Alliance for Human Relevant Science

Newsletter Summer 2024

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.

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

CERTARA EXPANDS THE SIMCYP™ SIMULATOR PLATFORM

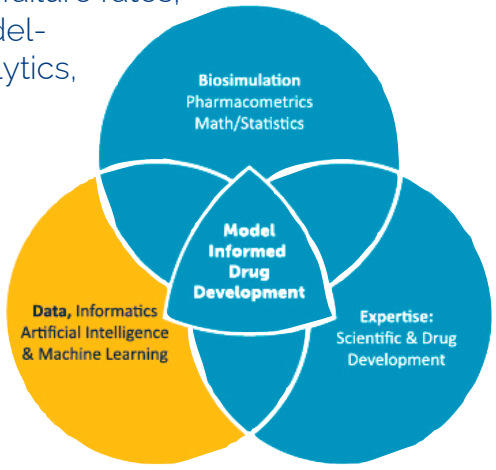
Certara has very recently announced the further expansion of its Simcyp™ Simulator Platform to advance *physiologically based pharmacokinetic (PBPK) modelling*. The latest version includes numerous advancements to support data driven decision making at every stage of drug development. The release of Simcyp Simulator Version 23 coincides with the recent announcement of the FDA establishing the new Quantitative Medicine (QM) Center of Excellence (CoE) within the Center for Drug for Drug Evaluation and Research (CDER). The centre will facilitate the application of quantitative modelling and simulation to drug development, regulatory decision-making, and patient care. PBPK is a cornerstone of these quantitative methods, enabling better predictions of tissue-by-tissue pharmacokinetics .

"*The adoption of biosimulation, particularly PBPK, continues to gain regulatory acceptance,*" Rob Aspbury, President Certara Predictive Technologies said. "*We continue to collaborate with our clients and consortium members to advance the Simcyp Simulator to deliver greater value to scientists supporting better decision-making through in-silico modelling and virtual trials that de-risk development and bring medicines to patients faster.*" Development of the Simcyp Simulator is guided by a consortium of 35 leading pharmaceutical companies and to date has contributed to over 110 FDA-approved novel drugs, informed more than 350 drug label claims and supported clinical trial waivers in many areas.

Certara also continues its training and outreach webinars, including presentation of case studies such as 'Hazard assessment of non-genotoxic carcinogen agrochemicals using New Approach Methodologies (NAMs) and in silico NAMs developed by Risk-Hunt3R's partners.' .

See more at www.certara.com

Certara also continues to work to dramatically reduce new drug failure rates, via development of safe and effective treatments through a model-informed drug development approach, combined with data analytics, artificial intelligence technology, and scientific and regulatory expertise.



While the growth of AI is incredibly promising, the life sciences industry continues to face challenges with nearly 73% of companies struggling to adopt appropriate AI technologies. Certara works to fill this gap with its Gen-AI technology and through its 'on demand' training and educational resources, is promoting Gen AI to help discovery scientists prioritize the right drug candidates and aid clinical trial teams to optimise study design and achieve the highest chance of regulatory success.

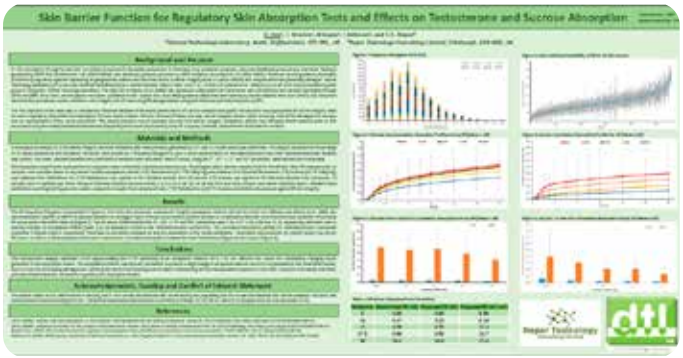
AXOL BIOSCIENCE POWERING MPS PLATFORMS WITH HIGH-QUALITY, FUNCTIONAL HUMAN IPSC-DERIVED CELLS

