



News

AUT: Ministry for Science overrides suggestion for ethics guideline

The Austrian Ministry for Science published a regulation for the evaluation of the ethical justification of proposals to perform animal experiments (*Tierversuchs-Kriterienkatalog-Verordnung* = TVKKV) on December 23, 2015 which entered into force on January 1, 2016. The regulation contains a questionnaire with the sections “General information on the project”, “Information on benefits” and “Information on harm” which is to be filled in by the applicant. The harm-benefit analysis itself is left up to the authority with no guidance as to how it is to be performed on the basis of the answers to the questionnaire or on whether the authority is to make its own assessment of the harms and benefits on the basis of the proposal.

Animal protection organizations such as *Vier Pfoten, pro-tier.at*, *Internationaler Bund der Tierversuchsgegner* and *Menschen für Tierrechte* criticize the regulation for not providing objective, transparent and reproducible procedures to determine the ethical justification of animal experiments.

The Ministry had commissioned the Messerli Research Institute at the University of Vienna to develop a detailed guideline by mid December 2015. In its response to the TVKKV, *Pro-tier.at* states that a draft of the Messerli guideline was presented at a meeting of the national committee on animal experimentation in 2014. It stated that only few of the questions developed by the Messerli Research Institute are contained in the TVKKV and claims that the Messerli guideline contained a harm-benefit analysis that was not incorporated in the TVKKV.

As reported by the *Kronen Zeitung* (November 5, 2015), the animal protection ombudsperson of Vienna Eva Persy, in a press conference on November 4 on the draft of the now published TVKKV regulation, stated that the regulation had not been discussed with the national committee on animal experimentation and that the committee had not been given the opportunity to comment on it. She questioned whether it therefore fulfilled the statutory requirements. The Ministry of Science defended its draft, stating that it had been developed in cooperation with relevant stakeholders, that it provided added objectivity and that it kept a fair balance between the legitimate interests of animal protection, research and industry. Further it was stated that the suggestions of the Messerli Research Institute for the quantification and the harm-benefit analysis had not fulfilled the objective requirements to allow a uniform calculation for all possible projects.

Full regulation: <http://bit.ly/1RWTTcf>

Response of pro-tier.at: <http://bit.ly/1YXjjWl>

EU: ECHA Board of Appeal states potential risk must justify animal test

The ECHA Board of Appeal has annulled ECHA’s requirement for an extended one-generation reproductive toxicity study (EOGRTS) following the substance evaluation of carbon tetrachloride (case A-005-2014). The decision clarifies that the Agency needs to be able to demonstrate that there is a potential risk, that the risk needs to be clarified and that the requested information has a realistic possibility of leading to improved risk management measures. The decision also examines the relationship between substance and dossier evaluation.

The Board of Appeal annulled the Contested Decision on the grounds that it was disproportionate as the EOGRTS is not, based on available information, necessary to clarify a potential risk to human health and the environment. Furthermore, the Board of Appeal found that the Agency had not adequately justified requesting information that was standard for only one registrant from several registrants.

ECHA e-News
September 23, 2015

EU: ECHA requests registrants show how they considered alternative methods

To further ensure that testing on animals is only done as a last resort, ECHA has started requesting additional information from registrants who submit new testing proposals for vertebrate animal tests. This follows the European Ombudsman’s recent decision about ECHA’s role in evaluating testing proposals.

ECHA has sent the first requests to registrants asking them to inform ECHA of their considerations of alternative methods to support their testing proposals involving vertebrate animals. This affects testing proposals made since 11 September 2015.

The information received will be published together with the testing proposals on ECHA’s testing proposals consultation web page. Third parties can take this into account when deciding whether to submit relevant information about the substance from alternative methods that may avoid the test. Registrants

sva



could consider this information instead of testing on vertebrate animals to fulfil the REACH information requirements. In such cases, the registrant must show that the main objectives of the REACH Regulation, to ensure a high level of protection of human health and environment, can be achieved without the performance of a vertebrate test.

ECHA has started a consultation with the Member States and stakeholders on the further practical steps to implement the Ombudsman's conclusions. The aim is for companies to be able to show their considerations in registration dossiers following the next update of the IUCLID tool in 2016. In the meantime, registrants will be contacted through REACH-IT.

