News

AUS: Bill to ban animal testing for cosmetics before parliament

A bill to enable a national ban on the use of new animal test data to support the introduction of chemicals used exclusively as cosmetic ingredients was put before the Australian House of Representatives in June 2017. The ban will be achieved through the new Australian Industrial Chemical Introduction Scheme (AICIS) and is planned to take effect on July 1, 2018. A stakeholder consultation process is currently underway.

The government has also proposed a respective ban on testing cosmetic ingredients in animals that will be triggered by changes to the National Health and Medical Research Council's *Australian code for the care and use of animals for scientific purposes* and will require incorporation into the states' and territories' legislation.

Countries with bans on animal testing include the European Union, Brazil, Norway, India, Israel, New Zealand, Turkey, United Kingdom, Switzerland, South Korea, Taiwan and Guatemala.

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CAN: Canadian Centre for Alternatives to Animal Methods launched

The establishment of the Canadian Centre for Alternatives to Animal Methods (http://bit.ly/2uNlC6m) was announced by the University of Windsor in Ontario on June 15, 2017. The Canadian Centre for Alternatives to Animal Methods (CCAAM) and its subsidiary, the Canadian Centre for the Validation of Alternative Methods (CCVAM), aim to develop, validate, and promote methodologies in biomedical research, education, and chemical toxicity testing that do not require the use of animals in partnership with Health Canada and other Canadian regulators. CCAAM will conduct multidisciplinary biomedical research to understand human health and disease using only human-based biomaterials and methods. CCAAM will also train the next generation of scientists, ethicists, and policy makers through its academic degree program in Animal Replacement Science at the University of Windsor. The centre is headed by Dr Charu Chandrasekera, executive director of the centre; Dr Philip Karpowicz, scientific director and Dr Andrew Hubberstey, academic director. It will host an inaugural conference October 2 and 3.

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DNK: Funding for research into alternatives to animal experiments announced

Forsøgsdyrenes Værn and Alternativfondet announce financial support for research into and development of alternatives to animal experiments. The overall amount of funding available is 1 million Danish kroner. To be considered for support it is not enough that your research is carried out without the use of animals. The research must genuinely contribute to the replacement of animals with other methods.

Application deadline: August 1, 2017
More information: http://forsoegsdyrenes-vaern.dk/ or http://alternativfondet.dk

EU: EURL ECVAM publishes recommendation on the use of non-animal skin sensitization tests

The JRC's European Union Reference Laboratory for alternatives to animal testing (EURL ECVAM) has published its recommendation on the use of non-animal approaches for skin sensitization (allergy) testing. This document builds on the progress made in the area since the publication of the EURL ECVAM strategy in 2013 and provides EURL ECVAM views on the latest two methods for skin sensitization, the LuSens and the U-SENS™, peer-reviewed by the EURL ECVAM Scientific Advisory Committee (ESAC), and on "defined approaches" which are based on the integration of different kinds of non-animal data.

EURL ECVAM is committed to play a leading role in the definition of international standards for assessing chemicals for their potential to elicit skin allergic responses. Three recommendations were issued by EURL ECVAM on non-animal methods for skin sensitization testing, the DPRA, the KeratinoSens™ and the h-CLAT. A major achievement was the OECD adoption of these first three *in vitro* methods (OECD Test Guidelines 442C, 442D and 442E) based on key chemical and biological mechanisms of the process that leads to development of skin allergies. Following independent peer review by the EURL ECVAM Scientific Advisory Committee (ESAC), EURL ECVAM now supports the use of two additional methods, the LuSens and the U-SENS™ when used in combination with other relevant information.

Since none of the regulatory adopted methods provides the same level of information as the traditional animal tests, a number of defined approaches, i.e., approaches based on the use of

different types of non-animal data, have been proposed for the identification of chemicals that may cause skin allergy. On behalf of the European Commission, the JRC's EURL ECVAM led the development of international guidance on the harmonized reporting of these approaches.

The defined approaches for skin sensitization have comparable performance to the standard animal test, the Local Lymph Node Assay (LLNA), for identifying potential skin allergens. In addition, some of them provide useful information to distinguish between strong and weak sensitizers. In the light of this evidence, EURL ECVAM recommends these defined approaches be used where applicable and adequate instead of LLNA data or together with the animal data if these are already available. EURL ECVAM recognizes the need to further evaluate the existing defined approaches in view of their possible translation into international standards to promote a global harmonized approach to the evaluation of chemicals for their skin sensitization potential and further reduce the number of animals used for this purpose.