Axol Bioscience attended the 2024 MPS World Summit to showcase their work on collaboratively building in vitro model systems with integration for higher throughput platforms (including MPS systems) and which incorporate their expertise in functional human iPSC-derived cells (axoCells™) to provide improved human relevant disease models. They also presented a poster on "The multiplatform utility of human iPSC-derived neuronal models to provide complex biological in vitro systems for drug discovery". Axol also continues its series of informative on demand webinars and has also recently joined the 3Rs Collaborative Microphysiological Systems Initiative., a collaboration of 82 representatives from 39 institutions, 28 that are providers of commercially-available MPS that are already translated into industry use as well as several end-users. Its principal goal is to increase the adoption of MPS technologies through stakeholder engagement, including fellow Alliance member C.N.Bio

RESEARCH ON OPTIMIZING SKIN BARRIER TESTS

DTL (Dermal Technology Laboratory) attended the 63rd SOT (Society of Toxicology) meeting to present their recently published research on '*Skin barrier function for regulatory skin absorption tests and effects on testosterone and sucrose absorption*'.

In vitro absorption through human skin is a critical component of chemical safety testing and OECD Test Guideline (TG)428 is used as a regulatory guideline. However, skin samples used can be damaged during collection, storage or transport and barrier integrity assays are used to identify samples which are potentially damaged. Therefore the objective of the DTL study was to evaluate its historical database of electrical resistance (ER) test values and to establish the most appropriate ER barrier limits for use in regulatory tests, to optimise test performance. The second objective was to evaluate how any new barrier criteria may influence direct measurements of skin absorption, since ER is a proxy (indirect) measurement of skin barrier function.



A retrospective analysis of almost 10,000 ER measurements was performed, to investigate cumulative absorption of two model substances, testosterone and sucrose. Test limits were identified which would provide suitable skin samples for regulatory skin absorption studies in the safety assessment of chemicals, crop protection products, consumer healthcare products and cosmetics.

Brackin, T., Gayes, H., Johnson, I., Fox, D., & Roper, C. (2024). Skin barrier function for regulatory skin absorption tests and effects on testosterone and sucrose absorption. *Toxicology in vitro : an international journal published in association with BIBRA*, 95, 105735. https://doi.org/10.1016/j.tiv.2023.105735

ANIMAL FREE RESEARCH UK LAUNCH CAMPAIGN FOR HERBIE'S LAW

On World Animal Free Research Day (May 27), Animal Free Research UK unveiled their new campaign for legislation that would support the long-term replacement of animals with human-specific technologies. Named after Animal Free Research UK's CEO's beagle who was bred for research but deemed not to be needed, 'Herbie's Law' would commit to the statute books the requirement for the UK to accelerate the transition to animal-free medical research. With provisions for funding, transition support and training for scientists, and with support from an Expert Advisory Committee, it represents a structured and considered approach to a 'decade of change' in which animal research and testing are replaced with cutting-edge, human-specific technologies.

Please visit Animal Free Research UK's dedicated Herbie's Law webpage to see action you can take to support the initiative.

THE HUMANE RESEARCH SYMPOSIUM

The Humane Research Trust invites you to their one-day symposium, **In vitro cell culture models; moving towards animal free**, on 17 September in conjunction with University of Manchester. It will be held at the Manchester Institute of Biotechnology and is open to all scientists interested in non-animal models in medical research. The event will include keynotes, flash talks and a poster prize. The Trust invite suppliers of animal-free research products and reagents to have a stand at the event. Follow the Trust on LinkedIn for event updates and make sure to register for free on Eventbrite: https://www.eventbrite.com/e/in-vitro-cell-culture-models-moving-towards-animal-free-tickets-918702954267

THE HUMANE RESEARCH GRANT-FUNDING ROUND

The Humane Research Trust is calling for applications for their animal-free research grants.