In closing its enquiry into a complaint, the European Ombudsman suggested that ECHA can require registrants that submit testing proposals on vertebrate animals to show that they have considered alternatives to animal testing. ECHA was also requested to share any relevant information concerning alternative testing methods for the registered substance with the registrant. As further measures may be necessary, the Ombudsman will review progress after six months.

Adapted from ECHA/PR/15/13
November 2, 2015

EU: Public consultation on consideration of alternatives to animal testing

ECHA has received the first consideration on alternative methods to an animal testing proposal from a registrant. The consideration about alternatives to genetic toxicity *in vivo* testing is included in the information on the testing proposal submitted for public consultation, which is open until January 14, 2016. Stakeholders are invited to submit scientifically valid information and studies on genetic toxicity testing, which ECHA will then forward to the registrant.

From September 11, 2015, ECHA has invited registrants with testing proposals involving vertebrate animals to provide their considerations on alternative methods to address missing information. This is a follow-up action of the European Ombudsman's conclusion in case 1606/2013.

Adapted from ECHA e-News
December 2, 2015

EU: EURL ECVAM publishes status report on alternative methods

EURL ECVAM (the European Union Reference Laboratory for Alternatives to Animal Testing) regularly publishes Reports providing an update on the development, validation and regulatory acceptance of alternative methods/approaches.

The last version – EURL ECVAM, status report on the development, validation and regulatory acceptance of alternative methods and approaches (2015) – provides an update on the development, validation and regulatory acceptance of alternative methods/approaches and their dissemination since the last report prepared in June 2014. The report describes primarily, but not exclusively, the activities that EURL ECVAM has undertaken or has been involved in since the publication of the last report in June 2014. It includes updates on research and development, validation studies, peer reviews, EURL ECVAM recommendations and activities to promote the regulatory acceptance and use of alternative methods and approaches.

Full report: <http://bit.ly/1Jk3kQn>

<https://eurl-ecvam.jrc.ec.europa.eu/eurl-ecvam-status-reports>

GER: Animal Protection Research Prize awarded

Minister of Consumer Affairs for Baden Württemberg Alexander Bonde awarded the Animal Protection Research Prize to Prof. Thomas Braunbeck representing the research team Aquatic Ecology and Toxicology at the Center for Organismal Studies at the University of Heidelberg on November 12, 2015 for their work on reducing animal experiments on fish. The team has been working for more than 20 years on testing environmental chemicals in water and has developed alternatives to fish tests which have been translated into DIN standards and included in OECD test guideline 236 in 2013. This has led to a reduction in the number and to a refinement of animal experiments as the tests are performed on fish eggs or fish embryos instead of on fully developed fish.

The €25,000 Animal Protection Research Prize of Baden Württemberg is awarded annually. It recognizes excellent contributions to research on reducing or refining animal experiments.

Ministry of Rural Affairs,
Food and Consumer Protection
Baden-Wuerttemberg
Press release
November 10, 2015



GER: Animal Use Statistics 2014 published

Directive 2010/63/EU, which was transposed into national German law in 2013, required changes in the German animal use statistics. These include the documentation of the use of cephalopods, larvae of vertebrates and animals used for breeding genetically modified animals. Furthermore, the severity of pain, suffering, or harm inflicted on the laboratory animals must be documented. The animal use statistics for 2014 report the animal numbers according to the new requirements for the first time. Therefore, comparisons to previous numbers must be made with caution.

2,008,537 vertebrates and cephalopods were used for experimental purposes in Germany in 2014 according to the data published by the Federal Ministry for Food and Agriculture (BMEL). More than 80% of these were rodents, especially mice (63% of the total number) and rats. Fish (11%), rabbits (5%) and birds (2%) were among the other commonly used species. In addition to the vertebrates and cephalopods 563,600 fish larvae were used for experimental purposes.

The severity of the experiments was categorized as follows: low (60%), medium (21%), high (6%); 13% of procedures were performed under terminal anesthesia.

