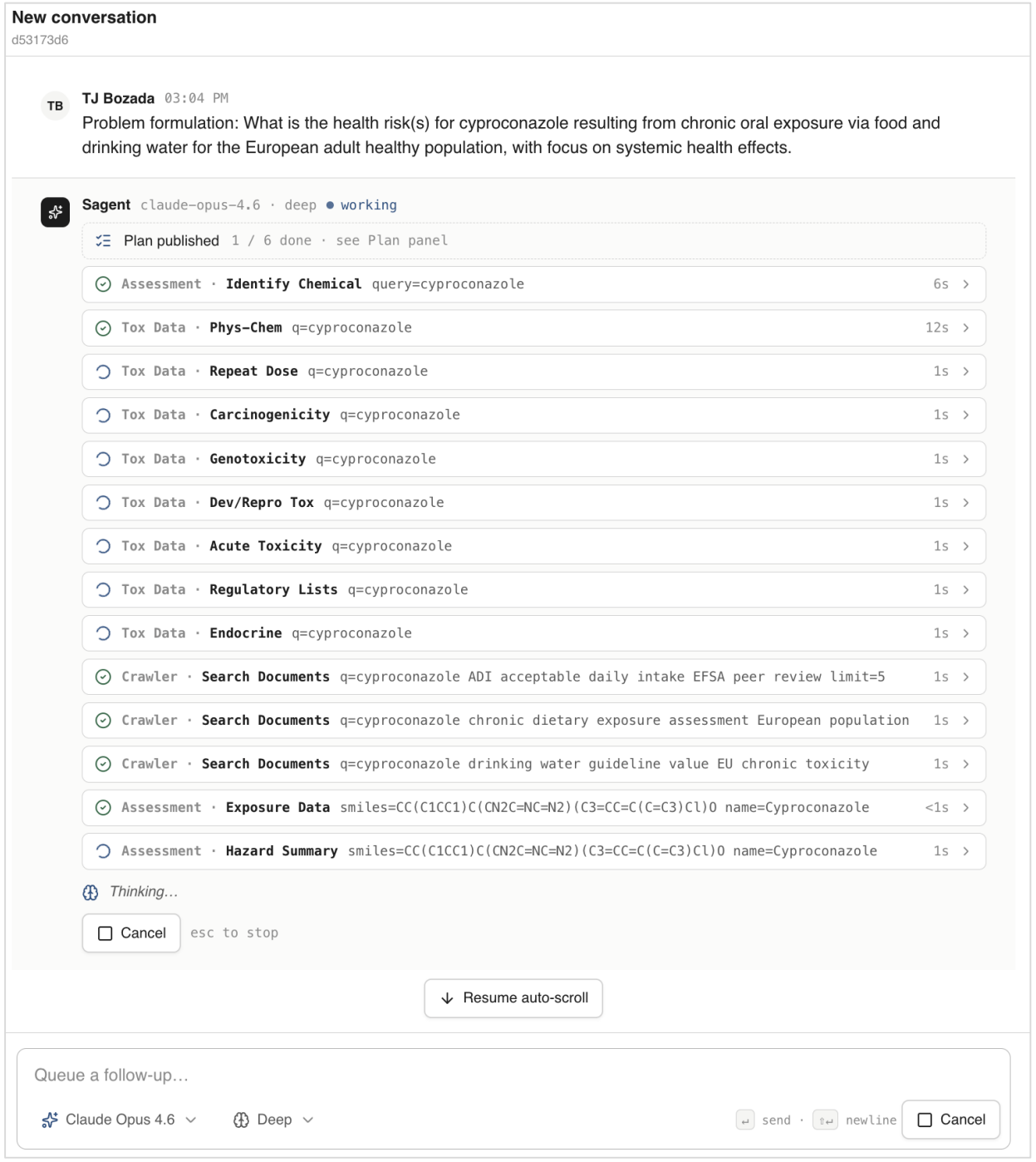
100 bln Data Points

90 mln Regulatory Documents

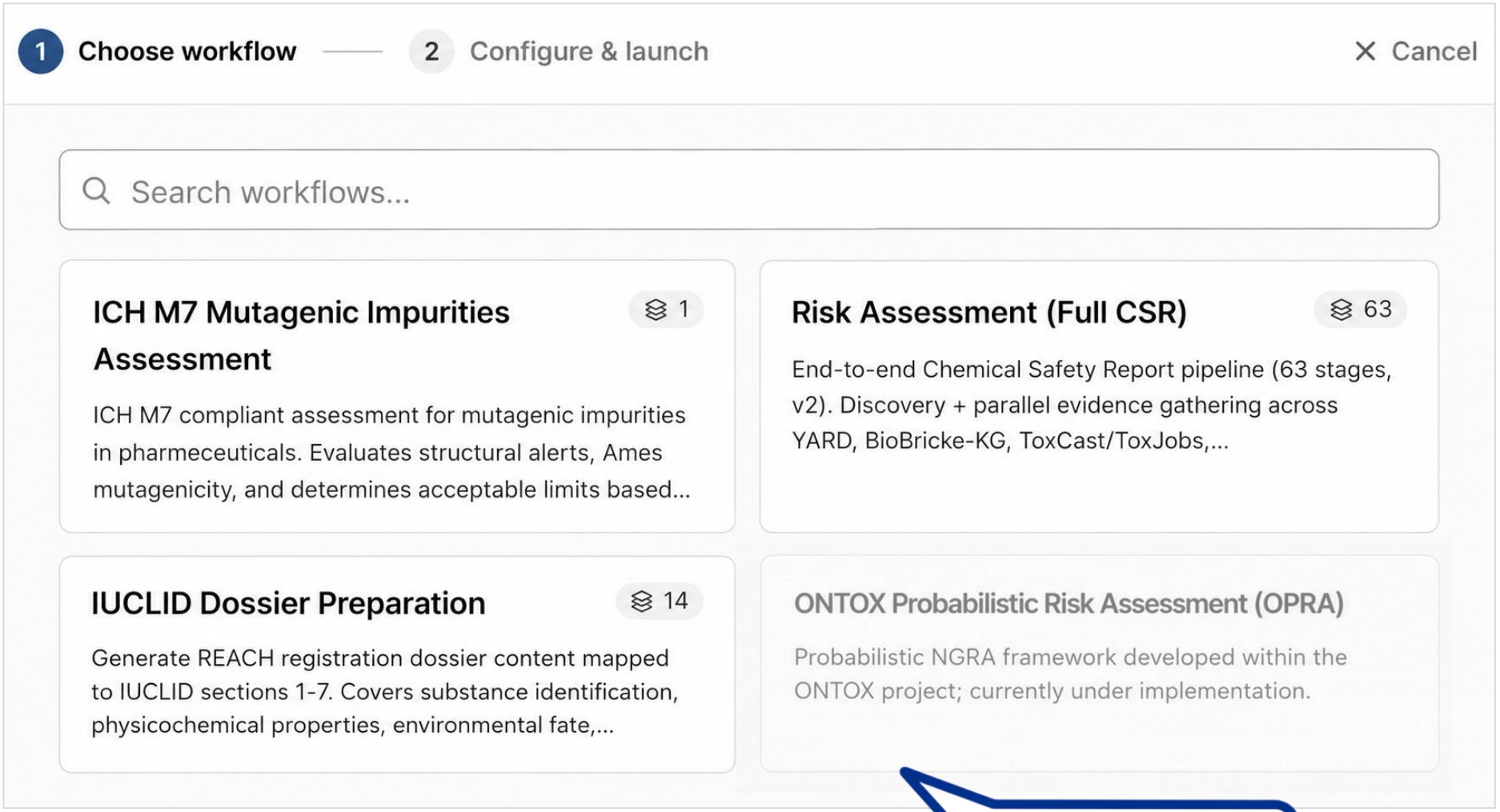
127 Computational Tools

Conversational AI





ONTOX Probabilistic Risk Assessment (OPRA): *An AI-enabled framework*



Working on it!

