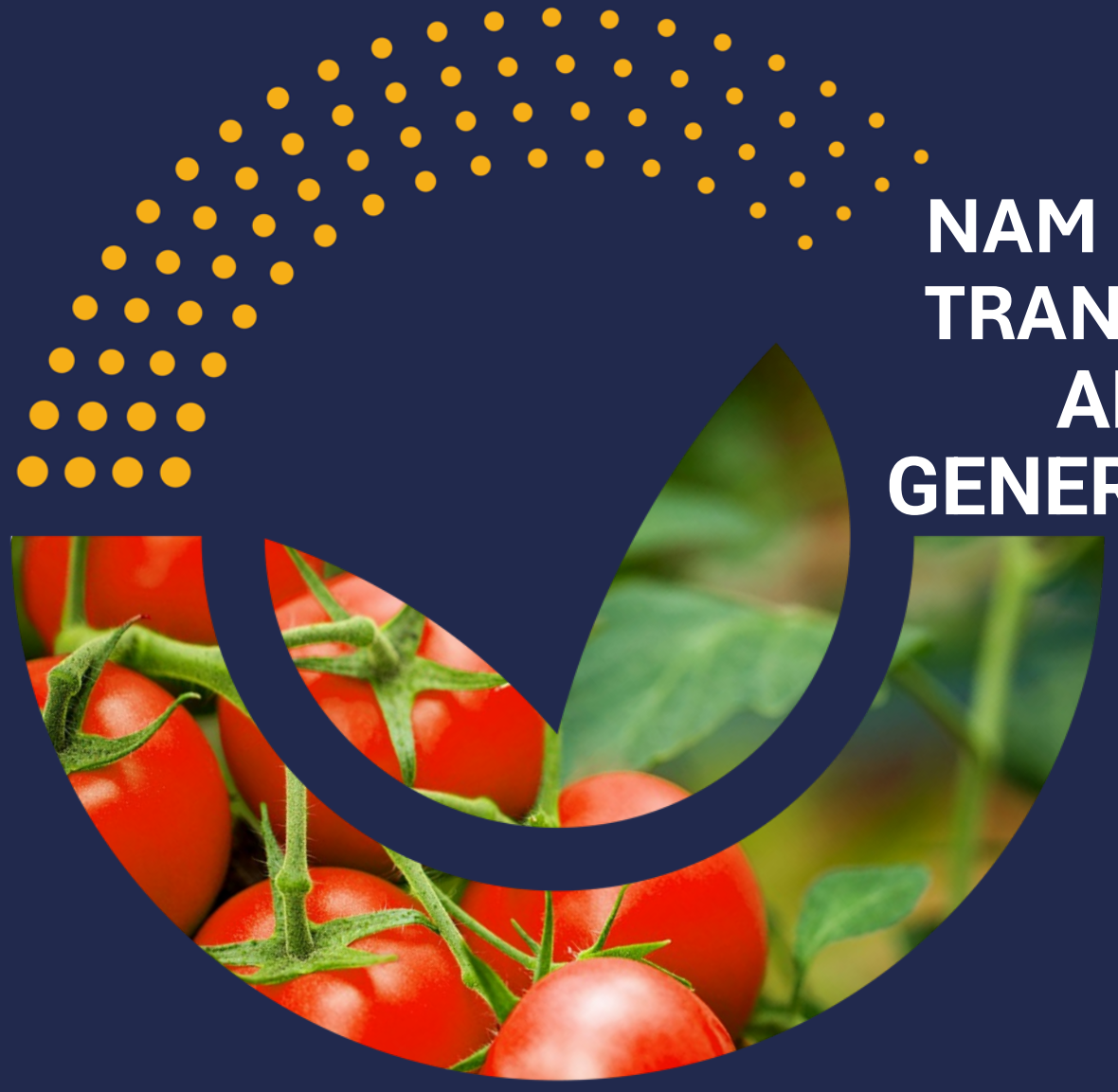
ECHA EFSA EC Road Map Meeting 21st October 2026



NAM PROJECTS@ EFSA : FROM TRANSLATIONAL RESEARCH TO APPLICATIONS IN NEXT GENERATION RISK ASSESSMENT

Jean Lou Dorne,
Lead Expert on NAMs,
Chief Scientist Office, EFSA

efsa
EUROPEAN FOOD SAFETY AUTHORITY

HOW AND WHERE CAN NAMS BE INTEGRATED IN NEXT GENERATION CHEMICAL RISK ASSESSMENT ?