The Trust typically funds UK-based PhDs and post-doctoral research projects that investigate human diseases using non-animal methods. For more information and how to apply, see the Trust's website.

The closing date for applications is 25 August 2024. Good luck!

The Alliance is delighted that two of its members, Safer Medicines Trust (represented by Dr. Pandora Pound, Research Director) and FRAME (represented by Celean Camp, Chief Executive Officer) are part of the Coalition to Illuminate and Address Animal Methods Bias, otherwise known as COLAAB, which was recently awarded the very first Lush Prize for Major Scientific Collaboration.

Here we include a blog by Pandora Pound on COLAAB's success so far:

LUSH PRIZE 2024 MAJOR SCIENCE COLLABORATION AWARD WINNER – COLAAB

Safer Medicines Trust is part of the Coalition to Illuminate and Address Animal Methods Bias, otherwise known as COLAAB, so we were delighted when COLAAB was recently recognised for its important work with a Lush Prize in the category of Major Science Collaboration!

COLAAB is an international coalition of researchers and advocates from a range of organisations, charities and universities worldwide. It was formed in 2022 following a workshop to discuss how the bias towards using animal methods plays out within scientific publishing. Workshop attendees from publishing, academia, industry, government, and non-governmental organisations discussed this phenomenon and the impact it could have on scientists' research and their careers. Two years later, COLAAB held another workshop, this one to explore the issue of bias in reviews of academic funding proposals.

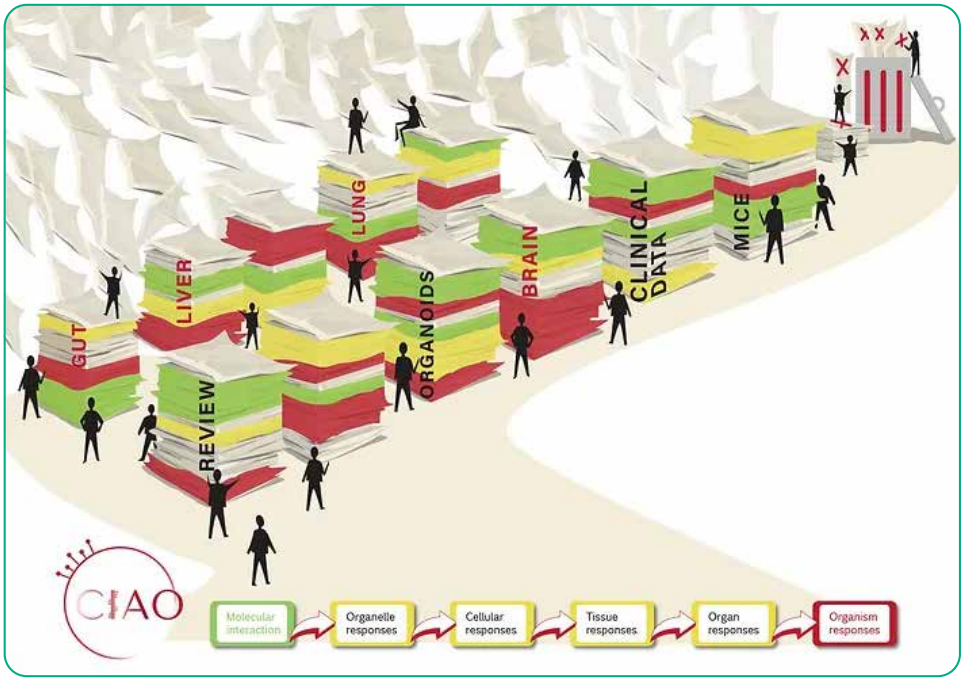
There has long been anecdotal evidence of a bias towards using animals within academia. But what COLAAB has done is two things. First, and importantly, it has named the phenomenon. Being able to talk about 'animal methods bias' makes the issue much easier to discuss and helps people recognise it and – crucially – challenge it when it arises. Second, the coalition is collecting empirical evidence about how this bias plays out and how it affects scientists' ability to get their studies published if they do not use animals. Not content with anecdote, COLAAB has conducted two surveys of scientists' experiences of animal methods bias in academic publishing. The first was an initial foray into this field and the second, which should be published later this year, is a much larger survey, together with an analysis of biomedical publications. Further research is planned, including a qualitative study of the experiences of PhD students and early career researchers, and – hopefully – an investigation into animal methods bias within biomedical funding.

