Corners

CAAT feed

EPA Awards Nearly $850,000 to Johns Hopkins CAAT to Advance Research on Alternatives to Animal Testing

The U.S. Environmental Protection Agency has awarded $849,276 to Johns Hopkins University in Baltimore, MD, as part of a total of $4.25 million in funding to five universities to research the development and use of alternative test methods and strategies that reduce, refine, and/or replace vertebrate animal testing.

"Johns Hopkins University has long been an important partner to EPA in conducting research to protect human health, as well as helping tackle global environmental challenges through their research and academic programs," said EPA Mid-Atlantic Regional Administrator Cosmo Servidio. "We congratulate the university for being selected to contribute to the field of research on alternatives to animal testing."

CAAT's Lena Smirnova is a recipient of the EPA STAR award on Advancing Actionable Alternatives to Vertebrate Animal Testing for Chemical Safety Assessment (EPA-G2018-STAR-C1). Her project, "Multiplexed human BrainSphere developmental neurotoxicity test for six key events of neural development" will be focused on development of a CRISPR/CAS9 modified fluorescently-tagged multi-fusion 3D BrainSphere model derived from iPSC to assess developmental neurotoxicity. It will be carried out in collaboration with Dr Cynthia Berlinicke, Wilmer Eye Institute (JHU), and Dr David Gracias, Whiting School of Engineering (JHU).

"For nearly 40 years, the Johns Hopkins Center for Alternatives to Animal Testing's mission has been to promote humane science and human-relevant, modern approaches in the field of toxicology and risk assessment. I'm glad to be part of the Center's team and working in the field of alternatives for a decade," said CAAT's Dr Lena Smirnova.

Administrator Wheeler has called for the EPA to aggressively pursue a reduction in animal testing. The memo states, EPA will reduce its requests for, and funding of, mammal studies by 30% by 2025 and eliminate all mammal study requests and funding by 2035. Any mammal studies requested or funded by EPA after 2035 will require administrator approval on a case-by-case basis. It directs leadership and staff in the Office of Chemical Safety and Pollution Prevention and the Office of Research and Development to prioritize ongoing efforts and to direct existing resources toward additional activities that will demonstrate measurable impacts in the reduction of animal testing while ensuring protection of human health and the environment.

In accordance with the memo, EPA will hold an annual conference on new approach methods beginning in 2019.

Read the full EPA memo here: https://www.epa.gov/environmental-topics/administrator-memo-prioritizing-efforts-reduce-animal-testing-september-20-2019

Next Generation Humane Science Award Winner: Danielle Ireland

Danielle Ireland, of the Department of Biology, Swarthmore College, is the recipient CAAT's 2019 Next Generation Humane Science Award. The award is presented annually to young scientists to acknowledge and encourage researchers who focus on replacing animal experiments.

EBTC Hamilton Workshop Available on YouTube

EBTC and the GRADE Working Group collaborated on a workshop, Integrating Evidence into Toxicology Systematic Reviews, which explored how mechanistic information can be better organized and integrated into systematic reviews of health risks posed by exposure to chemical substances. The workshop preceded the annual GRADE meeting on June 13-14 in Hamilton, Ontario.

Watch Now (YouTube): https://www.youtube.com/watch?v=Nna0r2qL4pI&t=7664s

Kathrin Herrmann at 12th Animal Research Conference

On June 20, Kathrin Herrmann, CAAT's Refinement Program Director, spoke at the 12th Animal Research Conference of the Swiss animal welfare organization Schweizer Tierschutz (STS). This year's theme was the 3Rs and non-animal approaches – better science and less animal suffering. Kathrin presented on ways to move beyond the 3Rs towards human-relevant science.

Lorna Ewart Joins CAAT as Senior Advisor for Microphysiological Systems

Lorna Ewart has joined CAAT as a senior advisor for its microphysiological systems research.

Lorna obtained an honors degree in pharmacology from the University of Aberdeen and a PhD at The William Harvey Research Institute, Queen Mary University of London. Twenty years ago, she joined the Respiratory and Inflammation research area within AstraZeneca as a lead biologist, bringing forward drug projects to candidate drug nomination before moving into preclinical drug safety, where she led a safety pharmacology team delivering GLP studies across multiple therapeutic areas. Lorna then spent two years in Gothenburg, Sweden as the therapy area lead toxicologist for Respiratory and Inflammation before moving to Cambridge, UK, where she established the Centre of Excellence for Microphysiological Systems within AstraZeneca's R&D Biopharmaceuticals Unit.

