Title: ECETOC-VHP4Safety-ONTOX: Application of Digital Infrastructures Leveraging AI in Human Health Risk Assessment

Date and Venue: 28-29 October 2025, Cardo Hotel, Brussels

Workshop Format: 2-day, in person (Face-to-Face)

Background and objectives: The integration of digital infrastructures and artificial intelligence (AI) in human health risk assessment is rapidly evolving, offering promising advancements in toxicology and exposure science. However, trust, transparency, and validation and ethical considerations, remain critical for their regulatory and scientific adoption.

Key Objectives:

- Explore how to build **trust and confidence** in AI tools used in toxicological risk assessment.
- Define what level of **transparency and clarity** is needed to make AI decision-making understandable.
- Discuss validation methods for AI tools for different uses.
- Examine the interoperability of different digital infrastructures, such as the platforms OPRA and VHP4Safety, and their alignment with other ongoing initiatives.
- Address **ethical concerns** related to using AI in health and safety assessments.
- Collect **-**multi-stakeholders' insights (regulators, scientists, and industry) **on needs, expectations, and** experiences.
- Foster dialogue on how AI models can be made understandable, **scientifically robust and practically useful**.

Participants: The workshop seeks to bring together 40 participants from regulatory bodies, industry and academia.

Workshop Outcome:

- Identify key challenges and opportunities in applying digital tools and AI in human health risk assessment.
- Propose practical solutions and next steps for trusted, transparent, and regulatory-usable digital platforms.

Background on AI tools and case studies:

A) OPRA (ONTOX AI)

OPRA decision tree will finally be an interactive digital model and will be integrated in the future ONTOX Hub platform. ONTOX Hub is a platform which will secure the sustainability of the ONTOX project results/outputs and thereby OPRA and will ensure long-term access to the results of the ONTOX project. The OPRA decision tree is being built as a diagram made up of several key components, with a high-level overview shown in Figure 1.

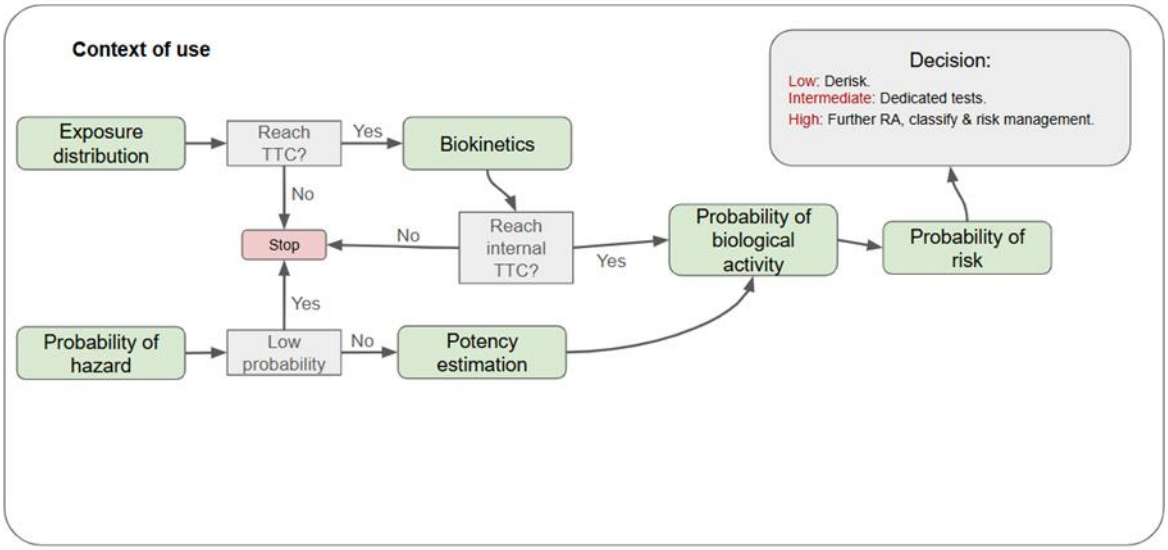

Fig. 1: OPRA high-level view. Exposure distribution from probability of exposure of individual. Biokinetics resulting range of active tissue concentrations. Probability of hazard from chemical features, from biological and chemical properties, and from perturbation of physiology. Potency estimation from in vitro and from in silico. Probability of risk for individual or population.

