



# Project overview

*Ontology-driven and artificial intelligence-based  
repeated dose toxicity testing of chemicals  
for next generation risk assessment*

---

**Mathieu Vinken**

*Project coordinator*



Funded by the Horizon 2020  
Framework Programme of the  
European Union



VRIJE  
UNIVERSITEIT  
BRUSSEL

3<sup>rd</sup> *In Silico* Toxicology Conference 2022

29 September 2022



# Scope



## Goal

Development of an animal-free and human-relevant strategy for the prediction of chemical-induced toxicity

## Focus

- Systemic repeated dose toxicity
- 6 case studies
  - Liver: steatosis and cholestasis
  - Kidney: tubular necrosis and crystallopathy
  - Brain: neural tube closure and cognitive function defects
- Drugs, cosmetics, biocides and food ingredients

## Driving principles

- 3Rs
- 21<sup>st</sup> century toxicity testing
- Next generation risk assessment





# Concept



## Rationale

- Rely as much as possible on available data, models and methods
- Fill data gaps by means of targeted *in vitro* and *in silico* testing

## Toolbox

- Human data and biological material
- *In vitro* methods and stem cell technology
- *In silico* methods and artificial intelligence



# Main deliverable



## New approach/non-animal methodology (NAM)

- ONTOX will deliver 6 NAMs:
  - Liver: steatosis and cholestasis
  - Kidney: tubular necrosis and crystallopathy
  - Brain: neural tube closure and cognitive function defects
- An artificial intelligence-based strategy linked with a battery of *in vitro* assays and *in silico* tools for hazard prediction to be combined with customized exposure assessment for the purpose of human risk assessment



# Main deliverable



Artificial intelligence system



Cell culture system



*In vitro* assays



*In silico* tools

*In vitro/in silico* test battery

NAM



# Artificial intelligence



## Definition

Simulation of human intelligence by means of computers

## Application 1: (big) data collection

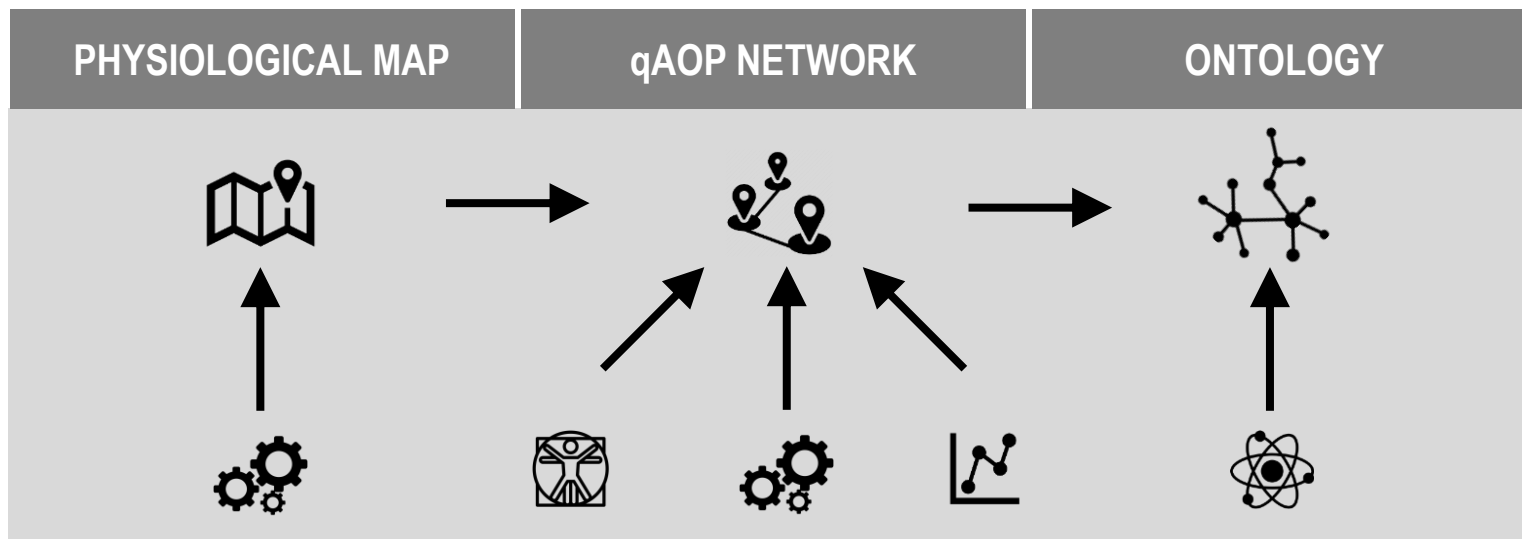
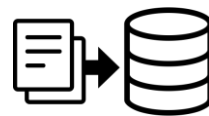
- Type: biology, toxicology, chemistry and kinetics (ontology)
- Sources: safety dossiers, databases, papers, text books, other projects, ... (FAIR principles)

