Session: The future of human health assessment

Using new methodologies for a better understanding of the health impacts of petroleum substances

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Ivan Rusyn (Texas A&M University)

Cat-App was initiated with the aim of minimizing the need for testing in vertebrate animals under regulatory programmes. This is achieved by grouping petroleum substances (PS) to make the most optimal use of the toxicological information on PS by read-across of the available data within and (where needed and justified) between these groups. A framework will be developed for grouping based on chemical-biological properties combining multiple streams of information comprising PS production type/refining process, physical-chemical properties, chemical analytical profiles, existing (eco)toxicological data and a comprehensive array of biological responses in a broad spectrum of in-vitro systems.

Direct implementation of the Cat-App framework in the Concawe REACH strategy by applying the approach and submitting the data in the petroleum REACH dossiers will fill data gaps in the already-existing in-vivo toxicological data on PS, and help to develop a pragmatic and informed testing approach only as a last resort when read across to fill data gaps is not possible.

This strategy will eventually address mandatory human health hazard end points under REACH while significantly reducing the use of vertebrate animals for toxicity testing without underestimating the potential hazards.

The intention is to inform a broad spectrum of stakeholders globally (commercial entities, regulatory agencies and non-governmental organizations), concerned with public health and well-being, and to promote application of the Cat-App framework which is expected to eventually have a wide and diverse applicability domain.

Cat-App work programme

Cat-App: New technologies to underpin the category approaches and read across in regulatory programmes
Project Management: Hans Ketelslegers / Concawe
Steering: Scientific Committee / Concawe

WP1

Organisation of data available on PS (Ivan Rusyn/AgriLife)

1.1 Obtain, process and share chemical samples
1.2 Collect available records (manufacturing process info., phys./chem. properties, analytical chemistry, existing toxicity data on mammalian, ecotox)
1.3 Digitise records into flexible and inter-operable databaseformat

WP2

Toxicity screening (Ivan Rusyn/AgriLife)

WP2.a (Ivan Rusyn/AgriLife)

- High content screening of iPS-derived cells
- Hepatocytes, neurons, cardiomyocytes, myo-fibroblasts, endothelial

WP2.b (Tim Gant/PHE)

- Toxicity phenotyping in 10 diverse cell lines (overlapping with LINCS)

WP3

High throughput genomics (Ivan Rusyn/AgriLife)

3.1 High-throughput transcriptomics profiling of 13,500 samples for TempO-seq

WP4

Perform data integration and chemical biological read across (Fred Wright/NCSU)

WP 4.a (Fred Wright/NCSU)
4a.1 Coordinate data management and workflow
4a.2 Perform uncertainty and variability analyses
4a.3 Process and analyse omics data
4a.4 Perform ToxPi analysis

WP4.b (Shu-Dong Zhang/Ulster)
4b.1 Perform connectivity mapping
4b.2 Develop and apply an-alysis algorithms to robust-ness testing, investigate grouping accuracy and profiling cost

WP5

Dissemination, project administration and Outreach (Klaus Lenz/SYNCOM)

5.1 Project Dissemination and website
5.2 Project Administration
5.3 Outreach

Advisory Board

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Institute abbreviations:
AgriLife: Texas A&M AgriLife Research - NCSU: North Carolina State University - PHE: Public Health England
Ulster: Ulster University - SYNCOM: SYNCOM R&D consulting GmbH

Timeline

MS1: All petroleum substances available as DMSO extracts for testing in in vitro assays

MS2: Quality control report of preliminary in vitro analyses

MS3: Initial workflow for Chemical-Biological Read-across and ToxPi visualisation available