Step 1
Hazard Identification

Step 2
Hazard Characterisation

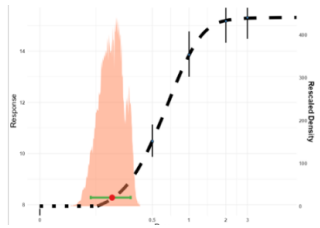
Step 3
Exposure Assessment

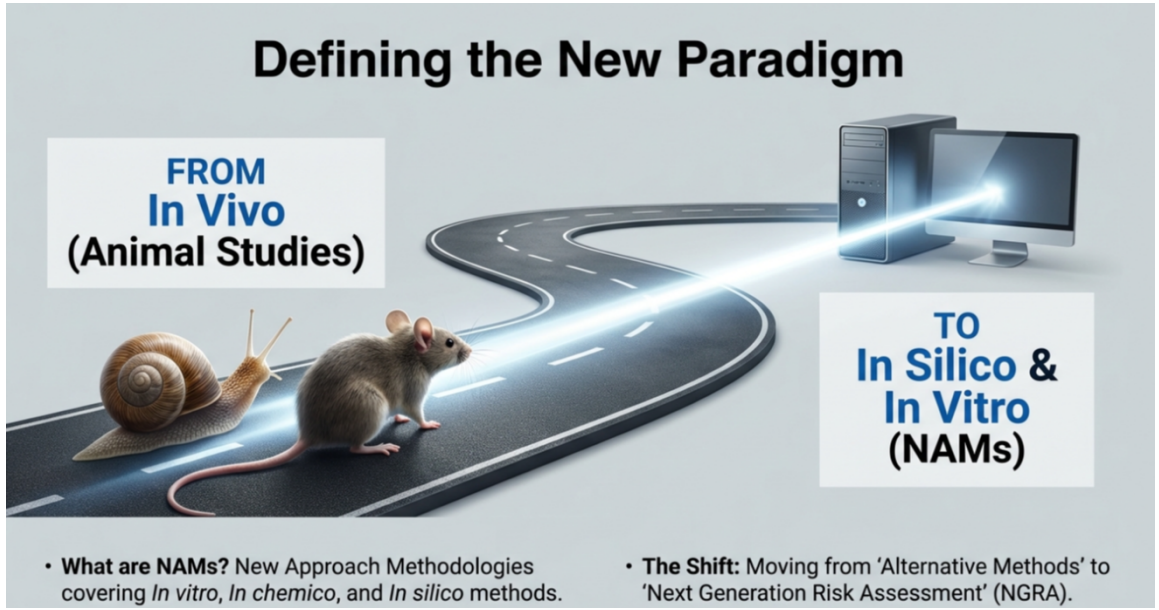
Step 4
Risk Characterisation

Classify chemicals for specific properties
e.g. Genotoxicity



Dose response Modelling:
Derive Points of Departure





CURRENT USE OF NAMs @EFSA

From regulatory flexibility to mechanistic evidence

WHERE NAMs ARE USED

- CONTAMINANTS
- FEED ADDITIVES
- FOOD ADDITIVES & FLAVOURINGS
- GMO
- NOVEL FOODS
- PESTICIDES HUMAN HEALTH
- PESTICIDES ERA

HOW NAMs CONTRIBUTE

NON-TESTING

Exposure • read-across • TTC • existing information

IN SILICO

ADME • BMD • PBK • (Q)SARs • population models

IN VITRO

Genotoxicity • ADME • DNT • ED • ecotoxicity

NAMs

integrated evidence for risk assessment

MECHANISTIC

AOP • MoA • pathway and protein-safety evidence

WEIGHT OF EVIDENCE

Omics • WGS • IATA • integrated assessment

REGULATORY FLEXIBILITY

Waivers • extrapolation • tiered strategies • safe-use history

KEY MESSAGE

NAMs are already embedded across EFSA domains, combining computational, experimental and mechanistic evidence with regulatory provisions.

Examples shown are condensed from the source matrix.

THE FIRST APCRA CASE STUDY (2020) : DERIVING POINTS OF DEPARTURE USING NAMS

- For 448 substances, 89% PoD_{NAMs} more conservative than $PoD_{Traditional}$

EPA Public Access
Author manuscript
Toxicol Sci. Author manuscript; available in PMC 2021 January 01.
About author manuscripts | Submit a manuscript

Published in final edited form as:
Toxicol Sci. 2020 January 01; 173(1): 202–225. doi:10.1093/toxsci/kfz201.

Utility of In Vitro Bioactivity as a Lower Bound Estimate of In Vivo Adverse Effect Levels and in Risk-Based Prioritization

Katie Paul Friedman*, Matthew Gagne†, Lit-Hsin Loo‡, Panagiotis Karamertzanis§, Tatiana Netzeva§, Tomasz Sobanski§, Jill Franzosa¶, Ann Richard*, Ryan Lougee*, Andrea Gissi§, Jia-Ying Joey Lee‡, Michelle Angrish‖, Jean-Lou Dorne‖, Stiven Foster‖‖, Kathleen Raffaele‖‖, Tina Bahadori‖, Maureen Gwinn*, Jason Lambert*, Maurice Whelan‖‖, Mike Rasenberg§, Tara Barton-Maclaren†, Russell S. Thomas*

