Corners

CAAT feed

Major Changes in Lab Animal Policy

We saw some significant policy shifts on animal testing over the past year. In the United States, both the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) announced plans to step back from animal models in favor of new approach methodologies. Canada, the UK, and the EU are also taking steps in favor of non-animal methods. These changes are the culmination of years of work by humane science advocates and forward-thinking researchers to make science more human-relevant, ethical, and effective.

12th 3Rs Symposium

This year the 3Rs Symposium saw some incredible presentations on artificial intelligence, musculoskeletal tissue engineering, animal research in education, and more. These meetings educate and encourage people from all over the life sciences, showing them ways they can refine, reduce, and replace animal experimentation.

Thomas Hartung Participated in EU Parliament Workshop on Data Sovereignty in Research!

CAAT director Thomas Hartung recently gave the keynote address at an EU Parliament-hosted workshop on data sovereignty in research. The high-level session was led by the Panel for the Future of Science and Technology or STOA and featured a diversity of voices, all of whom center data usage and privacy in their work. The full event, including Dr Hartung's presentation on "ScAInce vs science, dependencies and risks", was recorded and posted to the EU Parliament's site: https://multimedia.europarl.europa.eu/en/webstreaming/20251001-1400-SPECIAL-STOA

CAAT Faculty Traveled to Beijing for IUTOX!

Thomas Hartung, Fenna Sillé, Lena Smirnova, and Alex Maertens traveled to Beijing, China, to participate in and speak at this year's International Union of Toxicology annual meeting. Thomas Hartung delivered the Day 1 keynote address, providing an upper-level overview of CAAT's many active programs and initiatives. CAAT's core leadership members spoke on topics spanning green toxicology, MPS, and exposomics. It was a very productive trip for all!

CAAT Student Achievements

CAAT students have been busy presenting their research and winning exciting opportunities to expand their professional experience! Alex Rittenhouse presented on "Microglia activation in brain microphysiological systems harboring a 16p11.2 deletion and autism" at the World Congress in Psychiatric Genetics in Cancun as part of the GEARs Symposium. Aliyah Penn was selected to receive the Johns Hopkins Technology Ventures (JHTV) Commercialization Fellowship, an experiential opportunity that trains early researchers on the process of bringing new technologies to market. She also presented at the Annual Maryland Stem Cell Conference on "Using iPSC-Derived Brain Organoids as a Tool for Precision Medicine for Rare Neurodevelopmental Diseases". In September, Dowlette-Mary Alam El Din received the David Ray Award as part of the International Neurotoxicology Association Conference. International Foundation for Ethical Research (IFER), where Dowlette is a fellow, sponsored her travel to the conference.

Thomas Hartung makes headlines after bringing the Exposome to WCSJ 2025!

Thomas Hartung has returned from a very successful trip to Pretoria, South Africa for the World Conference of Science Journalists (WCSJ 2025). While there, Dr Hartung led and participated in numerous well-attended and extremely well-received talks. He spoke to the potential of the exposome to improve precision medicine, increase health equity, and generally remake the biomedical enterprise from reactive to proactive with the power of AI, better health analytics, alternative methods, and other similarly innovative technologies. The trip achieved its goal of engaging critical stakeholders in the Global South and amplifying the message of the Global Exposome Forum, a multi-stakeholder, annual event aimed at organizing a global effort around the Human Exposome Project. For the complete WCSJ 2025 program, visit: https://www.wcsj2025.org

Thomas Hartung Travels to California for Apple's Annual Green Chemistry Advisory Meeting

This marks the tenth year that Dr Hartung has served on this panel. The seven-person advisory group is Apple's only external board. Members include green chemistry leaders, academics, and researchers. The group assembles annually to provide Apple with strategies for reducing the company's climate impact and toxic substances – a strategy and company policy we hope more tech companies will consider adopting in the future!

Conferences and Conversations

Looking ahead, CAAT leadership will continue traveling regularly and speaking to specialized audiences on the role of AI in toxicology, the role the exposome has to play in medicine and scientific discovery, as well as the increasing urgency institutions and individuals should feel to shift away from animal models given the rapidly changing regulatory landscape. One prime example is the annual AAAS meeting: Thomas Hartung and other close collaborators will be speaking to mixed audiences on the rapidly evolving field of exposomics and CAAT's efforts to organize international momentum and collaboration. Thomas Hartung will also be traveling to Switzerland at the start of the year to discuss crucial scientific and technological changes at this year's World Economic Forum! This international event brings major players in politics, economics, science, and other areas into conversation with each other. Presenting at, participating in, and supporting external talks and conferences is a cornerstone of CAAT's strategy to facilitate the shift away from animal models and improve the safety and exposure sciences.