Regarded as a pioneer of the field, Lorna established AstraZeneca at the leading edge of industrial adoption of these models and as a valued partner in multiple external collaborations involving academic institutions, regulatory bodies, and technology developers. Scientifically, Lorna is passionate about the translation of preclinical science to patient outcome to improve lives. She has over 30 peer-reviewed publications, is a fellow of the Royal Society of Biology and British Pharmacological Society, and channels her infectious personality towards the development and mentoring of more junior scientists. Lorna has now established herself as an independent consultant in the field of preclinical drug discovery, translation, and application of technology to scientific advancement.

Vy Tran, Student at CAAT, Wins Tox21 Student Award

Vy Tran, a student at CAAT, received the Tox21 Student Award for her project "Comparing gene networks between MCF-7 cell line and human breast cancer." Dr Ray Tice, a leader in the development and use of high-throughput test methods and other alternatives, established the Tox21 Student Award, which will be awarded to the graduate student first author of a winning poster or oral presentation. The winner receives a $500 cash award to assist with travel and/or research expenses.

More information about the conference can be found here: https://www.ascctox.org/annualmeeting

CAAT Online Courses Pass 2,500 Learner Mark

CAAT's highly-rated online courses, offered by the Johns Hopkins Bloomberg School of Public Health on the popular Coursera education platform, have now passed the 2,500 learner mark. Toxicology 21: Scientific Applications and Evidence-based Toxicology are free and available to anyone.
More information about the courses can be found here:
https://www.coursera.org/learn/toxicology-21
https://www.coursera.org/learn/evidence-based-toxicology

Thomas Hartung Interviewed in *Live Science*

Lab-Made Mini Brains Produce Brain Waves Just Like Those of Preterm Babies

Excerpt:
This study shows "very nicely that you can make this [*sic*] reproducible experimental systems where you can address processes which are so fundamental for the development of a human being," said Dr Thomas Hartung, the director of the Johns Hopkins Center for Alternatives to Animal Testing who has also worked on developing mini-brains in the lab but who was not a part of the study.

The "inaccessibility of the embryonic brain is one of the reasons why these models are offering something different," he said. "But it also means you have very limited opportunities to say it's the real thing." While the EEG signals are similar to that [*sic*] of pre-term babies, they're slightly off in timing, he added.

While a human embryo is connected to the mother and thus receives signals from the outside, these lab-grown brains aren't connected to anything. "These cells have no input or no output they cannot recognize anything happening in the world," Hartung said. So they are "definitely not" conscious.

FullArticle:https://www.livescience.com/mini-lab-brains-produce-waves.html

Thomas Hartung and EBTC in *The Scientist*: Fixing the Flaws in Animal Research

Excerpt:
Poorly designed animal studies raise ethical concerns in addition to financial and scientific ones. Preclinical experiments, which often involve modeling aspects of human diseases in animals, can include procedures that may cause pain or otherwise inflict harm on the organisms under investigation. While most scientists may consider that harm to be justified in cases where well-conducted research leads to scientific advances, projects that generate irreproducible data on account of poor design create far more unease. According to toxicologist Thomas Hartung, director of the Center for Alternatives to Animal Testing, a group dedicated to promoting and improving the welfare of research animals, at the Johns Hopkins Bloomberg School of Public Health and the University of Konstanz in Germany, "Research that is not quality-controlled is unethical."

Researchers in the US and in Europe are working to implement these types of critical assessments for animal experiments more broadly. For example, the Evidence-Based Toxicology Collaboration that Hartung chairs at the Johns Hopkins Bloomberg School of Public Health has started using systematic reviews to evaluate toxicology studies, and the Netherlands-based organization SYRCLE (SYstematic Review Center for Laboratory animal Experimentation) provides tools, guidelines, and support for researchers to conduct reviews of animal studies in their own fields.

Full Article (The Scientist): https://www.the-scientist.com/careers/fixing-the-flaws-in-animal-research-66276

Thomas Hartung in *Wired*

Is the UK finally turning its back on mouse testing? It's complicated.