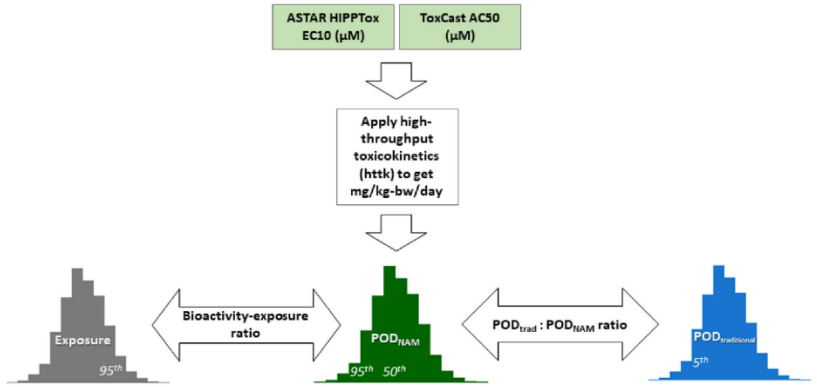
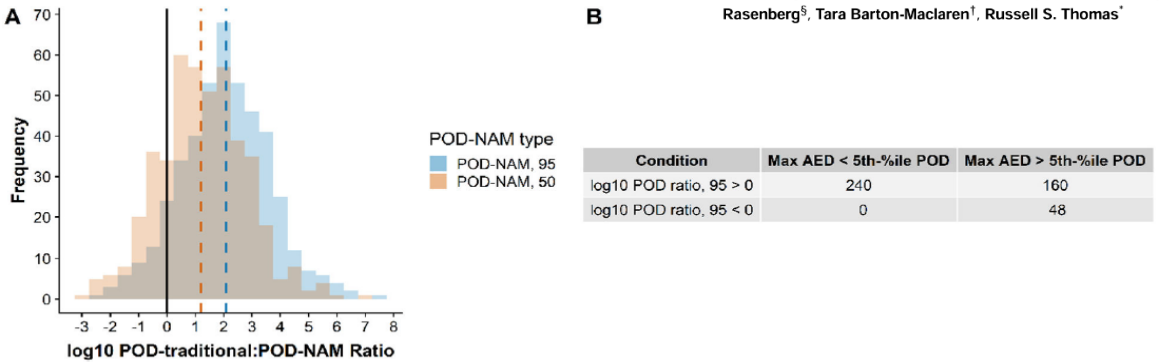


Figure 1. Overall workflow of the case study.
This case study includes 448 substances with exposure predictions, *in vitro* assay data, HTTK information, and *in vivo* hazard information. The 50th and 95th percentile from the Monte Carlo simulation of inter-individual toxicokinetic variability were used to estimate AEDs, and the minimum of either the ToxCast or HIPPTox-based AEDs were selected as the $POD_{NAM,50}$ or $POD_{NAM,95}$. The POD_{NAM} estimates were compared to the 5th percentile from the distribution of the $POD_{traditional}$ values obtained from multiple sources to obtain the log_{10}POD ratio. The log_{10}BER was obtained by comparing the POD_{NAM} estimates to exposure predictions. All values used for computation were in log_{10}-mg/kg-bw/day units



Condition	Max AED < 5th-%ile POD	Max AED > 5th-%ile POD
log10 POD ratio, 95 > 0	240	160
log10 POD ratio, 95 < 0	0	48

Figure 7. Further understanding of the POD ratio distribution.
(A) The log_{10}POD ratio is illustrated for the $POD_{NAM,95}$ and the $POD_{NAM,50}$. The solid black line indicates where the log10-POD $ratio_{95}$ is 0. Using the more conservative (i.e., lower) $POD_{NAM,95}$, 48 of the 448 substances (10.7%) demonstrated a log_{10}POD ratio < 0 (to the left of the dashed vertical line), whereas 92 of the 448 substances (20.5%) demonstrated a log10-POD ratio < 0 using the $POD_{NAM,50}$. The medians of the log10-POD ratio distributions are indicated by dashed lines for $POD_{NAM,95}$ and $POD_{NAM,50}$ as 2 and 1.2, respectively. (B) Maximum AED (max AED) was less than the $POD_{traditional}$ (5th-%ile POD) in 60% of the cases where the log_{10}POD $ratio_{95}$ > 0 (using $POD_{NAM,95}$). For the 48 chemicals with log_{10}POD $ratio_{95}$ < 0, the max AED was within the range of $POD_{traditional}$.

OVERARCHING OPPORTUNITIES FOR NEXT GENERATION RISK ASSESSMENT IN HH AND ERA

Building regulatory confidence in *in silico* predictions, *in vitro* methods and QIVIVE

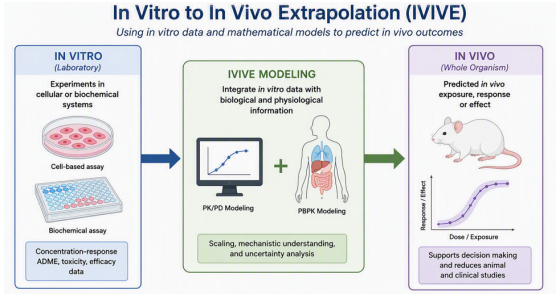
1 QSAR & QAF

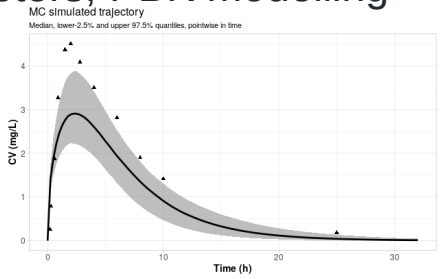
- Enhancing regulatory confidence through reliable QSAR predictions
- Enabling automated QAF-compliant reliability assessments



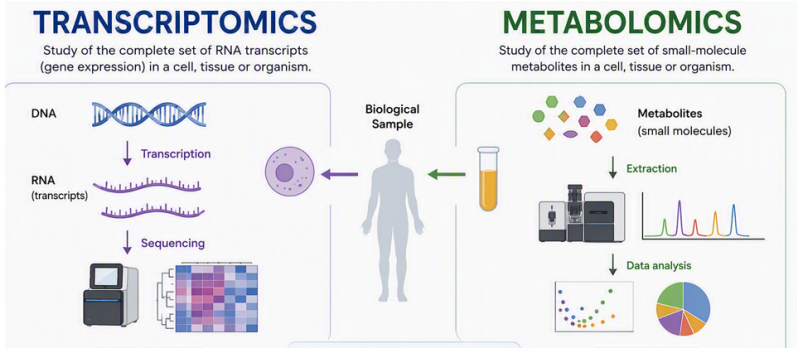
2 TK, ADME, PBK & QIVIVE

- Standardise *in vitro* TK parameters, PBK modelling





3 OMICS, PoD & SIGNATURES



4 Nanomaterials and nanoparticle risk assessment

- NMs as a complex materials requiring tailored risk assessment approaches and cross-disciplinary expertise.

