



Corners



Multiple Collaborations with the FDA Announced

CAAT is actively working to get alternative methods into the hands of regulators. Two projects are being advanced with this aim in mind. The first project, BrainMix-Tox, was initiated in September of 2021. “This project leverages the latest advances in the culture of human brain cells in 3D, also called brain organoids or brain microphysiological systems (bMPS), to test how exposure to different heavy metals (e.g., lead, arsenic, cadmium, and chromium) alter neural development and interact with autism-risk genes.”¹

The second collaboration was made official earlier this year with the signing of a Research Collaboration Agreement (RCA). “This new partnership will enable a close dialogue and collaboration between CAAT and FDA-CFSAN to explore the contexts of use under which these new testing approaches may be able to inform FDA’s thinking. Over the course of regular meetings, trainings, joint events and presentations, the partners will strategize on how to translate promising, highly specialized science and technology into actionable changes stakeholders can adapt to implement NAMs.” This collaboration will start with a focus on MPS application for food safety, beginning with a workshop around this topic, the details of which are forthcoming.

CAAT Members Participating in Three of 20 Teams Selected by the NIH!

“The NIH Common Fund Complement-ARIE program hosted this challenge as part of the strategic planning process to refine the Complement-ARIE program concept. This program will develop, standardize, and validate the use of new approaches that will more accurately model human biology and complement, or in some cases, replace traditional research models.”²

– *E-validation – Unleashing AI for Validation*: Artificial intelligence (AI) will be leveraged for several bottlenecks of the new approach methodologies (NAMs) validation process.

Team: Thomas Hartung’s Team

– *Organoid Intelligence (OI) – Learning in a Dish*: Brain organoids show simple forms of learning, which have the potential to replace cell-level behavioral studies in non-human primates.

Team: Lena Smirnova’s Team

– *NAMKG: LLM Powered Registry to Foster NAM Adoption*: Web-based NAM registry & knowledge graph for interoperability with public data assets and large language models (LLMs) to enable data discovery and tool automation.

Team: Insilica.co

Two CAAT Members Recognized by Lush Prize

Two CAAT members have been named as Lush Prize recipients or honorees. The Coalition to Illuminate and Address Animal Methods Bias (COLAAB) received the Major Science Collaboration Award. CAAT Program Director Kathrin Herrmann serves on and helps steer this coalition. Maren Schenke, a postdoc at CAAT, was commended by the Lush Prize jury for her project titled “Addressing sex differences in brain development without animals.” Congratulations to both members for this exciting achievement! The full list of awardees, including brief, informative videos, is available at: <https://lushprize.org/2024-prize/2024-prize-winners/>

Organoid Intelligence (OI) Selected to Join JHU’s SURPASS Initiative for a Second Year

CAAT’s research project into the dynamic field of organoid intelligence (OI) has been selected to join Johns Hopkins University’s SURPASS initiative for a second year! Born of a partnership between the Whiting School of Engineering and the Applied Physics Laboratory, SURPASS is a multimillion-dollar initiative funding projects that propose innovative solutions to complex problems. CAAT’s

¹ <https://www.fda.gov/science-research/advancing-regulatory-science/leveraging-human-brain-organoids-mixture-neurotoxicity-and-understanding-individual-susceptibilities>

² <https://commonfund.nih.gov/complementarie>



research project, “Organoid intelligence: Synthetic biological AI”, “*aims to uncover the complex dynamics underlying biological intelligence*,” says Thomas Hartung, JHU WSE, one of the leaders of the project. “*Success could enable breakthroughs from disease models to efficient biocomputing through hybrid approaches.*” To learn more about the SURPASS initiative, please visit the SURPASS website at: <https://surpass.jhu.edu/>

CAAT Launches OI Community News Bulletin

CAAT recently created a newsletter for members of the growing OI community to stay up to date on recent activities, publications, and events. “*Over the last few years, we aim to form a community for organoid intelligence (OI), i.e., establishing basic memory and learning in a dish by combining brain organoids with AI through microelectrode arrays. It is my pleasure to announce the start of a free bulletin.*” If you would like to receive the newsletter, please visit <https://jhsph.us4.list-manage.com/subscribe?u=066d5d7abe2de2d5e04d214bf&id=9af3a07e55> to subscribe.

