News

CH: Two researchers awarded the E. Naef prize

On 16th January 2010, the Fondation E. Naef pour la Recherche in Vitro awarded its annual prize to two researchers for developing new alternatives to animal research. The prize has been awarded each year since 2000. The general aim of the Foundation (www.fondation-naef.com) is to promote the development of methods replacing the need for animal experiments. The Foundation is based in Geneva (Switzerland).

The first prize was awarded to Eric Féraillé, from the Geneva Faculty of Medicine. He shared the first prize with his collaborator, Valérie Leroy. Eric Féraillé has established a new method to reconstitute a functional renal epithelium in vitro. This allowed him to study renal pathologies and to measure renal toxicity of compounds without the use of animals. This work is a significant step forward in the development of in vitro toxicology methods that could significantly reduce the use of animals.

Luca Fumagalli from Lausanne University received the second price for his work on non-invasive and non-destructive methods to analyze populations of wild animals. The basic principle of this approach is to replace capture of animals with analysis of biologic traces (hair, feathers and droppings) left in the environment. It is essential to follow wild populations to be able to ensure their optimal preservation, and these methods minimise the impact of analysis on the animals.

The award was widely reported in the media (press, radio and TV).

CH: Elisabeth Zbinden passed away

The Doerenkamp-Zbinden Foundation and ALTEX have the sad duty of announcing the death of Elisabeth Zbinden (1923-2009). Mrs Zbinden, one of ALTEX’s most loyal readers and widow of the late Gerhard Zbinden, who was the scientific founder of the Doerenkamp-Zbinden Foundation and passed away far too soon in 1993, died unexpectedly on Christmas Day 2009 after a short, severe illness.

Only in her last e-mail, a few days before her death, Mrs Zbinden mentioned how much she had enjoyed the ALTEX Abstracts of the 7th World Congress in Rome 2009. She was especially fascinated by the strategy “Toxicity Testing in the 21st Century”, as she recognised in it the direction in which her husband, the world-renowned toxicologist Gerhard Zbinden, always strove. Evidently, he was far ahead of his times. Fifteen years had to pass before toxicology was ready to embrace his ideas. She was deeply gratified that the Doerenkamp-Zbinden Prize 2009 went to this group of toxicologists.

We know that Elisabeth Zbinden supported her husband in the establishment of the Doerenkamp-Zbinden Foundation and in his work to replace the LD50 test with great enthusiasm. Animal protection was close to her heart and she generously also cared for physically challenged persons, acting as guidance counsellor in a home for the blind in Zurich for many years.

We will keep Elisabeth Zbinden in our hearts and remember her as a remarkable person.

Franz P. Gruber
President DZF and
Editor-in-chief ALTEX
GER: Legal dispute about primate experiments in Bremen

In October 2008, the Bremen Health Authority, competent authority for the regulation of animal experiments in the German city of Bremen, denied an animal experimentation license and so started a legal dispute, which centres on the weighing of animal suffering against the benefit to be gained from a research project. This legal dispute comes after more than ten years of heated public debate on this issue.

Professor Andreas Kreiter heads the Department of Theoretical Neurobiology at the Bremen University’s Brain Research Institute since 1997. In 1998, he was awarded a license to conduct animal experiments for his research proposal “Examination of Mammal Brain Function”. Consecutive licenses followed in 2001, 2004 and 2005, the last of which expired on 30th November 2008.

The subject of the experiments is invasive brain research in rhesus monkeys. The aim is the examination of cognitive mechanisms in the cerebral cortex – a problem of basic research. The research method is measuring electric activity of single brain cells by way of intracerebral electrodes – a method practiced since the 1950s.

Before the experiments, the monkeys are implanted, in two or more surgical procedures, with fixation bolts into the skull and electrodes around one eyeball and into the brain. During the run of experiments, a monkey spends several hours per day on five days per week at the research station in the so-called primate chair (an acrylic glass box just big enough for the seated monkey), with his head fixed by the bolt in his skull, performing visual tasks at a computer monitor. To ensure the animal’s compliance, he does not have free access to water on those days but must earn his fluid ration in the experiment: only for successfully performed tasks does he receive fluid through a drinking straw in tiny sips (about 0.2 ml). The experimental phase can be as long as several years for each monkey. At its end, he is killed to verify the exact position of the electrodes in his brain.