➡ Development of *in vitro/in silico* testing batteries, including for nanomaterial assessment

- **Harmonised OECD criteria**
- **Practical tools**

Stronger confidence in NGRA using NAMs

Overarching Opportunity 1 : QSARs

OPENFOODTOX 3.0: EFSA'S CHEMICAL HAZARDS DATABASE

Open-source database of toxicological information since EFSA's creation (2002)

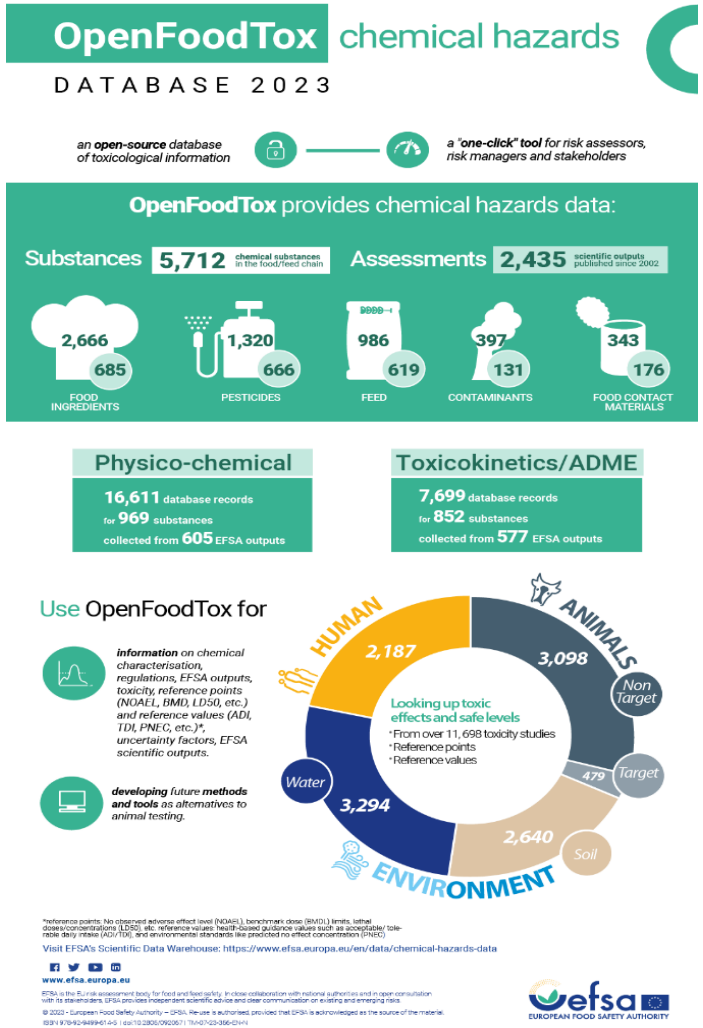
- "One-click" tool for risk assessors, risk managers and stakeholders

International data harmonisation and sharing

- OECD Harmonised Templates

Developing future methods and tools as alternatives to animal testing

- Basis for developing *in silico* models



https://www.efsa.europa.eu/it/data-report/chemical-hazards-database-openfoodtox

OPENFOODTOX: QSAR MODELS AVAILABLE IN VEGA PLATFORM

- **20+ QSARs for OECD test species:**
  - NOAEL/LOAEL- Rat
  - NOEC - bobwhite quail
  - LC_{50} – fish, NOEC -earthworms
  - LDC_{50} & MoA - Honey bees
  - NOEC - Harlequin fly and EC_{50} - swollen duckweed



- **Implemented in VEGA HUB** *in silico* platform and **OECD QSAR Toolbox** = *f*



https://www.vegahub.eu/portfolio-types/in-silico-models/

- **Next: Implement template of OECD QSAR reporting framework in risk assessment**