Lena Smirnova Selected to Receive Johns Hopkins Discovery Award

Please join us in congratulating CAAT Program Director Lena Smirnova, PhD, who just received the Johns Hopkins University’s Discovery Award! Smirnova and her team are conducting research on extracellular vesicle (EV) RNA as functional biomarkers of clinical autism spectrum disorder heterogeneity. Discovery Awards provide grant funding to projects that span multiple schools or affiliates across Johns Hopkins University, facilitating research between team members from different divisions. To learn more about the Johns Hopkins Discovery Award, please visit the JHU webpage on the program and its awardees: <https://research.jhu.edu/major-initiatives/discovery-awards/2024-awardees/>

2024 Next Generation Humane Science Award Recipients Announced

This award spotlights the bright, promising work of young scientists committed to replacing animals in experimentation. This year’s award supported this cohort of early career investigator’s participation in the 2024 MPS World Summit! Congratulations to:

- *S. Kim* for their work on “Evaluating the effects of amniotic fluid motion on the amnion membrane using an amnion membrane (AM) organ-on-chip (OOC)”
- *D. Nash* for their research titled “Investigation into the effect of APOE4 iPSC-derived astrocytes on the blood brain barrier through *in vitro* models”
- *K. Hawkins* for their project focused on “Human iPSC-CMT2s motoneuron model for characterization and drug development”
- *M. Grisales* for their investigation of “Development of a human-based cortical neuron model for Down syndrome”

International Call for Proposals

The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) is now accepting proposals for the 2024 Reduction and Humane Education Grants.

The Reduction Grant focuses on research projects that help reduce animal use by identifying areas of research and testing where animal models lack reproducibility and translational value. Hence, the grant is intended for researchers who conduct systematic reviews, meta-analyses, or citation analyses of animal studies or similar work with the goal to reduce animal use in science.

The Humane Education Award is given for the development of animal-free training resources for veterinary, medical or laboratory courses. The grant is intended for educators and training material developers with the goal to foster respect and compassion for animals.

Each grant is USD 6,000. There are no facilities and administrative costs allowed

on the grants. Preference will be given to studies that have broad applicability and a potentially large impact on animal protection and science.

The deadline for receipt of submissions is September 30, 2024 at 11.59 pm EST.

Applications should be submitted electronically to the Director of the Beyond Classical Refinement Program, Kathrin Herrmann, at: kherrma1@jhu.edu

Additional details are available at: <https://lnkd.in/dg5zxqyj>

Upcoming Events

3Rs Training Webinar

The next 3Rs Training Webinar will take place on *Tuesday, August 6*, at 1 pm EST/ 7 pm CEST and will be led by Dr *Nils Haep* from Charité Berlin. He will present his work focused on understanding genetic influences in non-alcoholic steatohepatitis and developing innovative disease models. Being aware of the limitations of animal models, Dr Haep is an advocate for humanized models to better mimic human disease states. His work underscores the importance of humanized disease models in translational research. Please register in advance at: https://jh.zoom.us/webinar/register/WN_9m6v86TqQweH_L0u8gJKpg

11th Annual 3Rs Symposium: Practical Approaches to Each of the 3Rs

This symposium will focus on reduction, refinement, and replacement methods to improve laboratory animal welfare while maintaining or improving scientific results. Sessions will discuss opportunities to do more with less, refinement techniques in research that involve pain and distress, and how to use the 3Rs to improve efficiency and rigor. Jointly organized by the Center for Alternatives to Animal Testing, Johns Hopkins University Bloomberg School of Public Health, the Department of Molecular and Compara-



tive Pathobiology, Johns Hopkins University School of Medicine, the USDA's Animal Welfare Information Center (AWIC) at the National Agricultural Library, and the Office of Laboratory Animal Welfare, National Institutes of Health, the goal of the symposium is to bring together experts and practitioners to share information and discuss new and practical approaches to the 3Rs.

The seminar will take place *September 4-5, 11-12, 2024, 10:00am-1:30pm ET* and will be offered virtually. This virtual event will be submitted for RACE Credits. Sessions are designed for investigators, laboratory animal veterinarians, care staff, and IACUC members and staff. Residents, students, and postdocs are also welcome! Please register here: <https://www.eventbrite.com/e/11th-annual-3rs-symposium-practical-approaches-to-each-of-the-3rs-tickets-936579373117>

WC13 to Be Held in Rio de Janeiro August 31 - September 4, 2025

WC13 will be held in Rio de Janeiro, Brazil at the end of Summer 2025. The theme of 2025's congress will be *3Rs Integrating 3 Worlds: Human, Animal, and Environmental Health* and session proposals are already open! To make a submission and learn more about requirements, please visit <https://www.wc13rio.org/proposal-submission/>. More information on WC13 as well as newsletter subscription, sponsorship options, and more information on the location can be accessed via <https://www.wc13rio.org>.

