CH: Doerenkamp Zbinden Award 2009 for Toxicology in the 21st Century team

The Doerenkamp-Zbinden Foundation for Alternatives in Biomedicine presented the 2009 Doerenkamp-Zbinden Award (with 25,000 CHF) to the individuals who were instrumental in launching the "Toxicity Testing in the 21st Century – a Vision and a Strategy" movement. The "Tox-21C" movement involves the elaboration of the NAS/NRC vision report, the alliance of various US federal agencies and the resulting new EPA toxicity testing strategy.

The individuals honored are: Daniel Acosta, Jr., University of Cincinnati; Melvin Andersen, The Hamner Institutes for Health Sciences; Henry Anderson, Wisconsin Division of Public Health; Chris Austin, National Institute of Health; John Bailar III, University of Chicago; Kim Boekelheide, Brown University; Robert Brent, Thomas Jefferson University; John R. Bucher, US EPA; Gail Charnley, Health Risk Strategies; Vivian Cheung, University of Pennsylvania; Ralph Cicerone, National Academy of Sciences; Francis S Collins, National Institutes of Health; Michael Firestone, United States Environmental Protection Agency (US EPA); George M. Gray, US EPA; Sidney Green, Howard University; Robert Kavlock, US EPA; Karl Kelsey, Harvard University; Nancy Kerkvliet, Oregon State University; Melissa Kramer, US EPA; Daniel Krewski, University of Ottawa; Abby Li, Exponent, Inc.; Ellen Mantus, National Academy of Sciences; Lawrence McCray, Massachusetts Institute of Technology; Otto Meyer, The National Food Institute; D. Reid Patterson, Reid Patterson Consulting; William Pennie, Pfizer, Inc.; Robert Scala, Exxon Biomedical Sciences (retired); Gina Solomon, Natural Resources Defense Council; Martin Stephens, The Humane Society of the United States; Raymond Tice, National Institute of Environmental Health Sciences/National Toxicology Program, James Yager, Johns Hopkins University; Lauren Zeise, California Environmental Protection Agency; Hal Zenick, US EPA

"Toxicity Testing in the 21st Century – a Vision and a Strategy" closely parallels the vision of the DZF's scientific founder, the late toxicologist Gerhard Zbinden, who long sought a paradigm shift in toxicology. This report calls for a collaborative effort across the toxicology community to rely less on animal studies and more on *in vitro* tests using human cells and lower organisms, as well as computational toxicology, to identify chemicals with toxic effects. "Tox 21C" was the center of discussions at WC7 in Rome.

Franz P. Gruber (President of the DZF) announced the award in Rome and conveyed the congratulations and sincere gratitude of Hildegard J. Doerenkamp, the co-founder of DZF, and Elisabeth Zbinden, the widow of Gerhard Zbinden, to the award winners.

The award sum of 25,000 CHF will be used for an EU-US meeting on implementation of the Toxicology in the 21st Century.

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CH: ALTEX awards for Marcel Leist et al. and Thomas Hartung

The article "The biological and ethical basis of the use of human embryonic stem cells for *in vitro* test systems or cell therapy" by Marcel Leist (Doerenkamp-Zbinden Chair for Alternative in vitro Methods, University of Konstanz, Germany), Susanne Bremer (Institute for Consumer Health and Protection, EU Joint Research Center, Ispra, Italy), Patrik Brundin (Wallenberg Neuroscience Center, Lund University, S-22184 Lund, Sweden), Jürgen Hescheler (Institute of Neurophysiology, University of Cologne, Germany), Agnete Kirkeby (Memorial Sloan Kettering Cancer Center, Developmental Biology, New York, USA; H. Lundbeck A/S, Valby, Denmark), Karl-Heinz Krause (Centre Medical Universitaire 1, Geneva, Switzerland), Peter Pörzgen (Hawaii Pacific University, Kaneohe, USA), Michel Pucéat (INSERM/Université-EvryUMR-861, Evry, France), Mathias Schmidt (Nycomed GmbH, Konstanz, Germany), André Schrattenholz (Proteosys AG, Mainz, Germany), Naomi B. Zak (CellCure Neurosciences Ltd., Jerusalem, Israel), Hannes Hentze (S*BIO Pte Ltd, Singapore), published in ALTEX 3/2008 was chosen for the ALTEX Prize 2009 by the editorial office and the advisory committee of ALTEX Edition.