In 2026, CAAT will accelerate this work by once again acting as host, organizing small-scale to multi-hundred-person convenings carefully designed to foster exchange and advance the latest, greatest, and most human-relevant technologies available.

Green Toxicology for a Sustainable Future Rescheduled for Spring of 2026

With official dates being announced at the start of the year, this event will bring together researchers, practitioners, and student innovators for a deep dive into the next generation of computational tools shaping the field of toxicology, safety testing, and related fields like exposomics.

This impact-driven session will focus on the practical application of cutting-edge, industry-defining technologies, including agentic research platforms, AI-driven modeling environments, and open-source analytics frameworks. Participants will gain exclusive, first-ever exposure to novel and transformative technologies, learning how to integrate them directly into their own work.

Tools attendees will be trained on include:

- BioBricks.ai: A data registry and ETL framework for building open, reproducible datasets ("biobricks") that power toxicology and environmental health research.
- ToxIndex: An agentic research platform for toxicology and risk assessment, integrating literature review, computational models, and inventory analysis into automated workflows.
- ChemTransformer: A multitask molecular property prediction model trained on millions of compounds for chemical safety assessment.
- Tidyexposomics: An open-source R package that provides an end-to-end, tidyverse-native workflow for integrating exposure and multi-omics data. It streamlines quality control, association testing, multi-omics integration, network analysis, and ontology-driven enrichment.

New Webinar Series Organized by UNESCO, the Human Cell Atlas, and GEF!

The Global Exposome Forum – a joint initiative co-led by CAAT and institutional partners across the US and EU – is thrilled to announce a new collaboration with UNESCO and the Human Cell Atlas! Our upcoming series, "Towards a Human Exposome Cell Atlas", launched December 9 with a deep dive into endocrine disruptors.

This exciting series will work to bridge connections between exposomics and single cell lines, shedding light on some of exposomics most pressing questions around exposure, health determinants, and much more! To learn more about the series, visit: https://events.humancellatlas.org/exposome/9816712

Applications Open for Summer Immersion on Innovative Approaches in Science

Apply now for the Summer Immersion on Innovative Approaches in Science, a free, in-person event designed to educate scientists on human-based non-animal methods in medical research and regulatory testing. Attendees will participate in scientific talks, career development workshops, poster presentations, technology demonstrations, case studies, networking opportunities, and more. CAAT is one of the organizing institutions and will be leading programing with on-site, lab-based trainings and tours designed to inspire and support the next generation of animal-free researchers.

NCATS recently named the Summer Immersion a winner of the NCATS Translational Science Education and Training Challenge, recognizing it as an exemplary educational event. The next program will take place at Johns Hopkins Bloomberg School of Public Health in Baltimore, MD, June 15-18, 2026.

To submit an application, visit: https://www.pcrm.org/ethical-science/summer-immersion

The Global Exposome Summit Registration Opens!

The Global Exposome Summit is the next event in a series launched as follow-up to the CAAT co-hosted event, the Exposome Moonshot Forum. It will be held in the coastal city of Sitges, Spain, a city known for its proximity to Barcelona and reputa-

tion as a small but lively beach town on April 27 - 29, 2026, and facilitate extensive discussion, ideation, and collaboration to continue building on the framework outlined during May's Moonshot Forum in Washington, DC.

Organized in partnership with the International Human Exposome Network (IHEN), the Global Exposome Summit will coincide with IHEN's own internal planning and development retreat. Numerous leaders in the spaces of science, society, and health policy will be participating in and leading specialized as well as big-picture discussions on exposomics, precision medicine and similar disciplines.

This is a fantastic opportunity to contextualize your research within the highly dynamic field of exposomics while making valuable connections and gaining new insight into the future of this project and discipline. Submit your application today and plan for a productive, impactful and sunshine-filled week on the Mediterranean!

For the event page and abstract submission form, please visit: https://www.globalexposomesummit.org/#abstracts

CAAT Mixer at SOT 2026!

Join CAAT at SOT for networking, apps, drinks, and exciting updates from Thomas Hartung, Fenna Sillé, and Alex Maertens, as well as updates from the Evidence-Based Toxicology Collaboration! Registration is free and open. The mixer will coincide with SOT 2026 in San Diego, California and be held at the Mission Hills room of the Marriott Marquis Marina hotel from 7:30pm-9:30pm PST. We hope to see you there!

To register, visit: https://www.eventbrite.com/e/caat-mixer-tickets-1976891701295?aff=oddtdtcreator

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Cruelty Free INTERNATIONAL
Ending animal experiments worldwide

NIH updates grant policy to permit funding for post-research animal rehoming

The U.S. National Institutes of Health (NIH) has updated its Grants Policy Statement to clarify that grant funds may be used to prepare for and facilitate the rehoming or retirement of animals at the conclusion of research, including placement in homes or sanctuaries.

