



# Alliance for Human Relevant Science

Newsletter Spring 2019

## WHO WE ARE

**The Alliance for Human Relevant Science** is an inclusive collaboration of like-minded companies, organisations and individuals. Working together, we will accelerate innovation and create positive change.

The UK is a world leader in life science research. Yet many breakthroughs are lost in translation from preclinical animal models to humans. There is now a tremendous opportunity to bridge the translational gap with human relevant technologies.

### It is time to focus on the human.



Simcyp



LORD DOWDING FUND  
FOR HUMANE RESEARCH



### AIMS OF THE ALLIANCE

- Support better science for better health
- Save lives – human and animal – through improved safety and efficacy testing of medicines and other chemicals
- Save money by promoting more scientifically relevant research

## FINDING SYNERGIES FOR 3RS – TOXICOKINETICS AND READ-ACROSS

A [recent publication](#) by the [EPAA Partners Forum](#), including Alliance member SimCyp and co-authored by Iain Gardner, provides an overview on research activities to develop *in vitro* toxicokinetics methods and physiologically-based

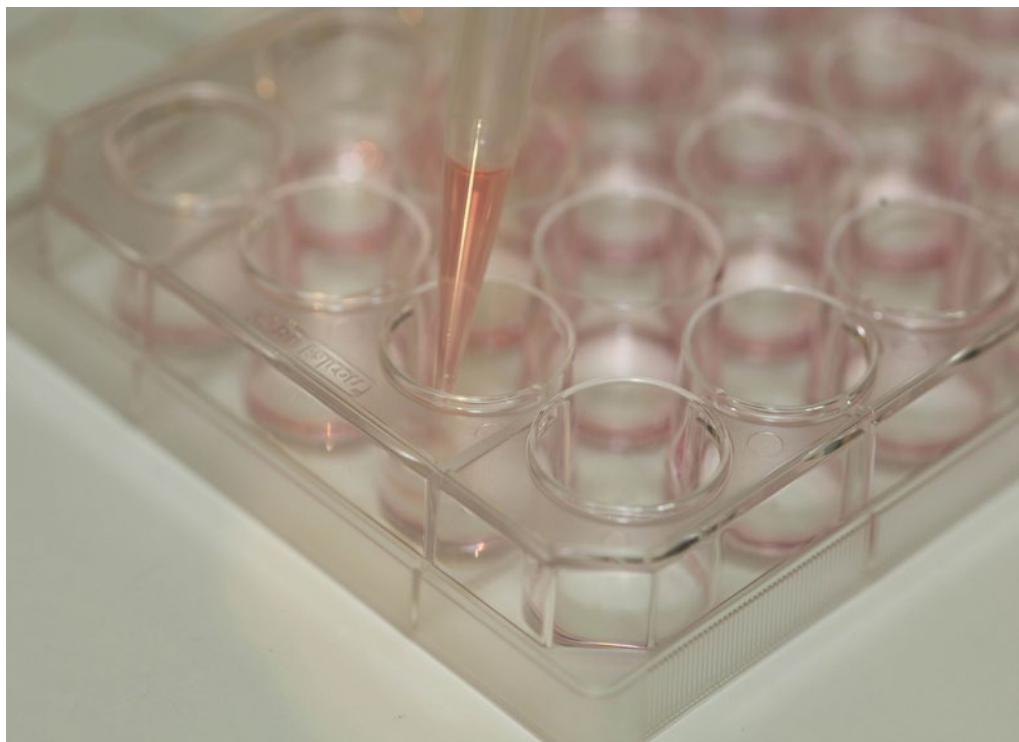


kinetic (PBK) models and to find synergies to enhance the use of toxicokinetic data to strengthen read-across and to promote the generation of human relevant toxicokinetic data using *in vitro* and *in silico* tools.