It's wonderful that Lush Prize has recognised the importance of this collaboration. Congratulations to everyone involved!

We are thrilled to be recognized for our work on animal methods bias with this 2024 Lush Prize win in the category of Major Science Collaboration! Thank you to everyone who has supported and contributed to this effort!

A SYSTEMATIC SCOPING REVIEW OF THE NEUROLOGICAL EFFECTS OF COVID-19

Our latest publication co-authored by Scientific Consultant Rebecca Ram, as part of the CIAO (Covid-19 Adverse Outcome Pathway) project, is a systematic scoping review of the neurological effects of COVID-19.

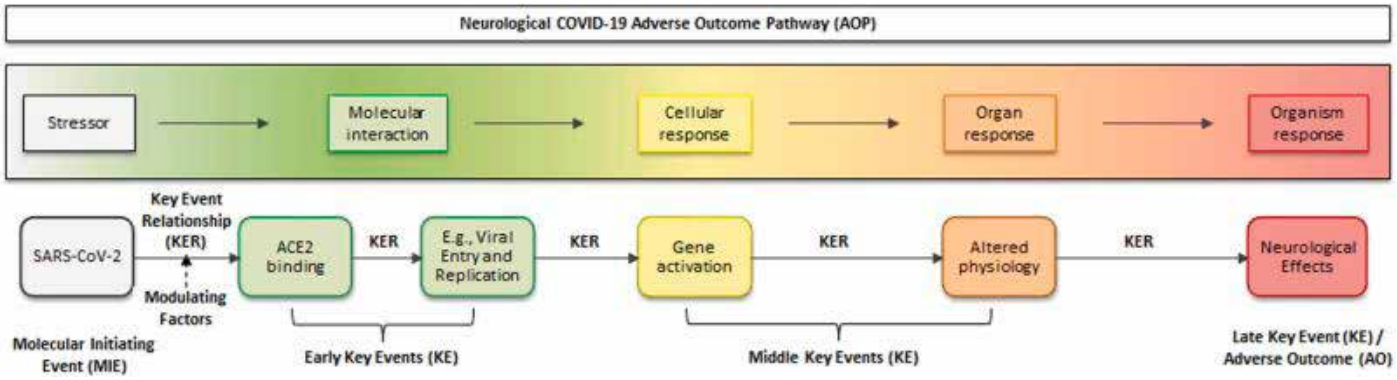


Congratulations to all involved from the International Collaboration on Cosmetics Safety (ICCS), the NTP (National Toxicology Program) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), the Evidence-Based Toxicology Collaboration (EBTC), the Center for Alternatives to Animal Testing (CAAT), Humane Society International (HSI) and others on acceptance and release of this publication.

In mid-2020 the CIAO (Modelling the Pathogenesis of COVID-19 Using the Adverse Outcome Pathway Framework) project was established, bringing together over 75 interdisciplinary scientists worldwide to collaboratively investigate the underlying biological mechanisms of COVID-19 and consolidate the data using the Adverse Outcome Pathway (AOP) Framework.

Within CIAO, a working group was formed to conduct a systematic scoping review of COVID-19 and its related neurological symptoms to determine which key events and modulating factors are most commonly reported and to identify knowledge gaps.