In Germany, vertebrates that are killed for scientific purposes without having undergone a procedure are also documented although this is not required by the EU Directive 2010/63/EU. The number totaled 789,926 animals in 2014.

Animal use was divided into 43% for basic research, 16% for disease research in humans and animals, 11% for production and quality control of medicinal products, 14% for toxicological safety assessments and 16% for other purposes such as education and training or for the breeding on genetically modified animals.

2,842 monkeys and prosimians were used for experimental purposes in 2014. Great apes were last used in Germany in 1991. Dogs (4,627) and cats (997) were used mainly for research on animal diseases and for regulatory toxicity tests of human and veterinary drugs.

At the time of going to press the pdf of the detailed animal used statistics was not available on the BMEL website. The numbers and percentages were taken from the introductory text on the website: <http://bit.ly/1OChYyi>.

Official statistics: <http://bit.ly/1OssEUz>

GER: *In vitro* test for Botulinum toxin receives European approval

The German Federal Institute for Drugs and Medical Devices has approved the *in vitro* test developed by the company Merz to determine the potency and stability of its products Xeomin and Bocouture, which contain botulinum neurotoxin A. The company now will be able to phase out its use of the animal LD₅₀ bioassay also in Europe over a number of years.

After the US Food and Drug Administration (US FDA) approved the alternative method developed by Merz in February 2015, the company received approval from the German Federal Institute for Drugs and Medical Devices in November 2015. This approval is recognized by all drug authorities in the European Union. The company announced that when the test is approved in all other countries, it will also be able to switch to the *in vitro* cell culture based method in these countries.

sva

GER: New chair for animalfree research in Berlin

In 2016 the first chair for research on alternatives to animal experiments shall be installed at the Free University Berlin. The chair will have the aim to develop disease models on the basis of human cells and reconstructed human organs. These models are to be used in basic and applied research, e.g. to determine the effectivity of drugs or the effects of environmental chemicals on the human organism. The chair will receive €400,000 start up funding from the State of Berlin and shall be filled in 2016. The chair will be attached to the *Berlin-Brandenburger Forschungsverbund* BB3R.

Free University Berlin
press release
November 4, 2015

KOR: Restrictions to animal testing for cosmetics by 2018

The National Assembly's Health and Welfare Committee of South Korea approved a bill banning the use of animal testing for cosmetics and cosmetic ingredients for certain endpoints on November 26. It will apply from 2018 and cover cosmetics produced in and imported into South Korea. However, the ban only applies to endpoints for which alternative tests have been accepted by the Ministry of Food and Drug Safety (MFDS). These currently do not include alternative tests for skin and eye irritation, repeated dose toxicity and skin sensitization.

sva



SUI: 3R Research Foundation will not award grants in 2016

The 3R Research Foundation has announced that it will award no new grants in 2016 but will respect its commitments to the recipients of running grants. The Foundation is financially supported by the Federal Food Safety and Veterinary Office (FFVO) and Interpharma. With a view to establishing a new 3R Competence Center by the FFVO in the near future, the two sponsors will discontinue the support of the 3R Research Foundation. Therefore, the 3R Research Foundation is unable to incur financial liabilities for future grants.

Four new projects which will receive a total of about CHF 550,000 were approved in 2015.

sva

SUI: Research on lung cancer distinguished

The Fondation E. Naef pour la Recherche in Vitro (FENRIV) awarded its 2015 prize to Dr Christophe Mas, co-founder of the Oncotheis biotechnology company, for developing new alternatives to animal research. The prize has been awarded each year since 2000. The aim of the Foundation (<http://www.fondation-naef.com>), which is based in Geneva, Switzerland, is to promote the development of methods decreasing the need for animal experiments. The prize of CHF 10,000 was awarded on March 2, 2015.

Dr Mas has developed and adapted new *in vitro* methods to study the development of lung cancer in human lung tissues reconstituted *in vitro*. For this, he used an *in vitro* model of human tissue and seeded it with lung cancer cells. This allowed following the gradual development of cancer with excellent detail and a perfect control of experimental conditions. Lung cancer is responsible for more than one million deaths worldwide each year, and despite 30 years of intense research no efficient treatment method has been developed to date. The use of sophisticated *in vitro* methods allows testing the effect of new molecules to combat cancer cells while avoiding unwanted side effects on the surrounding tissue.