Excerpt:
This disconnect between pharma and academia comes from increasing pressure on pharmaceutical companies to adapt to new approaches, says Thomas Hartung, professor at Johns Hopkins Bloomberg School of Public Health. However, he says researchers

in larger institutes, like the Harwell Insitute [sic], are slowly catching up and moving away from animal testing because big investments put them under pressure to innovate beyond the animal models' shortcomings.

"Top institutes have to be bold to stay on top because they're driven by pharmaceutical companies who have to bring in money to develop the next drug," he says. "They have to think about what tools will get them there – and in this case, they're much more sensitive to the shortcomings of what they have and the opportunities of new approaches."

Read the full article: https://www.wired.co.uk/article/mice-testing-uk

Upcoming Events

JHU Exposome Collaborative Launch Event

November 8, 2019
Johns Hopkins Bloomberg School of Public Health
Baltimore, MD

The Exposome Collaborative at Johns Hopkins was funded to congregate the intellectual and material resources housed under the various disciplines within the environmental health sciences and engineering, to evaluate the exposome in a holistic manner. The goals of The Exposome Collaborative at Johns Hopkins:

- Develop the needed tools and analyses for exposome assessment.
- Bring together expertise in all the different disciplines needed to better characterize the exposome in human health studies.

Details and registration: https://tinyurl.com/yynlkjc5

60 Years of the 3Rs: Lessons Learned & the Road Ahead

November 22, 2019
Johns Hopkins Bloomberg School of Public Health
Baltimore, MD

Join us as we celebrate the 60th anniversary of the publication of The Principles of Humane Experimental Technique by W. M. S. Russell and R. L. Burch.

We will have an exciting roster of the biggest names in the history of alternatives, celebrating the accomplishments of the past and forward to the breakthroughs of the future. Invited guests include Michael Balls, Rodger Curren, Alan Goldberg, Julia Fentem, Thomas Hartung, Nicole Kleinstreuer, John Pascarandola, Andrew Rowan, Horst Spielmann, Martin Stephens, Russel Thomas and more.

Information: https://tinyurl.com/3Rs60years

5th International Conference on Alternatives for Developmental Neurotoxicity (DNT) Testing

April 6-8, 2020
Konstanz, Germany

This conference will bring together diverse stakeholders from around the globe, including research scientists, regulators, industry representatives, academics, and pediatricians to discuss the actions to take for:

- improving the development of time-efficient and human-relevant predictive *in vitro* DNT methods, and;
- boosting their use in the risk assessment regulatory decision-making process.

Details and registration: https://www.uni-konstanz.de/en/dnt5/about-the-event/

7th Annual 3Rs Symposium: Practical Solutions and Success Stories

June 4-5, 2020
USDA National Agricultural Library
Beltsville, Maryland

The 7th Annual 3Rs symposium is co-hosted by the USDA Animal Welfare Information Center (AWIC), NIH Office of Laboratory Animal Welfare (OLAW), the Johns Hopkins Department of Molecular and Comparative Pathobiology, and the Johns Hopkins Center for Alternatives to Animal Testing (CAAT). The goal of this year's symposium is to bring together experts in replacement, reduction, and refinement of animal experimentation to exchange information with scientists, IACUC members, veterinarians, and animal care technicians about practical solutions and recent success stories to reduce the use of animals in research and improve their welfare.

The format includes 1.5 days of lectures and panel discussions with interactive breakout sessions in the afternoon on day two. These lectures give participants a strong foundation in the relevant research underlying breakthroughs in the 3Rs, while the breakout sessions allow participants to receive feedback specific to their own facilities from experts and colleagues. A half-day tour of labs and research centers at the Agricultural Research Service is planned for June 3, 2019 as an optional pre-symposium event.

Recent Event

Food Safety Symposium

September 5, 2019
The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
Hosted by CAAT and The Center for a Livable Future
This event is now available to view online here: https://youtu.be/5QMM9uIRjN8

New Publications

Hartung, T. (2019). Conference article on predicting toxicity of chemicals: Software beats animal testing. *EFSA J 17, Spec Issue 1*, e170710, 8 pp. doi:10.2903/j.efsa.2019.e170710

Hartung, T. (2019). La sperimentazione farmacologica sugli animali. In B. Fedi and M. Corsini, *L'Errore Antropocentrico – Uomo – Natura – Altri Viventi* (207-210). Milano, Italy: Mimesis Edizioni..