According to internationally accepted classifications of severity, these experiments are condemned not only by animal welfare specialists but also by researchers of natural monkey behaviour. Repeated surgical procedures, years of experiments five days a week for several hours per sitting, performing most unnatural tasks with a rigidly fixed head and coercion by water deprivation must all be classified in the highest category of severity. Ethicists confirm that the public benefits of this research are in no way commensurate to the suffering that the animals undergo. In addition, the techniques of non-invasive brain research are progressing at a rapid pace: questions of the physiology of cognition can be addressed with alternative methods in humans. For these reasons, the method of Kreiter’s research can no longer be justified.

Andreas Kreiter considers the severity of his experiments to be minor. He argues that the surgical procedures are well tolerated; and rhesus monkeys are animals of dry steppes, to which thirst poses no physiological problems. Incomprehensibly, Kreiter has equalled the rigid fixation in the primate chair and the computer tasks with the situation of social grooming as there, too, the animals sit still, concentrating for hours. Again and again Kreiter has declared his research to be fundamental for the development of effective therapies, even though this cannot be demonstrated either from his research or from that of many others using the same research method.

The German Animal Welfare Federation has objected to this research project since its beginning. It made sure that the general public were informed as thoroughly as possible and participated in the discussion about the suffering undergone by the laboratory animals. For years it maintained political pressure against Andreas Kreiter, the University and their supporters by means of several petitions signed by more than 100,000 eligible voters, by panel discussions, demonstrations and other initiatives. Additionally, the animal welfare community was encouraged by a change in the German constitution. In 2002, animal protection was incorporated as a state aim. In March 2007, the government of Bremen decided to abandon the research project by 2008.

In the summer of 2008, Andreas Kreiter applied for a renewal of his animal experimentation license in order to continue his research project. The application was denied in October 2008 by the Bremen Health Authority. Immediately, Andreas Kreiter and the University of Bremen filed an objection against this decision. At the same time, they applied to the Bremen Administrative Court for an interim court order to continue Kreiter’s research license until a decision is reached in his case. The Court granted this license, but limited its term to two months after the authority’s ruling on Kreiter’s objection.

In August 2009, the Bremen Health Authority conclusively denied Andreas Kreiter’s objection. Its reason for this decision was that the presumable public benefit of the research project could not justify the severe suffering of the laboratory animals. The provisional research license granted by the Administrative Court was thus set to expire in October 2009.

In September 2009, Kreiter filed suit at the Bremen Administrative Court against the denial of his animal experimentation license by the Bremen Health Authority. At the same time, he again applied for an interim court order to permit him to continue his research. On 19th October the Court granted his application with an interim decision: Kreiter may continue his research but not increase its scope; the number of monkeys in his project must stay constant. The final decision on the issue of continuing Kreiter’s animal experimentation license, allowing him to
continue his research, is expected in the first quarter of 2010, the same as the first hearing of Kreiter’s lawsuit against the Health Authority’s denial of the animal experimentation license.

In this lawsuit, the issue is not only the primates in Bremen. Rather, basic ethical and judicial questions regarding the recent constitutionally adopted state aim of animal protection need to be resolved:

- How much pain, suffering and distress of non-human primates in research be assessed, and how is it to be weighted in the ethical evaluation of research proposals?
- How is the importance of basic research for the general public to be evaluated?
- What is the effect of the constitutional state aim of animal protection in the licensing practice of animal experiments?
- Can animal welfare put limits on freedom of research by changing the ethical weight of animal suffering?
- Finally, must the German Animal Protection Law be changed?

GER: Support for project to develop in vitro model for blood-spinal cord barrier

A research project to develop an in vitro model of the blood-spinal cord barrier to examine pathomechanisms of barrier disruption and test pharmacological interventions shall be supported by the minister of the environment of Rhineland Palatinate, Margit Conrad, with € 40,000.