## EBTC TOX21 STUDY PRESENTED AT US SOT AND UK BTS EVENTS

An ongoing study by The Evidence Based Toxicology Collaboration (EBTC) Tox21 Working Group was accepted for a platform presentation during the 58th Annual Meeting of the Society of Toxicology (SOT), March 10-14, 2019 in Baltimore. The working group includes Safer Medicines Trust, John Hopkins University, the Norwegian Institute of Public Health and other stakeholders. The study aims to answer the following question: '*How well do the ToxCast in vitro tests predict the liver outcomes in animals (mice, rats, Beagle dogs and non-human primates) and humans?*'

To achieve this, the project is combining three main evidence streams (Systematic literature review of animal and human published studies; mechanistic 'in vitro'



data and human real world evidence (RWE)) to compare the observed adverse event profiles with the pathway signatures based on ToxCast and Tox21 data for five pairs of drugs. Each pair includes one drug which has caused human adverse effects and a pharmacologically related drug which has not caused those effects. At SOT, the group presented its work so far on the first

pair, the antidiabetic drugs Troglitazone (withdrawn) and Rosiglitazone.

The work was also presented by Gerry Kenna at the [2019 British Toxicology Society \(BTS\)](#) on 17 April in Cambridge, entitled 'Can we use *in vitro* data to predict human hazard? A comparison of three evidence streams for troglitazone and rosiglitazone'

SMT is delighted to welcome Dr Jan Turner as its new Director. Jan brings a wealth of experience in developing and promoting human-relevant in vitro technologies, including directing validation studies and influencing organisations such as the FDA to introduce such technologies into the early safety testing of drugs. After completing her BSc in Biochemistry & Pharmacology, followed by a PhD and postdoctoral research in Genetic Toxicology, Dr Turner worked for Amersham Biosciences, subsequently GE Healthcare Life Sciences. Her roles included Development Scientist, Project Leader, Global Product Manager and Product Management Operations Leader. For the past 18 months she has been Senior Product Manager at BBI Solutions, directing global cross-functional teams and driving adoption of innovative technologies.



## OVERCOMING OBSTACLES TO HUMAN RELEVANT SCIENCE

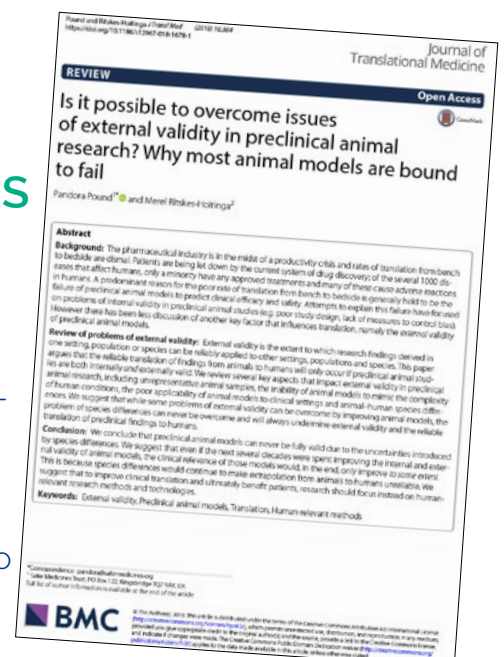
Dr Gerry Kenna of Safer Medicines Trust spoke at the second WIST (Wissenschaft statt Tierversuche- Science instead of Animal Experiments) Congress in Germany on October 2018 on the topics of 'Overcoming obstacles to human relevant science'. His [full presentation](#) and [slides](#) can be viewed here.



## PUBLICATION OF 'IS IT POSSIBLE TO OVERCOME ISSUES OF EXTERNAL VALIDITY IN PRECLINICAL ANIMAL RESEARCH? WHY MOST ANIMAL MODELS ARE BOUND TO FAIL'

In November 2018, the Journal of Translational Medicine published a paper by Dr. Pandora Pound of Safer Medicines Trust and Prof Merel Ritskes-Hoitinga of SYRCLE entitled '[Is it possible to overcome issues of external validity in preclinical animal research? Why most animal models are bound to fail](#)'.

