# News

## BRA: Brazil's São Paulo state bans animal testing

On January 23, the Brazilian state of São Paulo banned all animal testing for the cosmetics, perfume, and personal care industry, including both finished products and ingredients. Noncompliance by an institution or research center will be punished by a high fine and may lead to closure of the establishment. Professionals violating the ban will also be fined. The State of São Paulo hosts more than 700 cosmetics companies. São Paulo is the first state to issue a ban on animal use for cosmetics testing. A proposal for a national ban on animal testing for cosmetics has been submitted to the Conselho Nacional de Controle de Experimentação Animal. Cosmetics testing on animals is currently banned in the European Union, Israel, India (see p. 236) and Norway.

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## GER: Ethics committees have no discretion to perform ethical evaluation

The five year legal battle about the neurobiological experiments on macaques in the group of Prof. Kreiter in Bremen ended in January with a final ruling of the Federal Administrative Court in Leipzig. This confirmed a prior ruling by the Higher Administrative Court of Bremen that declared the experiments on macaques to be permissible and did not allow an appeal. The experiments involve the measurement of brain activity via electrodes inserted into the brain of the macaques, their fixation on a "primate chair" and their being tasked to respond to signals for which they are rewarded with drinking water.

Although the ruling only applied to the experiments performed between 2008 and 2011 and a further law suit about the experiments performed until 2014 is still active, the January ruling indicates that this will also be ruled in Kreiter's favor: The justification of the ruling stated that, based on the former and current German Animal Protection Law, the animal protection authority of Bremen, which had refused to renew permission for the macaque experiments in 2008, had no discretion to evaluate the severity of the animal experiment itself or to weigh the severity of the experiment against the importance of the research proposal. Thus it had no basis to refuse permission for the experiments to be performed as all formalities were fulfilled.

This decision led to the German Animal Welfare Federation (*Deutscher Tierschutzbund*) calling upon its representatives in all ethics committees to resign from these and calling on the Federal Minister for Food and Agriculture to initiate a reform of the Animal Protection Law, see also Comment by Ruhdel et al., p. 219

Federal Administrative Court ruling: http://www.bverwg.de/200114B3B29.13.0

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## GER: Competition for 3Rs prize of Hessen announced

Minister of the Environment Priska Hinz has announced the € 15,000 animal protection prize of the Federal State of Hessen. The prize will be awarded for exceptional contributions to the reduction, replacement, or refinement of animal experiments in research, education, or in the production of biomedical products, e.g., vaccines or antibodies.

Persons or groups that are scientifically active in Hessen as well as companies or institutes that are located in Hessen are eligible.

Deadline: July 15, 2014
More information: http://bit.ly/PmDG2E

## GER: Competition for 3Rs prize of Baden-Württemberg open

The Ministry of Rural Affairs and Consumer Protection of Baden-Württemberg has announced a competition for a € 25,000 prize for exceptional contributions to reducing or refining animal experiments in research or education. For the first time work performed in any state of Germany, not only in Baden-Württemberg, is also eligible for the prize.

Deadline: May 28, 2014
More information: http://bit.ly/1ijy5lT

## GER: Baden-Württemberg calls for applications for 3Rs research funding

The Ministry of Rural Affairs, Food and Consumer Protection Baden-Württemberg has published a call for applications for research funding in the field of alternatives to animal experiments. The total budget amounts to € 400,000. A prerequisite is that the research is conducted in Baden-Württemberg in part or in full. Refinement approaches are also applicable.

Deadline: May 28, 2014
More information: http://bit.ly/1ijy5lT and http://bit.ly/1pVg95L

## GER: BASF SE team receives another 3Rs Prize

After receiving the Animal Protection Research Prize of the German Federal Ministray of Food and Agriculture in December, the group of Dr Tzutzuy Ramirez Hernández and Dr Robert Landsiedel in February received the "Prize to support research on replacement and refinement methods for animal experiments" of the state of Rhineland-Palatinate for their animal-free strategy to test skin and eye irritation as well as skin sensitization of chemicals. The prize of € 20,000 has been awarded biannually since 2006.