Disruption of the blood-spinal cord barrier is a common complication of spinal cord injuries, which until now have been studied exclusively in rats, mice and rabbits. In these experiments, the spinal cord is usually injured mechanically, leading to severe suffering, pain and damage. The animals survive only a few hours to a few weeks. To contribute to replacing these severe animal experiments with an in vitro model, the project’s goal is to establish a long-lived murine endothelial cell line to investigate mechanisms of barrier destruction and potential pharmacological interventions.

Since 1992, the state has supported nine projects on alternatives with a total of € 580,000, six of these at the University of Mainz.

GER: Federal ministry evaluates research funding

Within the framework programme “Biotechnology – Using and Shaping its Opportunities” the Federal Ministry of Education and Research supports Research and Development (R&D) initiatives with the goal of replacing, reducing or refining animal experiments by alternative methods. According to the 3R concept of Russel and Burch, these are methods that either require no animals (replacement) or, if this is not possible – allow the experiment to be performed with fewer animals (reduction) or in a way that involves less pain and distress for the animals (refinement).

Guidelines on the funding of R&D initiatives in the area of “Alternatives to Animal Experiments” were published in December 1984, May 1989 and June 1998. With the help of the methods developed in this framework in the past, significant contributions could be made to limiting animal experiments in the sense of the 3R concept.

On the 14th of October 2009 the Ministry published a call for a service agreement on “Evaluation of Research Funding of Alternatives to Animal Experiments”. Next to the evaluation of the projects that started between 2001 and 2008, the task includes the development of ideas for an update of the research funding guidelines in this area. The Ministry further requests the development or definition of parameters by which the success of funded initiatives can be evaluated. These could consider changes in the level of pain and distress experienced by the animals or whether the targeted experiments are performed regularly, also including regulatory experiments. Further an exemplary appraisal of the expected implementation of the results into practice is requested. How and how much have potential users profited from the results of the programme, and to what extent have contributions to the 3Rs been realised? How has the research funding of the Ministry affected the number of animals used in experiments? Where applicable, the economic advantages of the new methods shall be evaluated, also with regard to their economic potential for Germany. Also, the funding modalities shall be evaluated.

The tender by the Fraunhofer-Institute for Systems and Innovation Research in Karlsruhe, Germany, has been accepted; the evaluation shall be performed within six months.

In the event of an adverse ruling, both parties in this lawsuit have announced their resolve to appeal through all levels of jurisdiction up to the German Constitutional Court.

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FPG
**LUX: In memoriam Anny Eck-Hieff (1930-2009)**

We were deeply moved when we learned that Anny Eck-Hieff passed away after an accident on 30th November 2009. Anny was founder and President of the Association Luxembourgoise pour la Protection des Animaux (Alpa) in Luxembourg and in 1986 she established the International Foundation for Ending Animal Experiments F.I.S.E.A.

Scientists at ZEBET have enjoyed the collaboration with Anny for 20 years, since she was an unusually warm hearted and charming person. At the same time she was the most prominent animal welfare activist in Luxembourg. She was well respected in the public from President Jean Claude Juncker to EU Parliament members of the Green Party. Anny realised as early as in 1986 that to end the suffering of experimental animals it is smarter to initiate funding of research on alternatives than attacking laboratory animal scientists and technicians and even animal facilities.

Due to her charming and convincing personality she managed to raise funding from European animal welfare organisations for the annual European FISEA award for scientist who had developed promising alternatives to animal experiments. She established an excellent scientific panel for evaluating the applications. The list of scientists, who received the European FISEA award, is quite impressive. Due to her close ties to the political hierarchy in Luxembourg the annual FISEA award ceremonies were quite memorable and well attended events. The venue was a theatre or the city hall, and usually the minister of health or science as well as representatives of the city of Luxembourg actively participated in the award ceremony and local media covered it. Anny was the most charming host and diplomat who took advantage of her warm Luxembourg dialect or French at these events, to make it quite clear that more research is needed to reach our common goal of ending animal experiments.

