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**IND02-05****The NeuroDeRisk toolbox: DeRisking chemical structures for neurotoxic adverse outcomes**

S. D. Bryant<sup>1</sup>, G. Ibis<sup>1</sup>, T. Seidel<sup>2</sup>, S. Kohlbacher<sup>2</sup>, J. Heider<sup>2</sup>, M. Ernst<sup>3</sup>, K. Bampali<sup>3</sup>, F. Koniuszewski<sup>3</sup>, V. Virvilis<sup>4</sup>, E. Lekka<sup>4</sup>, A. Persidis<sup>4</sup>, M.-A. Mayache<sup>5</sup>, D. Weissmann<sup>5</sup>, T. Langer<sup>2</sup>

<sup>1</sup>*Inte:Ligand Software Entwicklungs und Consulting GmbH, Vienna, Austria;*

<sup>2</sup>*University of Vienna, Department of Pharmaceutical Sciences, Vienna, Austria;*

<sup>3</sup>*Medical University of Vienna, Department of Pathobiology of the Nervous System, Vienna, Austria;*

<sup>4</sup>*Biovista, Inc., Athens, Greece;*

<sup>5</sup>*ALCEDIAG, Montpellier, France*

Prediction of adverse effects of compounds and pharmaceuticals on the central (CNS) and peripheral nervous systems (PNS) is a significant and unresolved challenge in preclinical research and development (R&D). To address this, we have developed the NeuroDeRisk Toolbox (<https://neuroderisk.eu/in-silico-toolbox/>). The NeuroDeRisk Toolbox offers a combination of innovative in silico tools for derisking compounds for neurotoxicity at an early stage of the development process [1–5]. It addresses unmet needs in preclinical drug discovery and development related to three of the most challenging neurotoxic adverse effects associated with chemicals and prescription drugs. Those include seizures, psychological/psychiatric changes, and peripheral neuropathies. It has been developed in collaboration with neurobiologists, safety toxicologists, pharmaceutical scientists, computational chemists and software engineers in the NeuroDeRisk | Neurotoxicity De-Risking in Preclinical Drug Discovery Consortium (IMI-2-821528). The NeuroDeRisk Toolbox supports the 3Rs approach (“Reduce, Refine, Replace” animal use) while at the same time increasing productivity towards the development of safer pharmaceuticals. Early assessment of risk for neurotoxicity will benefit human volunteers and patients through safer, preclinical candidates and pharmaceutical drugs. It supports clinical and preclinical researchers by understanding molecular initiating events (MIEs) and adverse drug events (ADEs), and the pharmaceutical industry by reducing attrition rates of candidate medicines in development at a much earlier stage in the compound development process. The NeuroDeRisk Toolbox is available for in-house installation and productive usage [1].

**References**

- [1] The NeuroDeRisk In Silico Toolbox: <https://neuroderisk.eu/in-silico-toolbox/>
- [2] The NeuroDeRisk IL Profiler: <https://docs.inteligand.com/ndr/il-profiler/>
- [3] The NeuroDeRisk IL Profiler Predictive Models: <https://docs.inteligand.com/ndr/models/>
- [4] The NeuroDeRisk FAERS Drug Selection Tool: <https://neuroderisk.biovista.com/doc/biovista-faers-drug-selection/>
- [5] The NeuroDeRisk Knowledge Base: <https://neuroderisk.biovista.com/doc/ndrkb/>

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**IND03 | WuXi AppTec: The Importance of Animal Welfare During Your Toxicology Program****IND03-01****The importance of animal welfare during your toxicology program**

J. Kelly

*WuXi AppTec, Cranbury, USA*

What is animal welfare and why is it important during your toxicology program? There are excellent opportunities to advance the welfare of animals by eliminating pain and distress, and systematically reducing the number of animals necessary for individual studies by implementing the 3Rs.

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**IND04 | Emulate, Inc.: Modernizing Drug Discovery & Development with Organ-Chip Technology****IND04-01****Modernizing drug discovery & development with organ-chip technology**

S. Berdichevski

*Emulate Inc., Boston, USA*

There is no doubt that scientific progress has accelerated the discovery and development of innovative medicines, a phenomenon acutely visible through the rapid advancement of vaccines against SARS-CoV-2. Outside of dealing with a global pandemic, the process of drug discovery and development remains painfully slow, extremely costly and can, despite appropriate measures, result in patient-safety concerns. Because only around 12% of drugs that enter clinical trials make it to approval, governments in the United States and Europe are taking steps towards modernizing the process of drug discovery and development. Whilst several solutions will ultimately be required, there are growing calls for the utilization of 21st century tools within drug discovery pipelines. One such tool is organ-on-a-chip technology that employs microfluidic systems engineering to recapitulate in vivo cell and tissue microenvironments in an organ-specific context. This is achieved by recreating tissue-tissue interfaces and providing fine control over fluid flow and mechanical forces, optionally including supporting interactions with immune cells and microbiome, and reproducing clinical drug exposure profiles.