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## GER: Thomas Korff receives Ursula M. Händel Animal Protection Prize

The German Research Foundation (DFG) awarded the Ursula M. Händel Animal Protection Prize worth € 100,000 for the fifth time. Prof. Thomas Korff, a physiologist at the University of Heidelberg, received the prize on March 20, 2014 in Berlin. Prof. Korff has developed procedures that contribute to refinement and reduction and alternative methods that replace animal use in vascular research. The prize is awarded to scientists who improve animal protection in research alternately every two or three years.

Korff develops cell culture systems to investigate the reaction of cells to biomechanically induced vascular changes and to study tumor induced angiogenesis. These combine umbilical cord endothelial cells with smooth muscle cells in three-dimensional aggregates. More complex changes in the vasculature are followed by observing the local outgrowth of new vessels in the murine ear instead of by systemic application. This prevents systemic effects of the active substances and allows non-invasive analysis of its effects.

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## EU: ECHA finds 69% of evaluated dossiers non-compliant

The European Chemicals Agency ECHA announced that it has checked 1,130 (5.7%) registration dossiers of substances produced in quantities of more than 100 tons per year and found 69% of these lacking important information on their safe use. 19,772 registrations covering approximately 2,700 unique substances were submitted by the 2010 deadline. The agency stated that it used both concern-based (809 cases) and random (321 cases) selection to choose which dossiers should be evaluated, and checked both lead and member dossiers. The compliance checks addressed 957 unique substances, i.e., approximately 35% of the 2010 phase-in substances.

The two main reasons for non-compliance were deficiencies in information regarding identification and composition of the substance, and insufficient justification for not submitting the required studies, or missing information in the chemical safety report. Registrants found to be non-compliant must provide the requested information by a deadline given in the decision.

It has not been stated whether the finding of this high rate of non-compliance will lead to further compliance checks on other dossiers.

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## EU: EURL ECVAM issues recommendations on Keratosens

The European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) has issued final recommendations on the use of the KeratinoSens™ assay for skin sensitization testing. EURL ECVAM recommended that KeratinoSens was useful in distinguishing sensitizers from nonsensitizers and could be used in an integrated approach with complementary information from other assays to determine skin sensitization potential. However, KeratinoSens should not be considered a stand-alone full replacement method. EURL ECVAM found the KeratinoSens assay to be transferable to laboratories experienced in cell culture and reproducible within and between laboratories.

More information: http://bit.ly/1i2HU6v

*Iccvam-all Digest*, Vol 88, Issue 2

## EU: EURL ECVAM survey and method solicitation for *in vitro* toxicokinetics

Toxicokinetics (TK) refers to the absorption, distribution, metabolism, and excretion (ADME) of chemical substances in the body. TK information is essential in regulatory safety assessment of chemicals. Aspects also include interspecies and route-to-route extrapolation, development of mechanistic understanding of TK processes, and better interpretation of systemic toxicity data.

Hepatic metabolic clearance plays a key role in the transformation and the elimination of chemicals from the human body and in recent times various *in vitro* methods for human hepatic metabolic clearance/stability have been developed. With the present survey, EURL ECVAM (the European Union Reference Laboratory for Alternatives to Animal Testing) seeks to identify *in vitro* human hepatic metabolic clearance/stability methods, which can contribute to the development of harmonized standards and associated international TK test guidelines.

Deadline: June 30, 2014
Survey: http://bit.ly/1gk2fmx

Posted on EU-NETVAL website
March 20, 2014

## India: End to animal testing of cosmetics and household products

In order to promote the use of validated non-animal research methods, PETA India works cooperatively with national bodies, such as the Bureau of Indian Standards (BIS) and the Indian Ministry of Health and Family Welfare, to reform government testing regulations. PETA India is the only animal rights organization to hold an official seat on both BIS committees that set the precedents for testing the safety of cosmetics and household products: the Cosmetics Sectional Committee (PCD 19) and the Soaps and Other Surface Active Agents Sectional Committee (CHD 25).

A major part of PETA India's focus has been to encourage the Indian government to follow the progressive examples of the European Union, which has banned animal tests for cosmetics as well as sales of animal-tested cosmetics, and Israel, which has banned testing on animals for both cosmetics and household products as well as selling cosmetics and household products that have been tested on animals. Following extensive efforts by PETA India, substantial progress was made on this issue in 2013 and early 2014.

