News

EU: REACH registrants to use alternative test methods for skin sensitization

The amended REACH annexes concerning skin sensitization are expected to enter into force in autumn 2016. The information needed for the classification or risk assessment of a substance will then be obtained through non-animal methods as a first step. *In vivo* methods can only be used if the *in chemico* or *in vitro* test methods are not adequate for the substance or cannot be used for classification and risk assessment.

With the amended requirements, if a substance is predicted to be a skin sensitizer based on the available data, skin sensitization potency should also be assessed. There is currently no standardized way to assess potency with the *in vitro* methods and therefore the *in vivo* test may still be necessary.

However, estimating potency is not necessary if an existing *in vivo* study does not allow potency estimation and the study has been performed according to internationally-adopted test methods and good laboratory practice.

The amended requirements will be implemented in the completeness check of IUCLID and REACH-IT in the autumn.

ECHA's draft guidance takes the amended information requirements into account and gives advice to registrants. Some minor changes might still occur in the final consultation process. The final guidance will be published in the autumn after the Annex amendment has been published in the Official Journal.

ECHA/NI/16/32

EU: Advice on skin and eye irritation testing helps reduce animal tests

The OECD test guidelines are relevant for many registrants preparing for the 2018 REACH registration deadline. The advice on using the guidelines has been updated taking into account the recent amendments of the REACH annexes, making non-animal test methods the default requirement.

For most substances, the use of the adopted OECD *in vitro* test guidelines for skin and eye irritation testing will provide results which are accepted under REACH.

Regarding skin corrosion/irritation, four adopted *in vitro* test guidelines are available:
- OECD 439: *in vitro* skin irritation (revised in 2013)
- OECD 431: *in vitro* skin corrosion (revised in 2013)
- OECD 430: Transcutaneous electrical resistance test (TER) (revised in 2013)
- OECD 435: *in vitro* membrane barrier test method (2006)

Regarding serious eye damage/eye irritation, five adopted *in vitro* test guidelines and one draft test guideline are available:
- OECD TG 437: The Bovine Corneal Opacity and Permeability test method (BCOP) (revised in 2013)
- OECD TG 438: Isolated Chicken Eye Test (ICE) (revised in 2013)
- OECD TG 460: Fluorescein leakage (FL) method (2012)
- OECD TG 491: Short Time Exposure (STE) (2015)
- OECD TG 492: Reconstructed human Cornea-like Epithelium (RhCE) (2015)
- Test Method Cytosensor Microphysiometer (CM) (draft under discussion)

In some cases, animal testing may still be necessary, as a last resort. For this, one revised test guideline is available:
- OECD TG 405: *in vivo* Acute Eye Irritation/Corrosion (revised in 2012)

Registrants must consider and use alternative methods where possible. Due to the sequential nature of the REACH standard information requirements, and irrespective of the annual tonnage of the substance, new data for skin and eye irritation needs to be generated with *in vitro* testing. If the *in vitro* results are adequate for classification and labelling or risk assessment, no further *in vivo* testing is needed. Registrants need to make sure that the chosen test method is suitable for the substance to obtain adequate information from the *in vitro* studies.

ECHA/NA/16/28

EU: ECHA updates guide on avoiding unnecessary animal tests

ECHA has published version 2.0 of "How to use alternatives to animal testing to fulfil your information requirements for REACH registration", which combines five practical guides on how to use alternative approaches and report data in the regis-

tration dossier. It aims to help applicants to better understand their obligations to avoid unnecessary testing on animals while still making sure that they have sufficient information on their substances for classification and risk assessment. It also highlights the many opportunities to use alternatives to animal testing and how the results can be reported correctly.

URL: https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals

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EU: European Court of Justice sharpens ban on animal tests for cosmetics

Animal tests on cosmetic product ingredients performed outside the EU cannot be used to claim safety of the ingredients for the purpose of marketing the product in Europe.