The policy update follows several years of advocacy by Cruelty Free International, including work with Members of Congress, to secure a U.S. Department of Health and Human Services (HHS) report examining the release and adoption of animals used in NIH-funded research. That report provided important insights into current practices while also highlighting inconsistencies in federal policy.

A key issue identified through this process was that the Grants Policy Statement previously did not permit the use of grant funds for post-research adoption or rehoming activities under the section on allowable costs and activities. This restriction limited the ability of institutions to support the rehoming of animals following completion of studies.

The updated policy addresses this issue by explicitly recognizing the "*rehoming/retirement of experimental animals*" as an allowable use of NIH grant funds. Further implementation could be supported through additional NIH guidance on post-research adoption practices and through measures such as those outlined in the Companion Animal Release from Experiments (CARE) Act of 2023 (H.R.2878), which proposed requirements for funded institutions to maintain transparent adoption policies and to report the number of animals released.

Replace Animal Tests Act (H.R. 6660) introduced in U.S. Congress

U.S. Congressman Jared Moskowitz recently introduced a new bill to reduce animal testing by requiring the use of scientifically valid non-animal methods where such methods are available. The Replace Animal Tests (Replace) Act (H.R. 6660) would apply across federal regulatory agencies including the Consumer Product Safety Commission, the Department of Agriculture, the Environmental Protection Agency, and the Food and Drug Administration.

The bill would make it unlawful for any regulated entity to submit data to these agencies that is derived from an animal test method where a non-animal test method is available to meet the regulatory requirement, or where the agency has issued a waiver exempting the entity from a requirement for data derived from an animal test method.

The bill includes a few exemptions, including animal testing data generated before the enactment of the Act and data generated from an animal test method conducted outside the United States for the purpose of complying with a foreign regulatory requirement.

Covered agencies are empowered to either refuse to accept animal testing data generated in violation of the Act or to impose a civil penalty of not more than $10,000 per violation.

In addition to mandating the use of accepted non-animal test methods, the bill would require agencies to provide clear guidance on approved non-animal methods and to publish annual reports on non-animal method usage and animal testing data, including the purpose for which animal tests were conducted. Where animal testing is still required, the bill would also require that the number of animals used and the pain inflicted is reduced to a minimum.

Cruelty Free International is working with Congressman Moskowitz's office to build bipartisan support for the bill, which was informed by evidence compiled through its Replace Animal Tests (RAT) List.

The text of the bill is available at: https://www.congress.gov/bill/119th-congress/house-bill/6660

ASRU report shows continued high levels of reported animal welfare non-compliance in UK laboratories

On December 12, the UK Home Office's Animals in Science Regulation Unit (ASRU) published its annual report for 2024, detailing cases of non-compliance with the Animals (Scientific Procedures) Act 1986 governing the use of animals for scientific purposes in Great Britain.

According to the report, 146 cases of non-compliance were recorded in 2024, involving a total of 22,204 animals. While the number of reported cases was lower than in 2023, the number of animals affected increased compared with earlier years, indicating ongoing animal welfare concerns.

The reported cases included failures to provide adequate care, animals being kept alive beyond authorised humane endpoints, equipment failures, and procedural errors resulting in injury or death. "Adverse welfare outcomes", defined as greater pain, distress, suffering or lasting harm than permitted under the licence, were reported for 189 animals.

Most cases of non-compliance were identified through self-reporting by establishments, with only a small proportion detected through audits or inspections. Enforcement action primarily consisted of advice from inspectors or letters of reprimand, with no cases referred for prosecution.

The report also noted an increase in the number of active project licences for animal use in 2024.

UK Animals in Science Committee (ASC) publishes recommendations to improve public transparency on animal testing

The UK Home Office has received recommendations on improving public transparency in the use of animals in science, set out in a report by the Animals in Science Committee (ASC), an advisory body to the UK government.

The ASC has reviewed two publicly available documents linked to licenses issued by the Home Office for the use of animals in experiments in the UK – non-technical summaries (NTS) and retrospective assessments (RA). These summaries and assessments are meant to provide the public with clear, accessible information about the procedures involved and the potential harms to animals.

The ASC reviewed 30 of these documents, as well as conducting a stakeholder survey. Common problems identified include the use of overly technical language, which can be difficult for the public to understand, and a lack of information on what the experiment involves and the pain the animals will experience.

