News

EU: EC approves LC-MS/MS replacement for detection of marine biotoxins

The biological test for the detection of Diarrhetic Shellfish Poisoning marine biotoxins (DSP) in bivalve molluscs like mussels, cockles, oysters, or scallops will soon be replaced by a chemical test, which will better ensure the protection of consumer health. Member States endorsed the relevant European Commission proposal during the meeting of the Standing Committee of the Food Chain and Animal Health (SCoFCAH) on 17 November 2010. The test, validated by the Union Reference Laboratory for marine biotoxins, maintains and ensures a full protection of consumer health without the shortcomings of the biological test, such as the high variability in results, the insufficient detection capability, and the limited specificity. In addition, the Commission estimates that the use of the chemical test will spare about 300,000 mice per year, which are used annually in biological testing for the detection of these marine biotoxins. In biological testing, mice are injected with a solution containing mollusc extract and, if toxins are present, the rodents die. As mice cannot be used twice for testing, they are humanely killed after the test, even if no biotoxins are detected. Chemical testing, on the other hand, is carried out mechanically – a procedure similar to blood testing – without the use of animals. Animal welfare associations have already expressed their satisfaction with the decision. Chemical testing is expected to start in July 2011. Bivalve molluscs are shellfish. Most of the familiar edible shellfish such as mussels, cockles, oysters, and scallops belong to this group of shellfish. The term bivalve refers to their two hinged shells. For more information, please visit: http://www.aesan.msps.es/CRLMB/docs/docs/metodos_analiticos_de_desarrollo/EU-Harmonised-SOP-LIPO-LCMSM_Version2.pdf

Press release
Europa Midday Express
18 November 2010

EU: First REACH registration closes

On 30 November, 2010, the registration of widely-used chemicals set by REACH, the Regulation for Registration, Evaluation, Authorization, and Restriction of Chemicals, was closed. This first deadline applied to the most hazardous substances (e.g., those that are carcinogenic, mutagenic, or toxic for reproduction) manufactured or imported in quantities of 1 ton or more per year per company, substances very toxic to the aquatic environment manufactured or imported in quantities of 100 tons or more per year per company, and substances manufactured or imported above 1,000 tons per year. 24,675 files were submitted to the European Chemicals Agency (ECHA).

The aims of REACH (Regulation No. 1907/2006) are to ensure safer use of chemicals, increased industrial competitiveness, promotion of alternative test methods, and a cleaner environment. REACH makes industry responsible for assessing and managing the risks posed by chemicals and providing appropriate safety information to their users. In parallel, the European Union can take additional measures on highly dangerous substances, where there is a need for complementary action at EU level. Under the REACH system companies cannot place a chemical substance they manufacture or import on the EU market unless it has been registered with ECHA within the applicable deadline. There are two further registration deadlines in 2013 and 2018 for chemicals produced or imported in lower volumes.

Europa press release
1 December 2010

GER: Animal Protection Research Prize awarded to *in vitro* test for residual toxicity of tetanus vaccine

On 15 December 2010 Federal Minister Ilse Aigner awarded the 29th Animal Protection Research Prize of the German Federal Ministry of Food, Agriculture and Consumer Protection to Dr. Heike Behrensdorf-Nicol, Ursula Bonifas, Dr. Beate Krämer, and Dr. Karin Weißer of the Paul Ehrlich Institute in Langen, Germany. They received the prize of € 15,000 for their work on "Development of an *in vitro* method to determine the residual toxicity of tetanus vaccines." With this method they aim to replace the guinea pig test on tetanus vaccines currently required by the European Pharmacopoeia. 2,000 animals per year are used for this test in Germany alone.

The ceremony took place at the Federal Institute for Risk Assessment in Berlin, Germany. The prize is awarded yearly to support methodological work aiming to reduce or replace animal experiments. The call for application for next year's prize has been published with a deadline of 31 March 2011.

Details at: http://www.bmelv.de/cln_173/SharedDocs/Downloads/Landwirtschaft/Tier/Tierschutz/30-Tierschutzforschungspreis.pdf?__blob=publicationFile

sva

GER: Ursula M. Händel Animal Welfare Prize for the automated FADU assay

Dr. Maria Moreno-Villanueva and Prof. Dr. Alexander Bürkle from the University of Konstanz, Germany were awarded the Ursula M. Händel Animal Welfare Prize by the German Research Council (DFG) for their work in developing the automated Fluorimetric Detection of Alkaline DNA Unwinding (FADU) assay, an *in vitro* genotoxicity assay. The Prize was presented by the president of the German Research Association, Dr. Matthias Kleiner, in a ceremony on 24 January 2011 in Berlin, Germany. The prize money of € 25,000 will be spent on research work related to the validation of the method.