Members of EFfCI, a trade association representing the manufacturers within the European Union of ingredients for use in cosmetic products, had conducted animal testing outside the EU in order to test the safety to human health of certain cosmetic ingredients. The data from those tests was required for the use of those ingredients in cosmetic products intended to be sold in Japan and China.

The European Court of Justice was asked to rule on whether the ingredients could now also be incorporated into cosmetic products placed on the EU market because the animal experiments had been performed with the intention to meet requirements of other countries' legislation and not those of the EU. The court decision explains that it is settled case-law that interpretation of EU law requires consideration of both the wording and the context in which it occurs and the objectives pursued. As Regulation No 1223/2009 sought to decrease animal experiments and actively promote non-animal alternative methods, it must be understood to make access to the European market conditional upon compliance with the prohibition of animal testing. Therefore, cosmetic products containing ingredients that have been tested on animals outside the EU may not enter the EU market if the resulting data is used to prove the safety of those products for the purposes of placing them on the EU market.

Full decision: http://bit.ly/2eRtDDJ

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GER: Prize awarded for BoNT/B BINACLE assay

The Ursula M. Händel Animal Protection Prize has been awarded to Birgit Kegel and Beate Krämer from the Paul Ehrlich Institut in Langen together with four further members of their team for developing an *in vitro* method to test botulinum neurotoxin potency. The method determines the potency of the BoNT serotype B used to treat different forms of dystonia and in cosmetic procedures. The assay takes into account the binding as well as the protease function of the toxin.

The biannual prize, which is endowed with €100,000, was awarded by the *Deutsche Forschungsgemeinschaft* (DFG) for the sixth time.

Reference

Wild et al. (2016). In vitro potency determination of botulinum neurotoxin B based on its receptor-binding and proteolytic characteristics. *Toxicol in Vitro 34*, 97-104. http://dx.doi.org/10.1016/j.tiv.2016.03.011

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IND: Seminar held on bioethics in medical and biological research

A national seminar on "Progression of Bioethics in Medical and Biological Research" was organized by the Department of Zoology, Dev Samaj College for Women (DSCW), Firozpur City, on February 24, 2016.

The seminar was inaugurated by Dr Madhu Prashar (National & State Awardee), Principal, DSCW. A key note address was presented by Prof. Dr Raj Bahadur, Vice-Chancellor, Baba Farid University of Health Sciences, Faridkot. Around 120 registered participants, 150 students, and 30 faculty members from different educational institutes, medical, dental and nursing colleges attended the seminar.

The seminar's aims included to increase the respect for living beings; to explore the morals/values, value analysis and its clarifications; to understand the equilibrium between benefits and risks of science and technology and their uses; to understand better the diversity of views of different persons; to study the development of reflective processes (individual/societal views); to develop the skills for "informed choice"; to realize the importance of bioethical decision-making; and to evaluate the direction and principles underlying scientific endeavours.

Invited lectures dealt with current bioethics in medical practice, cancer research, dental health, microbiology, biosystematics, cryopreservation and therapeutic approaches as well as bioethical concepts.

The organizers and participants are grateful to the Indian Council of Medical Research, New Delhi, for providing financial assistance for the seminar to all the resource persons, facilitators and chairpersons of the sessions.

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INT: OECD launches a new series on adverse outcome pathways

OECD launched its knowledge base on Adverse Outcome Pathways (AOPs) in collaboration with the U.S Environmental Protection Agency and the European Commission Joint Research Centre in 2014. Two years later, the first five endorsed AOPs have been published in a new OECD Series on Adverse Outcome Pathways, available free of charge on the OECD public website. These publications are the result of joint efforts between AOP developers and AOP reviewers through an established OECD AOP development and review process. The first publication in the Series proposes a user guide for developing AOPs. In the future, the publication of AOPs is likely to happen on a yearly basis, following the cycle of annual reviews and publications.