Quite recently Alpa/FISEA inherited a significant amount from Margot Reck-inger-Thome, a close friend of Anny, which she intended to use to establish a centre for research on alternatives at the Life Sciences Research Unit of the University of Luxembourg. Although Anny was not able to finalize this project, Alpa/FISEA will continue to collaborate with scientists and administration of the University of Luxembourg to establish an experimental unit for research alternatives to animal experimentation.

Anny Eck-Hieff was quite a special personality in the European animal welfare movement. She was an outspoken advocate for experimental animals, who did never hide, when it was necessary to speak up in the public. Scientists in Europe devoted to the 3Rs have lost a true friend and the experimental animals one of their strongest advocates. We really miss her and will always remember her affectionate, warm and stimulating personality.

Barbara Grune, Manfred Liebsch, Andrea Seiler and Horst Spielmann

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**RUS: The Ural region stops inhumane education**

On 4th February 2010 a formal agreement between Perm State Pharmaceutical Academy and the International Network for Humane Education (InterNICHE) was signed. Perm State Pharmaceutical Academy now becomes the tenth Russian higher education institution to sign a contract with InterNICHE concerning the introduction of alternatives to animal labs. According to the contract terms, InterNICHE grants the academy computer programs for use in the classroom as an alternative to dissection and animal experimentation, while the Academy guarantees to stop all animal labs for students and commits to alternatives. Active promotion of alternatives made by VITA (www.vita.org.ru) and InterNICHE (www.interniche.org/ru – Russian section) campaigners in Russia, Ukraine and Belarus has resulted in the introduction of alternatives in dozens of universities of CIS countries and the replacement of the annual use of thousands of animals. The progress of this curricular change is described in the new Russian film “Humane Education in the CIS countries” made by VITA and InterNICHE with the support of DAAE (Doctors Against Animal Experiments Germany, www.aerzte-gegen-tierterversuche.de/en). The first higher education institution to abolish animal labs in Russia was St Petersburg State Academy of Veterinary Medicine. It signed an historic agreement with InterNICHE on the cancellation of experiments in the departments of pharmacology and toxicology on 24th October 2005. The second institution was Velikie Luki State Agricultural Academy, which signed an agreement in 2006 that covers the whole Faculty of Animal Science. In both institutions there has been significant further progress since. The contract with Perm State Pharmaceutical Academy provides for an immediate cessation of all animal labs for students across all departments.
UK: FRAME chairman offers hope for an end to animal experiments

FRAME Chairman Prof Michael Balls has held out hope of an end to animal experimentation within two decades, in spite of the poor progress since legal changes in 1986.

Speaking on a BBC World Service broadcast, he said: “I believe that if we really wanted to, we could work steadily towards a day in 10 to 20 years time when animal experimentation will have disappeared.”

He said that new technologies enabled scientists to carry out much more work by using computers, or at a cell or molecular level, removing the need for many of the current animal tests. Recent developments meant that it was possible to carry out tests on human volunteers that it would not have been safe to do only a few years ago.

But he expressed dismay that the number of animal procedures carried out in the UK was still rising. FRAME was one of the organisations involved in proposals to reduce animal experiments that were put forward in 1983 and that formed the basis for the 1986 Animals (Scientific Procedures) Act.

“The idea was that there would be a progressive reduction in laboratory animal use, but all these years later, I am amazed that the number of animal procedures is higher than it was in 1987, when the 1986 Act came into force.”

Other participants in the broadcast were less optimistic, even suggesting that an end to animal experiments would not take place within the 21st century.

The programme was one of a series called One Planet. In a two-part broadcast called “Animals and Us”, documentary maker Victor Schonfeld looked back on progress since he produced The Animals Film, 28 years ago. At the start of the programme he admitted that he was a strong opponent of what he calls “animal exploitation” and that included experimentation in any form.

A number of organisations contributed to the recording, including the US bodies the Physicians Committee for Responsible Medicine and National Institutes of Health, the WHO and Yale Collaborating Center on Health Promotion Policy, and the Austrian Verein gegen Tierfabriken (Association Against Animal Factories).