Pierre Cosson
Centre Médical Universitaire
Dpt of Cell Physiology and
Metabolism
Geneva, Switzerland

UK: 3Rs global award winners announced

The Consortium for Innovation and Quality in Pharmaceutical Development (IQ) and the Association for Assessment and Accreditation of Laboratory Animal Care International (AAA-LAC) run a Global 3Rs Awards Program which recognizes bioscience research papers which make significant and innovative contributions to the 3Rs.

Entries from authors at academic and industry organizations around the world were judged by a prestigious panel, chaired by Dr Mark Prescott of the NC3Rs. Three winners were selected, one in each of three world regions – Europe, North America and the Rest of the World. The recipients received their awards of \$5,000 (USD) at the National Meeting of the American Association of Laboratory Animal Science in Phoenix, Arizona.

Dr Paulin Jirkof, University of Zurich, received her award for a study published in *Laboratory Animals* which established that a single injection of a sustained-release formulation of buprenorphine delivers long-lasting pain relief in mice undergoing laparotomy, and with fewer side effects compared with the standard protocol of repeated injections, requiring handling and restraint.

Dr Aleksander Skardal, Wake Forest School of Medicine in North Carolina, USA, was recognised for his work published in *Annals of Biomedical Engineering*, demonstrating the potential of *in vitro* 3D liver-tumor organoids to serve as a model for metastasis growth and for testing the drug response of tumor cells, thus reducing the need for *in vivo* animal studies.

The award in the Rest of the World category was won by Dr Nancy Oguiura at the Butantan Institute in Sao Paulo, Brazil. Her paper in *Toxicon* reports the development and use of an *ex vivo* method, using blood from chicken wing veins, to test the coagulant activity of poisons and toxins and the neutralizing capacity of antivenoms, reducing the need for lethality assays in mice.

NC3Rs newsletter
November 2015

UK: Animal use statistics published in common format

The Home Office published the Statistics of scientific procedures on living animals, Great Britain 2014, on October 22. Some changes have been made to the data reporting according to the requirements of European Directive 2010/63/EU, which sets out a common format for member states to submit information on the use of animals for scientific purposes.

The Directive was transposed into UK law in January 2013 through amendment regulations to the Animals (Scientific Procedures) Act 1986 and therefore the changes have first impacted on the 2014 figures.



Some of the key changes are:

- Actual severity of all procedures is now reported; therefore the data is on procedures completed and not on procedures started. The severity reported reflects the peak severity of the procedure.
- Species reported now include all cephalopods, free-feeding larval forms (e.g. tadpoles) and other species newly listed in the Act.
- Data on place of birth replace source of animals. For non-human primates, information is collected on whether animals were wild caught or captive bred and in which generation of captivity they were.
- For genetically modified animals separate breakdowns are now collected on animals which do or do not show a harmful phenotype (i.e. a harmful physical or biochemical defect).
- Specific information is now collected on regulatory use.

The Home Office warns that as a result of changes to the reporting requirements and the data collection format, the 2014 data and comparisons with previous years' data should be interpreted with some caution.

In 2014, a total of 3.87 million procedures were completed (6% less than in 2013). Of these, 1.94 million (50%) related to the creation/breeding of genetically altered animals that were not used in further procedures and the remaining 1.93 million (50%) were experimental procedures. Of the experimental procedures completed in 2014, the majority involved mice (60%), fish (14%), rats (12%) and birds (7%). There was a strong increase in procedures involving amphibians (likely due to reporting of free-feeding larval forms) and hamsters but decreases in procedures involving mice, rabbits, horses, dogs and reptiles. No great apes have been used since 1987 and their use has not been permitted since 2013).

The severity thresholds reported for the experimental procedures were 9% (180,000) sub-threshold; 7% (133,000) non-recovery; 51% (980,000) mild; 25% (483,000) moderate; and 8% (150,000) severe.