The recommendations include creating a list of key technical terms to make complex issues more understandable to the public; helping applicants include enough detail on the tests to be performed and the potential suffering they will involve; and developing a searchable database in which to publish the documents to improve public accessibility.

Many of these align with findings and recommendations from published research by Cruelty Free International on the quality of non-technical summaries (Taylor et al., 2018, 2024).

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The UK Home Office publish statistics on animal use in science for 2024

Official figures released in October on the number of animal tests in Great Britain showed a total of 2,637,578 uses of animals in laboratories in 2024 – a 2% decrease from 2023. Of the total uses of animals, 18% (488,255 uses) resulted in moderate or severe suffering.

Regulatory tests, which aim to assess the safety or effectiveness of products, ac-

counted for 10% of all uses in 2024. There were increases seen in the use of animals to meet requirements for chemicals and veterinary medicines legislation. Regulatory tests that took place in 2024 despite having approved non-animal replacements included three eye irritation and corrosion tests and 148 skin sensitisation tests.

The statistics also show changes in the use of different species. Compared with 2023, the use of dogs decreased by 30% and the use of non-human primates decreased by 11%. In contrast, the use of cats increased by 30% and the use of horses by 1%.

The UK government publish a strategy to replace the use of animals in science

The UK government has published a strategy, "Replacing animals in science: A strategy to support the development, validation and uptake of alternative methods". The strategy aims to seize opportunities to replace animal tests used to evaluate impacts on human health and the environment, covering medicines, chemicals, consumer products, food, and pesticides, and to support collaborative working and regulatory change.

The strategy set out clear targets and milestones including:

- Forming a cross-governmental ministerial group on alternative methods and publishing key performance indicators via a publicly accessible dashboard, in 2026
- Creating a preclinical translational models hub and a UK Centre for the Validation of Alternative Methods (UKCVAM), by the end of 2026
- Developing guidance permitting medicines trials based on non-animal data where relevant preclinical animal models do not exist, by the end of 2026
- Reducing pharmacokinetic studies on dogs and non-human primates by at least 35%, by 2030
- Time-bound commitments to end specific regulatory toxicity tests on animals, including the rabbit pyrogen test by the end of 2025; animal skin and eye irritation and corrosion and skin sensitisation tests by the end of 2026; and mouse potency tests for Botox and selected batch contamination tests for human medicines by 2027.

Detergents regulation

The EU is close to agreeing a new Detergents and Surfactants Regulation. Following formal approval by the European Council, the proposal will now move to plenary debate and vote in the European Parliament. This is expected in 2026 and will precipitate formal adoption of the regulation and its entry into force.

The revision will update the existing framework with new measures on labelling and digital sustainability. Another key change is the introduction of a ban on animal testing for the purposes of meeting the requirements of the Detergents and Surfactants Regulation (although a derogation is in place for exceptional circumstances), with only non-animal methods permitted.

The EPAA celebrates its 20th anniversary

The European Partnership for Alternative Approaches to Animal testing (EPAA), a partnership which brings together the European Commission and industry groups from across 9 industrial sectors, celebrated its 20th Anniversary in November 2025 starting with an event at the European Parliament, opened by President Roberta Metsola.

EUSAAT

European Society for Alternatives to Animal Testing

EUSAAT supported the Next Gener3Ration meeting on September 18-19, 2025 in Genova, Italy

EUSAAT was happy to financially support the Next Gener3Ration meeting at the University of Genova, which was organized by young researchers for young researchers. The aims were:

- inspiring new ideas to move towards the future of biotech and biomedical sciences;
- promoting networking and collaboration among different research fields, contributing to the growth of 3Rs in basic, applied and translation science;
- emphasizing the great opportunity offered by application of the 3Rs to different fields of research.

EUSAAT was proud to foster this meeting and future researchers in the 3Rs field.

More information: https://www.centro3r.it/it/events/next-gen3ration-research

EU3Rnet – The European network of 3Rs centers and institutions is online – www.eu3Rnet.org

Following several meetings after the EUSAAT 2018 congress and the two recent workshops on 3Rs centers in Linz (September 2024, https://cost-improve.eu/outcome/open-workshop-3rs-centres/) and Genova (September 2025, https://cost-improve.eu/outcome/improve-3rs-centres-workshop-brought-together-european-experts-in-genova/) under patronage of the COST Action IMPROVE, major outcomes were the development of a common Memorandum of Understanding and the establishment of working groups addressing key challenges in the field and on the organization, communication, funding, and sustainability of EU3Rnet.