Lanzoni, A., Castoldi, A. F., Kass, G. et al. (2019). Advancing human health risk assessment. *EFSA J 17, Spec Issue 1*, e170712. doi:10.2903/j.efsa.2019.e170712

Cruelty Free INTERNATIONAL
Ending animal experiments worldwide

Poll reveals nearly 9 in 10 US adults support law requiring medical researchers to prioritize non-animal testing methods

According to a new nationwide poll conducted by SurveyUSA on behalf of Cruelty Free International, 88% of US adults across party lines would support a federal law to require medical researchers to use non-animal alternatives before resorting to animal experiments.

The poll also reveals high levels of support for priority investment in non-animal research. When it comes to allocation of tax-payer funds for medical research, 79% said that the National Institutes of Health (NIH) should prioritize research proposals that utilize scientifically valid alternatives to animal testing. Similarly, 80% said that medical researchers seeking funding for animal tests should first be required to show that an alternative is not available.

A bill currently pending in the US Congress, The HEARTS (The Humane and Existing Alternatives in Research and Testing Sciences) Act, prioritizes NIH funding for non-animal methods and would require NIH grant applications to more fully evaluate such methods. The bill, H.R.1209, was introduced by Reps. Lucille Roybal-Allard (D-Calif.) and Ken Calvert (R-Calif.) in February this year and now has multiple cosponsors.

The poll also shows that 70% of American adults support a federal law to end animal testing for cosmetics. Bills in California, Nevada and Illinois that will end the sale of newly tested cosmetics in those states from January 2020 are also increasing pressure for federal action.

Pressure mounts on UK government as it prepares to leave the EU

The scheduled date for Brexit – October 31 – is fast approaching and the UK government has yet to honor its commitment to sentience legislation. Without this, animals will no longer be legally recognized as sentient beings, and there will be no legal requirement for government to pay regard to their needs when formulating and implementing policy.

Alongside 40 animal protection organizations, Cruelty Free International is supporting the #BetterDealForAnimals campaign, calling on the UK government to urgently incorporate recognition of animal sentience into UK law.

The UK government is also yet to reach an agreement with the EU to share REACH safety data, which would prevent the need for duplicate chemical tests on animals. The decoupling of UK chemical safety rules from EU law also raises the prospect of even higher levels of testing chemicals in animals beyond that which is required in the EU.

Earlier this year, Cruelty Free International worked with cross-party MPs to coordinate a letter to government asking it to rule out duplicate chemical testing on animals as a result of a no-deal Brexit and UK-REACH. To date, the concerns raised by those MPs have not been answered.

Two ethics reviews into genetic modification

Cruelty Free International has responded to a call from the UK's Nuffield Council on Bioethics for evidence to inform its inquiry into the use of genome editing techniques in farmed animals. The deadline for responses was September 20 and the evidence will be used to develop the working group's first report.

According to the evidence submitted by Dr Jarrod Bailey, Senior Research Scientist at Cruelty Free International, gene editing – even the "new improved" CRISPR technology – is not anywhere near being capable enough to be applied to the creation of genetically modified farmed animals without causing significant, serious, and widespread suffering and should not be permitted on both animal welfare and scientific grounds.

The European Commission's European Group on Ethics in Science and New Technologies is also looking into the issue of gene editing of humans, animals, and plants. On October 16, 2019, they will convene a public round table in Brussels; Dr Jarrod Bailey will be attending on behalf of Cruelty Free International. Perspectives and conclusions from the roundtable will feed into the preparation of the EGE's Opinion on the Ethical Implications of Gene Editing, requested by the European Commission, and due to be issued beginning 2020.

Impact assessment needed for REACH annex changes affecting animals

In June, the European Chemicals Agency (ECHA) and the European Commission (EC) published a REACH Evaluation Joint Action Plan to improve the compliance of REACH chemical registration dossiers. Included in the actions is a mandate for review whether the information requirement annexes in REACH (Annexes VI to XI) need to be updated to provide "clarity" for registrants.