Opportunity 2 : TK, ADME, PBK & QIVIVE

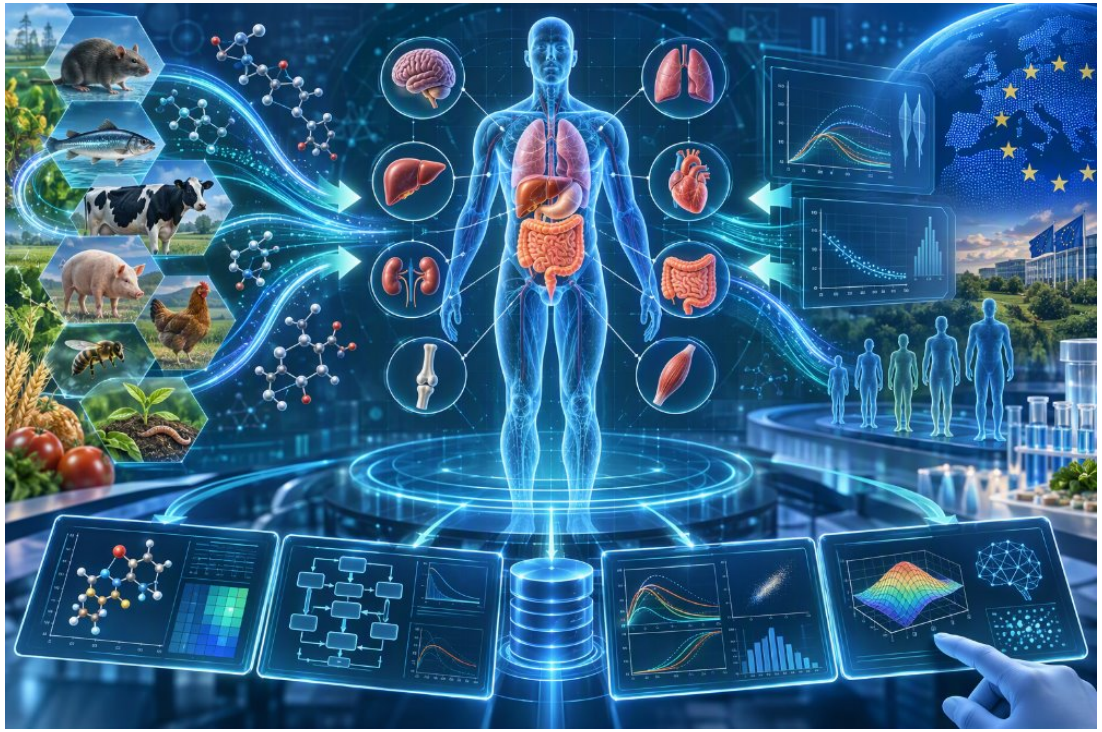
TKPLATE 1.0: IMPLEMENTING TK AND TD MODELLING IN EFSA'S RA

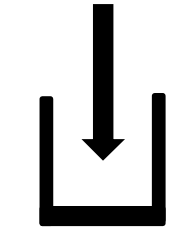
Approved: 12 October 2023
DOI: 10.2903/j.efsa.2023.e211101

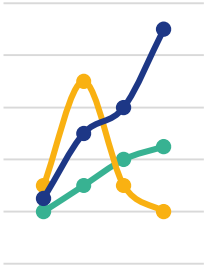
EDITORIAL

efsa JOURNAL

TKPlate 1.0: An Open-access platform for toxicokinetic and toxicodynamic modelling of chemicals to implement new approach methodologies in chemical risk assessment









INPUT

- Select Model and Species
- Select Chemical and Data
- Set Exposure Settings and Time scale

MODELS

- Forward Dosimetry
- Reverse Dosimetry
- Toxicodynamic Modelling
- Dynamic Energy Budget
- MixTox Calculator

OUTPUT

- Download Automated Report
- Summary Inputs and Outputs
- Download Data and Graphs

DELTA 9 AND DELTA 8 THC AS CONTAMINANTS

- **Delta-9-tetrahydrocannabinol**

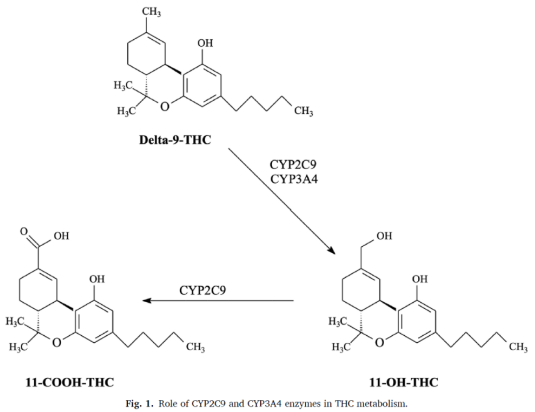
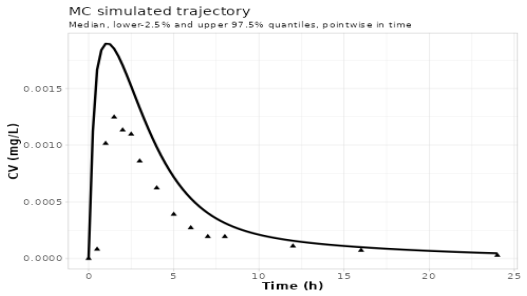


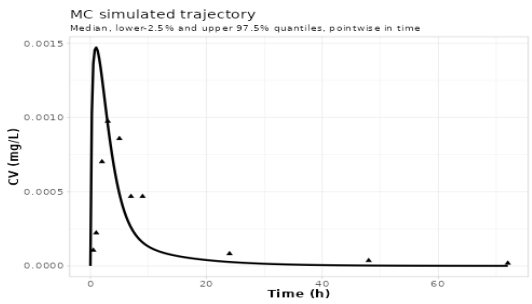
Fig. 1. Role of CYP2C9 and CYP3A4 enzymes in THC metabolism.

- D-9-THC metabolised by CYP2C9 : Polymorphic enzymes
- In vitro data and in vivo for each phenotype for D-9-THC
- Extrapolation in vitro in vivo for kinetics in vivo
- Compare with in vivo data
- Refine uncertainty factors for polymorphic subgroups
- BMDL modelling if dose response data for each phenotype ?