In an ongoing ethical debate opinions of different groups are based on varying sets

of religious, historical, cultural and scientific arguments as well as on widely differing levels of general information. In this article the authors give an overview of the biological background for non-specialists, and address all issues of the current stem cell debate that are of concern in different cultures and states. Thirty-five chapters address embryo definition, potential killing and the beginning of human life, in addition to matters of human dignity, patenting, commercialisation and potential alternatives for the future, such as induced pluripotent (reprogrammed) stem cells. All arguments are compiled in a synopsis, and compromise solutions, e.g. for the definition of the beginning of personhood and for assigning dignity to embryos, are suggested. Until recently, the major application of hESC was thought to be transplantation of cells derived from hESC for therapeutic use. The authors discuss that the most likely immediate uses will rather be *in vitro* test systems and disease models. The full article can be downloaded from www.altex.ch.

Again an honorary certificate is presented to Thomas Hartung for his "Food for thought ..." series. Food for thought ... on animal tests in 1/08, ... on the evolution of toxicology and phasing out of animal testing in 2/08 (together with Marcel Leist), ... on alternative methods for cosmetics safety testing in 3/08 and ... on food safety testing (together with Herman Koëter) in 4/08 made ALTEX famous all over the world. All these articles can also be downloaded from www.altex.ch.

ALTEX Edition is proud to have such authors and congratulates.

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CH: Roche joins forces to innovate toxicity testing and to reduce animal experimentation

In May 2009, Roche opened the Joint Science & Technology Laboratory in Basel, Switzerland, where Roche Pharma scientists are using the innovative xCELLigence real-time Cell Analyzer system of Roche Diagnostics to investigate hepatic and cardiac toxicities *in vitro*. This new technology will improve the predictive value of *in vitro* assessments of organ toxicity and help to reduce animal testing in toxicity research.

Cell-based *in vitro* assays are a key tool for early assessment of drug candidates. Toxicology routinely employs these assays, for example to determine genotoxicity. The non-clinical safety community is developing other assays especially for prediction of organ-specific toxicity.

"New techniques such as real-time cell analysis with the xCELLigence system will accelerate the ability to identify the toxic potential of a compound at an early stage of drug development, which supports also Roche's 3Rs concept of Reducing, Refining, and Replacing animal experimentation", stated Thomas Singer, Head of Global Non-Clinical Safety at Roche Pharma.

"This project is yet another example for the advantage of having pharma and diagnostics under one roof", added Manfred Baier, Head of Roche Applied Science. "We are in the process of identifying more and more opportunities in working together for more efficient processes and in the development of treatments that are tailor-made for the patients."

The uniqueness of the non-invasive and label-free xCELLigence technology is based on measuring the impedance of cells: The variations in electrical resistance are caused by changes in numbers, adhesion or shape of the cells. In conjunction with its user-friendly data collection and analysis capabilities, the xCELLigence system makes a unique platform for continuous, real-time cell-based assays and provides a huge opportunity for cellular and molecular biology.

The data from the xCELLigence real-time impedance measurement, combined with molecular profiling of the toxic effects of compounds on cardiomyocytes and hepatocytes, will be compared to conventional cell biology assays and molecular endpoints. Based on this platform, the goal is to develop new prediction methods for target organ toxicity *in vitro* and identify new cellular biomarkers for toxicity prediction.

Press release, 18th May 2009
Roche Diagnostics
www.roche.com

EU: EFSA's Scientific Committee promotes alternatives to animal testing

The European Food Safety Authority (EFSA) Scientific Committee has underlined the importance of risk assessment approaches in the area of food and feed safety that not only minimise the use of experimental animals and their suffering but also lead towards the replacement of animal testing. The committee's published opinion reviews the state-of-the-art concerning the use of experimental animals in different areas of EFSA's risk assessment activities, and outlines strategies to reduce the number of animal studies needed.

The opinion stresses that animal testing should be conducted in line with guidelines endorsed by the European Commission, EU agencies or other international bodies such as the OECD. It also recommends a dialogue between EFSA and the European Commission on the best ways to address the inclusion of new, validated testing methods in existing guidelines based on the replacement, reduction and refinement of animal testing. Further-

more, it stresses the importance of good communication in this area among the different agencies dealing with chemical risk assessment.