In its response to the action plan, Cruelty Free International raised concerns that not all of the clarifications were benign and some could in fact lead to an increase in animal testing even for already registered substances. For example, there was an indication that text waiving a reproductive-developmental toxicity screening study when a prenatal developmental study is already available is to be deleted. A single screening study alone uses at least 400 animals including the pups, and it had already been decided when REACH was created that, in that case, doing both tests was unnecessary. Cruelty Free International are calling for the Commission to be more transparent in its intentions for the REACH Annexes and to commit to a full impact assessment of any changes. Proposals are expected to be presented by the end of 2019.

Quantity does not always mean quality, but during the second halftime of the EU-ToxRisk project, we will show that maximization of both aspects is possible.

The ambition of EU-ToxRisk is to generate a sustainable platform of NAMs (New Approach Methods) that will be used for chemical risk assessment in the near future. To allow a real application of this platform and to increase the confidence in its use, quality assurance (QA) procedures and application of the FAIR principles (Findable, Accessible, Interoperable and Reusable information) are key aspects. For this scope, the project has established an in-house strategy to collect in a formal, accessible and searchable way extensive information on the developed methods and the produced data.

To date, the consortium has produced and deposited almost 800 datasets (on the open platform of Biostudies[1]) derived from more than 150 different methods. These have been extensively characterized and described, adhering to high-level parameters of quality, leading to a publicly-accessible methods database[2]. The information included in the method description is also used to assess the readiness level for each method, depending on its regulatory purpose, indicating the validity of test systems and their application domains. The extensive documentation and the pre-validation of the EU-ToxRisk toolbox allow its application in industry. To test the selected NAMs in a relevant environment, some industry-driven practical case studies are already running. Based on all the information obtained from this experience, a final selection of tests will be made to derive a core service package that will be rolled out in a new collaborative service platform that is currently being developed.

Since the start of the project, the development and applications of the methods have been described in more than 80 publications in important peer-reviewed journals and presented at more than 15 dedicated sessions at international conferences. The latest occasion was the international conference EUROTOX 2019 in Helsinki (Finland) in September 2019. The EU-ToxRisk project was present with two dedicated sessions focused on the application of NAMs to develop an integrated testing strategy applicable to regulatory risk assessment. Furthermore, project experts contributed to the session's speaker panel on knowledge-based computational approaches in predictive toxicology.

EU-ToxRisk publications

In the current issue of the project newsletter[3], an overview on different key aspects of the EU-ToxRisk QA process is given, as applied to (i) chemical handling, (ii) method descriptions, (iii) data handling, (iv) data processing, and (v) test relevance.

The described approach is applied by the partners for the development and use of different novel *in vitro* and *in silico* testing tools. Here are some of the most recent examples.

In the publication by Delp et al. (2019), the authors described the development of a neurotoxicity assay specifically tailored to detect mitochondrial toxicants. The combination of the high throughput neurotoxicity screening assay with the mechanistic follow-up of target site identification allowed both more sensitive detection of neurotoxicants and a sharper definition of the mode of action of mitochondrial toxicants. The authors Ramme et al. (2019) presented a four-organ-chip developed to interconnect miniaturized human intestine, liver, brain, and kidney equivalents. All four organ models were pre-differentiated from induced pluripotent stem cells from the same healthy donor and integrated into the microphysiological system. This model platform will allow the development of autologous co-culture cross-talk assays, disease induction, and subsequent drug testing. Finally, in Karremann et al. (2019), a free and highly interactive image analysis program SUIKER (program for SUperImposing KEy Regions) was described. The program allows the quantification of co-localized proteins or other features over an entire image field.

Aspects of test method evaluation are part of the QA and are described in the review by Sachinidis et al. (2019). Here the authors proposed a road-map for the development of stem cell-based alternative test methods with the aim to facilitate test system development, including a description of the most useful performance metrics. The review includes an interesting discussion on the limiting factors and the possibilities for improvement, with a focus on hepatocytes, cardiomyocytes, tubular epithelial cells, and developmental toxicity.