The programme is available on the BBC iPlayer on http://www.bbc.co.uk/programmes/p005nhv5

Press release FRAME, 8th January 2010

UK: Survey of the quality of experimental design, statistical analysis and reporting of research using animals

British authors published the findings of a systematic survey of reporting, experimental design and statistical analysis in published biomedical research using laboratory animals. Medline and EMBASE were searched for studies reporting research on live rats, mice and non-human primates carried out in UK and US publicly funded research establishments. Detailed information was collected from 271 publications, about the objective or hypothesis of the study, the number, sex, age and/or weight of animals used, and experimental and statistical methods. Only 59% of the studies stated the hypothesis or objective of the study and the number and characteristics of the animals used. Appropriate and efficient experimental design is a critical component of high-quality science. Most of the papers surveyed did not use randomisation (87%) or blinding (86%), to reduce bias in animal selection and outcome assessment. Only 70% of the publications that used statistical methods described their methods and presented the results with a measure of error or variability. This survey has identified a number of issues that need to be addressed in order to improve experimental design and reporting in publications describing research using animals. Scientific publication is a powerful and important source of information; the authors of scientific publications therefore have a responsibility to describe their methods and results comprehensively, accurately and transparently, and peer reviewers and journal editors share the responsibility to ensure that published studies fulfil these criteria.

Carol Kilkenny et al., http://www.plosone.org/article/info:doi/10.1371/journal.pone.0007824
CAAT Europe Inauguration

CAAT-EU will be inaugurated on March 30th, 2010 in a celebration to be held at 1:00 pm in the Senatsaal of the University of Konstanz. The Center for Alternatives to Animal Testing – Europe (CAAT-EU) was founded as a joint venture between the University of Konstanz and the Johns Hopkins Bloomberg School of Public Health. CAAT-EU activities will complement those of its sister organization, the Johns Hopkins Center for Alternatives to Animal Testing (CAAT) in Baltimore, USA. CAAT-EU will act as a communications platform for science, industry, and the regulatory authorities in Europe and will serve also as a central communications hub for transatlantic exchange.

As a transatlantic cooperation center, CAAT-EU will consolidate its activities in the field of alternatives and toxicology at the University of Konstanz and combine them strategically with the activities of CAAT-US. This transatlantic interchange will promote the application and teaching of humane science, raise funds from industry and private sponsors for this purpose, and participate in and/or coordinate EU funded projects. For details see the article in this issue of ALTEX.

The inauguration program includes Thomas Hartung, Director of CAAT-US and Co-Director of CAAT-EU, Ulrich Rüdiger, Rector of the University of Konstanz, Michael Klag, Dean of the Johns Hopkins Bloomberg School of Public Health, Baltimore, Alan Goldberg, Founder of CAAT-US, Marcel Leist, Co-Director of CAAT-EU, Gerd Ganteför, professor at University of Konstanz and Johns Hopkins University, Michael Balls, Emeritus Professor for Medical Cell Biology, University of Nottingham and Trustee of Fund for the Replacement of Animals in Medical Experiments, Horst Spielmann, retired Head of the Department of Scientific Services and of the National German Centre for the Documentation and Evaluation of Alternatives to Testing in Animals and Professor for Regulatory Toxicology at the Freie Universität Berlin, Adela Lopez De Cerain Salsamendi, President of the European Consensus-Platform for Alternatives, and Kirsty Reid, Eurogroup for Animals. Inaugural sponsors, including the Doerenkamp-Zbinden Foundation (Franz Gruber, President), BASF (Robert Landsiedel), Beiersdorf (t.b.d.), L’Oréal (t.b.d.), and others will address the meeting.

The inauguration will be followed by a reception, and the inaugural board meeting will be held the next day.