Hogberg, H. T., Tsaioun, K., Breidenbach, J. D., Elmore, B., Filipovska, J., Garcia-Reyero, N., Hargreaves, A. J., Joshi, O., Omeragic, E., Plant, S., Ram, R., Virmani, I., Waspe, J., & Macmillan, D. S. (2024). A systematic scoping review of the neurological effects of COVID-19. Neurotoxicology, 103, 16–26. Advance online publication.



EXPLORING TRANSPORT AND METABOLISM THROUGH TISSUE BARRIER MODELS

At the 2024 MPS World Summit , C.N. Bio presented their work during an educational session on 'Utilizing a microphysiological system (MPS) to explore transport and metabolism through tissue barrier models'. Dr. Anthony Berger and Dr. Audrey Dubourg provided hands-on training with focus on the importance of human-relevant models in drug transport and metabolism research; how MPS (microphysiological systems) tissue barrier models work; what to consider when generating tissue barrier models in MPS. Attendees learned about the limitations of traditional methodologies when modelling tissue barriers as well as how to characterize tissue barrier maturity and functionality and analyse using the CN Bio MPS platform drug transport and metabolism using the CN Bio Physiomimix platform. See more at https://cn-bio.com/event/mps-world-summit-seattle-2024/

KEYNOTE SPEAKER

We are excited to announce Prof. Linda Griffith as our keynote speaker for the CN Bio User Group Meeting 2024 - The founder of the technology commercialized into the PhysioMimix OOC system, a MacArthur Genius Award recipient, a TIME100 Health Leader, and a pioneer in tissue engineering and women's health.

Don't miss this chance to hear Prof. Griffith speak

CN BIO USER GROUP MEETING 2024 (UGM24)

17TH OCTOBER 2024
14:00 - 16:30 (GMT)

In this year's event, we will focus on the value of predictive human organ models in today's drug discovery, development and research workflows. You will have the opportunity to:

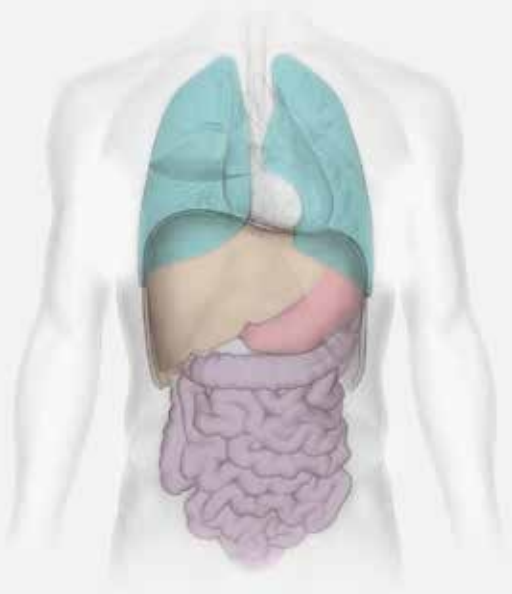
Gain insights into the successes and challenges of adopters

Learn about the benefits of incorporating OOC/MPS into your toolbox

Equip yourself with practical knowledge to get started

Take part in insightful conversations and network with industry professionals across the globe from the convenience of your home or office. Stay tuned for the full conference agenda and speaker information.

https://cn-bio.online/



CN BIO'S NASH ASSAY ADVANCES DRUG DEVELOPMENT

Further recent developments at CN Bio include that the PhysioMimix® non-alcoholic steatohepatitis (NASH) assay has provided data to support an IND submission for Inipharm's INI-822 - now in clinical testing.

The submission represents the first example of an organ on a chip (OOC) provider's data supporting the clinical progression of a drug for metabolic, fibrotic liver disease.

Why is this news important? The use of in vitro OOC for early evidence of efficacy for INI-822 demonstrates the transformative potential of in vitro OOC models to provide human-relevant data within preclinical programmes. The assay overcomes the limitations of existing approaches that lack human relevance, bridging the gap between human 2D cell culture and expensive animal models, which are ineffective in mimicking the full spectrum of the disease.