Outlook

The EU-ToxRisk project is organizing the 3rd EU-ToxRisk Open Symposium, which will take place on February 11-12, 2019 in Egmond aan Zee, The Netherlands. The

[1] https://www.ebi.ac.uk/biostudies

[2] https://eu-toxrisk.douglasconnect.com/public

[3] https://www.eu-toxrisk.eu/media/articles/files/EU-ToxRisk_Newsletter_No-6_FINAL.pdf

event program will be structured around two main subjects: (i) NAM-enhanced read-across regulatory applications, with a focus on the EU-ToxRisk read-across advisory guidance document and the linked web-based tools; (ii) the launch of an integrated NAM-based testing platform developed by the project. On this occasion, a strong interaction between the project partners and the participants will be promoted, in order to exchange knowledge and experience related to the application of NAMs in chemical safety assessment for future regulatory applications.

References

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Ramme, A. P., Koenig, L., Hasenberg, T. et al. (2019). Autologous induced pluripotent stem cell-derived four-organ-chip. *Future Science OA 5,* FSO413. doi:10.2144/fsoa-2019-0065

Sachinidis, A., Albrecht, W., Nell, P. et al. (2019). Road map for development of stem cell-based alternative test methods. *Trends Mol Med 25*, 470-481. doi:10.1016/j.molmed.2019.04.003

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement n° 681002.

Giorgia Pallocca and Marcel Leist

LUSH
PRIZE

SUPPORTING ANIMAL-FREE TESTING

Lush Prize 2020 reviews its science criteria and opens for nominations

The Lush Prize has grown to become the largest global awards program to recognize scientists and campaigners working to replace animals in chemical safety testing. Now in its eighth year, it has provided more than £2 million to 113 projects and campaigns in 28 countries. It has also bought an unusually glitzy and left-field sensibility to the area of animal-replacement science.

In 2019, Lush Prize announced that it would become a biennial event with its next awards scheduled for May 2020. Nominations for the May 2020 prize opened on September 9, 2019 and will close on December 6. 2019.

This year, as part of these changes, the Lush Prize has also reviewed all its awards criteria to take account of some of the significant scientific advances that have taken place in the relatively short time that it has been operating. At the core of its new strategy is to focus attention on projects most likely to lead to practical non-animal tests that could be accepted by regulators.

When the prize began in 2012, its science prizes focused particularly on projects working in the area of "adverse outcome pathways" (AOPs) or on developing pathway understandings generally. This was demonstrated most dramatically in 2015 when a special £250,000 Black Box Prize was awarded for the elucidation of the skin sensitization AOP and the acceptance of regulatory tests based upon it.

Changes to science criteria

Since then, it has become clear to the Prize judges and advisors that, in terms of developing practical test replacements – often based upon these new pathway understandings – two other emerging technologies are also going to play an increasingly import-

ant role: these are "organ-on-a-chip" and "computational toxicology".

2020 science winners (in Science, Training or Young Researcher categories) are therefore now likely to be working in one of three fields.

- adverse outcome pathways
- organs on chips, and
- computational toxicology

Within AOPs and replacement tests the judges have noted the high levels of attention now being paid to skin and eye sensitization pathways generally. In 2020 they will therefore be looking to identify and reward projects in the less well studied areas of AOPs for systemic toxicology and developmental toxicology.

This refocusing has also had an impact on other areas of the prize. The Black Box breakthrough award is now looking for either:

- the first, fully accepted, human relevant adverse outcome pathway for systemic toxicology or developmental toxicology OR
- the first regulatory acceptance of a new substance using entirely non-animal methods.

More specific details and criteria for this award appear on the Lush Prize website.

The Lush Prize Young Researcher Awards, which are open to scientists up to 35 years at the time of application, award bursaries of £10,000 to a selection of winners each year. From 2020, Lush Prize hopes to make at least one of the young researcher awards for work on computational toxicology.

Dr Xing from Qinghai University in China accepts a Young Researcher Prize for her work on a successful chemical toxicity test using human stem cells

Changes to other criteria

In years when a breakthrough award is not being made, Lush Prize will still be making awards in its five main areas as before:

1. Public Awareness: public awareness-raising of on-going testing
2. Science: for the development of replacement non-animal tests
3. Training: training researchers in non-animal tests
4. Lobbying: policy interventions to promote the use of replacements
5. Young Researcher: to researchers specializing in replacement research

Within the Lobbying Prize: In addition to the £50,000 award for lobbying, from 2020 Lush Prize have introduced a non-financial "Political Achievement Award". This is in recognition of the essential work politicians do to create lasting legal change for animals and science.