Main NGRA-related challenges (II)

Monte Carlo simulation is a useful method for estimation when it is difficult to obtain an analytical solution (Vose, 1996). To estimate the expected value of the quantity of interest, let $\theta_1, \ldots, \theta_M$ be random samples drawn from the posterior distribution $f(\theta \mid \mathbf{x}, t_0)$. For each $j \in \{1, \ldots, M\}$, let $x^j_{n+1}, \ldots, x^j_{n+N}$ be random samples drawn from the assessment variable conditional on θ_j. Then, $\widehat{h}(\theta_j)$ is a Monte Carlo estimate for $h(\theta_j)$:

$$h(\theta_j) \approx \widehat{h}(\theta_j) := \frac{1}{N}\sum_{i=1}^{N} \mathbf{1}_{\left\{g\left(x^j_{n+i}\right) \geq g^*\right\}}. \tag{6}$$

Thus, sample j of the quantity of interest $\widehat{h}(\theta_j)$ is not directly computed from θ_j, but from the samples $x^j_{n+1}, \ldots, x^j_{n+N}$.

The posterior expected value of the frequency of exceeding a threshold can be estimated by

$$\mathrm{E}(h(\Theta) \mid \mathbf{x}, t_0) \approx \frac{1}{M}\sum_{j=1}^{M} \widehat{h}(\theta_j). \tag{7}$$

Extension to more than two evidence sources is straightforward. For example, the ground probability masses needed for combination of three DST structures are

$$q(f_k) = \sum_i \sum_j \sum_l m_1(f_i) m_2(f_j) m_3(f_l) \text{ for any } f_k \neq \varnothing \tag{40}$$
$$f_i \cap f_j \cap f_l = f_k$$

$$q(Y) = m_1(Y) m_2(Y) m_3(Y) \tag{41}$$

$$q(\varnothing) = \sum_i \sum_j \sum_l m_1(f_i) m_2(f_j) m_3(f_l) \tag{42}$$
$$f_i \cap f_j \cap f_l = \varnothing$$

Dempster's combination rule

In the original DST combination rule proposed by Dempster, the joint basic probability mass m_D associated with each joint focal element f_k is obtained by

$$m_D(f_k) = \frac{q(f_k)}{1 - q(\varnothing)} \text{ for all } f_k \neq \varnothing \tag{43}$$

$$m_D(\varnothing) = 0 \tag{44}$$

Eq. (43) also applies to the universal set, so

$$m_D(Y) = \frac{q(Y)}{1 - q(\varnothing)} \tag{45}$$

In standard Bayesian analysis, the posterior probability for this event can be written as the integral of the quantity of interest for a given value of the parameter θ, times the posterior distribution of θ:

$$P(g(X_{n+1}) > g^* \mid \mathbf{x}, t_0) = \int P(g(X_{n+1}) \geq g^* \mid \theta) f(\theta \mid \mathbf{x}, t_0) d\theta. \tag{3}$$

If we define the quantity of interest as a function of assessment parameters θ:

$$h(\theta) := P(g(X_{n+1}) \geq g^* \mid \theta), \tag{4}$$

and Θ the random variable corresponding to uncertainty in the parameter θ, Equation (3) can be written as:

$$\int h(\theta) f(\theta \mid \mathbf{x}, t_0) d\theta = \mathrm{E}(h(\Theta) \mid \mathbf{x}, t_0). \tag{5}$$

With the MVE approach, the prediction of a model is not a definite number but a random variable. Given a model with weights $\boldsymbol{\theta}$ and input x, the conditional expectation and variance of the prediction $\hat{y}$ are:

$$E[\hat{y}|\boldsymbol{\theta}, x] = \mu(\boldsymbol{\theta}, x) \tag{8}$$

$$var(\hat{y}|\boldsymbol{\theta}, x) = v(\boldsymbol{\theta}, x) \tag{9}$$

where $\mu(\cdot)$ and $v(\cdot)$ are two deterministic functions. Under the Bayesian perspective, the weights of a trained model are also random variables following posterior distribution $p(\boldsymbol{\theta}|\mathcal{D}^A)$:

$$p(\boldsymbol{\theta}|\mathcal{D}^A) = \frac{p(\boldsymbol{\theta}) p(\mathcal{D}^A|\boldsymbol{\theta})}{\int p(\boldsymbol{\theta}) p(\mathcal{D}^A|\boldsymbol{\theta}) d\boldsymbol{\theta}} \tag{10}$$

where $p(\boldsymbol{\theta})$ is the prior and $p(\mathcal{D}^A|\boldsymbol{\theta})$ is the likelihood. Combining Eqs. 8–10, the posterior distribution of the prediction is:

$$p(\hat{y}|x, \mathcal{D}^A) = \int p(\hat{y}|\boldsymbol{\theta}, x) p(\boldsymbol{\theta}|\mathcal{D}^A) d\boldsymbol{\theta} \tag{11}$$

whose expectation and variance are:

$$E[\hat{y}|x, \mathcal{D}^A] = E[\mu(\boldsymbol{\theta}, x)], \boldsymbol{\theta} \sim p(\boldsymbol{\theta}|\mathcal{D}^A) \tag{12}$$

$$var(\hat{y}|x, \mathcal{D}^A) = E[v(\boldsymbol{\theta}, x)] + var(\mu(\boldsymbol{\theta}, x)), \boldsymbol{\theta} \sim p(\boldsymbol{\theta}|\mathcal{D}^A) \tag{13}$$

Error propagation through ensembles is also useful to estimate errors on derivatives of the model target with respect to a continuous parameter λ that characterizes the samples—e.g. forces acting on atoms, that are derivatives of the potential with respect to atomic coordinates. Defining derivative errors based on a direct variance estimator is not trivial [32], whereas a calibrated ensemble allows to do so straightforwardly, as we shall discuss later

$$\bar{y}'(A) = \frac{1}{n_{\text{ens}}} \sum_{k=1}^{n_{\text{ens}}} \frac{\partial y^{(k)}(A)}{\partial \lambda}$$

$$\sigma_{y'}(A) = \frac{1}{n_{\text{ens}} - 1} \sum_{k=1}^{n_{\text{ens}}} \left[\frac{\partial y^{(k)}(A)}{\partial \lambda} - \bar{y}'(A)\right]^2. \tag{13}$$

$$\bar{V}(A) = \sum_{A_i \in A} \frac{1}{n_{\text{ens}}} \sum_k v^{(k)}(A_i) = \frac{1}{n_{\text{ens}}} \sum_k V^{(k)}(A)$$

$$\sigma^2_{\bar{V}}(A) = \frac{1}{n_{\text{ens}} - 1} \sum_k \left[\sum_{A_i \in A} v^{(k)}(A_i) - \bar{V}(A)\right]^2.$$

force errors can be readily computed based on the derivatives of the committee members

$$\bar{f}_{i\alpha}(A) = \frac{\partial \bar{V}(A)}{\partial r_{i\alpha}} = \frac{1}{n_{\text{ens}}} \sum_k \frac{\partial V^{(k)}(A)}{\partial r_{i\alpha}}$$

$$\sigma^2_{\bar{f}_{i\alpha}}(A) = \frac{1}{n_{\text{ens}} - 1} \sum_k \left[\frac{\partial V^{(k)}(A)}{\partial r_{i\alpha}} - \bar{f}_{i\alpha}(A)\right]^2. \tag{16}$$

Due to conjugacy, the posterior distribution for these parameters is also a normal-gamma distribution with hyperparameters $\alpha^A_k, \beta^A_k, \gamma^A_k$, and δ^A_k:

$$\tau^A_k \mid \mathbf{a}_k \sim \text{Gamma}(\alpha^A_k, \beta^A_k), \tag{22}$$

$$\mu^A_k \mid \tau^A_k, \mathbf{a}_k \sim \mathcal{N}(\gamma^A_k, \delta^A_k \tau^A_k), \tag{23}$$

ONTOX Probabilistic Risk Assessment (OPRA): An AI-enabled framework

Theory (understand frameworks)

Food for Thought ...

Probabilistic Risk Assessment – The Keystone for the Future of Toxicology

Alexandra Maertens[1], Emily Golden[1], Thomas H. Luechtefeld[1,2], Sebastian Hoffmann[1,3], Katya Tsaioun[1] and Thomas Hartung[1,4]

[1]Center for Alternatives to Animal Testing (CAAT), Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA; [2]ToxTrack, Baltimore, MD, USA; [3]seh consulting + services, Paderborn, Germany; [4]CAAT Europe, University of Konstanz, Konstanz, Germany

t⁴ Workshop Report*

From Cellular Perturbation to Probabilistic Risk Assessments

Alexandra Maertens[1], Breanne Kincaid[1], Eric Bridgeford[2], Celine Brochot[3], Arthur de Carvalho e Silva[4], Jean-Lou C. M. Dorne[5], Liesbet Geris[6,7], Trine Husøy[8], Nicole Kleinstreuer[9], Luiz C. M. Ladeira[6], Alistair Middleton[10], Joe Reynolds[10], Blanca Rodriguez[11], Erwin L. Roggen[12], Giulia Russo[13], Kris Thayer[14] and Thomas Hartung[1,15,16]