Full article: Casati, S., Zuang, V. and Whelan, M. (2017). EURL ECVAM Recommendations on the use of non-animal approaches for skin sensitization. EUR 28553 EN, Publications Office of the European Union, Luxembourg. doi:10.2760/588955

Adapted from EU Science Hub
May 3, 2017

EU: SCHEER updates opinion on non-human primate use

The Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) has issued an updated opinion on the need for non-human primates in biomedical research, production, and testing of medical products and devices (http://bit.ly/2sPOedX). The opinion, which updates a 2009 version, finds that a proposal of a timetable for phasing out non-human primate use in Europe is not feasible at this time. However, the opinion provides recommendations on how to advance the 3Rs for non-human primate use, such as through alternative methods, training, improvement of techniques and protocols, sharing of knowledge, and removal of barriers. It also formulates current research needs.

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EU: ECHA publishes report on the use of alternatives for REACH

The third report on "The use of alternatives to testing on animals for the REACH Regulation" was published by the European Chemicals Agency in June 2017. It is based on registration dossiers for 6290 substances submitted to ECHA between 2008 and 2016.

ECHA states that 98% of substances are registered jointly, i.e., registrants work together to compile one registration dossier per substance and that usually all existing information on the substance is first combined to determine which studies are still required. 89 % of dossiers contained at least one endpoint where an adaptation or other argument was provided instead of a study result; the most common alternative methods used were read-across (63%), weight of evidence (43%) and QSAR prediction (34%). Data from new vertebrate animal studies were used in 11% of all endpoints for all substances.

Although read-across is the most commonly used alternative method, the report states that its quality is often insufficient and needs to be improved. ECHA has recently published the read-across assessment framework (https://echa.europa.eu/documents/10162/13628/raaf_en.pdf) to guide registrants in providing high quality read-across studies.

56% of the new studies performed for skin corrosion/irritation and serious eye damage/eye irritation were *in vitro* studies, used either alone or in combination with existing *in vivo* or read-across studies; the use of *in vitro* skin sensitization studies was rare.

Full report: http://bit.ly/2rCpllA

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EU: ECHA reports on Member State investigations on vertebrate testing proposals

Following its 2015 report of information on 295 new "higher-tier" studies on vertebrate animals submitted in registration dossiers without first submitting a testing proposal and awaiting a prior regulatory decision from ECHA (or the European Commission) to conduct the testing, ECHA undertook a survey to identify the possible reasons – apart from incompliance with the REACH regulation – why registrants had submitted the studies (http://bit.ly/2sOZozQ), e.g., the study had been required by another regulation and therefore had been justified and included in the dossier. Of the 295 cases, 121 were considered by ECHA to be of potential interest to the Member States' national enforcement authorities, the rest being considered of low interest.

ECHA in May 2017 published feedback from national enforcement authorities on their investigations submitted by April 2017 (http://bit.ly/2tTxUOl). Only 7 of the 15 contacted nation-

al enforcement authorities reported back to ECHA. Six of these reported on investigations into a total of 25 cases of potential interest, while the German national enforcement authority reported that it had not had any response from the companies it contacted and that German national laws do not allow sanctions in relation to these specific REACH violations.

The six national authorities reported only one confirmed violation; one inspection was not concluded.

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EU: Report on Scientific Conference Non-Animal Approaches – The way forward online

The European Commission has published a conference report as well as presentations and video recordings (http://bit.ly/2p3l7Fx) of its December 2016 conference aimed to engage the scientific community and relevant stakeholders in a debate on how to exploit cutting edge advances in biomedical and other research in the development of scientifically valid non-animal approaches. The conference was held as a response to the 2016 European Citizens Initiative "Stop Vivisection".

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GER: New chair for "Animal Welfare with Focus on Refinement in Laboratory Animal Science" in Berlin

The Federal Institute for Risk Assessment (BfR) and Freie Universität Berlin have appointed Dr Lars Lewejohann to the newly created chair for "Animal Welfare with Focus on Refinement in Laboratory Animal Science", which is assigned to the competence area "Reduction of severity and improvement of living conditions of laboratory animals". The field of research comprises all measures to reduce the burden on laboratory animals and determines objective criteria to estimate the distress to which animals are exposed during experiments.

Professor Lewejohann conducted biological research on refinement at the University of Münster using methods from behavioral biology with different strains of mice. In addition to heading a unit at the BfR, he will be teaching undergraduate and postgraduate students at the Faculty of Veterinary Medicine at the Freie Universität Berlin in his capacity as professor for "Animal Welfare and Refinement".