Conferences and Conversations

Spring at CAAT was largely dominated by preparations for the final CAAT-organized MPS World Summit, but CAAT members were also kept busy speaking at local, domestic and international conferences. In May of this year, CAAT Program Director Lena Smirnova spoke at the 1st Annual

Maryland Spring Stem Cell Symposium and Workshop organized by the University of Maryland School of Medicine. CAAT Director Thomas Hartung and CAAT Program Directors Lena Smirnova and Kathrin Herrmann all participated in the 2024 Summer Immersion Program in Washington, DC organized by the Physicians Committee for Responsible Medicine. Kathrin Herrmann also served on the organizing committee and contributed considerably to the production and promotion of the highly interactive, multi-day event. Thomas Hartung served on the organizing committee and as a keynote speaker for Keystone Symposia on AI in Biomedicine. This virtual event offered a unique opportunity for participants to gain a better understanding of AI's impact on the biomedical field, the many opportunities AI integration presents, and important practical and ethical considerations.

Thomas Hartung and Yifan Gao, who recently joined CAAT's Computational Toxicology team, attended the ONTOX Hackathon in Utrecht, The Netherlands. Yifan's presentation on "How to drive the use of AI in chemical risk assessment" received the Best Pitch award, which came with the opportunity to attend ESTIV 2024. Multiple CAAT members gathered in the culturally rich city of Prague, Czech Republic for the multi-day conference organized by the European Society of Toxicology in Vitro (ESTIV). CAAT members also participated in and contributed to FENS Forum 2024, EUROTOX Molecular Toxicology course, the 5th International Cell & Gene Therapy China Summit & Exhibition, as well as many others.

In June, the MPS World Summit, organized by CAAT and its team in collaboration with hosts Elaine Faustman, Thomas Neumann, and Danilo Tagle, took place in Seattle, WA, welcoming attendees from more than 30 countries to the iconic US city. Going forward, the Summit will officially be managed by iMPSS, a society formed under the leadership of CAAT to eventually lead the development and organization of this annual event. This year's

conference marked a rewarding and energizing conclusion to a concept that has been three years in the making. The event saw high attendance, with academia (402 attendees), industry (406 attendees), and government sectors (129 attendees) all well-represented, as well as a remarkable presence of students and trainees (190 attendees).

As CAAT transitions the MPS World Summit to the capable hands of iMPSS, we want to acknowledge and appreciate the many contributions made since 2022 by organizers, partners, vendors, and volunteers. Special thanks to the steering group consisting of over 60 organizations, jointly promoting the field and the Summit, scientific advisory committee, program committee, fundraising committee, and to all our hosts through these past 3 years (Don Ingber, Suzie Fitzpatrick, Thomas Hartung, Peter Loskill, Uwe Marx, Marcel Leist, Elaine Faustman, Thomas Neumann, and Danilo Tagle). This project would not have been possible without your dedication and hard work.

Publications

- Pamies, D., Ekert, J., Zurich, M. G. et al. (2024). Recommendations on fit-for-purpose criteria to establish quality management for microphysiological systems and for monitoring their reproducibility. *Stem Cell Reports* 19, 604-617. doi:10.1016/j.stemcr.2024.03.009
- Krebs, C. E. and Herrmann, K. (2024). Confronting the bias towards animal experimentation (animal methods bias). *Front Drug Discov* 4, 1347798. doi:10.3389/fddsv.2024.1347798
- Hartung, T. (2024). The (misleading) role of animal models in drug development. *Front Drug Discov* 4, 1355044. doi:10.3389/fddsv.2024.1355044
- Kagan, B. Mahlis, M., Bhat, A. et al. (2024). Toward a nomenclature consensus for diverse intelligent systems: Call for collaboration. *The Innovation* 5, 100658. doi:10.1016/j.xinn.2024.100658



Cruelty Free INTERNATIONAL Ending animal experiments worldwide

New update on the quality of EU non-technical summaries published in ALTEX

All countries of the European Union (EU) are required to publish non-technical summaries (NTS) of research projects that involve the use of animals. To improve transparency, the public must have easy access to NTS and be able to understand their content.

Cruelty International's previous review (Taylor et al., 2018) found that the information provided in the NTS was lacking in many cases, preventing a full understanding of what animals experience during experiments. In particular, the NTS often failed to fully describe what procedures the animals would be subjected to, how often they would take place, how long they would last, and the harm they would cause.

Cruelty Free International has conducted a follow-up review of the NTS, published in this issue of ALTEX (Taylor et al., 2024), to see if recent legislative changes in the EU, including the requirement for NTS to be published in a central database using a standard template, have made a difference.

While there has been some improvement in reporting, many NTS still fail to adequately describe the harm that animals will experience. Unless the NTS improve further, their utility as a tool for sharing of good practices in the 3Rs or to support evidence-based policy making will remain limited.