Of the 1.94 million procedures in 2014 relating to the creation/breeding of genetically altered animals that were not used in further procedures, nearly all involved mice (91%), zebrafish (8%) and rats (1%). The severity thresholds reported for these procedures were 46% (898,000) sub-threshold; 0.1% (1,900) non-recovery; 48% (934,000) mild; 4% (74,000) moderate; and 2% (34,000) severe.

Full text: <http://bit.ly/1LHe19Y>

UK: First Black Box LUSH Prize awarded

Now in its fourth year, in 2015 The Lush Prize awarded a record £450,000 in prizes to 18 outstanding winners from 9 countries. The awards were presented at a gala ceremony in London in No-

vember. In addition to £200,000 being shared by the winners of the lobbying, training, public awareness, science and young researcher awards, this year the judges decided to present the first ever Black Box award, totalling £250,000, to winners involved in mapping the first ever “human toxicity pathway”.

Black Box Prize

Key breakthroughs in human toxicity pathways research
The Lush Prize judges believe that mapping the “human toxicity pathway” represents a breakthrough moment marking the first step into a future where a superior molecular science replaces the old, imprecise, technology of testing on animals in laboratories. The award recognizes the work conducted on the “skin sensitization pathway” and was divided between five winners.
£150,000: The OECD's Adverse Outcome Pathway programme, France
£25,000: David Basketter, UK
£25,000: Frank Gerberick, USA
£25,000: Andreas Natsch / Roger Emter, Switzerland
£25,000: Terry Schultz, USA

Lobbying Prize

Policy interventions promoting the use of alternatives
Mojo Mathers MP, New Zealand
(Declined financial part of prize)

Public Awareness Prize

Policy interventions promoting the use of alternatives
£20,000: SOKO Tierschutz EV, Germany
£20,000: Beagle Freedom Project, USA

Science Prize

21st century Toxicology
£25,000: Oncotheis, Switzerland
£25,000: Prof Michael L. Shuler & Team, USA

Training Prize

Training researchers in non-animal methods
£25,000: PETA International Science Consortium Ltd., UK
£25,000: Dmitry Leporsky, Ukraine

Young Researcher Prize

Post-doctoral students specialising in alternative research
£10,000: Laura Bray, Leibniz Institute of Polymer Research, Germany
£10,000: Jeremy Caplin, Hashemi Labs, Iowa State University, USA
£10,000: Elena Kummer, Università degli Studi di Milano, Italy
£10,000: Bianca Marigliani, The Federal University of São Paulo, Brazil
£10,000: Ilka Maschmeyer, TissUse, Germany
£10,000: Dr Lena Smirnova, Center for Alternatives to Animal Testing, USA

sva



UK: NC3Rs launches Experimental Design Assistant

The NC3Rs has launched its new online tool – the Experimental Design Assistant (EDA) – to help improve the design of *in vivo* experiments (<http://bit.ly/1ZGHA1C>). The EDA consists of a website plus innovative technical software that provides tailored advice on specific experimental designs as well as tools for randomization and blinding and for power calculations for determining group sizes.

The EDA was developed to guide researchers through the design of their experiments, helping to ensure that they use the minimum number of animals consistent with their scientific objectives, methods to reduce subjective bias, and appropriate statistical analysis.

NC3Rs newsletter
November 2015

UK: Roadmap to wider use of non-animal technologies published

The NC3Rs and Innovate UK in partnership with four other organizations – the BBSRC, EPSRC, MRC, and Dstl – has published a roadmap on developing and applying non-animal technologies (NATs) to improve the methods and tools available for the safety and efficacy testing of pharmaceuticals, veterinary products, chemicals, agrichemicals and consumer products.

The roadmap sets out a vision for the UK as a market leader in NATs and the steps to delivering this. It brings together a unique collaboration between the major public funders of the underpinning science and technologies for NATs, with the capabilities of those driving innovation in the UK economy, and the 3Rs “know-how” and leadership of the NC3Rs.

The roadmap is part of a wider program which has already seen the launch of an online NATs forum and £10 million invested in business-led NATs R&D.

Full text: <http://bit.ly/1LvSOzx>

NC3Rs press release
November 10, 2015