This seminar will showcase the Emulate Organ-Chip platform and will present the findings of the first of its kind Organ-Chip study which utilized the pharma consortium Innovation and Quality (IQ) roadmap for developing in vitro liver models for the prediction of drug-induced liver injury<sup>1</sup>. Using 780 Liver-Chips across a test set of 27 small molecule drugs, data will be presented indicating that the Liver-Chip has a 87% sensitivity and 100% specificity, thus making it a highly predictive tool compared to animal models and prior preclinical in vitro models. The seminar will complete with an overview on how such a tool can be implemented into drug discovery workflows whilst providing adopting organizations a significant productivity gain.

**Reference**

[1] Baudy *et al.* 2020. Liver microphysiological systems development guidelines for safety risk assessment in the pharmaceutical industry. *Lab Chip*, 20, 215.

<https://doi.org/10.1016/j.toxlet.2022.07.241>

## IND05 | SenzaGen AB: *In vitro* skin sensitization testing: new opportunities for hazard and quantitative potency assessment using genomics and machine learning technology

**IND05-01**

***In vitro* skin sensitization testing: new opportunities for hazard and quantitative potency assessment using genomics and machine learning technology**

**A. Forreryd**

*SenzaGen AB, Lund, Sweden*

The field of *in vitro* skin sensitization assessment is rapidly evolving, and novel methods are developed to increase predictivity, broaden the applicability and to provide reliable quantitative and qualitative potency assessments. This symposium will introduce the audience to GARD<sup>®</sup>, the genomic-based technology, and discuss the new opportunities it brings to the field of *in vitro* skin sensitization testing.

The session will start with an introduction to the key elements of the GARD technology followed by reviewing the performance and applicability of the GARDskin assay for *in vitro* skin sensitization testing. Results from the assessment of “difficult-to-test” samples including metals, complex mixtures, pre- and pro-haptens, surfactants and hydrophobic substances will be presented. Moreover, the capability of GARD for quantitative skin sensitizing potency assessment will be exemplified by several industry-sponsored case studies.

In summary, this symposium will highlight the performance and applicability domain of GARD and discuss its potential for addressing remaining challenges within R&D and regulatory skin sensitization testing.

**Learning objectives**

The participants will have the opportunity to learn more about the following:

- Key elements of the GARD technology.
- Quantitative potency assessments on a continuous scale for use as point-of-departure in already established risk assessment procedures.
- The applicability domain of GARDskin and its performance for “difficult-to-test” samples including metals, complex mixtures, pre- and pro-haptens, surfactants and hydrophobic substances.
- User cases from industry-sponsored studies to exemplify how GARD can be used for R&D and regulatory testing.

About the GARD technology platform.

GARD – Genomic Allergen Rapid Detection<sup>®</sup> – is a next-generation, non-animal-based testing platform for identification and potency

assessment of chemical sensitizers. The GARD platform brings novel elements to the field of regulatory toxicology, and integrates state-of-the-art technological components, including human immunological cells, specific genomic biomarker signatures and machine learning-assisted classification models. As a result, GARD comprises an accurate, cost-effective and efficient method for assessment of skin sensitizing properties of neat chemicals, complex mixtures and medical devices and may successfully be applied throughout the product life cycle.

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## IND06 | Lunch Industry Symposium

**IND06-01**

**Predicting human responses to drug toxicants using liver-on-a-chip technology**

**T. Kostrzewski**

*CN-Bio Innovations Ltd, Cambridge, UK*

Liver-on-a-chip technology can recapitulate human tissue level function, using multi-cellular 3D liver microtissues cultured in a microfluidic platform. We will demonstrate how these microtissues can be exposed to hepatotoxic substances, to determine mechanisms of human hepatotoxicity and enhance predictivity in the drug development process.

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**IND06-02**

**Enhancing the early detection of safety liabilities of new therapies to advance drug development**

**S. Prill**

*Astra Zeneca, Mölndal, Sweden*

Enhancing the early detection of safety liabilities of new therapies would advance drug development. The simplicity of current pre-clinical *in vitro* assays and species differences from animal studies means there is often a lack of predictivity for the patient. Microphysiological systems (MPS) aim to recapitulate the architecture, cell-cell interactions, and tissue microenvironment more representative of their complex *in vivo* biology than standard two-dimensional (2D) culture. Thereby human MPS provide an opportunity to improve preclinical-to-clinical translation and have the potential to improve the drug development process at multiple points.

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