References

- Taylor, K., Rego, L. and Weber, T. (2018). Recommendations to improve the EU non-technical summaries of animal experiments. *ALTEX* 35, 193-210. doi:10.14573/altex.1708111
- Taylor, K., Rego, L. and Weber, T. (2024). Have the non-technical summaries of animal experiments in Europe improved? An update. *ALTEX* 41, 382-394. doi:10.14573/altex.2310181

Sharp rise in reports of non-compliance with laws protecting animals in UK laboratories

On April 25, the Animals in Science Regulation Unit (ASRU) – the regulator overseeing the use of animals in research and testing in Great Britain – released its annual report for 2022, which details cases where animal users have failed to comply with the Animals (Scientific Procedures) Act (ASPA) on the protection of animals used for scientific purposes in the UK.

According to the report, a total of 16,062 animals were involved in 175 cases of non-compliance, including a horse, two dogs, 53 monkeys, hundreds of rats, and thousands each of chickens, fish and mice. This represents a 43% increase in breaches of the law since 2021.

A total of 1,063 animals suffered “adverse welfare outcomes”. For example, the report described multiple cases of failing or faulty equipment leading to hundreds of deaths, including by drowning and poor ventilation. Consistent with previous years, the report also detailed numerous cases of animals dying as a result of being left without food and/or water – these cases have increased by 420% since 2018.

Most cases of non-compliance are reported by the individuals or establishments themselves, with just a handful each year identified by the ASRU. It is therefore likely that there are cases that remain unreported and unidentified.

While the ASRU does have the authority to refer cases of non-compliance for prosecution, it chose not to take this course of action for any of the cases reported, instead issuing letters of reprimand and/or advice from an Inspector. Just two cases resulted in re-training of staff, but neither of these were recognised as having caused harm or death to the animals involved.

“Forever Against Animal Testing” wins campaign award

Cruelty Free International's “Forever Against Animal Testing” partnership with The Body Shop to end animal testing for cosmetics in Canada has won the silver award in the “Best Advocacy or Policy Initiative” category at the 2024 Engage for Good Halo awards.

The decade-long campaign ended on December 22, 2023, when the ban came into effect and made Canada the 44th country to pass laws to end or limit cosmetics animal testing and/or sales.

This is the second time that Cruelty Free International's work in Canada has been recognized by The Halo Awards, after a 2018 silver award for delivering the largest petition to Ottawa's Parliament Hill in over 70 years, with over 630,000 Canadian signatures supporting a ban on cosmetic animal testing. That was soon followed by the delivery of a petition signed by eight million global citizens to the United Nations.

SAFRireland announced as the second recipient of the 2024 Geoffrey Deckers Award

The Geoffrey Deckers award honors the much-loved former Chair of Cruelty Free Europe, who tragically passed away in June 2020. The award is given annually to groups demonstrating a commitment to ending animal tests and projects likely to make the most effective use of funds towards this goal.

On June 26, Cruelty Free Europe announced SAFRireland as the second recipient of this award. The group plans to use the funds to work towards ending botulinum toxin (Botox) testing in Ireland, which is a main hub for these tests in the EU.

Approximately 270,000 tests are still conducted on mice to measure the potency of Botox in the EU every year (based on official statistics for the EU and Norway



for 2020) despite the availability of a validated cell-based replacement. In this test, which is officially classified as “severe”, the highest category of suffering (according to EU Directive 2010/63), mice are injected into their abdomens with the botulinum toxin and, over the following three days, become increasingly paralyzed. If left, mice in the higher dose groups will suffocate to death. Approximately 50% of the mice die per test, and survivors are killed at the end.

Botox testing is included in Cruelty Free International’s RAT (Replace Animal Tests) list, which describes ten animal tests that are still being conducted in the EU despite the availability of non-animal replacements and calls on regulators to end experiments on animals where valid non-animal methods already exist.

NGO-led roundtable on the European Commission’s plans for phasing out animal testing for chemicals

An NGO-led roundtable discussion on the European Commission’s plans to phase out animal testing for chemical safety assessments was held in June.

In 2022, over 1.2 million people signed the European Citizens’ Initiative (ECI) “Save Cruelty Free Cosmetics – Commit to a Europe Without Animal Testing”, which was launched by a coalition of European animal protection groups and demanded the protection and strengthening of the EU ban on animal testing for cosmetics, the transformation of EU chemicals regulation, and the modernization of science in the EU. In response, the European Commission committed to deliver a roadmap for the phase-out of all animal testing for chemicals.

The roundtable discussion was held in Brussels and was led by a group of animal protection groups including Cruelty Free Europe. The day brought the Commission together with key stakeholders with expertise from across the chemicals sector, including pharmaceuticals, with attendees including representatives from European Union institutions, national regulators, industry, academia, environmental protection, and human health.