8TH INTERNATIONAL CONFERENCE ON BIO-SENSING TECHNOLOGY

Prof. Richard Luxton of the Institute of Bio-Sensing Technology(IBST) spoke at the 8th International Conference on Bio-Sensing Technology held in May 2024 in Seville. The conference is a global platform on the latest developments in bio-sensing technology, including a diverse range of presentations in advancements in novel biomarkers, binding technologies, applications of new materials, integration of new transducers and instrumentation, and data analysis and interpretation.

The ever-growing demand for faster, more sensitive, and reliable testing methodologies, as evidenced by numerous COVID-19-related funding calls, highlights the demand for advancements in biomarker-based detection technologies. This extends beyond coronavirus detection and encompasses diverse applications of bio-sensing technology in healthcare, agri-food, environment, and security. Prof. Luxton presented on 'Novel biomarkers' and ' Real world applications and commercialisation'.

KIRKSTALL ANNOUNCE TWO EXCITING NEW FIELDS OF APPLICATION OF THE QUASI VIVO® SYSTEM IN CANCER RESEARCH

In this recently published report, Dr. Eija Mäki-Mikola and a team at the University of Helsinki demonstrated the application of the Quasi Vivo® system to establish a dynamic in vitro cell culture model to more accurately mimic the lung cancer microenvironment.

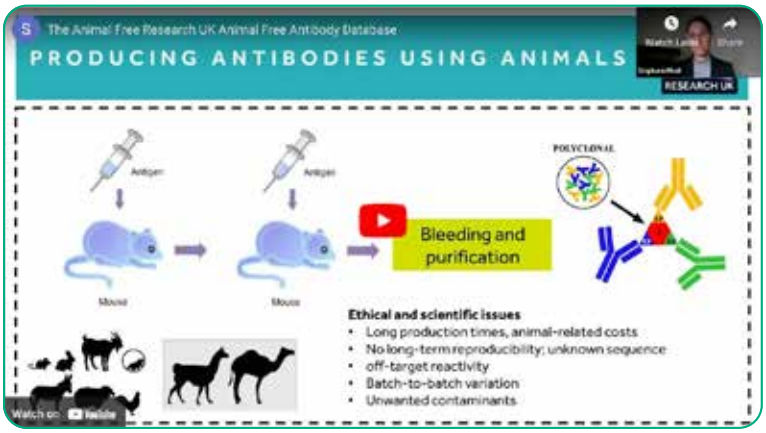
Mäki-Mikola, E., Lauren, P., Uema, N. et al.(2023) Establishing a simple perfusion cell culture system for light-activated liposomes. Sci Rep 13, 2050 (2023). https://doi.org/10.1038/s41598-023-29215-6

Dr Hannah Harrison of the University of Manchester, UK, utilised the Quasi Vivo® system to model lung colonisation of breast cancer cells in a two-organ dynamic culture of lung and breast cancer. ''With the Quasi vivo system, it was possible to investigate for the first time the movement via fluidics and the interactions of breastcancer cells with those which make up a distant tissue'' said Dr Harrison.