A website as official communication and contact platform was generated and went online in November 2025. It informs about activities of the members of EU3Rnet and can be reached at: https://eu3Rnet.org/

COST Action IMPROVE – update

As a common outcome of the *COST Action CA21139 – 3Rs concepts to improve the quality of biomedical science (IMPROVE)* a paper entitled "Building Bridges: Involvement of Animal Care Staff and Laboratory Technicians in Experimental Planning and Conduct of Animal Studies for Better Job Satisfaction and Science" has recently been accepted by *Laboratory Animals*, and several others are in the submission and revision process.

A training school in Porto, Portugal on October 8-10, 2025, gave 3Rs trainers opportunity to learn about concepts in education science applied to higher education and professional training and to discuss how to train researchers best for high-quality research with respect to the 3Rs. A detailed report can be found at: https://cost-improve.eu/outcome/training-school-teaching-the-3rs-train-the-trainers/

A series of webinars co-organized by the COST Actions IMPROVE, AFFECT-EVO, and LIFT was dedicated to improving animal welfare in research and promoting the 3R principles. The sessions featured leading experts discussing best practices, innovative approaches, and ethical considerations in laboratory animal science. The recordings are now available:

- Dr Tom Smulders, Reader in Evolutionary Neuroscience, University of Newcastle: "Adult hippocampal neurogenesis as a valence marker", 28.5.2025, https://www.youtube.com/watch?v=TuzKz0jZob4
- Prof. Georgia Mason, Department of Integrative Biology, University of Guelph: "Proxy measures for animal feelings: How to validate indicators of affective state or cumulative affective experience", 15.7.2025, https://www.youtube.com/watch?v=qK_1GlQG9kk
- Assoc. Prof. Laura Webb, Animal Production Systems Group, University of Wageningen: "Animal Happiness: Understanding and Assessment through Behaviour, Cognition and Physiology", 15.10.2025, https://www.youtube.com/watch?v=p_1vveS7UHs

Events in 2026

- 13-15 May 2026: Workshops in Split, Croatia on "Practices of Care: A Path to Enable Integrity and Open Communication" and "Balkan 3Rs centre"
- 16-17 June 2026: Workshop in Porto, Portugal on "Improving the quality and reproducibility of both NAMs and animal studies"
- 28 September - 1 October 2026: Workshop on "A multi-disciplinary approach to human-relevant modelling" and a final conference in Pisa, Italy

Website: https://www.cost-improve.eu
LinkedIn: https://www.linkedin.com/company/improve-3rs-concepts-to-improve-the-quality-of-biomedical-science-ca21139/
X: https://X.com/caimprove
Facebook: https://www.facebook.com/profile.php?id=100094711647507

COST Action Members can apply for Short Term Scientific Missions (STSMs) of up to 3 months in a host lab (https://cost-improve.eu/calls-grants/#section-3).

ITC nationals can apply for an ITC grant to visit a conference (https://cost-improve.eu/calls-grants/#section-1).

EUSAAT Board election in early 2026

The next EUSAAT Board will be elected early in 2026. The election procedure was agreed upon at the EUSAAT AGM on December 17, 2025 and sent to the EUSAAT members by e-mail. We are looking forward to a large number of candidates and good voter turnout for the 2026 EUSAAT Board election. The next EUSAAT congress is planned for February 2027 in Linz, Austria.

IPAM, the Italian Platform on Alternative Methods

The Italian Platform on Alternative Methods (IPAM), established in 2003, is committed to promoting research and disseminating information on alternatives to animal experimentation in accordance with the 3Rs principle (replacement, reduction, refinement). IPAM seeks to foster synergies among all relevant stakeholders to accelerate the development, validation, and regulatory acceptance of alternative methods in basic, applied, and regulatory research. The concept of a national platform – as outlined in the Final Declaration of the Third World Congress on Alternatives and Animal Use in the Life

Sciences (Bologna, 1999) – is based on the recognition that the implementation of the 3Rs requires a multidisciplinary approach to combine different interests and areas of expertise. The representation of the four stakeholder groups academic research, industry, government institutions, and organizations for animal welfare ensures a balanced and comprehensive perspective on issues related to animal experimentation, the application of the 3Rs principle, and the development of new approach methodologies (NAMs). This comprehensive approach extends beyond academic and technical considerations to include ethical aspects, legislative frameworks, and societal concerns. At present, the elected stakeholder representatives are Francesca Caloni and Cristina Maria Failla (academic research), Maurilio Calleri and Michela Kuan (organizations for animal welfare), Giancarlo Melato and Francesco Nevelli (industry), Isabella De Angelis, Augusto Vitale, and Stefano Lorenzetti (government institutions). Stefano Lorenzetti is the current president. IPAM's website (www.ipamitalia.org) and Facebook page (www.facebook.com/IPAMITALIA) provide updates on IPAM's activities and are points of contact for interested parties.