Participants recognized that the roundtable played a critical role in challenging the Commission to be ambitious and, by bringing various stakeholders together in one room, supporting the Commission in the delivery of a successful and impactful roadmap.

Cruelty Free International makes final push for candidate pledges at UK general election

With just a couple of days to go before UK voters go to the polls, Cruelty Free International is making its final pitch to parliamentary candidates for their support of three policy pledges which would: strengthen the UK cosmetics testing ban; end the use of animals in chemicals testing; and initiate a transition away from the use of animals in all science and education. So far, over 150 candidates have made a commitment to champion these policies if they are successfully elected to represent their constituencies.

The UK Labour party is the strong favorite to win the election and form the next government, so analysts have been paying close attention to their manifesto announcements. Cruelty Free International has welcomed the Labour Party’s manifesto pledge to phase out animal testing and the Green Party’s commitment to work to-

wards an outright ban on all animal testing. Whichever party wins, they will continue to push the government towards ambition in order to secure a roadmap with clear targets, milestones, and action to phase out the use of all animals in experiments.

Cruelty Free Europe calls on incoming MEPs to keep the goal of ending animal testing on the political agenda

As the impact of shifting political dynamics ripples across Europe following European Parliament elections, Cruelty Free Europe is urging incoming MEPs to ensure that animal testing stays on the political agenda. During the election several candidates signed the Cruelty Free pledge, giving their commitment to policies which will: protect cruelty-free cosmetics; end the use of animals in the regulatory system; and promote EU-wide action for animal-free science. Key animal champions such as Tilly Metz MEP and Anja Hazekamp MEP have been re-elected for another five years, but campaigners will be looking to all MEPs to take heed of clear resolutions from the previous Parliament, commitments from the Commission, and the support of 1.2 million EU citizens who signed the ECI, which together show there is a strong mandate to pursue changes across all elements of animal testing in the EU. However, with the emergence of new political forces across Europe and shifting priorities, Cruelty Free Europe will be preparing to work with its associate members from across Europe to make sure that the shared goal of ending animal testing remains on the agenda.



Fachbereich Veterinärmedizin
der Freien Universität Berlin



Survey of Berlin 3R Open Access Online Seminar shows continued high demand for 3Rs education

Webinars on the 3Rs are a barrier-free opportunity to acquire knowledge about the 3R principle, to stay updated on current scientific developments, and to learn about the professional opportunities within the 3R field. The Institute of Animal Welfare, Animal Behavior and Laboratory Science at the Free University of Berlin has been running an open access online seminar titled “Alternatives to animal use in research and education – Refine, Reduce & Replace” since 2016. The seminar offers scientists, students, animal welfare officers, authority representatives, and other

interested individuals the opportunity to engage with a diverse array of topics within the domain of the 3Rs. The series was initiated by the Berlin-Brandenburg research platform BB3R, integrated into the information and education platform “3R SMART”, and extended to the Berlin Einstein Center 3R. An overview of the seminars between the years 2016 and 2018 was provided by Hohlbaum et al. (2020); the topics covered between 2020 and 2023 are given in Table 1. Between 800 and 900 participants from Europe and the United States attended the individual seminars.

82 participants answered a survey in 2023. These included scientific researchers (n = 37), doctoral candidates (n = 19), veterinarians (n = 12), technical assistants

(n = 11), students (n = 10), animal welfare officers (n = 3), animal house managers (n = 3), and an animal caretaker (n = 1) (multiple answers possible). More than 20% of the participants reported they did not have extensive knowledge on the topics presented ahead of the seminar. The satisfaction with the seminar (> 80%) and the interest in further training (75%) in the 3Rs was high, which was consistent with the report by Hohlbaum et al. (2020). 71% of respondents expressed that the knowledge acquired during the seminars could be applied in their work (compared to 55% in Hohlbaum et al., 2020). These numbers suggest a growing practical application of the 3Rs and potentially signify an increasing awareness of the 3R principles.

Tab. 1: Topics covered in the online seminar between 2020 and 2023

Ethics, law, education, and training	Replacement	Reduction	Refinement	Culture of care
<ul style="list-style-type: none"> - Ethical justification of animal experimentation - Regulating animal testing - Legal classification of animal testing - The legal governance on animal experiments - Approaches for the implementation of the 3R principles in education and training - Simulation-based education 	<ul style="list-style-type: none"> - Alternative methods for inflammatory diseases, genetic disease, stroke, neurodegeneration, and brain diseases - Biomimetic robots - 3D bioprinting of humanized organ models - Organoids for personalized medicine approaches - Online tool to retrieve potential alternatives from scientific literature 	<ul style="list-style-type: none"> - Animal study registry - Robustness, registration and reporting of animal experiments - <i>In-vitro</i> modeling - Assembloids - 3R-schooling for methodological approaches to reduce animal tests - Cross-species comparability and validity 	<ul style="list-style-type: none"> - Animal training - Assessment and improvement of well-being - Investigating intelligence - Simulators - Non-aversive animal handling techniques - Social enrichment methods - Behavioral phenotyping – refinement strategies 	<ul style="list-style-type: none"> - Cooperative care training - Caring for those who care - Transparent communication about animal testing as a basis for a social discourse



The substantial number of suggested topics underscores an ongoing demand for informative events in the field of the 3Rs (Tab. 2). Among these, there is keen interest in addressing critical subjects like refinement in large animal models, optimization of breeding practices, and ethical aspects surrounding experimental animals.