There are currently three standards for the safety evaluation of cosmetics and household products in India:
– IS 4011: Methods of Test for Safety Evaluation of Cosmetics; requires the skin sensitization test on guinea pig, the acute oral toxicity limit test, and the oral mucosal irritation test on rat
– IS 11601: Methods of Safety Evaluation of Synthetic Detergents – Tests for Skin Irritation and Sensitization Potential of Synthetic Detergents; requires the skin sensitization test on guinea pig
– IS 13424: Safety Evaluation of Bathing Bars and Toilet Soaps – Methods of Test; requires the skin sensitization test on guinea pig

During BIS meetings, PETA India proposed replacing the aforementioned tests with the following non-animal methods:
– Skin Sensitisation Test: Direct Peptide Reactivity Assay (DPRA); Human Cell Line Activation Test (hCLAT); KeratinoSens™ ; SenCee Tox®; Quantitative structure-activity relationship (QSAR) approach
– Acute Oral Toxicity Limit Test: Balb/c 3T3 neutral red uptake (3T3 NRU) assay; Normal human keratinocyte neutral red uptake (NHK NRU) assay; CeeTox's (now Cyprotex) AcuteOralTox-LD50 in vitro screen; Novaleads' EvaTOX assay; QSAR models
– Oral Mucosal Irritation Test; MatTek's EpiOral tissue model; SkinEthic's reconstructed human oral epithelium (RHOE) model

The human repeat insult patch test was also proposed as a non-animal method for determining the safety of known chemicals.

At the 23rd meeting of the Cosmetics Sectional Committee (PCD 19) held on June 28, 2013, the Drug Controller General of India (DCGI) decided to delete the requirement of tests on animals from the IS 4011 and to replace them with suitable non-animal methods. He emphasized the need to end animal testing of cosmetics without compromising consumer safety. The DCGI also said that when it is necessary to evaluate cosmetics products in order to exonerate oral toxicity and/or oral mucosal irritation, manufacturers should submit safety data based on non-animal testing methods. During the meeting it was also decided that the following sentence would be included in the standard: "*Prior to initiating the test involving novel ingredients or products containing novel ingredients, preliminary safety assessment using Quantitative Risk Assessment (QRA) tools and/or non-animal methods followed by Skin Irritation Test (Patch Test in humans) should be carried out*." The working group in charge of revising the IS 4011 was also asked to submit a quarterly report to the BIS Secretariat documenting the changes that other countries are making with respect to the oral toxicity test.

"*The European Union has imposed prohibition of the marketing of the cosmetics and their ingredients which have been tested on animals in March, 2013. In India also, following various representations regarding the ban on use of animals in testing of cosmetics in several countries, the Sectional Committee in its last meeting held on 28th June, 2013 finalized an amendment to delete the requirements for animal based test methods from the standard to align with global practices*," reported the Minister for Health and Family Welfare, Government of India, to the Parliament on December 17, 2013.

In November 2013, at the 65th meeting of the Drugs Technical Advisory Board, which operates under the Ministry of Health and Family Welfare, the Board proposed that a suitable provision be added under the Drugs and Cosmetics Rules, 1945, to prohibit import of cosmetics tested on animals abroad. In January 2014, the Ministry of Health and Family Welfare published a draft notification inviting public comments on the proposed amendment to the Drugs and Cosmetics Rules, 1945: "148-C. *Prohibition of testing of cosmetics on animals. – No person shall use any animal for testing of cosmetics*." Later that month, at the 20th meeting of the CHD 25 Committee of the BIS, the DCGI decided to remove the tests on animals from the IS 11601 and the IS 13424 and asked that they be replaced with suitable non-animal methods.

PETA India's campaign to end testing of cosmetics and household-products in animals has been endorsed by the Animal Welfare Board of India and the Mahatma Gandhi-Doerenkamp Center (MGDC) for Alternatives to Use of Animals in Life Science Education, established in India by the Doerenkamp-Zbinden Foundation. In addition to Member of Parliament Mrs Maneka Gandhi (also Founder, People for Ethical Treatment of Animals – PfA), several other senior politicians also advised the relevant ministries to look into PETA India's request for an end to these animal tests. President of the Congress Party Mrs Sonia Gandhi, Bharatiya Janata Party leader Shri Lal Krishna Advani, Member of Parliament Shri Abhijit Mukherjee, and the Ministers of State for Health and Family Welfare, Labor and Employment, Agriculture and Food Processing Industries, among others, sent appeals to the Ministries of Health and Family Welfare and Consumer Affairs of the Government of India to consider PETA India's request. In addition, PETA has held programs to protest testing of cosmetics on animals and push for a ban on sales of animal-tested cosmetics and household products, made a cruelty-free logo available to companies that do not test on animals and started an online database to make it easier for consumers to determine which companies' products are tested on animals and which are not. The MGDC and caring citizens from all over India also responded to PETA India's call for appeals to the ministries.