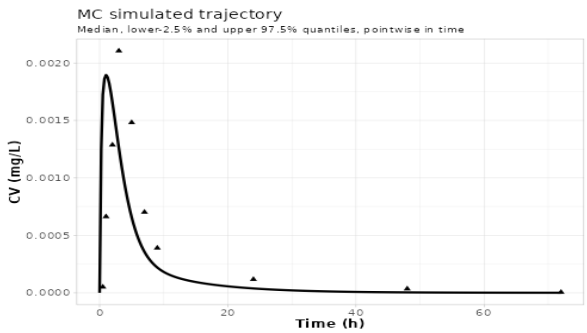
Non-phenotyped individuals



CYP2C9 phenotype *1/*3



CYP2C9 phenotype *1/*3



ALTERNARIA TOXINS AND PARC RAPID RESPONSE MECHANISM ADOPTED 30 SEPTEMBER 2026

Tenuazonic acid

PARC Filling gaps: Rapid Response mechanism

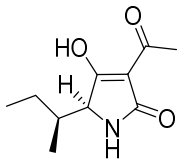
In vitro dose Response metric

Internal exposure metric in liver blood

Parameterise Generic Human PBK model TKPlate

Reverse dosimetry in TKPlate

Margins of Exposure

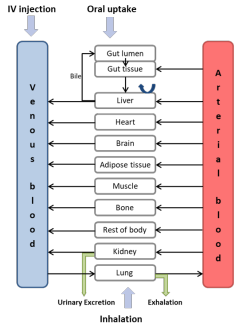


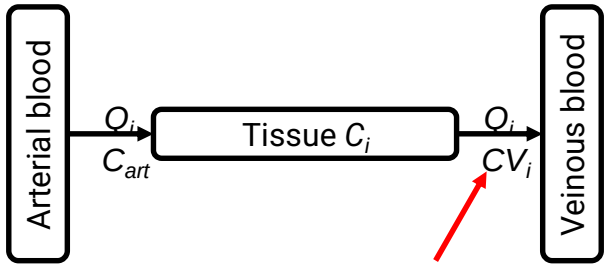




Dose response data 10 days
3D HepaRG cells steatosis :
Lipid accumulation

Concentration Response

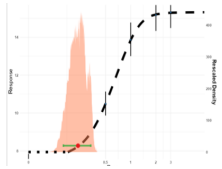




Analysis in EFSA CONTAM Opinion as Annex

QIVIVE : PBK
Concentrations in liver blood to external doses

External dose for each concentrations

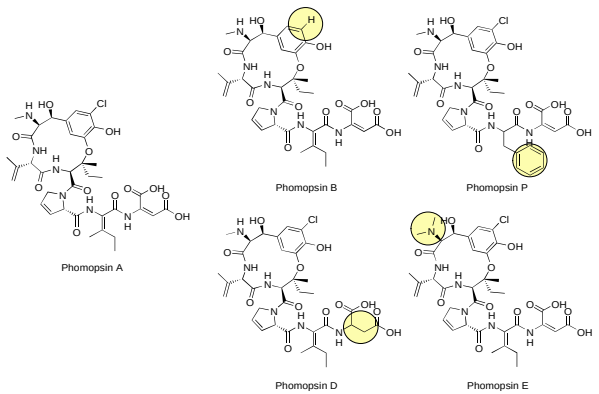


BMDL for each subgroup

Not used for Hazard and risk characterisation

TTC instead but approach in Annex

PHOMOPSINS : CONTAM ASSESSMENT ADOPTED 30 SEPTEMBER 2026



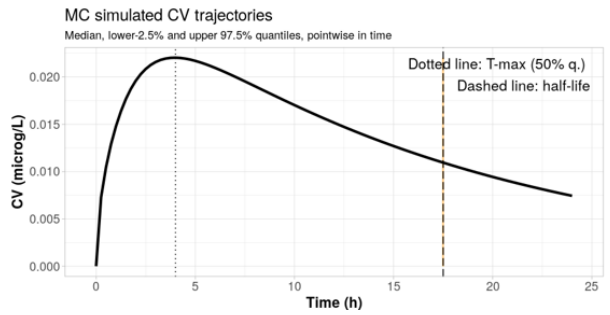


ADME parameters

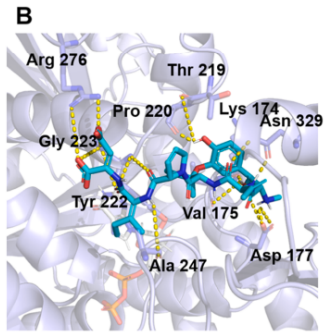
TKPlate

TK profile

- **No in vivo TK data**
- ✓ **QSARs to predict ADME parameters**
  - Open access QSAR platforms (OPERA, VEGA etc..)
    - Moderate reliability (Application domain) for fraction unbound, absorption, Clearance
- ✓ **Predict PK profiles in TKPlate**



	0%-quantile	2.5%-quantile	50%-quantile	97.5%-quantile	100%-quantile
T-max (h)	4.00E+00	4.00E+00	4.00E+00	4.00E+00	4.00E+00
C-max (microg/L)	2.20E-02	2.20E-02	2.20E-02	2.20E-02	2.20E-02
Half-life (h)	1.35E+01	1.35E+01	1.35E+01	1.35E+01	1.35E+01
AUC (h * microg/L)	1.85E-01	1.85E-01	1.85E-01	1.85E-01	1.85E-01