For 2010/11, CAAT awarded seven grants relating to refinement, developmental toxicology, immunotoxicology, and translational toxicology

The CAAT research grants program makes approximately $250,000 per year available and is funded entirely through contributions from companies and foundations. The CAAT grants program is aimed directly at bringing toxicology into the 21st century. For more information and to see previously funded projects and abstracts, please see: http://caat.jhsph.edu/programs/grants/preproposal

In 2010, CAAT funded the following seven research grants to develop in vitro or refinement alternatives:

- The 3-Dimensional MAME Culture Model: An In Vitro Screen for Agents Affecting Mammary Gland Development, John Reiners, Wayne State University
- Biological Pathway Analysis in Human Dendritic Cells after Exposure to Sensitizing Chemicals, Greet Schoeters, VITO NV
- A Microassay Analysis Software Package for Comparisons and Extrapolations Relevant to Toxicology, Thomas Sutter, Vinhthuy Phan, University of Memphis
- Use of High Throughput Screening Methods Improves Computational Models for In Vivo Acute Toxicity Tests, Hao Zhu, University of North Carolina at Chapel Hill
- Human Culture Model as Replacement to the Animal Assays for Assessing the Potential of Cosmetic Ingredients to Cause Non-immunological Contact Urticaria (NICU), Francesca Levi-Schaffer, The Hebrew University of Jerusalem
- Innovative Micro RNA-based Differentiation Strategy to Develop Metabolically Stable Long-term Hepatocyte Cultures Applicable in Early Pre-clinical Drug Research, Tamara Vanhaecke, Vrije University, Brussels
- A Novel Anterior Stromal Construct for In Vitro Ocular Irritancy Testing, Walter Petroll, University of Texas Southwestern Medical Center


Proposals relating to Toxicology, with a maximum grant amount of $25,000 per year, should be developed to provide understanding of mechanism/mode of action and to consider how one would be able to translate the mechanism to a method that can be used to evaluate/predict health consequences.

Proposals Relating to Developmental Toxicology, with a maximum grant amount of $50,000 per year, can be either in vitro, involve embryonic stem cells, or utilize species such as C. elegans

CAATfeed
USA: IIVS Update

A New Scientific Society

IIVS, in cooperation with the Physicians Committee for Responsible Medicine (PCRM), announces the formation of a new scientific society dedicated to the advancement of in vitro, in silico and other toxicological testing methods, especially as replacements for animal-based tests. The American Society for Cellular and Computational Toxicology (ASCCT) will function as an American counterpart to similar societies in Europe and Asia and will capitalize on the growing interest in advancing toxicology for ethical, scientific, and practical reasons.

Since the release of the US National Academy of Sciences’ 2007 report Toxicity Testing in the 21st Century: A Vision and Strategy, interest in “alternative” toxicological methods has increased exponentially. It is this enthusiasm specifically for non-animal toxicology that the ASCCT wishes to harness: by bringing together scientists and professionals from a variety of backgrounds and sectors, we hope to create opportunities for discussion and collaboration that will foster the advancement of research into and development of new toxicology testing methods.

The Society will host regular meetings and offer an e-newsletter to encourage member collaboration. Sharing the diversity of experience that participants bring to the Society is essential to its mission; therefore special attention will be paid to encouraging membership and attendance of scientists from cellular, molecular, and computational disciplines. As many in this field know, the post-validation period for a new testing method can sometimes be as challenging as development and validation. A key mission of the ASCCT, then, must be to foster the routine application and use of computational and cellular methods for prioritization, classification, and risk assessment purposes.

To learn more about the ASCCT and its mission, please contact Erin Hill at ehill@iivs.org. More information about the society will be given during a special morning session of the 2010 In Vitro Alternatives Forum.

2010 In Vitro Alternatives Forum
18-19 October, 2010
Old Town Alexandria, VA, USA

Sponsored by the Institute for In Vitro Sciences (IIVS)
Endorsed by the Society of Toxicology (SOT)

The emergence of new national and international programs mandating increased toxicological safety testing of products and ingredients is a major driving force for the development of a “new toxicology.” From the REACH program in Eu-
Why are animal experiments not “validated?”

Having followed the development of validation standards for animal-free test methods for a long time, I understand that high expectations are placed on the science here, and rightly so, as the health of patients and consumers is at stake. But I do not understand why, in contrast to animal-free methods, animal experiments are not required to undergo validation, and especially why their relevance for medicine is not questioned. Is that simply because animal experiments have been accepted by liability insurances and regulatory bodies for a long time and there is thus no incentive to question their dubious relevance?

Erwin Kessler,
Verein gegen Tierfabriken Schweiz,
VgT.ch