[1]Center for Alternatives to Animal Testing (CAAT), Johns Hopkins Bloomberg School of Public Health and Whiting School of Engineering, Baltimore, MD, USA; [2]Dept. of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA; [3]Certara, Canterbury, Kent, UK; [4]University of Birmingham and Michabo Health Science Ltd, Birmingham, UK; [5]European Food Safety Authority (EFSA), Parma, Italy; [6]Molecular and Computational Biology, University of Liège, Liège, Belgium; [7]Mechanical Engineering, KU Leuven, Leuven, Belgium; [8]Food Safety/ Centre for Sustainable Diets, Norwegian Institute of Public Health (NIPH), Oslo, Norway; [9]National Institutes of Health, National Institute for Environmental Health Sciences, DTT/NICEATM, Durham, NC, USA; [10]Safety & Environmental Assurance Centre, Unilever, Colworth Science Park, Sharnbrook, Bedfordshire, UK; [11]Computer Science, University of Oxford, Oxford, UK; [12]ILeMC ApS, Kongens Lyngby, Lyngby, Denmark; [13]Drug and Health Sciences, University of Catania, Catania, Italy; [14]Chemical & Pollutant Assessment Division (CPAD), US Environmental Protection Agency (EPA), Durham, NC, USA; [15]Doerenkamp-Zbinden Chair for Evidence-based Toxicology, Johns Hopkins Bloomberg School of Public Health and Whiting School of Engineering, Baltimore, MD, USA; [16]CAAT-Europe, University of Konstanz, Konstanz, Germany

Uncertainty in toxicological assessments in the era of artificial intelligence

Karolina Kopańska[1] and Thomas Hartung[1,2,3,4]

[1]Johns Hopkins University, Bloomberg School of Public Health and Whiting School of Engineering, Center for Alternatives to Animal Testing (CAAT), Baltimore, MD, USA; [2]CAAT-Europe, University of Konstanz, Germany; [3]Doerenkamp-Zbinden Chair for Evidence-based Toxicology, Baltimore, MD, USA; [4]CAATevents, Solingen, Germany

t⁴ Workshop Report*

The Probable Future of Toxicology – Probabilistic Risk Assessment

Alexandra Maertens[1], Eric Antignac[2], Emilio Benfenati[3], Denise Bloch[4], Ellen Fritsche[5], Sebastian Hoffmann[6], Joanna Jaworska[7], George Loizou[8], Kevin McNally[8], Przemyslaw Piechota[1], Erwin L. Roggen[9], Marc Teunis[10] and Thomas Hartung[1,11]

[1]Johns Hopkins University, Bloomberg School of Public Health and Whiting School of Engineering, Center for Alternatives to Animal Testing (CAAT), Baltimore, MD, USA; [2]L'Oréal, Research & Innovation, Clichy, France; [3]Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano, Italy; [4]Department of Pesticides Safety, German Federal Institute for Risk Assessment (BfR), Berlin, Germany; [5]IUF-Leibniz Research Institute for Environmental Medicine, Duesseldorf, Germany; [6]seh consulting + services, Paderborn, Germany; [7]Procter & Gamble, Brussels Innovation Center, Brussels, Belgium; [8]HSE Science and Research Centre, Harpur Hill, Buxton, UK; [9]3Rs Management and Consulting ApS, Kongens Lyngby, Denmark; [10]Institute for Life Sciences & Chemistry, Dept. Innovative Testing in Life Sciences & Chemistry, Hogeschool Utrecht, Utrecht, The Netherlands; [11]University of Konstanz, CAAT-Europe, Konstanz, Germany

Uncertainty assessment of proarrhythmia predictions derived from multi-level in silico models

Karolina Kopańska[1] · Pablo Rodríguez-Belenguer[1,2] · Jordi Llopis-Lorente[3] · Beatriz Trenor[3] · Javier Saiz[3] · Manuel Pastor[1]

TOXTRUST: a tool leveraging the Dempster-Shafer Theory for robust integration of NAM results in decision-making considering uncertainty