"This opinion is a thorough review of the guiding principles on the use of animals for experimental purposes. It summarises possibilities for replacement, reduction and refinement of animal testing within the different areas of EFSA's activities. We hope it will help EFSA in further developing a proactive approach to animal welfare in its risk assessment activities based on sound scientific principles", said Professor Vittorio Silano, Chair of EFSA's Scientific Committee.

Most of the risk assessments conducted by EFSA require experimental data. It is currently not possible to obtain all the necessary data and information required to ensure a high level of consumer protection without some use of animal experiments.

This opinion lists the type of internationally-recognised alternative methods to animal testing which are available for different types of studies used in risk assessment – e.g. acute toxicity, skin irritation and eye irritation testing – and says that these should be used in line with existing Community legislation1. For areas where alternative methods cannot provide all of the necessary information, such as reproductive and developmental toxicity, the opinion describes integrated testing and risk assessment strategies which can help to reduce the need for animal experiments.

The opinion also proposes ways to better implement animal welfare practices within EFSA's work. The Scientific Committee notes that, in line with existing EU legislation, applicants submitting dossiers to EFSA should use accepted alternative methods to animal testing whenever possible. Moreover, the opinion emphasises the importance of fully reflecting the use of such methods in any guidelines for applicants developed by EFSA. The Scientific Committee also recommends that, when carrying out risk assessments, all existing data should be reviewed before any additional animal studies are requested.

This opinion is in line with EFSA's commitment to continuing to improve animal welfare when conducting risk assessments. The Scientific Committee recommended that EFSA should follow up on this opinion with a review of progress in the field of alternatives to animal testing in three years' time.

Press release, 8th June 2009
EFSA, European Food Safety Authority
www.efsa.europa.eu

EU: Two open calls for scientists at ECVAM

The European Centre for the Validation of Alternative Methods (ECVAM) is currently renewing its Scientific Advisory Structure.

In the context of this renewal ECVAM is publishing two open calls for the expression of interest addressed to experts in

- life and environmental sciences,
- medicine,
- chemistry,
- toxicology,
- test method and test strategy validation,
- risk assessment,
- other areas such as statistics, biometry, epidemiology, modelling approaches.
- The first call is dedicated to the new ECVAM Scientific Advisory Committee (ESAC). The 19 ESAC members, preferably senior scientists with a generalist profile, will be in charge of advising ECVAM on all scientific aspects of its work and, in particular, with regard to the scientific validity of methods that replace, reduce, or refine animal experiments. Deadline for submitting an expression of interest in the ESAC is 30 September 2009.
- The second call concerns the formation of an ECVAM Expert Pool (EEP) to support ECVAM's mission through direct expert advice to ECVAM and ESAC (e.g., through participation in ESAC Working Groups, task forces, or workshops). Preference will be given to experts with profound specialist knowledge in one or more areas. The call will be published mid-September. No deadline is foreseen at present.

All relevant information, including the application procedure, can be found on http://ecvam.jrc.ec.europa.eu/index.htm

ECVAM Scientific Advisory Committee (ESAC)

The ESAC, well known through its many published statements on the validity of Alternative Test Methods, will be renewed through an open call. Its members, senior scientists with a generalist profile, will be selected solely on the basis of their scientific and other qualifications and must act independently of any third party interest. The new ESAC will continue to work as a standing committee and will focus on providing scientific advice to ECVAM, e.g. through issuing published opinions on the scientific validity of ECVAM-evaluated Alternative Test Methods and other aspects related to alternatives to animal testing.

ECVAM Expert Pool (EEP)

Scientists from the ECVAM Expert Pool (EEP), a roster of highly specialised ECVAM associated experts, will support the ESAC through their participation in dedicated ESAC working Groups, each chaired by an ESAC full member. The EEP will be created through an open call. Scientists listed in the EEP may also contribute to other project-related working groups of ECVAM, such as task forces or validation management groups and specific ECVAM workshops.