Through a fruitful collaboration with ecopa (European consensus-platform for alternatives; https://ecopa.eu/), IPAM has contributed to promoting a shared European vision of the application and governance of the 3Rs principle (Lorenzetti et al., 2020) developed in close collaboration with other ecopa-associated national platforms, namely Fincopa (Finland), 3RCC (Switzerland), Francopa (France), Norecopa (Norway), REMA (Spain), and SET foundation (Germany). This collaboration represents a unique framework that brings together various cross-sector entities, each contributing distinct perspectives on scientific debate and progress at regulatory, political, and social levels to discuss strategies to reduce, and ultimately replace, animal testing. These activities are reinforced by the presence of other 3Rs institutes and centers established across many European countries, which constitute a further significant network for the dissemination and implementation of the 3Rs principle (Neuhaus et al., 2022).

IPAM regularly organizes national and international events and meetings targeting different stakeholder groups, such as students, researchers, and citizens (Caloni et al., 2018, 2022; Lorenzetti et al., 2020, 2021, 2025; Nagy et al., 2016; Rovida et al., 2013; Vitale et al., 2024). Two online *in silico* schools addressing innovative theoretical and practical aspects of computational methods in pharmaco-toxicology were held in 2020 (Lorenzetti et al., 2021) and 2022. Since 2022, IPAM has organized an online event in English titled 3Days for 3Rs (Caloni et al., 2022; Vitale et al., 2024), which aims to present different applications and theoretical perspectives for each of the three Rs. Each day includes talks by three invited national or international speakers. The IPAM Annual Meeting focuses on emerging topics related to alternative methods and animal experimentation. IPAM also maintains continuous communication with national and international regulatory bodies, and IPAM's members frequently share their expertise in training initiatives organized by universities, industry, and public institutions.

The IPAM-Farmindustria award, a biennial event established in 2007, which recognizes young researchers who have authored a scientific article and/or a thesis relevant to the application of 3Rs in pharmacological research, alternates with the IPAM thesis award, established in the early 2000s, which rewards doctoral and master's theses inspired by the 3Rs principle. The latter also considers humanistic disciplines.

In conclusion, the uniqueness of the national platform lies in its commitment to achieving consensus and collaboration of four different stakeholder groups, all actively involved in promoting the responsible use of animals in scientific and regulatory research, yet often with divergent perspectives and priorities.

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IPAM (Italian Platform on Alternative Methods) Board of Directors, Bologna, Italy

The third project period of RISK-HUNT*3R* has now ended. After 4.5 years of work, the consortium is entering its final year with several major goals achieved.

An Alternative Safety Profiling Algorithm (ASPA) expert workshop was held in Berlin (May 27-28, 2025), co-organized by RISK-HUNT*3R* with BfR, EFSA, ECHA, OECD, JRC, EPA, NIH/NIEHS, ONTOX, and PrecisionTox. Regulators, scientists, and industry representatives were invited to actively comment on ASPA and its usability. Participants provided constructive feedback on ASPA, focusing on how to further improve its use in practice and underlining its potential for regulatory application. The workshop marked a significant milestone for RISK-HUNT*3R* and emphasized the need to align ASPA with evolving regulatory expectations for NGRA. A final workshop report summarizing the feedback and next steps is in preparation.

A RISK-HUNT*3R* delegation also presented recent advances in next-generation risk assessment (NGRA) at the 13th World Congress on Alternatives and Animal Use in the Life Sciences (WC13) in Rio de Janeiro (August-September 2025), creating valuable opportunities to exchange with colleagues from across the globe.

Another major milestone is the first scientific publication on ASPA (Leist et al., 2025). The paper presents a broad-purpose, transparent and reproducible risk assessment workflow designed to make NGRA more structured, traceable and applicable in regulatory contexts. Developed within the ASPIS cluster, this work represents an important step towards the practical implementation of NGRA.

In 2025, three RISK-HUNT*3R* case studies were submitted to the OECD for the 11th review cycle of the IATA Case Studies Project, which aims to assess the practical applicability of NAM-based IATA approaches for regulatory decision-making. The overall feedback was very positive, and all three case studies will be finalized and published by the OECD as exemplary cases in 2026.

The next RISK-HUNT*3R* General Assembly will be held in January 2026 in Egmond aan Zee, NL. A central topic will be the outcome and main learnings from the OECD review of RISK-HUNT*3R* IATA case studies. On this occasion, an NGRA training course on building NGRA case studies using ASPA will be offered. The course is open beyond the project, including ASPIS members and external industry stakeholders, and will provide two days of hands-on training, case examples, and peer exchange. For more information and registration, please visit https://www.risk-hunt3r.eu/training-building-next-generation-risk-assessment-ngra-case-studies-using-the-alternative-safety-profiling-algorithm-aspa/.