Unravelling breast cancer metastasis in the lab

ONLINE EVENTS PROMOTING THE USE OF NAMS

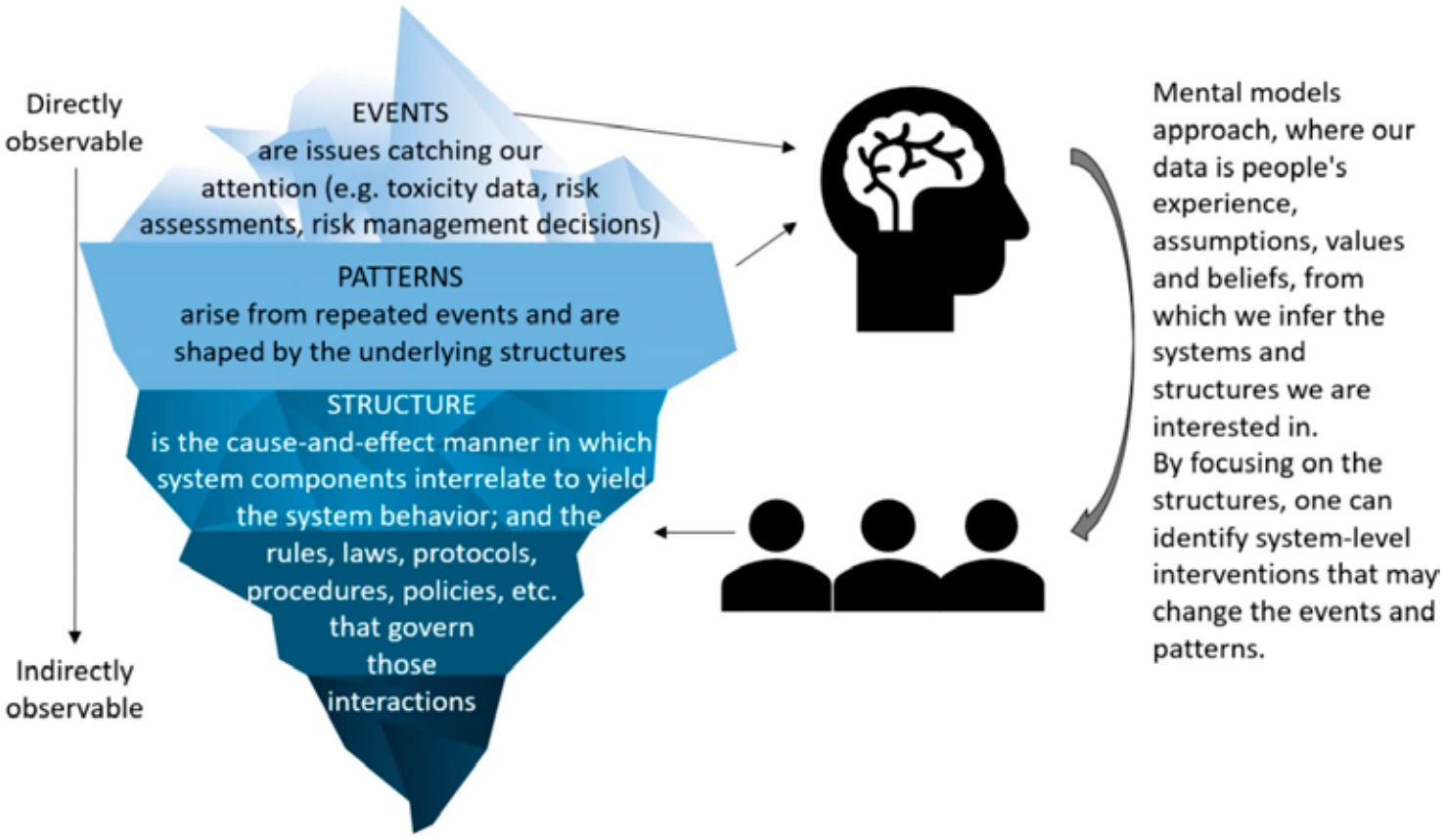
The Alliance Exchange continues to host its series of online events promoting the use of New Approach Methodologies (NAMs) which are presented by expert Alliance members throughout the year. 2024 events have so far included webinars on 'Modernising drug discovery research – an introduction to microphysiological systems (MPS)' and 'The Animal Free Research UK Animal Free Antibody Database' hosted by CN Bio and Animal Free Research respectively. These and all previous Alliance Exchange events are available to view on the Alliance website. More events will be released over the coming months and are free to register. Please follow the Alliance for Human Relevant Science and Exchange pages to stay updated.