Adapted from BfR
press release
June 27, 2017

GTM: Guatemala bans animal testing for cosmetics

The Congress of Guatemala approved an anti-animal cruelty bill to provide protection to animals in laboratories, circuses, homes, and in the wild in February 2017. The new set of laws was drafted and submitted by The Humane Society International (HSI). Among numerous animal welfare improvements, the law completely bans animal testing for cosmetics and creates an official government platform to address animal welfare for the first time.

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INT: 2016 3Rs Prize awarded for study on natural lab rat behavior

Joanna Makowska and Daniel Weary from the University of British Columbia, Canada, were awarded the 2016 3Rs prize by the UK's National Centre for the 3Rs (NC3Rs), sponsored by GlaxoSmithKline (GSK), for their work assessing the importance of simple and natural behaviors such as burrowing and standing upright (rearing) to rat welfare. They compared the occurrence of these behaviors in large and enriched semi-naturalistic cages with standard laboratory caging.

The international 3Rs prize is awarded for a piece of primary research published in the last three years that has significant impacts on the numbers and/or welfare of laboratory animals. The prize consists of a £28,000 prize grant and a £2,000 personal award.

Winning research paper:
Makowska, I. J. and Weary, D. M. (2016). The importance of burrowing, climbing and standing upright for laboratory rats. *Royal Society Open Science 3*, 160136. doi:10.1098/rsos.160136

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INT: EMA releases waiving criteria for animal batch safety tests for veterinary vaccines

The European Medicines Agency (EMA) has published two new guidelines on harmonisation of criteria to waive target animal batch safety testing for live vaccines for veterinary use (VICH GL55, http://bit.ly/2tgolYf) and for inactivated vaccines for veterinary use (VICH GL50, http://bit.ly/2uoTtmZ), which will both come into effect in May 2018. Their implementation will reduce the number of animals used for batch release testing in VICH regions in which the test is currently still required, e.g., the US and Japan.

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INT: OECD releases version 4.0 of QSAR Toolbox

The Organisation for Economic Co-operation and Development (OECD) has released version 4.0 of QSAR Toolbox. The QSAR Toolbox is a software application intended to increase the regulatory acceptance of (Q)SAR methods.

New features of the QSAR Toolbox:

- Automated and standardized workflows for skin sensitization and short-term toxicity to fish,
- Improved customizable reports,
- Modernized and renewed IT system,
- Expansion of databases and the introduction of the reliability score for alerts and databases,
- Enhanced ADME information and improved presentation.

The QSAR Toolbox can be downloaded at http://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm. This page includes the recording of a webinar on the new features.

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INT: OECD group approves proposal for test guideline development

A committee of national coordinators from member countries of the Organisation for Economic Co-operation and Development (OECD) has approved a proposal to develop a performance-based test guideline for defined approaches for skin sensitization. If ultimately adopted by the OECD, this test guideline will make it easier to validate and implement non-animal testing methods for skin sensitization.

Skin sensitization testing, currently primarily performed using mice and guinea pigs, is required by regulatory agencies worldwide for a variety of chemical products. Skin sensitization is a complex process, and replacing animal testing with non-animal methods currently requires data from several methods to be combined to adequately predict toxic effects. Defined approaches are a means by which data from several non-animal test methods can be considered in combination. They combine input data from several specific sources, such as non-animal test methods or computational models, using an objective data interpretation procedure such as a machine-learning model, flowchart, or decision tree.

The test guideline proposal was developed by NICEATM and ICCVAM scientists working with Canadian and European collaborators from the International Cooperation on Alternative Test Methods. The proposal was approved by the Working Group of National Coordinators of the OECD Test Guidelines Programme at its meeting in April.

Approval of the proposal allows for the coordination of expert groups and conduct of meetings to develop a performance-based test guideline for defined approaches for skin sensitization. Performance-based test guidelines describe standards that constitute acceptable performance for a general class of test methods that, while differing in protocol details, are intended to measure the same biological effect. Approval of a performance-based test guideline for defined approaches for skin sensitization is expected to allow regulatory authorities to more readily accept defined approaches for skin sensitization testing, which will advance the goal of elimination of animal use for skin sensitization testing worldwide.