## Application 2: hazard identification / prediction

- Goal: create a blueprint of toxicological effects
- Technique: machine learning (advanced read-across structure-activity relationship)



# Data collection tools



# *In vitro* / *in silico* tests



## Definition

- *In vitro*: cell culture methods
- *In silico*: computer-based methods

## Set-up

- Mapping of mechanisms underlying physiological functions
- Mapping of mechanisms underlying adverse effects and identification of key events
- Selection / optimisation of 1 or more *in vitro* and / or *in silico* tests per key event
- Battery of *in vitro* and *in silico* tests for each adverse effect



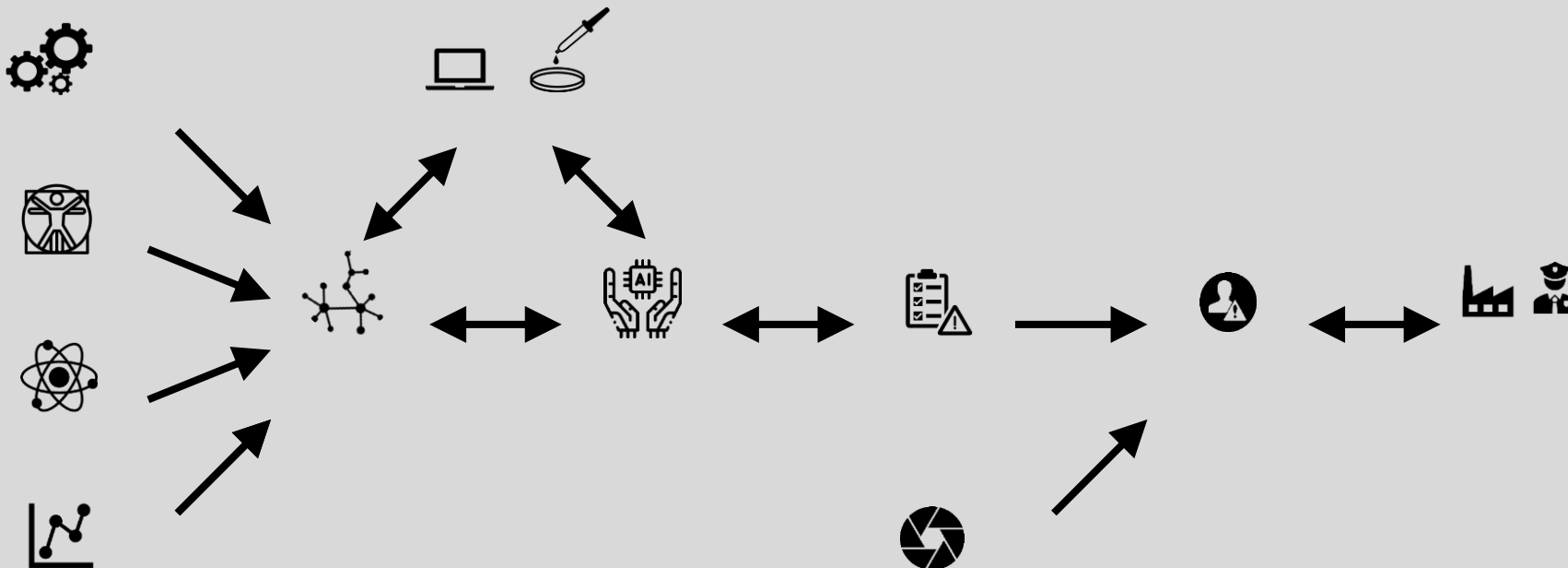
# Workflow



**TIER 1:**  
DATA COLLECTION

**TIER 2:**  
DATA INTEGRATION AND TESTING

**TIER 3:**  
RISK ASSESSMENT AND IMPLEMENTATION



Funded by the Horizon 2020  
Framework Programme of the  
European Union



3<sup>rd</sup> *In Silico* Toxicology Conference

# Workflow



## Phase I

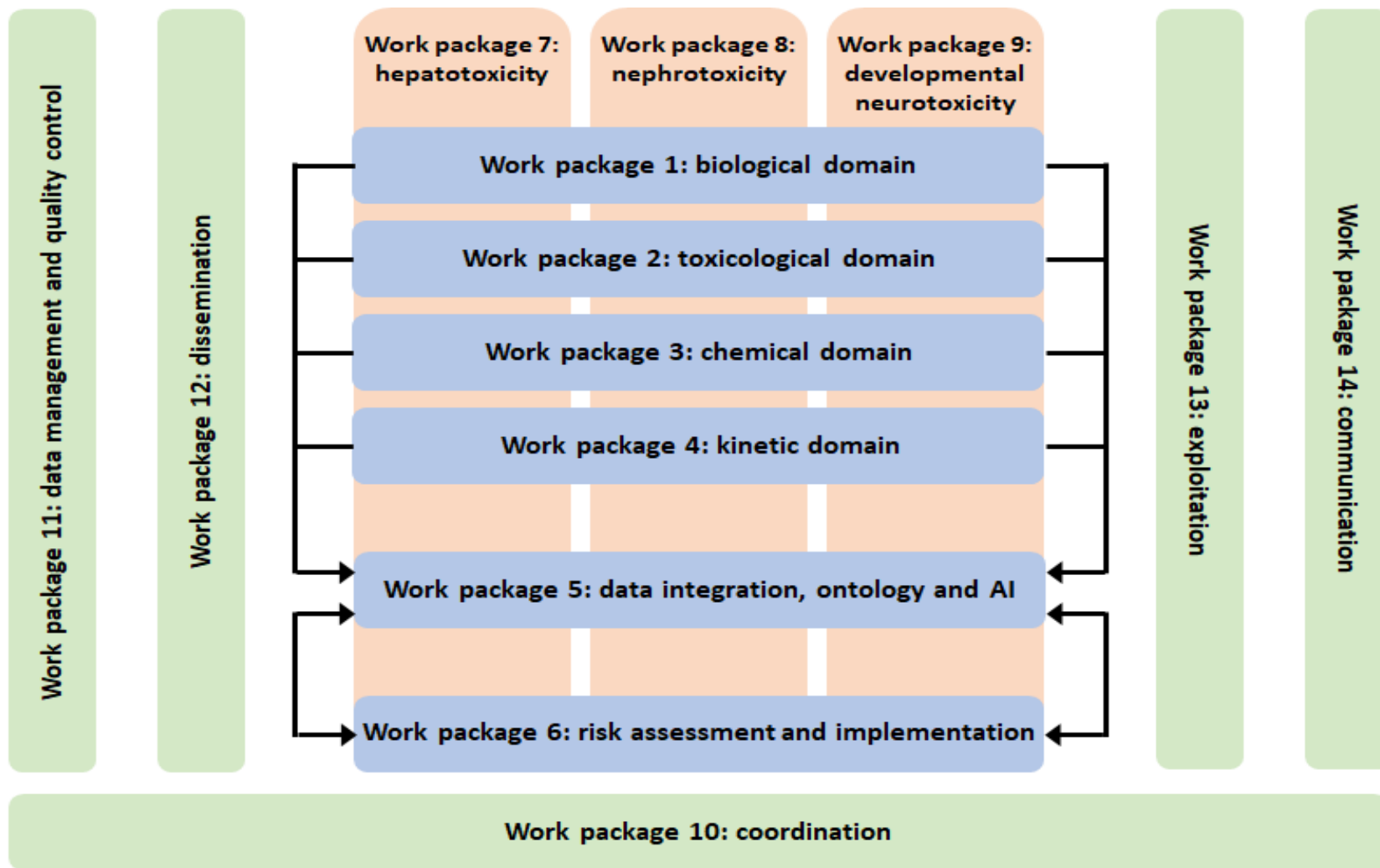
- Data-rich chemicals with well-known toxicological profiles
- Optimisation of the artificial intelligence system and the *in vitro* and *in silico* tests