The FADU assay detects the formation and repair of DNA strand breaks upon exposure to chemicals. The original FADU assay, published in 1981, was very demanding technically and required large numbers of cells. Alexander Bürkle and co-workers established an automated version that renders this assay more convenient and reproducible, increases throughput, and reduces the number of cells required. The assay is based on the use of cells from human blood and thus better reflects the human response. It does not require the use of fetal calf serum.

sva

GER: Award of research prize "Alternative and Complimentary Methods" 2010

On 29 November 2010 Secretary of State Friedlinde Gurr-Hirsch awarded the Research Prize "Alternative and Complimentary Methods" 2010 worth € 25,000 jointly to Dr. Elisabeth Schültke from Freiburg and Professor Marcel Leist from Konstanz.

Dr. Elisabeth Schültke, a medical doctor in Stereotactic Neurosurgery at the Neurocentre of the University Hospital Freiburg, developed a method to tag cells with gold nanoparticles in cooperation with a group from Trieste (Italy). The behavior of the tagged cells can be followed in the animals by special X-rays over a long period of time. This method could be employed to investigate therapeutic strategies for Alzheimer's disease, Parkinson's disease, and cancer while significantly decreasing the use of experimental animals.

Prof. Dr. Marcel Leist, Doerenkamp-Zbinden Chair for alternative *in vitro* methods at the University of Konstanz, developed a procedure to investigate changes and damage to dopamine-containing human nerve cells, which may be of genetic origin or be a consequence of exposure to a toxin. Until now, such research has been done using experimental animals. The new *in vitro* method allows the study of these processes using human cells. The results are both more relevant to the potential human patients and replace numerous animal experiments.

The ceremony took place in Stuttgart, Germany.

Press release
Ministry for Food and Rural Areas Baden Württemberg
Germany

INT: Draft One-Generation Reproductive Toxicity Study Test Guideline approved by OECD

On 19 November 2010, the Organisation for Economic Cooperation and Development (OECD) announced that the draft Extended One-Generation Reproductive Toxicity Study (EOGRTS) test guideline was approved by the Joint Meeting of the Working Party on Chemicals, Pesticides and Biotechnology and the Chemicals Committee. While the test guideline still requires official adoption by the OECD Council, the approval by the Joint Meeting represents a critical milestone towards reducing and refining animal use for reproductive and developmental toxicity testing.

The EOGRTS is an integrated protocol that can comprehensively assess reproductive and developmental toxicity within a single study using the same set of animals while using fewer animals than the current "gold standard" two-generation test. Central to its design is a key refinement that makes much better use of the first generation offspring and allows a major reduction in animal use due to the evaluation of one generation rather than two. The EOGRTS also provides more flexibility than the two-generation test, particularly with respect to the assessment of postnatal developmental toxicity, including developmental neurotoxicity (DNT) and developmental immunotoxicity (DIT).

These enhancements are accomplished in the EOGRTS by the retention of up to three times more of the first generation offspring for assessments at juvenile and/or young adult life stages, as compared to the two-generation study, in which 86% of the offspring are terminated before three weeks of age (weaning) and 43% are evaluated only until they reach four days of age. Furthermore, the pre-weaning offspring data in the two-generation study are limited to general measures, such as survival and body weight, whereas the additional offspring retained in the EOGRTS are evaluated for a variety of more specific developmental and functional end points. Thus, the quality and quantity of data obtained from the animals is greatly enhanced in the EOGRTS.

The other key design feature of the EOGRTS, namely evaluating one generation instead of two, yields an unparalleled reduction in animal numbers used for toxicity testing. Conducting separate two-generation reproductive toxicity (DNT and DIT) studies would consume ~5000 rats, whereas similar information can be achieved with the EOGRTS using ~1300 rats. Omission of the second generation is scientifically supported by several retrospective analyses that evaluated up to 498 existing two-generation reproductive toxicity studies and concluded that the second generation data had a minimal impact on risk assessment or chemical classification and labelling (Piersma et al., *Reprod. Toxicol.*, epub ahead of print, 2010).

Several companies in the industrial chemicals and crop protection sectors already have conducted their own EOGRTS studies in an effort to assess feasibility and effectiveness. For example, BASF conducted an EOGRTS study on vinclozolin and confirmed the ability to detect reproductive/development effects (Schneider et al., *Reg. Tox. Pharm.*, epub ahead of print, 2010). Bayer Crop Sciences has run a study on methimazole to assess DNT effects, and Syngenta sponsored an EOGRTS on lead acetate to address DIT. In addition, the first EOGRTS run for regulatory purposes was conducted by Dow Chemical on behalf of the 2,4-D Task Force. Dow is already receiving new requests for additional EOGRTS studies, and it is suspected that other companies are seeing similar activity. Given the comprehensive nature of toxicity testing requirements for crop protection compounds, this sector is likely to be among the first to implement the EOGRTS on a regular basis.