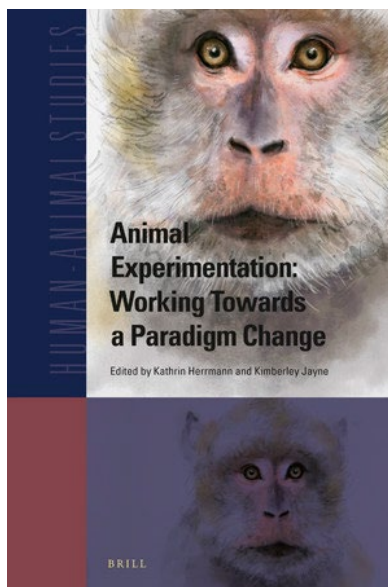
A [follow up article](#); 'Species Differences: The Elephant in the Room' was published in January this year and includes a link to the original paper.





## UK LAUNCH FOR ANIMAL EXPERIMENTATION: WORKING TOWARDS A PARADIGM CHANGE

On the 8th March 2019 the UK launch for Animal Experimentation: Working Towards a Paradigm Change, a new open access and peer reviewed book, was held in London. The event, sponsored by Animal Defenders International and supported by the Lord Dowding Fund, was attended by international delegates, and focused on critically evaluating animal use in science and the solutions for phasing out and replacing their use with human relevant methods. Presentations were given from Alliance members, Kathy Archibald, Jan Creamer, Christina Dodkin, Kimberley Jayne, Rebecca Ram, Jan Turner and Malcolm Wilkinson, who gave their unique visions for shifting the paradigm towards an animal free world of science. The



event also saw the launch of the Declaration for Advanced Science, spearheaded by Animal Defenders International, to "support research and legislative measures which accelerate the realisation" of a goal set out in European Directive 2010/63 to replace "procedures on live animals for scientific and educational purposes as soon as it is scientifically possible". Individuals or organisations wishing to support the declaration can contact [research@ldf.org.uk](mailto:research@ldf.org.uk) for further information. The book, edited by Kathrin Herrmann and Kimberley Jayne, is now available for free download or to purchase online through [Brill.com](http://Brill.com).

## UPM BIOFORE BEYOND FOSSILS



[UPM Biomedicals](#) are a member of the Alliance for Human Relevant Science and advance bio-innovations from renewable resources, by offering their patented 3D hydrogel technology for use in a wide number of applications. GrowDex is an animal free, ready to use hydrogel that mimics the extracellular matrix (ECM) and supports cell growth and differentiation with consistent results. Bridging the gap between in vitro and in vivo studies, GrowDex can be used for 3D cell culture for spheroid and /organoids, in personalised medicine, regenerative medicine,

organ-on-a-chip models, drug release studies, 3D printing and much more.

The technology has an ever increasing number of [applications](#). Recent success includes studies at the University of Zurich School of Applied Sciences, where SaOS-2 and HDF were successfully co-cultured in GrowDex with different cell ratios. Studies concluded that co-culturing of SaOS-2 tumor cells with stroma cells (HDF) in 3D hydrogel results in physiologically more relevant microtissues that could be used as an in vitro model

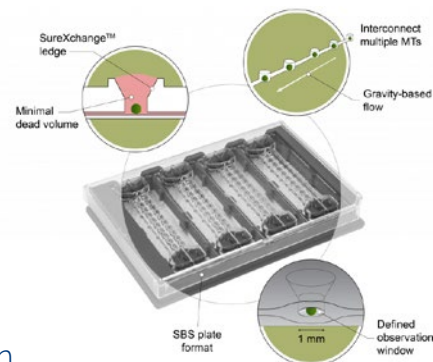
e.g. [in osteosarcoma drug development](#).

[Further recent success at the University of Helsinki demonstrated how MCF7 breast cancer cells form 3D spheroid structures in Growdex, to offer improved functionality and relevancy of 3D cultures, offering better in vitro models for disease modelling, drug development and toxicity assessment.](#)

Further information on these and other successful applications are available on the [UPM Biomedicals website](#).

### AKURA™ FLOW ORGAN-ON-A-CHIP SYSTEM BY INSPHERO

InSphero has been working over the past year to set new standards with their [Akura Flow system](#), involving scalable organ-on-a-chip networks which connect multiple human tissue systems and advanced liver disease models to more faithfully mimic the human response to drug dosing. Their work was presented at the Society for Laboratory Automation and Screening (SLAS) [2019 conference](#) in February.