We would like to thank all the speakers, moderators, organizers, and participants

who made this seminar possible. Additionally, we would like to thank BB3R and the Einstein Center 3R for their ongoing support. We eagerly anticipate organizing future webinars. The seminar program can be found on the website of the Institute of Animal Welfare, Animal Behavior and Laboratory Animal Science (<https://www.vetmed.fu-berlin.de/en/einrichtungen/vph/we11/index.html>).

Reference

Hohlbaum, K., Kral, V., Zoschke, C. et al. (2020). Open access webinars bring 3R experts to your web browser: The Berlin experience. *ALTEX* 37, 300-303. doi:10.14573/altex.2002091

Stephanie Schneidewind, Karolina Krehl, Christa Thöne-Reineke

Tab. 2: Topics for future 3R webinars suggested by participants in evaluations conducted between 2020 and 2023

Ethics, law, education, and training	Replacement	Reduction	Refinement	Culture of care/other
<ul style="list-style-type: none"> - Planning animal experiments - Animal research required by law and legal interpretation - Challenges of applying new alternative methods in the regulatory environment - Training on how to assess/write ethical justifications - Animal welfare law, application submission, communication with the approval authority - How science can help influence policies on the 3Rs - Severity assessment including genetically modified and phenotypically potentially burdened lines - In-depth talks on ethics 	<ul style="list-style-type: none"> - Embryoids/ (iPSC-derived) organoids - Lab-on-a-chip - 3D bioprinting - 3D culture and co-culture with immune cells, 3D neuron cultures, brain slice cultures - <i>In vivo</i> imaging techniques - Replacement of epilepsy models, dog models, bone metabolism/healing, education and training including surgical training - Transferability of findings from cell culture models to the whole organism – Presenting this in a publication/answering reviewer challenges - Literature searches for alternative models - Alternative methods to animal testing such as BCOP, HET-CAM 	<ul style="list-style-type: none"> - Biostatistics - Reduction of variability in animal experiments - Tracking the course of individuals over an extended period - Collaborations to share tissue/data 	<ul style="list-style-type: none"> - Analgesia and anesthesia in rodents - Refinement of animal-appropriate housing - Imaging techniques as a refinement - Refinement as a positive factor for reproducibility - Animal handling methods and their effects - Refinement for non-rodents including zebrafish, sepsis models, fibrosis models, euthanasia - Better breeding strategies, alternatives to hygiene sentinels - The impact of elevated stress hormone levels on experiments - Monitoring animals in experiments, animal care protocol, score sheet - Evidence-based training methods with defined training goals 	<ul style="list-style-type: none"> - Rehoming laboratory animals - Dialogue with the public - Where are the 3R principles already being implemented and where is improvement necessary? - Specific issues in the pharmaceutical industry - Farm animals (ruminants, pigs, poultry), non-human primates and fish, and amphibians - 3R implementation in laboratory animal husbandry - The 6Rs and their implementation - The 3Rs in wildlife studies - Mouse cancer models



EUSAAT

European Society for
Alternatives to Animal Testing

COST Action IMPROVE – update

Currently, over 230 members of the COST Action “CA21139 – 3Rs concepts to improve the quality of biomedical science (IMPROVE)” are working on different projects and publications.

After the successful participation of animal care staff and lab technicians, it is the turn of the researchers who work with animal research to take part in our international survey, “Framing the Role of Animal Care Staff and Lab Technicians in Experimental Planning and Conduct of Animal Studies”. The survey is available in eight languages, takes about 15 minutes, and is open until the end of July 2024: <https://umfragen.unimedizin-mainz.de/index.php/583131?lang=en>

A training school about 3D cell culture methods in Kaunas, Lithuania, took place on May 9-10, 2024. It included talks from different stakeholders (e.g., MatTek, IVTech, Biou Technology & Life, etc.) and practical courses on the generation and handling of organotypic models and spheroids. The detailed program and pictures can be found via: <https://cost-improve.eu/outcome/training-school-3d-cell-models-for-3r-research-in-kaunas-on-may-9-10-2024/>