ONTOX is developing several AI-based tools, called AI agents, which support various parts of the OPRA system. These AI agents can access relevant data and tools, guide users through tasks, and use large language models (LLMs) to help turn insights into practical actions. This improves the **transparency** and **traceability** of the information they use.

To work effectively, these agents follow clear, logical workflows, for example, they can help process and review large numbers of scientific publications. An internal demonstration of the AI agents is planned for the ONTOX consortium in summer 2025, with the goal of fully integrating them into OPRA during its initial phase.

AI-agent used in OPRA will be fully documented and will be featured in a real-world case study on the chemical PFOA to show how it works in practice. Importantly, these tools must be **explainable and transparent**, avoiding the so-called 'black box' problem, so that regulators and other users can trust their results.

AI agents that are not yet ready will be further developed in future projects. Ultimately, OPRA, along with its AI agents, must be presented and discussed with stakeholders, especially regulatory bodies, and industry risk assessors, to ensure it meets their needs and earns their confidence.

B) VHP4Safety

In the Virtual Human Platform for Safety Assessment (VHP4Safety) project, we develop the Virtual Human Platform (VHP) to support risk assessment of chemicals and pharmaceuticals. The VHP is a digital research infrastructure which enables human relevant safety assessments through interactive workflows that integrate FAIR data and containerized tools and services. For more information on the VHP4Safety project, see our project video and project paper.

The workflows, tools and services of VHP are developed using expert input, systematic reviews, dedicated models, including large language models and agent-based retrieval systems. Dedicated user research through stakeholder engagement, forms the foundation for developing a user-interface and an application programming interface (API) layer to enable execution of workflows that combine data from in vitro experiments, human studies (epidemiological, clinical and pharmacovigilance data), and various other knowledge resources. Prioritized users of the VHP include scientists and risk assessors from government and industry. This way, the platform can serve as a gateway to relevant computational models and databases, including the recommended international data collections connected by ELIXIR, in the European infrastructure for biological data. Built as a Docker-based platform, the VHP ensures data and tools are reusable and interoperable, for which objective quality criteria and verification processes are in place.

On the VHP, we collect and improve in silico tools for toxicokinetics to enable the translation of in vitro data obtained in human-relevant bioassays to the in vivo situation. We also deploy and integrate key in silico tools to describe computational toxicodynamics, including machine learning, structure-based modelling, and bioinformatics. Adverse outcome pathways (AOPs) play a key role in the toxicodynamic part on the platform and will serve as the basis to describe and understand results from case studies that represent the demonstrators of the VHP.

Together, the way we build the VHP not only ensures availability, quality control, and interoperability, it also effectively makes efforts to build the platform more sustainable and facilitates collaboration with other cloud- and container-based platforms, including those in other toxicology projects and in the European Open Science Cloud (EOSC).