To read more about our OECD IATA case studies, check out our latest Newsletter (https://www.risk-hunt3r.eu/wp-content/uploads/Newsletter-issue-8-_final-version.pdf), and learn more about the ASPA workflow at https://www.risk-hunt3R.eu/aspa/.

RISK-HUNT3*R* press review

Recent noteworthy publications from RISK-HUNT*3R* partners:

Determining the relationship between alterations in renal gene expression and adverse outcomes in humans is a key challenge. The publication by Kunnen et al. (2025) applied weighted gene co-expression network analysis (WGCNA) to rat kidney toxicogenomic data from 180 compounds to identify groups of genes (modules) linked to stress, injury, and inflammation. Many of these modules were associated with renal pathology and were preserved across datasets and in human kidney data, supporting the use of TXG-MAPr gene modules for broader toxicogenomic analyses and for improving human safety assessment.

Understanding how early liver cell changes translate into tumor formation is essential for quantitative adverse outcome pathways (qAOPs). In their publication, Veltman et al. (2025) quantified the link between hepatocyte proliferation and liver tumors in AOP #220, which is driven by CYP2E1 activation. By combining BrdU labelling (a specific method to detect cell proliferation) with lesion data, they improved carcinogenicity prediction and point-of-departure estimates and propose standardizing BrdU use in sub-chronic studies to support the development of qAOPs for regulatory purposes.

Compounds that need to be metabolized to exhibit toxicity pose a challenge for NGRA. Since many of the currently available non-animal new approach methodologies (NAMs) lack xenobiotic metabolizing activity, their use may lead to an underestimation of the true hazard to humans (false negative predictions). The publication by Suess et al. (2025) explores strategies to deal with metabolite-mediated toxicity in three assays for developmental neurotoxicity. It also assembles and characterizes exemplary parent-metabolite sets and gives an overview on strategies to further develop such approaches.

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Silvia Tangianu and Marcel Leist

The 3Rs Collaborative

3RsC & IQ MPS Webinar Series: ISTAND Program and MPS in Drug Development

In a continuation of past workshops on MPS models and various organs (https://3rc.org/mps/presentations/), the 3Rs Collaborative and IQ-MPS initiative hosted the third and fourth webinars in our 2025 series on September 30 and December 3.

ISTAND Program webinar

On September 30, the 3RsC hosted York Tomita from FDA's Center for Drug Evaluation and Research (FDA-CDER) to give an overview of the ISTAND (Innovative Science and Technology Approaches for New Drugs) program. The webinar began with a short introduction to the 3Rs Collaborative by Program Manager, Aleeza Stephens. This was followed by an introduction to the IQ-MPS by David Kukla. During his presentation, York Tomita described how FDA-CDER recognizes the value of NAMs but highlighted the importance of robust evidence in order for them to replace existing methods. The ISTAND program provides a clear regulatory pathway for innovative technologies not covered by existing qualification pathways. The program involves a multi-step submission process, beginning with a Letter of Intent (LOI), followed by a Qualification Plan (QP), and a Full Qualification Package (FQP). Once qualified for a specific context of use, the NAM can be incorporated into any drug development program for that purpose without needing the FDA to re-confirm its suitability each time. The webinar concluded with questions from the audience answered by York Tomita. The full webinar recording is available on the 3RsC's YouTube channel: https://youtu.be/FSvNzf_59w?si=RHYOU5_anqJTVld7

MPS in Drug Development webinar

On December 3, the 3RsC hosted a webinar on the use of MPS in drug development, specifically cases where data from MPS were used to support regulatory submissions. Representatives from eight companies gave 15-minute presentations, followed by a roundtable Q&A with all presenters. The webinar began with a short introduction to the 3Rs Collaborative by Program Manager, Aleeza Stephens. This was followed by an introduction to the IQ-MPS by David Kukla.

Bruno Filippi, VP Liver Safety, InSphero, introduced liver microtissues – 3D spheroids of human or animal liver cells – as a scalable, consistent *in vitro* model for drug safety testing. He presented a case study with Sanofi, where these microtissues helped clarify species-specific hepatotoxicity observed in dogs during preclinical trials of a drug being developed for breast cancer. Transcriptomic analysis revealed cholestasis-related gene signatures in dogs but not humans, supporting regulatory decisions and reducing reliance on animal models.