URL: http://bit.ly/1Av6cj0

OECD
20/09/2016

INT: OECD publishes guidance on waiving mammalian acute toxicity tests

In August the Organisation for Economic Co-operation and Development (OECD) published "Guidance document on considerations for waiving or bridging of mammalian acute toxicity tests" (ENV/JM/MONO(2016)32). It explains how acute toxicity testing can be waived based on scientific criteria, such as physico-chemical properties of the test chemical or the potential for little or no exposure to the test chemical by a specific route, or based on existing hazard information that is informative for the acute toxicity endpoint, e.g., hazard information from similar test chemicals which can be used for read-across, recognized calculation approaches and bridging concepts. The approaches used must be properly justified to provide regulatory authorities with the required basis for decision-making and to ensure the integrity of the hazard information.

URL: http://www.oecd.org/env/ehs/testing/mono%202016%2032.pdf

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INT: OECD publishes new *in vitro* test guidelines

The OECD has published the following new *in vitro* Test Guidelines:

- Test No. 458: Stably Transfected Human Androgen Receptor Transcriptional Activation Assay for Detection of Androgenic Agonist and Antagonist Activity of Chemicals
- Test No. 442E: *In Vitro* Skin Sensitisation

The OECD also published several updated versions of existing *in vitro* Test Guidelines, including:

- Test No. 431: *In vitro* skin corrosion: reconstructed human epidermis (RHE) test method
- Test No. 455: Performance-Based Test Guideline for Stably Transfected Transactivation *In Vitro* Assays to Detect Estrogen Receptor Agonists and Antagonists
- Test No. 473: *In Vitro* Mammalian Chromosomal Aberration Test
- Test No. 476: *In Vitro* Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes
- Test No. 487: *In Vitro* Mammalian Cell Micronucleus Test
- Test No. 490: *In Vitro* Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene

URL: http://bit.ly/1Fa8QOZ

INT: EU-ToxRisk and Tox21 to collaborate

The EU-ToxRisk project and the Toxicology in the 21st Century (Tox21) initiative in the US have agreed to collaborate on efforts to reduce the use of animals and achieve more efficient chemical safety assessments. A total of 28 representatives from both projects gathered in a workshop held in Mainz (Germany) on September 12-14, 2016 to initiate collaboration across areas

of mutual interest within the field of risk assessment. The following areas were agreed upon for mutual practical cooperation.

- Develop practices of cross-consortium data sharing with particular emphasis on the ongoing EU-ToxRisk case studies
- Develop core methodology in read-across and the application of high-throughput transcriptomics for safety assessment
- Create synergies across overlapping chemical subsets
- Utilize ongoing developments of *in vitro* tissue models and computer-based predictions of drug concentrations for risk assessment
- Develop joint case studies focused on innovations in the application of alternative approaches

The workshop, organized at the behest of the EU-ToxRisk project following the initiatives of the EU-ToxRisk Coordinator Bob van de Water (University of Leiden), features as a crucial part of the strategy implemented by the project to advance international cooperation on the topic of new approaches to chemical risk assessment. Exchange and cooperation with many like-minded international initiatives on approaches, data exchange and knowledge harmonization within the field of alternative toxicity testing will help drive this field forward and evolve towards a new era of safety sciences to the benefit of citizens worldwide.

EU-ToxRisk/Tox21
Workshop Press Release
28/09/2016

INT: New journal on animal feeling announced

The Humane Society Institute for Science and Policy has announced *Animal Sentience (ASent),* the world's first journal focused on animals' capacity to feel. *ASent* is a peer-reviewed, interdisciplinary, fully online and open-access journal with no subscription fees. The journal distinguishes sentience (the capacity to feel) from sapience (the capacity to think). It welcomes submissions relating to animal consciousness and cognition as these are integral to feeling. *ASent* encourages empirical studies, theoretical modeling, integrative reviews and syntheses, and peer commentaries from any academic discipline within the sciences, humanities, or further afield. If it clearly relates to animal sentience, it is appropriate for *ASent*. As part of the journal's broader mission of fostering respect and compassion for animals, it does not publish research that intentionally causes harm to the animals studied.