ECVAM News, 28.08.2009

EU: Open Call for Tender at ECVAM

The Institute for Health and Consumer Protection (IHCP) has launched an open call for tender for ECVAM of the In Vitro Methods Unit. The aim of the call is to invite laboratories to participate in the initial phase (phase III prevalidation) of the evaluation of three test methods designed for the assessment of the skin sensitisation potential of substances. The three methods are: 1) the Direct Peptide Reactivity Assay, 2) the Myeloid U937 Skin Sensitisation Test (MUSST) and 3) the human Cell Line Activation Test (h-CLAT). Within this project, the selected laboratories will work in close contact with multinational companies as well as the European Commission's Joint Research Centre.

Access to the official notice:
Document no: 2009/S 166-239612 (pdf) available from the Tenders Electronic Daily Homepage

Deadline for submitting offers:
13 October 2009

Contact Address:
Further information, including the relevant tender documents, can be obtained from jrc-ihcp-procurement@ec.europa.eu,
Tel: +39-0332-789197;
Fax: +39-0332-789434

In Vitro Methods Unit/ECVAM
Institute for Health & Consumer Protection (IHCP)
European Commission - Joint Research Centre (EC-JRC)

GER: Toxicologist wanted for commenting animal test proposals under REACH

The registered non-profit association Doctors Against Animal Experiments Germany is looking for a toxicologist for commenting animal test proposals within the 45 day REACH review period.

Job description:
The proposals are to be examined in order to determine whether the data required already exist or can be obtained by other (animal-free) testing methods.

Prerequisites:
- Dedication to animal welfare.
- Experience in regulatory processes, especially in the registration of chemical substances.
- Experience in researching animal-free testing methods.
- Excellent (professional) written and spoken English.

Time frame:
Commencing early 2010, initially for at least half a year. An extension is possible.

Place of work:
Free choice of location. A workplace will not be supplied.

Salary:
Full-time or part-time employment or payment on a fee basis are possible. Voluntary collaboration is also welcome.

The financial possibilities of our non-profit organisation are limited.
Please send a short application with curriculum vitae and salary or fee expectation by November 30th 2009 to:

Ärzte gegen Tierversuche e.V.
Landsbergerstr. 103
80339 München
Germany
Phone +49 (0)89 3599349
Fax +49 (0)89 35652127
e-mail:
info@aerzte-gegen-tierversuche.de
www.aerzte-gegen-tierversuche.de

GER: 20 years ZEBET

The Centre for Documentation and Evaluation of Alternatives to Animal Experiments (ZEBET) was established in 1989. For twenty years ZEBET has actively contributed to ensure the implementation of the 3Rs principle described by William Russel and Rex Burch in 1959 into administrative and scientific practice. To celebrate the 20th Anniversary of ZEBET and the 50th Anniversary of the publication of "The Principles of Humane Experimental Technique" by Russell and Burch, a two-day conference will be held at the BfR in Berlin on 26-27 October 2009. ALTEX is invited to print the abstracts of this conference in the next issue 4/2009.

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IND: Mahatma Gandhi-Doerenkamp Center for alternatives to animal use in life science education and *in vitro* toxicology

A Mahatma Gandhi-Doerenkamp Center for alternatives to animal use in life science education and *in vitro* toxicology was established as a national center for alternatives in India at Bharathidasan University, Tiruchirappalli, Tamil Nadu. The Bharathidasan University is a renowned university under the University Grants Commission of the Government of India. The mandate of the Center is to synergise the Gandhian philosophy of "Ahimsa" or "Non-Violence" with the teaching/research of life sciences. The Center was established with the generous financial support of the Doerenkamp-Zbinden Foundation, Switzerland, and includes the establishment of a "Gandhi-Gruber-Doerenkamp Chair" for alternatives in biomedical education. The Center was established in the belief that promoting humane science is an imperative scientific, legal, psycho-social, ecological and economic need. The Center will strive to create a strong positive presence of alternatives to the use of animals in India, thereby promoting quality and excellence in life science education, research and testing by way of continuous training programmes, an alternatives knowledge base, a library and a certificate/diploma/post-graduate diploma programme in alternative methods.

The Center will also bring together stakeholders in the 3Rs, i.e. academia, scientific community, industry, government and animal welfare personnel from national/international levels, to raise the awareness and facilitate the exchange of information and ideas on alternatives to translate the vision of the 3Rs into policy and curricular changes in India as relevant to education and research. The Center will also help by way of funding the research and development of environmentally friendly pedagogical tools and *in vitro* alternative methods for life science teaching and research. The twin approach will be to encourage the use of e-tools, to help establish virtual learning centres for teaching, and to establish a state-of-the-art cell culture laboratory for training in non-animal methods of research and product testing. The Center will essentially be a service provider for non-animal methods in learning, research and testing.