A virtual workshop on the use of the TATA-Box was given by Alvertox with research groups in Prague, Rome and Vienna on May 21, 2024. Details can be found on the IMPROVE outcomes website via: <https://cost-improve.eu/outcome/tata-box-online-workshop/>

The management committee meeting and meeting of working groups 1 & 2 took place in Utrecht on June 17-18, 2024. Over 50 members of the COST Action partici-

pated in these meetings organized excellently by the 3Rs Centre Utrecht. Significant progress was achieved in the preparation of several publications and initiatives. In addition, COST Action members Nuno Henrique Franco, Jeffrey Bajramovic, and Winfried Neuhaus gave lectures in the session “Improving uptake and validation of NAMs” during the conference “3Rs and NAMs – all inclusive” on June 19, 2024 in Utrecht, which was organized by the 3Rs Centre Utrecht and Transitie Proefdiervrije Innovatie (TPI).

One major aim of the COST Action IMPROVE is to disseminate 3Rs related concepts in basic science, especially in the areas of neuroscience, oncology, and cardio-vascular diseases, since most animals are used in these fields (next to immune system research). In this regard, Winfried Neuhaus participated in the panel discussion of the networking event “How to organize and respond to pressure to phase out animal experimentation in neuroscience” at the biggest European neuroscience conference, the FENS FORUM, with over 7000 participants, in Vienna on June 25-29, 2024. Presentations by Roger Adan, Roman Stilling, Sabine Hölter-Koch, Suzanne L. Dickson and Livia D’Angelo set the scene for a lively discussion, in which it became clear that transparent communication about animal studies targeted to specific stakeholder groups is key to increase the understanding of the value of animal experiments in neuroscience, but also that an all-inclusive approach using the best models available for the specific scientific questions could be the future way to also implement NAMs in basic research. Furthermore, polarization should be avoided in communication (“us” vs. “they”).

Do not miss the next meetings of the COST Action IMPROVE:

- A cross-WG workshop on “Ethics and 3Rs” will take place in Istanbul, Turkey, on September 2-3, 2024 organized on-site by Profs Yesim Isil Ulman and Augusto Vitale. The aim of the workshop is to discuss whether the use of animals can be morally and ethically permissible, and if or only when the study is scientifically structured on a sound and robust basis and it complies with the 3Rs principles (replace, reduce, refine). The main objective of the workshop is to reflect on the ethical dimension of animal experiments in the age of emerging sciences, new awareness on animal welfare, and in the perspective of new approach methodologies. The program, registration and the possibility of reimbursements can be found via: <https://cost-improve.eu/event/ethics-3rs-one-health-workshop-by-cost-action-improve-x-over-ethics-group/>
- Moreover, IMPROVE is co-organizing with EUSAAT a 3R centers workshop in Linz, Austria on September 17, 2024, ahead of the EUSAAT Congress on September 18-20, 2024. The meeting will be funded by CA21139-IMPROVE. The main objectives are i) to coordinate the 3R centers (currently most centers are part of the network “EU3RNet”); ii) to support emerging 3R centers; iii) to dialogue and collaborate with other relevant actors and stakeholders. The program, registration and the possibility of reimbursements can be found via: <https://cost-improve.eu/event/3rs-centres-workshop/>
- In addition to these in-person meetings, an online webinar series dedicated to



young researchers and innovators is being organized, and some other activities at online webinar series and basic science conferences will be supported by the COST Action IMPROVE in 2024.

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>

Anyone can apply to participate in the working groups. COST Action Members can apply for Short Term Scientific Missions (STSMs), which are stays of up to 3 months in a host lab, and young scientists from ITC countries can apply for ITC grants to visit conferences. Please check the website for further information on STSMs: <https://cost-improve.eu/calls-grants/#section-3> and ITC grants: <https://cost-improve.eu/calls-grants/#section-1>

EUSAAT/EU3Rnet at the 1st International Conference of the Würzburg Initiative 3R (WI3R)

Winfried Neuhaus gave the keynote “3Rs – past and progress” to open the scientific program at the 1st International Conference of the Würzburg Initiative 3R (WI3R) in Würzburg, Germany, on June 5-7, 2024. The conference offered several sessions with different topics highlighting several novel developments on NAMs, tissue engineered models, and microphysiological systems (MPS). More information: <https://wi3r.de/>.

Within the 1st WI3R symposium, the German Research Foundation (DFG) awarded the Ursula M. Händel Animal Welfare Prize to Peter Loskill and Silke Riegger from the University of Tübingen for their work on organ-on-chips. The Ursula M. Händel Animal Welfare Prize recognizes scientists who have made exemplary and sustained efforts to improve the welfare of animals in research. The €80,000 prize is currently the largest prize of its kind in Germany and is awarded bi-annually.