- **Target Tubulin : 3D Docking studies to assess interaction : Support MoA**

Opportunity 3 : OMICs

ONGOING AND PLANNED EFSA OMICS PROJECTS

1 TXG-MAP

2023-2027

Validating in vitro model responses against human tissue samples for regulatory decisions

Knowledge Gap Addressed:
How to interpret and translate transcriptomics data into actionable regulatory information

2 Multi-Omics Workflow

2022-2027

Organ-on-chip with multi-omics integration and standardized workflows for PoD derivation

Knowledge Gap Addressed:
Lack of standardized workflows for deriving human reference points from multi-omics data

AI Chemical Grouping

2027-2028

PLANNED

Automated pipeline using public omics data for cumulative assessment groups

Gap :
Need efficient methods to group data-poor chemicals

2 Brain Health

2023-2027

Developing neurotoxicity AOPs for glial cell toxicity using single-cell transcriptomics

Knowledge Gap Addressed:
Glial cell responses to chemicals are understudied compared to neuronal toxicity

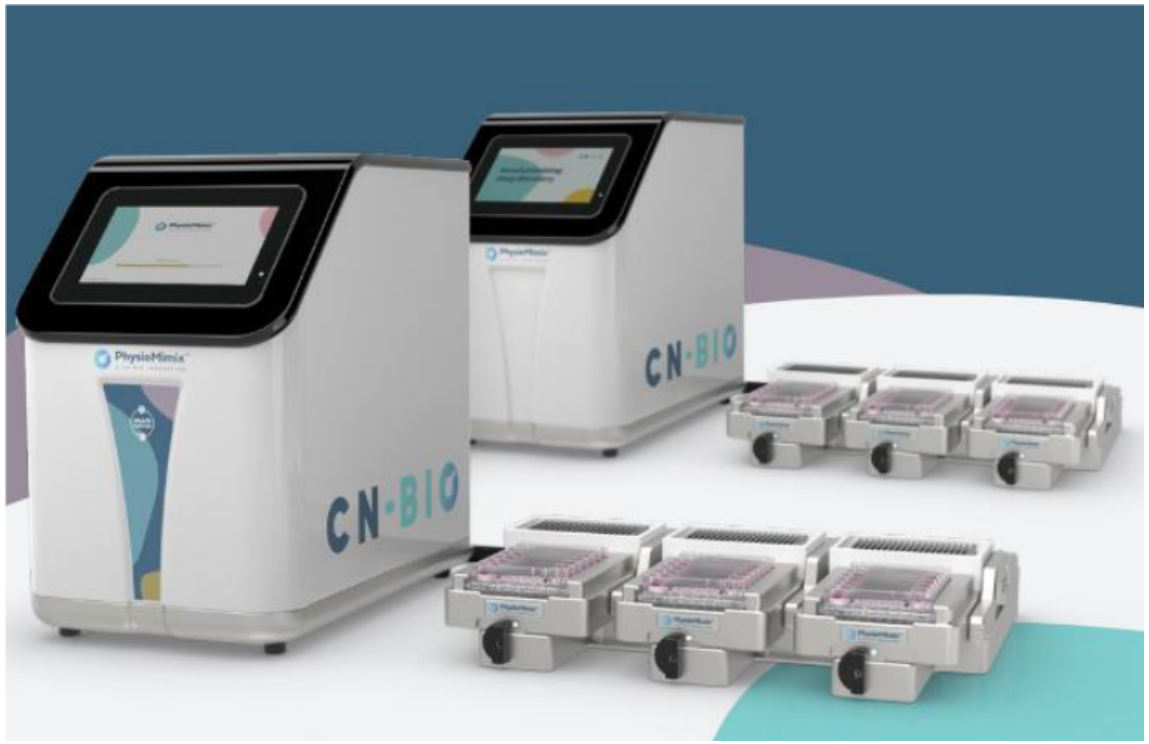
4 TD-TRAQ

2021-2026

Characterising human variability in toxicodynamics using transcriptomics

Gap Addressed:
Are current uncertainty factors adequately protective of population variability?

MULTI-OMICS (PROCUREMENT, 3M, 3Y, TAMPERE UNI, LUXEMBURG SCI&TECH)



- Push forward the Organ on Chip technology and knowledge in EU
- Push forward the use of Epigenetics in Toxicogenomics
- Improve upon existing software for toxicogenomics PoDs (e.g. BMDexpress)
- Standardize workflows (experimental & computational)



AMBITIOUS, NON-ROUTINE PROJECT

PUBLIC OMICS DATA FOR CHEMICAL GROUPING



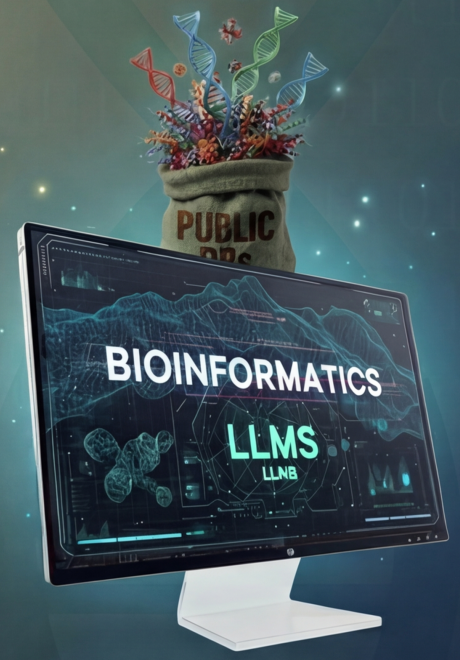
CUMULUTATIVE ASSESSMENT GROUPS

Grouping chemicals that are likely to contribute to the same toxic effect.