NICEATM News
May 11, 2017

INT: Refinement of zebrafish experiments included on Humane Endpoints website

The 3Rs-Centre Utrecht Life Sciences has published information on zebrafish that could contribute to the refinement of experiments with these animals. It helps researchers who work with zebrafish in the laboratory to prevent unnecessary pain and distress in these animals. The information is freely accessible on the Humane Endpoints website: https://www.humane-endpoints.info/en

The Humane Endpoints (HE) website helps to recognize humane endpoints in laboratory animals. A humane endpoint is the earliest indicator in an animal experiment of pain or distress in the animal. Researchers can use these indicators to avoid or limit pain and distress in laboratory animals. The website contributes to refinement, since it teaches scientists, animal-technicians and animal caretakers how to prevent unnecessary pain and distress in laboratory animals.

Newsletter 3Rs-Centre Utrecht Life Sciences
April 11, 2017

UK: NC3Rs publish guidance for university web pages on the 3Rs in animal research

To help establishments provide useful and informative animal research web pages, the NC3Rs has prepared a guidance document (http://bit.ly/2tPmb2p) that provides structured advice on the recommended content, especially in relation to the 3Rs, and considerations for designing, updating, and maintaining such pages. The guidance is not intended to be used as a checklist, nor to harmonize content between establishments, but rather to act as a framework for establishments to create pages that are personalized to local policies and practices on the 3Rs.

NC3Rs News & Blog
May 18, 2017

USA: US Pharmacopeia publishes revision to allow *in vitro* pyrogen test methods

A revision to the US Pharmacopeia and the National Formulary (USP-NF) now allows the use of *in vitro* pyrogen tests in place of the *in vivo* rabbit pyrogen test (RPT). Effective May 1, 2017, this change appears in general chapter 151, "Pyrogen Test," USP 40 – NF 35. This revision cites the US Food and Drug Administration (FDA) Guidance for Industry: Pyrogen and Endotoxins Testing Questions and Answers (http://bit.ly/2uNbGtH), which provides examples of *in vitro* pyrogen assays, including monocyte activation tests and the recombinant horseshoe crab factor C assay.

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USA: NIEHS to fund small business phase II grants for alternative methods development

The National Institute of Environmental Health Sciences (NIEHS) has published a Funding Opportunity Announcement (FOA) soliciting Small Business Innovative Research (SBIR) grant applications from small business concerns (SBCs) to develop medium- to high-throughput assays to evaluate the effects of toxicants on pluripotent or induced pluripotent cells with respect to cell differentiation and the resulting differentiated cell populations. The ability to incorporate genetic diversity in these assays would be useful. These assays will provide information on mechanisms of chemically-induced biological activity, help to prioritize chemicals for more extensive toxicological evaluation, support more predictive models of *in vivo* biological response, and potentially inform on the role of genetic diversity in toxicological effects.

Deadline for letters of intent: September 4, 2017
Deadline for applications: October 4, 2017
More information: https://grants.nih.gov/grants/guide/rfa-files/RFA-ES-17-007.html

USA: Bill requiring reporting of animal species and numbers used by federal agencies introduced

In February 2017, Congressman Ken Calvert (R-CA) introduced the Federal Accountability in Chemical Testing (FACT) Act (HR 816) into US Congress. The FACT Act requires that EPA, FDA, NIH, DOD, USDA and other federal agencies that conduct or require toxicity testing report the number of animals used, their species and what tests they were used for. The bill strengthens biennial reporting requirements in Rep. Calvert's 2000 law (Public Law No: 106-545) that created the federal program ICCVAM, mandating that agencies work to replace animal tests with more effective and cost-saving cell-based and computerized tests. The FACT Act will help measure agencies' compliance and progress towards ending animal testing. The FACT Act is the first animal testing-related bill of the 115th Congress.

Mice, rats, birds and most reptiles are not covered by the US Animal Welfare Act and therefore their use in laboratory tests does not need to be reported. The bill was written in partnership with the White Coat Waste Project (http://www.whitecoatwaste.org/).

Full text: https://www.congress.gov/115/bills/hr816/BILLS-115hr816ih.pdf

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Correction

The Hesse Animal Protection Prize 2016 (reported in ALTEX 34(1), 180) was awarded jointly to Christina Spohr of the Paul-Ehrlich Institute in Langen and to Rüdiger Hack and his team from Sanofi-Aventis Deutschland GmbH for the development of an *in vitro* test for batch release testing of the insulin glargine drug substance. The test, which measures the activation of human insulin receptors, has been accepted by the US FDA as an alternative to the rabbit blood sugar bioidentity test.

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