EUSAAT Congress 2024

The EUSAAT Congress 2024 will take place on September 18-20, 2024. We hope for an extensive turnout like in 2022 and that stakeholders and researchers from all areas of the 3Rs community will participate. Again, we especially want to attract young scientists by offering not only an attractively low participation fee but also the EUSAAT travel awards for young scientists via the YSTA (Young Scientist Travel Awards) Program.

We are offering attractive sessions on a wide spectrum of 3Rs topics on the EUSAAT Congress 2024 website: <https://eusaat.eu/eusaat-congress-2022/highlights/announcements/eusaat-congress-2024-practical-info-tentative-topics/>

We are delighted that a unique, thematically diverse, and scientifically excellent team of colleagues have joined the scientific committee: <https://eusaat.eu/eusaat-congress/24th-edition/scientific-committee-2024/>

In addition, we are very pleased that a huge number of co-organizers and sponsors will once again support the EUSAAT Congress 2024: <https://eusaat.eu/eusaat-congress/24th-edition/organizers-sponsors-2024/>

Information on registration is provided on the website: <https://eusaat.eu/eusaat-congress/24th-edition/registration-2024/>

EUSAAT and the organizers and sponsors are very much looking forward to hosting the 3Rs Community at the European 3Rs Congress 2024 at the University of Linz and to meeting you there!



LUSH PRIZE



SUPPORTING ANIMAL-FREE TESTING

Lush Prize 2024 winners announced

The winners of the 2024 Lush Prize have been announced. The £250,000 prize was shared across eight categories, three of which are non-financial and include the first award in a new category for “Major Science Collaboration”. There are a total of 14 winning projects from 9 countries and two commendations. You can learn more about all the winners and see videos about their projects or watch a recording of the awards ceremony held in May on the Lush Prize website (<https://lushprize.org>).

Winners of the Lush Prize 2024

- *Andrew Tyler Award* (non-financial): *Liz White*, Animal Alliance and the Animal Protection Party, Canada
- *Lobbying Prize*: £50,000. The *International Organisation for Standardisation (ISO) Working Group 8 team (ISO/TC-194/WG8)*, Switzerland, for work to build the consensus for regulatory acceptance of non-animal methods (NAMs) for medical devices.
- *Major Science Collaboration* (non-financial): *Coalition to Illuminate and Address Animal Methods Bias (CO-LAAB)*, USA
- *Political Achievement Award* (non-financial) – joint winners:
 - Jean-Yves Duclos, Liberal Party, Canada
 - Emma Hurst, Parliament of New South Wales, Australia
- *Public Awareness Prize*: £50,000. *Animal Aid*, UK, for their campaign to ban lethal dose animal tests including the LD50.
- *Science Prize*: £50,000. *Emulate Inc.*, USA, for their work to validate a human liver chip for preclinical toxicology.
- Also commended in the Science category was the *Comparative Toxicogenomics Database*, USA, for providing computational solutions that fill mechanistic knowledge gaps for toxic adverse pathways.
- *Training Prize*: joint winners, £25,000 each:
 - *Massey University School of Veterinary Science*, Aotearoa, New Zealand, for their work in replacing terminal surgical practical classes in animals with model-based skill instruction in veterinary undergraduate training.
 - *School of Public Health, China Medical University*, China, for their national workshops in computational toxicology training and application.
- *Young Researcher Awards*: £10,000 each
 - 1 *Lauren Dalat de Sousa Coelho*, Universidade Federal de Goias, Brazil – Multi-organ-on-chip platform for human teratogenicity screening of cosmetics.
 - 2 *Martina Iulini*, Università degli Studi di Milano, Italy – Advancing immunotoxicity studies through innovative *in vitro* human models: A focus on primary antibody production.
 - 3 *Barbara Jozef*, Eawag, ETH Domain, Switzerland – Exploring early neurotoxic effects: Phenotypic profiling of rainbow trout brain cells for identifying distinct modes of action in chemicals.

(Note: Project involves use of immortalised cell lines with an indefinite lifespan and which do not require the use of “new” animals for production, so these meet the strict eligibility criteria for Lush Prize.)
 - 4 *Chao Ma*, New York University, USA – Bioengineering *ex vivo* human leukaemia bone marrow precision immuno-oncology platform: Preclinical screening for personalized CAR T-cell immunotherapy.
 - 5 *Zheng Tan*, University of British Columbia, Canada – Establishing a multi-organ co-culture in an organ-on-a-chip setup to emulate the human atopic march.
- Also commended in the Young Researcher category was *Maren Schenke* of Johns Hopkins University, USA, for her project on addressing sex differences in brain development without animals.