Leopold Koenig, Senior Scientist, TissUse, introduced TissUse's Human Chip 2 platform, an advanced microfluidic system designed to model human bone marrow and hematopoiesis *in vitro*. The chip uses a ceramic scaffold seeded with stromal and hematopoietic stem cells to enable long-term cultivation and lineage differentiation, including natural killer (NK) cells. In a case study, the team evaluated an anti-IL-15 antibody's impact on NK cell development, showing dose-dependent, reversible inhibition of late-stage NK cells without affecting early progenitors, while maintaining cell functionality. These findings aligned with IL-15's known role and

supported investigational new drug (IND) submissions by providing human-relevant data complementary to traditional toxicology studies.

Lorna Ewart, Chief Scientific Officer, Emulate, presented a study performed at the Wyss Institute using human alveolar epithelial Organ-Chips to model viral infections and identify therapeutic targets. The team demonstrated that mechanical breathing motions reduced viral titers and cytokine responses, leading to the discovery of S100A7 as a potential target. They repurposed azeliragon, a RAGE inhibitor previously tested for Alzheimer's disease, and showed it reduced pro-inflammatory cytokines in flu-infected chips, supporting its use in COVID-19 clinical trials by Cantex Pharmaceuticals. Combining azeliragon with molnupiravir further enhanced efficacy. Lorna also provided a progress update on Emulate's FDA ISTAND qualification process for their Liver-Chip as a regulatory tool within drug-induced liver injury.

Paola Occhetta, CEO & Co-Founder, BiomimX, showcased BiomimX's UBeat technology for applying mechanical stimulation to 3D tissue models, enabling both tissue maturation and induction of pathological phenotypes. She focused on an osteoarthritis-on-chip model developed to mimic mechanical dysregulation, a key driver of the disease. In collaboration with Synartro, the team redesigned the platform to test an injectable therapy (SYN321), combining hyaluronan and diclofenac for sustained pain relief. The study confirmed SYN321's anti-inflammatory effects, reduced matrix degradation, and partially restored cartilage markers, while demonstrating drug release was influenced by mechanical stimulation. These human-relevant data complemented animal studies and supported regulatory approval for a first-in-human trial now in progress.

Gareth Guenigault, Lead Scientist, CN Bio, described how CN Bio's PhysioMimix liver-on-a-chip platform was used to evaluate the efficacy of an HSD17B13 inhibitor (INI-678) for treating metabolic-associated steatohepatitis (MASH). The model recreated key disease features – steatosis, inflammation, and fibrosis – using primary human liver cells under dynamic flow. Testing showed INI-678 reduced fibrotic markers, inflammation, and triglyceride levels consistent with protective human genotypes, without toxicity. Further screening identified a lead candidate (INI-822) with superior efficacy, supporting progression to Phase 1 clinical trials. These human-relevant data complemented *in vivo* studies and strengthened the IND submission.

Lizzy Crist, Business Development Manager & Technical Lead (USA), AIM Biotech, introduced AIM Biotech's 3D blood-brain barrier (BBB) model built on AIM's idenTx 40 platform, which uses vasculogenesis to form physiologically relevant BBB networks with endothelial cells, pericytes, and astrocytes. The model demonstrated accurate morphology, tight junctions, efflux transporter activity, and permeability values comparable to *in vivo* data, outperforming traditional transwell systems. In a case study, the BBB model was used to assess whether a monoclonal antibody binding to astrocytes caused off-target disruption to BBB barrier function. Results showed no disruption of BBB integrity, permeability, or morphology – even at 100× therapeutic dose – providing critical evidence that was included in a biopharma regulatory submission.

James Hickman, Chief Scientist, Hesperos, presented Hesperos' multi-organ-on-chip systems designed for clinically relevant functional readouts without serum, enabling advanced imaging and integrated PK/PD modeling. He highlighted neuromuscular junction (NMJ) models used for amyotrophic lateral sclerosis, myasthenia gravis, and rare disease applications, including patient-specific precision medicine, where data supported IND and orphan drug designations. Case studies showed efficacy testing for complement inhibitors, antibody therapies, and antisense oligonucleotides, as well as safety assessments that helped avoid long-term animal studies. Hickman also demonstrated multi-organ systems for cardiac toxicity, conduction velocity, and CNS models for Alzheimer's disease, emphasizing their role in replacing animal models and supporting regulatory submissions.

Pauline Zamprogno, Product Manager, Alveolix, discussed a technology using specific human cells to assess the safety of new immunotherapeutic compounds. This approach addresses limitations of traditional animal models and provides more reliable data for drug development and regulatory submissions. She highlighted a successful case where the method supported IND filings and safe initiation of a first-in-human clinical trial.

More about the 3RsC

Information on our individual initiatives can be found on our website https://3rc.org/; more information about how to join can be found here: https://3rc.org/mps/faq-how-to-join/