EU non-animal projects brought together for ASPIS cluster

11 November 2021
By Emma Davies
https://chemicalwatch.com/370080/eu-non-animal-projects-brought-together-for-aspis-cluster

Progress on selecting test chemicals

The EU has linked three ongoing EU projects on new approach methodologies (NAMs) to form a cluster called ASPIS, which had a kick-off meeting in Brussels on 4 November.

ASPIS is led by the European Commission and aims to pick out common areas across the NAMs projects. It has a goal to "synergise efforts" to increase the visibility of EU-supported research to improve safety assessment without animal testing. Involving a total of 70 institutions, and with around €60m of funding from Horizon2020, the ASPIS projects are:

- PrecisionTox (€19m);
- Risk-Hunt3R (€23m); and
- Ontox (€17m).

Work package leaders from the three projects have defined collaborative areas and are setting up ASPIS working groups on:

- chemical selection;
- kinetics and exposure;
- omics;
- quantitative adverse outcome pathways (qAOPs);
- computational approaches; and
- risk assessment.

As well as the working groups, ASPIS will have a regulatory forum of international experts to ensure that projects have global regulatory relevance.

The chemical selection group's main goal is to identify "commonalities" across projects. "Chemical selection is a high priority and can't be delayed," said Jonathan Freedman from the University of Louisville, US, during an ASPIS session at the EU-ToxRisk final symposium in Brussels on 3-4 November.

Chemical selection working group members have so far set up two ASPIS-wide initiatives. The first uses artificial intelligence to mine literature and toxicology databases for substance information. The second involves developing a common database for ASPIS test chemicals.

Quantitative AOPs are a "key topic" for ASPIS, said Bob van de Water from the University of Leiden in the Netherlands, who heads Risk-Hunt3R. The qAOP working group will look at how case studies can be combined to have "more impact" for designing and establishing them, he said.

The final working group on risk assessment will ask: "How can we together impact on changing the paradigm of [safety] testing?" said Professor van de Water. "We need to come to a common strategy to convince stakeholders that the approaches that we have been using are fit for purpose," he said.

ASPIS projects

During the ASPIS session, Jonathan Freedman from the University of Louisville, US described how PrecisionTox is first working on five "well-studied" chemicals, including arsenic and cadmium, to identify any issues with, for example, assay development, data generation and analysis. The chemicals are being used for a "run-through of the entire project to see where the problems are going to be before we start looking at a large number of chemicals," he said.

PrecisionTox aims to uncover molecular toxicity pathways shared across the animal kingdom, using human cell lines and a set of model organisms, including fruit flies, water fleas and round worms. Coordinated by the University of Birmingham, UK, its goal is to "establish causation" between chemicals and adverse health effects. Next, project partners will select a group of 50 data-rich chemicals for analysis, based on adverse outcomes and molecular initiating events. A third test group will contain

150 data-rich and data-poor substances. Finally, a fourth group of around 50 substances will be used for cross-ASPIS studies and to fill in gaps in AOP development.

Risk-Hunt3R – risk assessment of chemicals integrating human centric next generation testing strategies promoting the 3Rs – began in June and builds on EU-ToxRisk. The project promises to develop integrated testing strategies for assessing whether chemicals cause a range of human health effects, including developmental neurotoxicity and non-genotoxic carcinogenicity. It involves industry and regulators and will carry out a series of case studies.

Ontox is coordinated by Vrije University in Brussels and aims to create NAMs to predict systemic repeated dose toxicity effects. It focuses on six NAMs addressing adverse effects in the liver, kidneys and developing brain. The NAMs have computational systems fed by biological, mechanistic, toxicological, epidemiological, physico-chemical and kinetic data. Data gaps identified by artificial intelligence will be filled with *in vitro* and *in silico* testing. The plan is for the six NAMs to be evaluated and applied in collaboration with industrial and regulatory stakeholders.

ASPIS is an acronym for animal-free safety assessment of chemicals: project cluster for implementation of novel strategies.