Karolina Kopańska [a,1,b], Adrian Cabrera [a], Manuel Pastor [a,*]

[a] Research Programme on Biomedical Informatics (GRIB), Department of Medicine and Life Sciences, Universitat Pompeu Fabra, Hospital del Mar Research Institute, Barcelona, Spain
[b] Center for Alternatives to Animal Testing (CAAT), Johns Hopkins University, Baltimore, USA

Practice (find and pool tools)

nonconformist 2.1.0 documentation

This website contains the API documentation for the nonconformist Python package, generated using Sphinx. For an introduction to the basic usage of nonconformist, please refer to README.ipynb.

Source is available on GitHub.

TOXTRUST

TOXTRUST is a flexible package allowing for a probablistic evaluation of toxicological evidence as well as for the combination of individual evidence pieces using rigorous rules based on the Dempster-Shafer theory (DST).

phi-grib / TOXTRUST Public

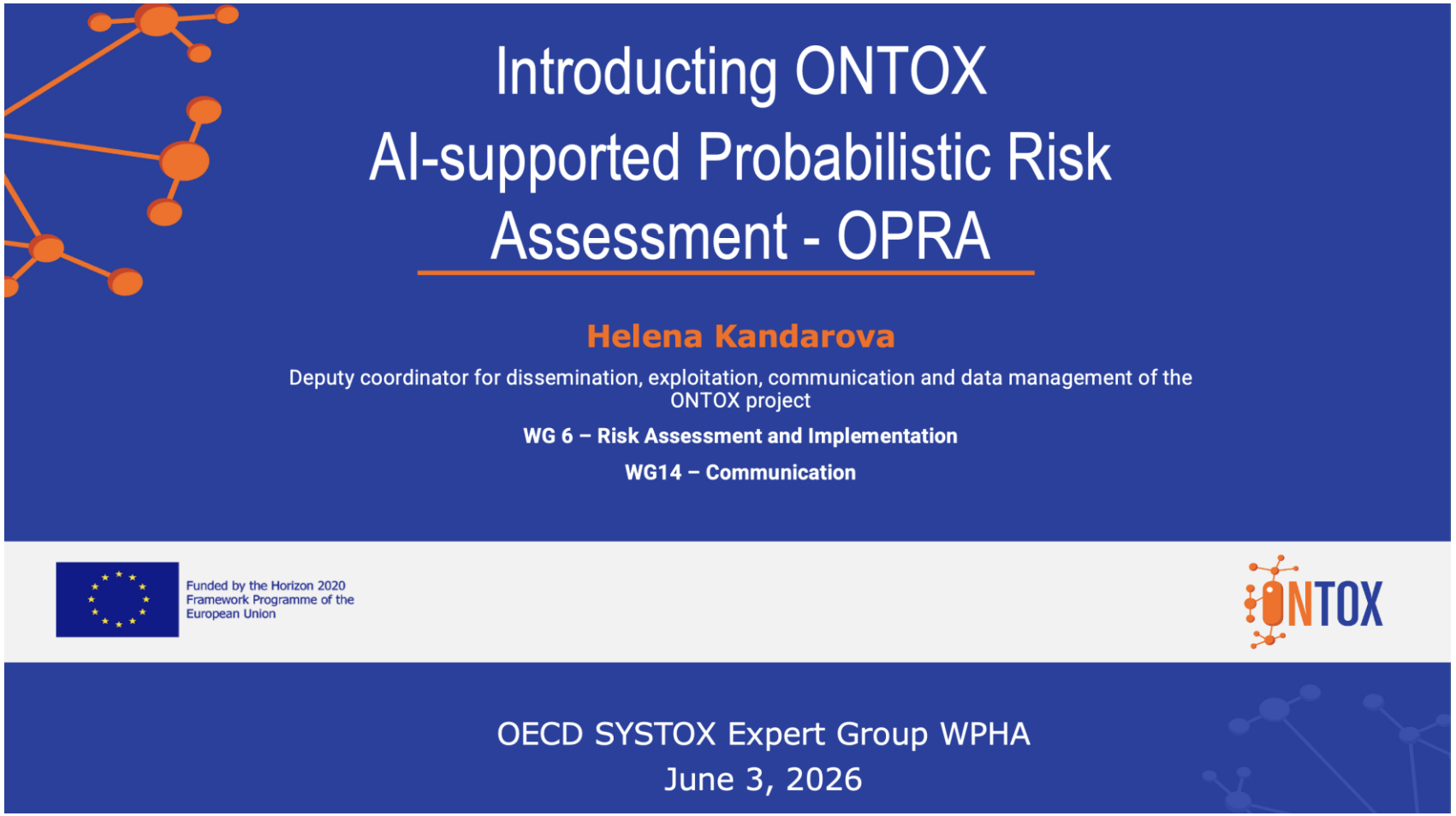
Unilever-NGRA-LCL

NGRA Case Study using LCL for population variability

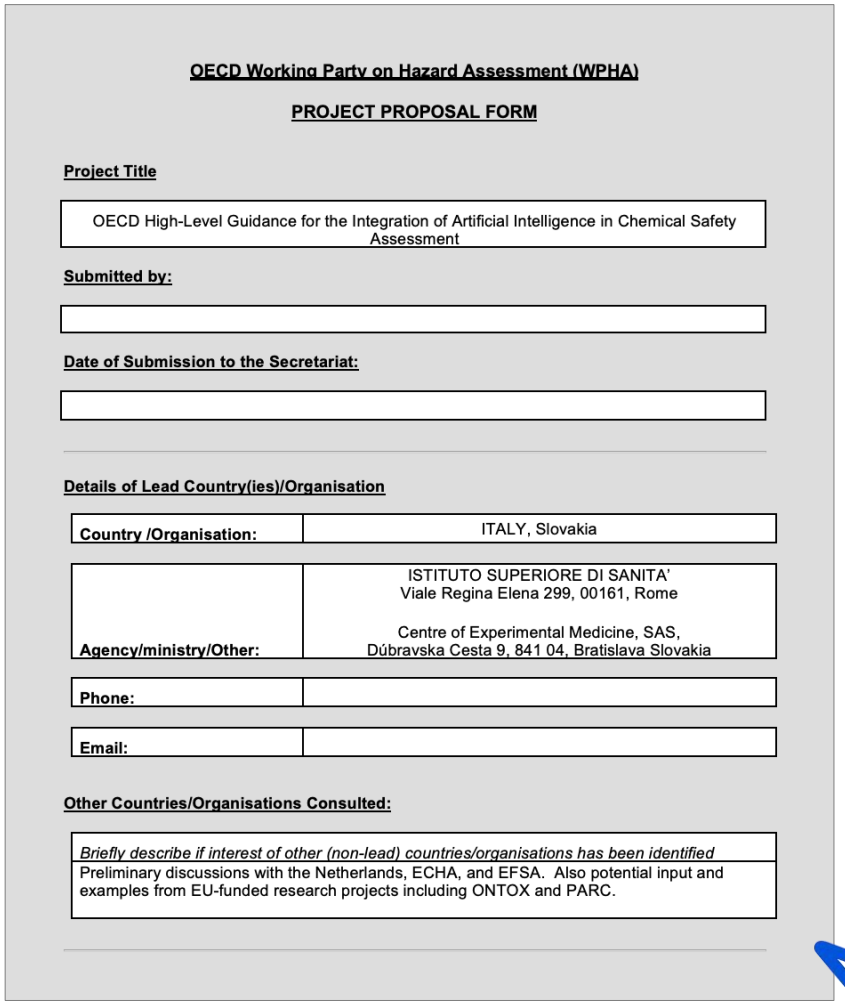
This repository contains the R code used for Alshammari et al. 2026 "Quantitative Estimates of Toxicodynamic Variability for New Approach Methodologies-Based Systemic Safety Toolbox Using a Population-Based Human in Vitro Model". Note that GWAS analysis was not conducted in R so is not included here.