## Phase II (*ab initio* case studies)

- Data-poor chemicals with less clear-cut toxicological profiles
- Step 1: apply the artificial intelligence system
- Step 2: fill data gaps with *in vitro* and *in silico* testing
- Step 3: exposure assessment / modelling
- Step 4: probabilistic risk assessment



# Organisation



# Consortium, budget and advisory board

## Consortium

- 19 partners from 9 countries
- 100 researchers
- 11 academic institutions
- 6 SMEs and 1 large company
- 1 public health institution

Budget: €17.211.050

## Scientific advisory board

- Patience Browne (OECD-France)
- Paul Carmichael (Unilever-United Kingdom)
- Sandra Coecke (JRC-Italy)
- Stéphane Dhalluin (L'Oréal-France)
- Mariana Novič (National Institute of Chemistry-Slovenia)
- Freddy Van Goethem (Janssen Pharmaceutica-Belgium)
- Paul Whaley (Lancaster University, United Kingdom)

Ethical advisor: Signe Mezinska (University of Latvia-Latvia)





## Animal-free safety assessment of chemicals: project cluster for implementation of novel strategies

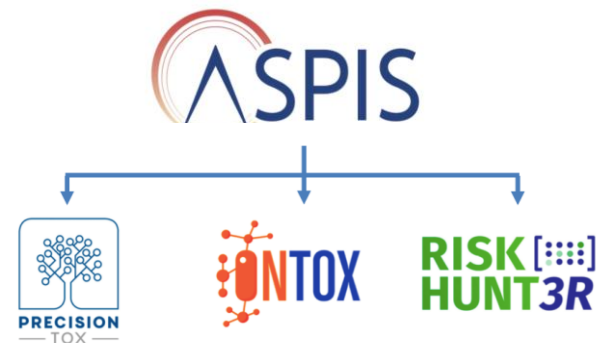
- 3 projects
- 70 partners in 17 countries
- €60 million

### RISK-HUNT3R

- Coordinator: Bob van de Water
- Goal: human-centric chemical safety assessment utilizing systems toxicology

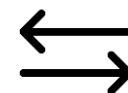
### PrecisionTox

- Coordinator: John Colbourne
- Goal: leveraging evolutionary diversity to reveal the molecular basis of toxicity





Forum meetings



ASPIS regulatory forum



Teleconferences, annual cluster meetings

ASPIS international scientific/regulatory advisory board

- Russell Thomas (US EPA)*
- Warren Casey (NIEHS)*
- Suzy Fitzpatrick (US FDA)*
- Patience Browne (OECD)*
- Thomas Steger-Hartmann (Bayer)*
- Christopher Portier (EDF)*

Research collaboration



EU and international toxicology programs (PARC, Tox21, US-FDA, NIH Japan, ICCVAM, ...)

Workshops, conferences



ASPIS stakeholder group



# Webpage and social media



[www.ontox-project.eu](http://www.ontox-project.eu)

Do you want access to Members area?

[Home](#)

[The project](#)

[Consortium](#)

[Contact](#)

[Members area](#)

Search ...

Search

The vision of the ONTOX consortium is to provide a functional and sustainable solution for advancing human risk assessment of chemicals without the use of animals in line with the principles of 21st century toxicity testing and next generation risk assessment.

SCIENTIFIC MEETINGS



PUBLICATIONS



PUBLIC DELIVERABLES



NEWS



LinkedIn, Twitter and Facebook accounts are accessible *via* the website

Subscription to the newsletter *via* the website



Funded by the Horizon 2020  
Framework Programme of the  
European Union



3<sup>rd</sup> *In Silico* Toxicology Conference

Mathieu Vinken  
VUB

mathieu.vinken@vub.be  
+32 2 477 45 87



[www.ontox-project.eu](http://www.ontox-project.eu)