LAUNCH OF THE COLLABORATION TO HARMONISE THE ASSESSMENT OF NEXT GENERATION EVIDENCE (CHANGE)

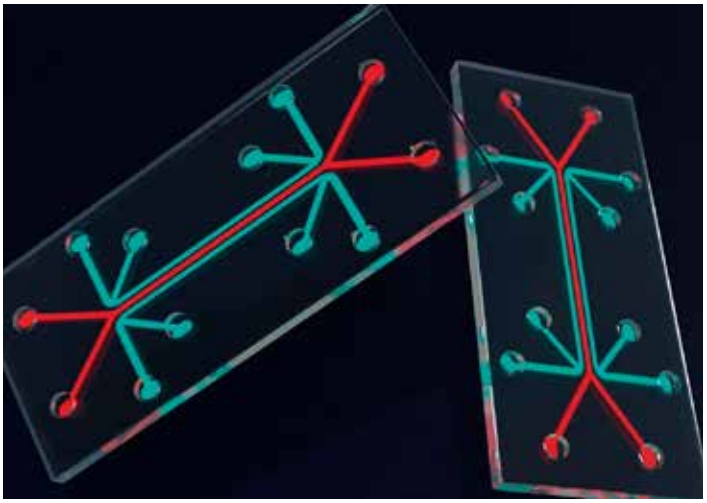
In June 2024 an exciting new initiative was launched: the Collaboration to Harmonise the Assessment of Next Generation Evidence (CHANGE). In an article published in Archives of Toxicology, the international stakeholder initiative – partly funded by the European Food Safety Authority (EFSA) and including research teams from academia, industry and government agencies across the USA, Europe and Japan – describes the considerable work over the past 20 years to achieve the urgently needed paradigm shift in regulatory toxicology from decisions based on data from animal studies to a "Next Generation Risk Assessment" (NGRA) system based on more human relevant New Approach Methods (NAMs). The launch publication also highlights different interpretations of the defintion of NAMs in that "*Whilst all NAM definitions include in silico, in vitro, ex vivo and in chemico approaches some also cover in vivo reduction and refinement approaches. The perceived potential benefits of NAMs that are driving the paradigm shift include better protection of humans and the environment, the reduction of animal testing, and ultimately, a faster and more cost-effective test systems for evaluating chemical safety*"

Mathisen, G.H., Bearth, A., Jones, L.B. et al. Time for CHANGE: system-level interventions for bringing forward the date of effective use of NAMs in regulatory toxicology. Arch Toxicol (2024). https://doi.org/10.1007/s00204-024-03802-6



CFI ENGAGES IN KEY STAKEHOLDER MEETINGS IN EUROPE AND BEYOND

CFI continues its work in Europe and beyond, by recently participating in three high-level European Commission meetings. At the biannual meeting of the National Contact Points (NCP) for the Directive on the protection of animals used for scientific purposes, CFI discussed the European Commission's roadmap to transition towards more human relevant, new approach methodologies (NAMs) in regulatory chemical testing. This roadmap is a direct result of the 2021 European Citizens' Initiative which received over 1.2 million verified signatures. A National Contact Point is a group of representatives from each EU member state ensuring that a specific Directive, in this case the use of animals in scientific research, is upheld. CFI continues to present at these meetings, as NGO stakeholders. CFI also attended the OECD (Organisation for Economic Co-operation and Development). Based in Paris, the OECD is a union of 38 of the world's industrialised countries, including the United States, Japan, Australia, Canada, Chile, Mexico and much of Europe. This facilitates progress to end animal testing to be discussed at a global level. Non-animal testing methods must be developed and accepted to fulfil regulatory requirements for the safety testing of chemicals, under a standardised validation process. Work continues in the OECD group responsible for updating these validation guidelines. CFI also recently attended the European Regulatory Summit conference in Brussels, to discuss chemicals regulations with regulators and other stakeholders, including those working in the manufacturing of chemicals and other NGOs.



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