MILLIONS OF TRANSCRIPTOMIC SAMPLES

A large amount of data that could be used to derive additional weight of evidence for chemical grouping



OMICS FOR GROUPING



Future opportunities

TOXCODE4ONEGRA: STRUCTURE HAZARD DATA AND MODEL CODES IN PARC

- Structured NAM-based Hazard Database using OECD harmonised Templates (OHTs)



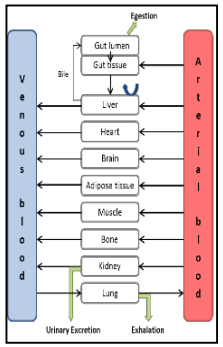






- Structured Model Codes (FAIR)









- Optimise Direct use of PARC NAM data in EFSA/ECHA
- 10 partners incl. ANSES/BfR, EFSA, ECHA, OECD
- Structure NAM data (vitro incl OMICs) and model codes (QSAR, PBK) in EFSA ECHA RA
- Support implementation EC roadmap
- EFSA and ECHA–relevant case studies (DNT, emerging chemicals, mycotoxins)

FUTURE OPPORTUNITIES TO INTEGRATE NAMS IN HUMAN, ANIMAL HEALTH AND ENVIRONMENTAL RA

HARMONISATION

- Assessing Quality of NAM data (i.e. in silico models, in vitro methods, AOPs, IATAs)
- Structuring NAM-based Data and model codes and Integration in RA workflows

GUIDANCE DEVELOPMENT

- Harmonised guidance for NAM integration in RA for food and feed chemicals

FURTHER DEVELOPMENT, QUALIFICATION AND VALIDATION

- QSAR models for missing test species and specific endpoints
- QIVIVE Tools for handling in vitro data and qAOPs
- Derivation of Reference Points of departure from NAM data incl. OMICs

TRAINING EFSA STAFF AND EXPERTS

FUTURE DEVELOPMENTS AND INTEGRATION OF NAMs

From promising methods to routine regulatory use



↔ Cross-agency alignment

- Human RA /ERA
- QSARs
- In vitro TK + PBK
- OMICS ongoing

◆ Implementation

MAKE IT USABLE

- QSAR reporting template
- PBK / QIVIVE : TKPlate and WGs
- Bioaccumulation + metabolites
- OMICs workflow

✓ Regulatory uptake

MAKE IT ROUTINE

- FAIR NAM structures
- OECD IATA case studies
- Dose-response OMICS → PoDs
- Train Risk assessors and Experts

Direction — **Connect methods → standardise evidence → build confidence → enable routine use**

THANKS TO ALL@ EFSA !

- **CSO :** Carlos, Claudia H, Yann, Kostas, Maia, Stef, Estefania, Alessia, Anna, Amelie
- **IRMA and DEEP**: Claudia P, Nik, Benedicte, Ioannis, Ketty, Massimo, Federico
- **MESE :** Jose, Alicia, Claudia RC, Bruno, Alexis, Sara, Claudia C, Maria Chiara, Irene, Maria B
- **iDATA**: Edoardo, Andrea, Giovanni, Adrian
- **PREV :** Jochem, Sofia, Andrea, Juan, Anna L,, Marco, Iris, Martina,
- **PLANTS** : Allessio, Alberto, Maria A
- **FEEDCO** : Chantra, Maria A, Anna C, Luisa, Mary, Paola, Maria Vittoria
- **NIF** : Georges, Maria G, Oceane
- **GMO** : Antonio, Reinhilde
- **FIP** : Josef, Katarina, Blanka, Eric
- **KNOW:** Raquel, Bernard, Angelo, Eileen, Didier
- **COMM :** Tony, Patrick,
- **Procurement** : Cristina, Muriel, Laura

STRONGER TOGETHER TO IMPLEMENT NAMS

EU MS Food Safety Agencies

European Commission

PARC

食品安全委員会
Food Safety Commission of Japan
内閣府
Cabinet Office

EFSA Stakeholders

Global Coalition for Regulatory Science Research

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

epaa
The European Partnership for Alternative Approaches to Animal Testing

World Health Organization

efsa
EUROPEAN FOOD SAFETY AUTHORITY

ECHA
EUROPEAN CHEMICALS AGENCY

FDA

ASPIS

EUTOXRISK

OECD
BETTER POLICIES FOR BETTER LIVES

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CFSA 国家食品安全风险评估中心
China National Center for Food Safety Risk Assessment

ILMERAC

APCRA
ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

STAY CONNECTED

SUBSCRIBE TO
efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss
Careers.efsa.europa.eu – job alerts

LISTEN TO OUR PODCAST
Science on the Menu –Spotify, Apple Podcast and YouTube

FOLLOW US ON TWITTER
@efsa_eu @methods_efsa
@plants_efsa @animals_efsa

FOLLOW US ON LINKEDIN
Linkedin.com/company/efsa

FOLLOW US ON INSTAGRAM
@one_healthenv_eu

CONTACT US
efsa.europe.eu/en/contact/askefsa

EUROPEAN FOOD SAFETY AUTHORITY