The much larger challenge, but also the greater opportunity, is the acceptance and use of the EOGRTS as an alternative to the two-generation reproductive toxicity study under the European Union's REACH program. REACH ultimately will require an estimated several hundred new two-generation reproductive toxicity studies on a wide variety of industrial chemicals, consuming a staggering number of animals. If the EOGRTS were to be accepted by the European Chemicals Agency (ECHA) as an alternative to the two-generation study, a reduction on the order of several hundred thousand animals could be achieved.

In addition to ECHA acceptance, another hurdle relates to the cost of the EOGRTS, which is considerably more expensive than the two-generation reproductive toxicity study. Costs can be reduced, however, if the DNT and DIT cohorts of the EOGRTS can be waived when scientifically justified and/or when the data are not required to meet regulatory requirements. This inherent flexibility of the EOGRTS allows study designs to be tailored to the specific regulatory framework in the most effective and efficient manner possible, making it far preferable to a one-size-fits-all approach in which the two-generation study is the only option.

Ed Carney, PhD
The Dow Chemical Company
posted on alttox.org
on 4 January 2011

Peru: Alternatives to animal use in education

The APEH group from *Unidos por los Animales* was invited to give presentations and a multimedia exhibition at the International Congress of Veterinary Science in Andean Valleys at the Micaela Bastidas National University, Abancay, Peru. The three lectures were "Alternatives to Animal Use in Teaching," "Use of Ethically Acquired Animals in Education – Experience in the Faculty of Veterinary Medicine, San Marcos University, Lima, Peru," and "Importance of Teaching Animal Welfare in Education." The exhibition included the display and explanation of CDs and DVDs on physiology and pharmacology, biology, anatomy, surgery, and the InterNICHE Loan System as well as the display and explanation of models, simulators, and manikins (simulator for suturing skin and injections, Koken rat, PVC rat (microsurgery), Jerry manikin). Visits were also made to the Faculty of Biological Sciences and Human Medicine, San Antonio de Abad National University, Cusco, and to the Faculty of Health Sciences of the Andean University of Cusco, who were also provided with written materials and CDs on relevant subjects. The professors were very grateful and satisfied with the donated and loaned material and showed great willingness to use the material in class to reduce the use of animals.

Milagros Ramos Munar
Coordinator working group APEH
Unidos por los Animales
Peru

SUI: Pharmaceutical industry sets global standards of animal protection

Swiss global research organizations have jointly signed a charter to improve standards of animal experiments in accordance with the 3Rs principles. Their efforts and aims apply to their worldwide operations and to all partner organizations that perform contract research for the companies.

Although the Swiss research organizations already are bound by stringent animal protection laws in that country, members of the inter-trade organization Interpharma – Novartis, Roche, Merck Serono, Actelion, Bayer Schering Pharma Schweiz, Cilag, and Vifor – by jointly signing the charter have committed to improving and expanding protection of experimental animals in their global sphere of influence. They plan to promote the 3Rs by developing and upgrading the training and education of their employees and by demanding the same additional efforts from all companies they contract to breed animals or to perform animal experiments. The organizations promise strict audits and evaluation processes to measure and control their performance on a global level. They aim to improve their communication with the public about animal-based research and animal protection. Further, the organizations commit to report annually on their progress.

Thomas B. Cueni
General Secretary Interpharma iph
www.interpharma.ch a

SUI: Basel Declaration on animal-based research adopted

At the two-day conference, "Research at a Crossroads," held in Basel on 29-30 November 2010, more than sixty scientists from Switzerland, Germany, the UK, France, and Sweden signed the Basel Declaration. This declaration calls for more trust, transparency, and better communication with regard to animal experimentation. By signing, the scientists aim to contribute constructively toward implementing the new Directive on Animal Experiments and enacting it into national law. They also commit to a responsible attitude towards experimental animals and to better and more active cooperation with the public.

Although very few people question the successes of biomedical research, which has led to improved life expectancy and quality for many patients, scientific methodology increasingly is being criticized by the public. Animal experiments, as a particularly emotional subject, only seldom are discussed objectively. This leads to growing limitations on animal-based research – limits that are not based on ethical or objective criteria but, rather, on public sentiment.

With the Basel Declaration, the participating scientists want to show that science

and animal protection are not contradictory. The signees commit to employing animal experiments only to obtain fundamentally important insights when no alternative methods are available. To make their motivation and methods more understandable to the public, they plan to work together more closely with the media and with schools. In return, the scientists ask the public to be more open-minded with regard to scientific topics. They also hope to build a cooperative relationship with the decision-makers based on both trust and reliability.