In recognition of PETA India's work to change government policies regarding animal testing and its efforts to help consumers choose cruelty-free products, international cosmetics company LUSH awarded PETA India its 2012 prize for excellence in lobbying.

PETA India is currently working to persuade the DCGI and the Ministry of Health and Family Welfare to ban the import of cosmetics and household products tested on animals.

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## INT: Updated ICCR Inventory of Validated Alternative Methods Applicable for Cosmetics

The International Cooperation on Cosmetics Regulation (ICCR) has released and "Inventory of Validated Alternatives to Animal Testing Applicable for Cosmetic Products and Their Ingredients in all ICCR Regions." The inventory should serve as a starting point for companies wishing to identify alternative methods for testing cosmetic products and ingredients. The list comprises methods developed and/or validated by the regional validation organizations of ICATM (ICCVAM, ECVAM, JaCVAM, HC, and KoCVAM). Most methods are also accepted as OECD test guidelines. The list does not include methods that were neither developed nor validated by ICATM partners and is therefore not exhaustive. The lead industry associations represented in ICCR are Cosmetics Europe (EU), CCTFA (Canada), JCIA (Japan), PCPC (US).

ICCR report: http://1.usa.gov/1fO8BeC
Annex: http://1.usa.gov/1i3HI6J

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## SUI: Research on nanoparticles distinguished by the Fondation E. Naef

On January 18, 2014, the Fondation E. Naef pour la Recherche in vitro (FENRIV) awarded its annual price to Prof. Barbara Rothen-Rutishauser for developing new alternatives to animal research. The prize has been awarded annually since 2000. The general aim of the Foundation (http://www.fondation-naef.com) is to promote the development of methods to reduce the need for animal experiments. The Foundation is based in Geneva (Switzerland).

Prof. Barbara Rothen-Rutishauser, from the Adolphe Merkle Institute in the University of Fribourg, has developed and adapted new *in vitro* methods to study the complex interactions between nanoparticles and lung tissues. For this, she notably assembled *in vitro* the various cells types found in human lungs, then assessed how nanoparticles interacted with this tissue. Pollution and nanotechnologies release nanoparticles into the atmosphere, and it is critical today to understand how these particles enter the human body and to determine their potential toxic effects. The use of sophisticated *in vitro* methods allows precise and well-controlled studies of human tissues and represents a promising alternative to animal experiments.

The FENRIV also announced on this occasion a collaboration with the Philanthropia Foundation. For the next three years,

the Fonds Carlo hosted by the Philanthropia Foundation will support the research work of scientists previously selected by the FENRIV. Accordingly, in 2014, the Philanthropia Foundation will support financially the 2013 laureate of the FENRIV prize, Dr Luc Stoppini, *Haute école du paysage, d'ingénierie et d'architecture de Genève*; Hepia/HESSO, for his *in vitro* studies on neurotoxicity.

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## UK: NC3Rs GSK Prize for Meritxell Huch

Dr Meritxell Huch from the Gurdon Institute at Cambridge University received the UK's international prize for scientific and technological advance with the most potential to replace, reduce, or refine the use of animals in science (the 3Rs) on February 26, 2014.

Dr Huch developed a method to enable adult mouse stem cells to grow and expand into fully functioning three-dimensional liver tissue. The model has potential as a high throughput screen for compounds to treat liver disease. Dr Huch and colleagues at the Netherlands' Hubrecht Institute isolated Lgr5$^+$ stem cells responsible for liver regeneration and cultured them to grow into small liver organoids, which survive and expand for over a year *in vitro*. When implanted back into mice with liver disease they continued to grow, ameliorating the disease and extending the survival of the mice. Having further refined the process using cells from rats and dogs, Dr Huch is now moving onto testing it with human cells, which would not only be more relevant to research into human disease, but also translate to the development of a patient's own liver tissue for transplantation.