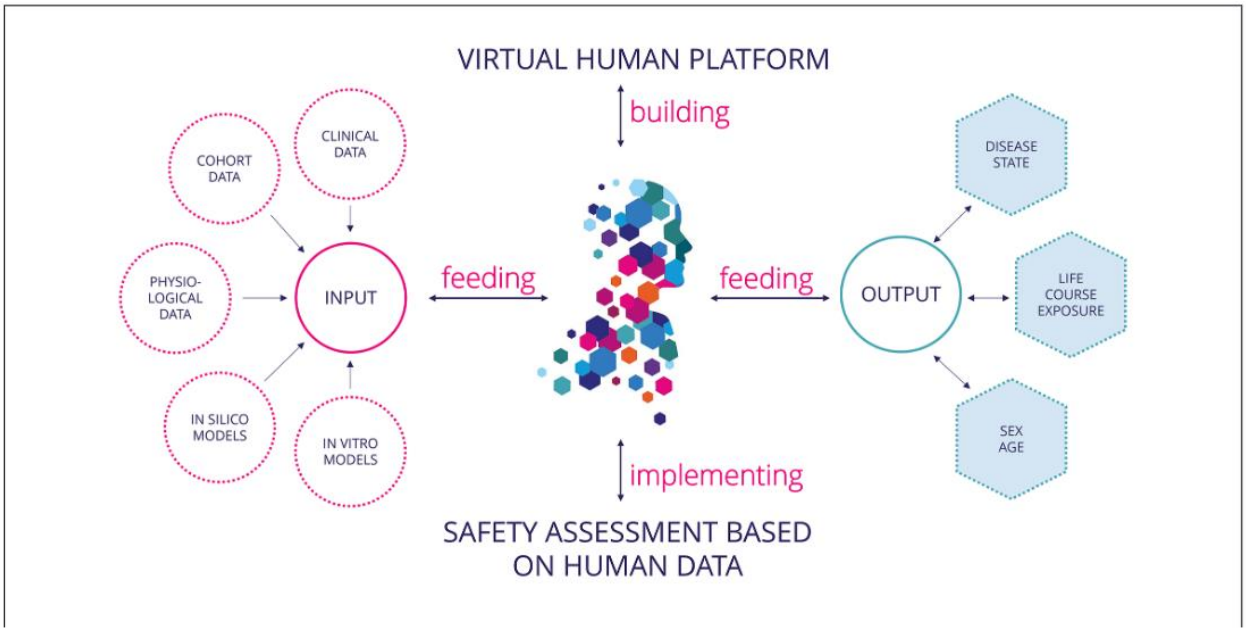

Fig. 2: Conceptual overview of the Virtual Human Platform for Safety Assessment (VHP4Safety) project

Workshop programme

Day 1: 28th October 2025		
8:30 – 9:00	Arrival and registration	
9:00 – 10:00	PLENARY SESSION: ▪ Introduction by OC representatives – Objectives of the WS, and expected outcome of the workshop. *(10 minutes)* ▪ Keynote – to be considered *(20 minutes)* ▪ OPRA overview *(20 minutes)* ▪ VHP4Safety overview *(20 minutes)* ▪ Introduction to breakout groups *(10 minutes)*	**OC Representatives (TBD)**
10:00 – 11:30	***Coffee break***	
11:30 – 13:00	**BREAKOUT SESSIONS PART 1 – work in respective breakout groups.**	**Participants**
13:00 – 14:00	***Lunch***	
14:00 – 15:00	**BREAKOUT SESSIONS PART 2 – Multiple group discussions by case study e.g., OPRA and VHP4Safety.**	**Participants**
15:00 – 16:30	**BREAKOUT SESSIONS PART 3 - work in respective breakout groups.**	**Participants**
16:30 – 17:00	***Coffee break***	
17:00 – 18:00	**BREAKOUT SESSIONS PART 4 – Initial mutual presentation for opposing group.** Paired group presentation (regulatory vs. industry). Presenting initial ideas to overcome identified barriers, having feedback from opposing groups – pros/cons.	
19:00	***Evening event***	

Day 2: 29th October 2025		
9:00 – 9:15	Welcome and overview of Day 2	
9:15 – 10:45	**BREAKOUT SESSIONS PART 5 - work in respective breakout groups.** Refining proposals after feedback from opposing groups.	**Participants**
10:45 – 11:15	***Coffee break***	
11:15 – 12:15	**BREAKOUT SESSIONS PART 6** Final preparation for group presentation	

12:15 – 13:30	***Lunch***	
13:30 – 15:30	Plenary presentation and discussion: ▪ Breakout group presentation 5 minutes per group and 10 minutes Q/A ▪ General discussion and conclusion (60 minutes)	
15:30 – 16:30	Overall Conclusion, way ahead & closing remarks	

Abstracts and Speakers' bios

Title **Speaker**	
Abstract:	
	Bio
Title: Introduction to OPRA **Speaker: Alexandra Maertens (To be confirmed)**	
Abstract:	
	Bio
Title: Introduction to VHP4Safety **Speaker**	
Abstract:	
	Bio

Organising Committee

Anne	Kienhuis	RIVM
Aniek	De Winter	Utrecht University
Maryam	Zare Jeddi	Shell
Mathieu	Vinken	Vrije Universiteit
Michael Guy	Diemar	3Rs Management
François	Busquet	Altertox
Monicah	Kirathi	Altertox
Francois	Doulliard	Altertox
Chantal	Smulders	Shell
Blanca	Serrano	ECETOC
Andrea	Lopez	ECETOC