OPRA at OECD – formal request of feedback

Working Party on Hazard Assessment (WPHA) and WPHA Systemic Toxicity Expert Group



OECD proposal (& project) on AI integration into RA



OECD Working Party on Hazard Assessment (WPHA)

PROJECT PROPOSAL FORM

Project Title

OECD High-Level Guidance for the Integration of Artificial Intelligence in Chemical Safety Assessment

Submitted by:

Date of Submission to the Secretariat:

Details of Lead Country(ies)/Organisation

Country /Organisation:	ITALY, Slovakia
Agency/ministry/Other:	ISTITUTO SUPERIORE DI SANITA' Viale Regina Elena 299, 00161, Rome Centre of Experimental Medicine, SAS, Dúbravska Cesta 9, 841 04, Bratislava Slovakia
Phone:	
Email:	

Other Countries/Organisations Consulted:

Briefly describe if interest of other (non-lead) countries/organisations has been identified
Preliminary discussions with the Netherlands, ECHA, and EFSA. Also potential input and examples from EU-funded research projects including ONTOX and PARC.

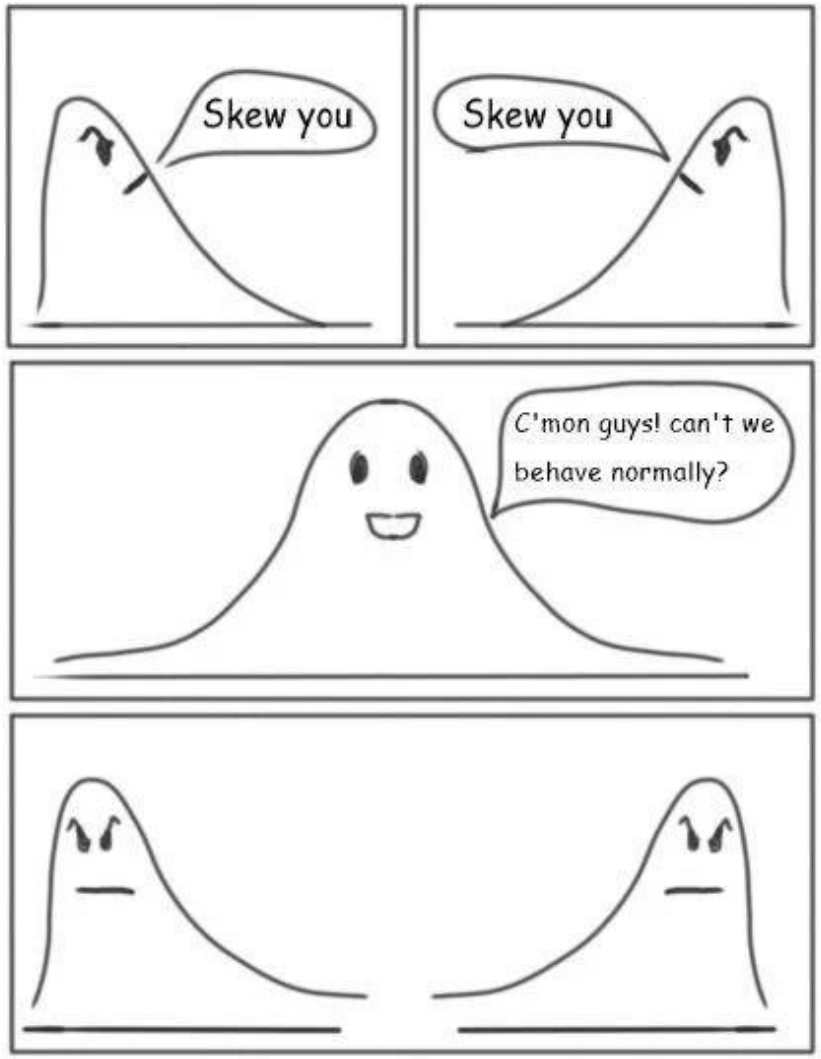
The aim of the project is to develop a practical **Framework for Trustworthy AI** to translate general OECD AI Principles into concise, sector-**specific guidance.**

The proposed high-level guidance will be **aligned**, to the greatest extent possible, with the **evolving requirements of major regulatory authorities.**

This project ensures all AI applications remain "**human-in-the-loop**" where AI acts as a "co-pilot" for expert risk assessors rather than a standalone decision-maker.

Aligned with the EU AI Act and OECD AI Principles

Thank you!



https://coolinfographics.com/news/2021/10/4/statistic-joke

Our **OPRA team**:

Thomas Hartung, Alexandra Maertens, TJ Bozada, Thomas Leuchtefeld, Eliška Kuchovská, Susana Proença, Trine Husøy, Helena Kandarova, Mathieu Vinken