The NC3Rs awards an annual prize for an original contribution to scientific and technological advances in the 3Rs (replacement, reduction and refinement of animal use) in medical, biological or veterinary sciences published within the last three years. Sponsored by GlaxoSmithKline, the prize consists of a prize grant of £ 18k, plus a personal award of £ 2k, and is part of the NC3Rs' commitment to recognize and reward high quality research that has an impact on the use of animals in the life sciences. Highly-commended prizes consist of a grant of £ 4k, plus a personal award of £ 1k.

Huch, M., Dorrell, C., Boj, S. F., et al. (2013). In vitro expansion of single Lgr5$^+$ liver stem cells induced by Wnt-driven regeneration. *Nature 494*, 247-250. http://dx.doi.org/10.1038/nature11826

Adapted from NC3Rs website
Posted February 26, 201

## UK: Institutional framework for the 3Rs

Institutional responsibilities for providing a framework and culture for the 3Rs should not be onerous or resource intensive. The NC3Rs has compiled a simple checklist of seven related principles to help institutions ensure that the 3Rs are developed and applied at all stages of the research process. The framework is internationally applicable.

http://www.nc3rs.org.uk/document.asp?id=2064

NC3Rs website
Posted February 24, 2014

## USA: Bill to End Cosmetics Testing on Animals proposed

The Humane Cosmetics Act (H.R. 4148) was introduced in US Congress by Congressman Jim Moran. The Act would ban conducting or commissioning animal use for cosmetics testing in the US and would prohibit the sale or transport of cosmetics if the final product or any component was developed or manufactured using animal testing. The bill is endorsed by The Humane Society of the United States, Humane Society Legislative Fund,

and Humane Society International, along with members and stakeholders of the personal care products industry. The use of animals for testing of cosmetics ingredients or final products is currently banned in the European Union, Israel, Norway, India (see p. 236), and the State of São Paulo, Brazil (see p. 234), with the European Union, Israel, and Norway also prohibiting the sale of animal-tested cosmetics.

However, the Safe Cosmetics and Personal Care Products Act of 2013 introduced in March 2013 by Jan Schakowsky and Ed Markey (H.R. 1385) would require a safety assessment of all cosmetics ingredients currently in use and could increase animal used for cosmetics ingredients testing in the US to up to 1.1 million animals per year for the next ten years (see Knight and Rovida, p. 177 - 208).

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## USA: Merck and other companies commit to end chimpanzee research

The major pharmaceutical company Merck & Co. has committed to no longer conduct or financially support research using chimpanzees. It has joined 26 other pharmaceutical companies and contract laboratories[1] in phasing out chimpanzee research or restricting their use of chimpanzees by following the principles set forth by an Institute of Medicine report released in 2011 that assessed the necessity of chimpanzee research[2]. This report also led to the announcement of the National Institutes of Health in June 2013 that 90% of chimpanzees owned by the US government would be retired to sanctuaries (see *ALTEX 30(3)*, 406).

Although their use is restricted but not banned by Directive 2010/63/EU, no great apes have been used for experimental purposes in the European Union since 1999.

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[1] http://www.humanesociety.org/issues/chimpanzee_research/tips/companies_chimpanzee_policies.html#.Uz0uM1fn1D2

[2] http://www.iom.edu/Reports/2011/Chimpanzees-in-Biomedical-and-Behavioral-Research-Assessing-the-Necessity.aspx

## USA: NIAID calls for proposals for *in vitro* models of enteric diseases

The National Institute for Allergy and Infectious Diseases (NIAID) is funding a program intended to advance understanding of enteric diseases by developing *in vitro* models that mimic biological structures, recapitulate human physiology and disease pathology, and incorporate components critical to disease and human host response. These models should facilitate studies that span the pipeline from basic research (pathogenesis) to product development. Grants will be awarded to multidisciplinary research teams with expertise spanning the fields of infectious disease and bioengineering. Eligible entities include U.S. for-profit and nonprofit organizations and government entities, including eligible agencies of the Federal government.

Application deadline: May 29, 2014
More information: http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-14-011.html

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