### HORIZON 2020 ORCHID ROADMAP RELEASED



In November 2018, the Horizon 2020 initiative published its interim roadmap report: '[ORCHID \(Organ-on-Chip in Development\): Towards a European roadmap for Organ-on-Chip](#)' during the

International Organ-on-Chip Symposium on November 8-9 2018 in Eindhoven, the Netherlands.

### NC3RS CRACK IT AWARDS £1 MILLION GRANT FOR IN SILICO ASSESSMENT OF DEVELOPMENTAL AND REPRODUCTIVE TOXICITY

The University of Applied Sciences in Utrecht has been awarded £1 million by the NC3Rs to deliver Phase 2 of the 2017 [DARTpaths CRACK IT Challenge](#). More details are available on the [CRACK IT website](#)

### VANDA PHARMACEUTICALS TAKES A STAND AGAINST UNNECESSARY ANIMAL RESEARCH



In February, US drug company Vanda filed a complaint against the U.S. Food and Drug Administration (FDA) requesting that the court lift a partial hold on the clinical development of its new drug Tradipitant - a potential treatment for several human conditions including gastroparesis. The hold (which Vanda is also challenging as being illegal) prohibits the company from studying Tradipitant in humans for more than 12 weeks, unless Vanda carried out what it considers to be 'unnecessary and unethical animal studies'. The dispute concerns Vanda's refusal to conduct nine month dog studies, on the basis that numerous previous animal studies have shown no clinically relevant safety

signals in humans. Critically, clinical studies of Tradipitant in humans have also suggested that it is well-tolerated, as have clinical and preclinical studies of drugs in the same class as Tradipitant. In addition, Vanda states how scientific literature has shown that nine-month studies in dogs are unlikely to identify clinically relevant safety signals that are not already identified in three-month studies. The company has also published an [open letter](#) to the FDA and asks other companies to support its position to reject unnecessary animal studies and request the FDA to conduct a review of the data it holds. Further details are available on the [VANDA website](#)

## ECVAM PUBLISHES LATEST 'STATUS REPORT ON THE DEVELOPMENT, VALIDATION AND REGULATORY ACCEPTANCE OF ALTERNATIVE METHODS AND APPROACHES (2018)'



The 133 page report provides updates on a number of ongoing projects, such as EU-ToxRisk, as well as projects on the assessment of chemical mixtures and endocrine disruption and status updates on a number of test method submissions. It also includes ECVAM's [Database Service on Alternative Methods](#) and

[TSAR –the Tracking System for Alternative Methods towards Regulatory Acceptance:](#)

The authors of the report, Valerie Zuang and Maurice Whelan of the JRC also discuss the latest developments in [an interview with the EU Science Hub](#).

## LAUNCH OF INDIAN SOCIETY FOR ALTERNATIVES TO ANIMAL EXPERIMENTS

In November 2018, India joined other nations working to replace the use of animals in research with the launch of the Indian Society for Alternatives to Animal Experiments (ISAAE) during the country's second national conference on alternatives in New Delhi, sponsored by the BioMed21 Collaboration. The conference created a platform for national

and international scientists from various backgrounds to engage in discussions on current - as well as the future of - human relevant technologies in research and testing. In addition, the BioMed21/ HSI India collaboration also recently offered funding grants to early career/ PhD scientists to support



the development and open-access publication of scientific literature towards a human-relevant roadmap for research into diseases in India.

## EVENTS

**4-5 June 2019, Cardiff**

Kirkstall ACTC (Advances in Cell and Tissue Culture) 2019

**10-13 Oct 2019, Linz Austria**

UK EUSAAT (European Society For Alternatives to Animal Testing)

**8-11 Sep 2019, Helsinki, Finland**

EUROTOX (European Toxicology Society) 2019

The [FDA website](#) provides a number of upcoming events and workshops on various topics, including drug development, validation and consultation on ICH guideline updates

## JRC SPECIAL ISSUE ON TESTING CHEMICALS FOR DEVELOPMENTAL NEUROTOXICITY USING ALTERNATIVE METHODS

More information at <https://ec.europa.eu/jrc/en/science-update/testing-chemicals-developmental-neurotoxicity-using-alternative-methods>