URL: http://animalstudiesrepository.org/animsent/

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IRL: SFI Investigators Programme to fund alternatives to animal research

For the first time, as part of the SFI Investigators Programme 2016 call, SFI is providing applicants with the opportunity to seek funding to support the development and validation of new tests, models and approaches not involving the use of live animals and/or addressing the principles of the 3Rs (Replacement, Reduction and Refinement). It is envisaged that this development and validation work related to the 3Rs would complement the hypothesis-driven research program and would run alongside the main research activities. Until now there has been no dedicated funding of research on alternatives to animal research in Ireland.

Deadline: December 9, 2016
Call document: http://bit.ly/2e0qoak

Adapted from SFI
Investigators
Programme 2016

UK: NC3Rs adds new statistics functionality to Experimental Design Assistant

An updated version of the Experimental Design Assistant (EDA) (http://bit.ly/2ers4rV) has been released. The EDA is a free tool built by the NC3Rs to help researchers design robust and reproducible experiments using the minimum number of

animals. Researchers build a diagrammatic plan of their proposed experiment within the EDA and the system provides a tailored critique, including suggestions on optimizing the design.

The latest release includes advice on which statistical test to use as well as links to the software for running the tests. Improvements have also been made so that the EDA now provides feedback on experimental plans within a few seconds.

NC3Rs News
July 27, 2016

UK: Annual experimental animal use statistics published

The Home Office published its statistics on the use of animals for experimental purposes in 2015. Changes in data reporting had been made in accordance with Directive 2010/63/EU the previous year. The report calls attention to quality issues with reporting of the 2014 data, and compares 2015 data with 2013 data.

In 2015, a total of 4.14 million procedures were completed. Of those, 2.08 million (50%) were experimental procedures and 2.06 million (50%) related to the creation/breeding of genetically altered animals that were not used in further experimental procedures.

Between 2006 and 2013, the total number of procedures increased by 37% (1.11 million procedures). The creation/breeding of genetically altered animals primarily accounted for this rise (1.00 million procedures) whilst the increase in the number of experimental procedures was much smaller (107 thousand procedures).

When comparing 2015 with 2013: the total of 4.14 million procedures in 2015 represents an increase of 1% or 21 thousand procedures compared with 2013; the 2.08 million experimental procedures in 2015 represents an increase of 3% or 63 thousand procedures compared with 2013; the 2.06 million genetically altered animals created/bred but not used in further procedures in 2015 represents a decrease of 2% or 41 thousand procedures compared with 2013.

Of the 2.08 million experimental procedures completed in 2015, the majority involved mice (61%), fish (14%), rats (12%) and birds (7%). Experimental procedures involving specially protected species (i.e. horses, dogs, cats, and non-human primates) accounted for 0.8% of procedures in 2015.

Comparing 2015 with 2013 by species, there were notable changes to the number of experimental procedures involving fish, up 14%; amphibians, up 15%; primates, up 12%; guinea pigs, down 17%.

Of the severity assessments undertaken for the 2.08 million experimental procedures completed in 2015 13% were assessed as sub-threshold (compared with 9% in 2014); 6% were assessed as non-recovery (compared with 7% in 2014); 51% were assessed as mild (compared with 51% in 2014); 24% were assessed as moderate (compared with 25% in 2014); 6% (123 thousand) were assessed as severe (compared with 8% in 2014).

Of the 2.06 million procedures in 2015 relating to the creation/breeding of genetically altered animals that were not used in further procedures, nearly all involved mice (86%), zebrafish (13%), rats (1%), and Xenopus (0.4%). Of the severity assessments undertaken for these 2.06 million procedures: 55% (1.13 million) were assessed as sub-threshold (compared with 46% in 2014); 0.2% (3,300) were assessed as non-recovery (compared with 0.1% in 2014); 39% were assessed as mild (compared with 48% in 2014); 3% (65 thousand) were assessed as moderate (compared with 4% in 2014); 3% (62 thousand) were assessed as severe (compared with 2% in 2014).

URL: http://bit.ly/29T9KLl

Adapted from Annual Statistics of Scientific Procedures on Living Animals Great Britain 2015