The Public Awareness Prize from 2020 will be divided into two sections: rewarding successful recent projects as before, and a new "future projects award" to help fund innovative public awareness initiatives. Up to 50% of the £50,000 prize will hopefully be given to a future project.

Within the Training Prize, Lush Prize hopes to give at least £10,000 in this category to a project in the Global South, to enable us to support the development of work in these countries.

More information about how to nominate for an award and about previous winners appears on the Lush Prize website at https://lushprize.org/

The Lush Prize is a partnership between Lush Cosmetics and the Ethical Consumer Research Association to support animal-free toxicology and is designed to help bring about an end to animal use in product safety testing.

How ethics, law and philosophy of science can help make progress in the development and use of alternative methods

The German research unit *R2N – Reduce and Replace based in Lower Saxony* aims at "developing scientifically-sound alternative methods on all levels of biomedical science to either minimize the quantity of animals used, or to fully replace existing animal experiments" (https://r2n.eu/home-2/). It is well known by now that the development and use of alternative methods is not only dependent on scientific and technological aspects. A number of non-scientific, "normative" aspects are additionally involved that, in many cases, have an inhibiting effect on progress. Examples include legal barriers, status quo biases in the scientific community, and conflicting value judgements of stakeholders at different levels (e.g., researchers, authorities).

To gain a deeper understanding of these and related issues and how to address them, *R2N* has included two research groups that investigate the normative aspects of the development and use of alternative methods as integrated parts of the research unit. These groups are conducting ethical, legal and social issues (ELSI) research on the development and use of alternative methods. ELSI research has been instrumental in analyzing normative aspects of cutting-edge life science research and novel health technologies, such as personalized medicine and genome editing. It uses a wide variety of approaches and methods from philosophy (e.g., conceptual analysis), law (e.g., policy analysis) and the social sciences (e.g., empirical social research) to explore the normative landscapes in which science and technological development takes place. In line with ELSI research, the normative research groups in *R2N* explore topics related to the ethics of animal research and the 3R principle, the legal framework for alternative methods in conjunction with regulatory practice, and social aspects of scientific (self-)regulation, including the social epistemology of scientific research.

One research group, led by Marcel Mertz and Hannes Kahrass, focusses on analyzing the decision-making processes of researchers for using or not using alternatives, shedding light especially on ethically relevant, but in many cases "hidden", value judgments that affect decisions both consciously and unconsciously. These value judgments can be influenced by a plethora of epistemic, ethical, legal, or practical considerations that stem from, e.g., scientific reasoning, internal and legal regulations, funding practices, processes of publishing and peer review, disciplinary culture and academic traditions, career perspectives, or personal moral standpoints. The ELSI research of this group will ethically assess the way such value judgments are constituted, with the final objective of providing a decision aid tool for supporting decisions regarding the possible use of alternative methods.

The second normative research group, led by Simon Lohse and Nils Hoppe, integrates ELSI research with a philosophy of science approach. It focuses on mechanisms in the broadly construed regulation of alternative methods, i.e., including self-regulation in basic science. The group aims at analyzing factors that influence the development and use of alternative methods at the interface of science and policy-making. These factors include legal requirements in translational research settings, social and infrastructural aspects of research, and "socio-epistemic" issues in science – such as different criteria for the validity of new approaches. The final goal of this analysis is to identify potential for improvement of the existing regulatory regime in basic and applied science.

Both groups work in close cooperation with each other and use conceptual methods (ethical or legal analysis) as well as empirical methods (social-scientific qualitative interviews). In doing so, they attempt to achieve three main goals: (1) A deeper understanding of ethical, legal, and social (including socio-epistemic) factors that influence the development and use of alternative methods achieved by close scrutiny of actual regulatory and scientific practices, as opposed to a purely theoretical analysis; (2) knowledge transfer between science and decision-/policy-making by way of direct engagement; (3) sound policy advice and support of decision-making, which will be based on the groups' empirical findings and conceptual work. All three of these goals can be considered as important steps in making progress in the development and use of alternative methods.

Lisa Hermann, Nils Hoppe, Hannes Kahrass, Simon Lohse, Marcel Mertz and Ines Pietschmann