For more information: www.basel-deklaration.org

Press release Basel Conference
30 November 2010

UK: Björn Ekwall Memorial Award 2010 for Richard Clothier

Richard Clothier, former Director of the FRAME Alternatives Laboratory (FAL), was presented with the Björn Ekwall Memorial Award at a special ceremony at the Kennel Club on 4 November 2010. He was a co-founder of the FAL, at the University of Nottingham Medical School, and was its director from 1997 to 2005.

For many years, Richard collaborated with Björn Ekwall on the Multicenter Evaluation of In Vitro Cytotoxicity (MEIC) programme, aimed at the evaluation of the ability of *in vitro* basal cytotoxicity assays to predict human acute systemic toxicity.

The award recognises his outstanding contributions in the field of *in vitro* toxicology, and in particular, the development, implementation, and validation of alternative toxicity test methods. He was presented with it by Prof. Ada Kolman of the Björn Ekwall Memorial Fund. He then delivered the memorial lecture entitled "Experience in the Development and Evaluation of In Vitro Alternative Assays." Dr. Clothier generously donated the award prize money of £ 1,600 to FRAME.

Press release FRAME
8 November 2010

USA/EU: EPA and ECHA sign agreement to enhance chemical safety

The US Environmental Protection Agency (EPA) and the European Chemicals Agency (ECHA) have announced a partnership that will promote enhanced technical cooperation on chemical management activities. The partnership is part of EPA's commitment to improve chemical safety. ECHA is the agency that implements the EU's chemical management program known as REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals).

The partnership was formalized through a statement of intent and was highlighted at the Transatlantic Economic Council (TEC) meeting in Washington, D.C. The TEC, established to advance transatlantic economic integration between the US and the EU, issued a statement stressing the importance of enhanced cooperation on chemicals. The statement of intent provides the first concrete result of this effort. The statement puts in place a process for working together on a range of issues of mutual interest including toxicity testing, the hazard and risk assessment of chemicals, risk management tools, scientific collaboration, and information exchange.

One of the major anticipated areas of collaboration will be on the exchange of data and information. For example, the statement of intent will promote the exchange of non-confidential information on hazards, uses, and substance identification between ECHA and EPA, including data collected under REACH. The two agencies will also share criteria for managing confidential business information with the goal to increase the availability of chemical information to the public. The statement also enables the agencies to share information on approaches to more efficiently address chemicals of concern that are prioritized for regulatory action.

EPA News release
17 December 2010

USA: Workshop calls for more strategic action on NRC vision

The Human Toxicology Project Consortium, a group formed to promote implementation of the "vision" for 21st century toxicology proposed by a National Research Council (NRC) committee in 2007, hosted a workshop on "Accelerating Implementation of the NRC Vision for Toxicity Testing in the 21st Century" in Washington, DC on 9-10 November 2010. The Consortium, composed of a research institute, non-governmental organizations, and diverse corporations, has proposed a human genome-type project as the mechanism for implementing the NRC vision.

Speakers presented data generated using a variety of high-tech tools and approaches, including ultra high-throughput, pathway-based, robot-assisted methods yielding hundreds of thousands of data-points interpreted and graphically depicted using high-speed computers. The 21st century tools are being applied for a variety of sometimes overlapping purposes, including prioritization of chemicals for follow-up testing in animals, screening of chemicals to quickly gain at least some insight into potential toxicity, and prediction of results in animals without resorting to animal testing. These and other purposes are all worthwhile and will also serve to extend the capabilities of these tools and our experience with them.

But where does this leave us with respect to implementing the pioneering 2007 National Research Council (NRC) report on "Toxicity Testing in the 21st Century," which gave us the label of "21st Century Toxicology" and energized the field? The report proposed a vision and strategy for using the new tools and approaches to predict a chemical's effects on human beings, not rodents, and to use them directly in risk assessment, not hazard identification. Workshop participants felt this was best achieved through enhanced coordination of existing efforts and a more strategic focus on human risk assessment. There was a clear call for an over-arching steering committee to look for potential synergies across current efforts and to foster new initiatives that complement current efforts by focusing on NRC vision elements that are not yet being fully addressed. Without such coordination and targeted efforts, full implementation of the widely heralded NRC proposal could be delayed a decade or more beyond the one or two decades already envisioned in the report.

For information on the workshop visit http://htpconsortium.wordpress.com/resource-materials/

adapted from AltTox Digest
November/December 2010

Message to members of EUSAAT

Dear members of EUSAAT,

The EUSAAT board decided at the board meeting in Linz 2010 that ALTEX Edition shall continue to send the invoices for the membership fees. ALTEX Edition will also keep account of the member address database. Please inform ALTEX of any change in your address via fpg@altex.ch. The invoices for the 2011 membership fees will be sent out in February 2011.

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