The Center is the fruitful culmination of a decade's work of People *for* Animals, Chennai, and I-CARE, Chennai, in promoting the concept of the 3Rs in India.

Prof. Akbarsha, Trichy, India

NL: Dieter Lütticken award 2008 recognizes development of new vaccine quality control assay

The Dieter Lütticken Award 2008 for alternatives in animal testing goes to Dr. Ivo Claassen for a project that he has managed at the Central Veterinary Institute (CVI), Lelystad (The Netherlands). The announcement was made by Prof. Coenraad Hendriksen, chairperson of an independent expert jury panel and Professor of Alternatives to Animal Testing at Utrecht University (The Netherlands).

Dr. Claassen had a leading role in an interdisciplinary team with Dr. Riks Maas and Dr. Hok Oei from the CVI in close collaboration with Dr. Jean Marc Spieser and Dr. Catherine Milne of the European Directorate on Quality of Medicines (EDQM), Strasbourg (France). The team developed an *in vitro* potency test for the routine quality control of inactivated Newcastle Disease Virus (NDV) vaccines. Previously, quality control of NDV vaccines included an *in vivo* potency assay in chickens. The new method allows avoiding the use of chickens and has now been included in the respective European *Pharmacopoeia* monograph as an additional potency assay to release NDV vaccines. The research project was largely funded by the Department of Agriculture, Nature and Food Quality in the Netherlands.

"The new *in vitro* potency test is an attractive alternative for the existing *in vivo* potency tests especially with regard to the objective of the European regulatory authorities to replace, reduce and refine (3R) the use of laboratory animals for production and quality control of immunobiologicals", said jury chair Prof. Hendriksen.

Intervet/Schering-Plough Animal Health, a leading global animal health company, sponsors the international Dieter Lütticken Award for alternatives in animal testing to support individual scientists and life science research institutions that make significant contributions to the 3R concept, i.e. reducing, refining and/or replacing the use of animals in testing for development and manufacturing of veterinary medicines. The Company recently became a member of EPAA, the European Partnership for Alternative Approaches to Animal Testing.

The total amount of the award is € 20,000 and was presented to Dr. Claassen on September 3, 2009 during the

award session at the 7th World Congress on Alternatives and Animal Use in the Life Sciences.

Candidates for the Dieter Lütticken Award are selected by a jury panel composed of experts from public institutions in the animal health and animal testing sector. Applications for the Dieter Lütticken Award 2009 can be submitted until November 15, 2009.

For submissions and more details, please contact Intervet/Schering-Plough Animal Health – Global Communications Animal Health (communications@intervet.com).

Press release, 7th April 2009
Intervet/Schering-Plough Animal Health
www.intervet.com

OECD/USA: Animalfree testing of severe eye irritation

The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Center on the Validation of Alternative Methods (ICCVAM) are pleased to announce that two ICCVAM-recommended nonanimal safety testing methods have been officially adopted as Health Effects Test Guidelines by the 30 member countries of the Organisation for Economic Co-operation and Development (OECD). These methods, the bovine corneal opacity and permeability (BCOP) and isolated chicken eye (ICE) test methods, can now be used around the world for identification of substances that may cause severe irritation or permanent damage to eyes without the use of animals.

Following an extensive review of their validation status by NICEATM and ICCVAM, the BCOP and ICE test methods were accepted last year by U.S. Federal agencies. (See NIEHS press release, "Newly Approved Ocular Safety Methods Reduce Animal Testing", June 23, 2008). NICEATM and ICCVAM, in collaboration with validation organizations in Europe and Japan, then drafted test guidelines based on the ICCVAM recommendations for submission to OECD. The new test guidelines, which have been designated Test Guidelines 437 (BCOP) and 438 (ICE), were formally adopted by the OECD Council this past Monday, September 7. This represents the fastest ever adoption of new test guidelines by OECD. The prompt acceptance was due in large part to the comprehensive ICCVAM evaluation of the test methods and the involvement of international validation partners in the development of the test guidelines.

Final versions of Test Guidelines 437 and 438 are expected to be published in late October and will be available on the NICEATM-ICCVAM (http://iccvam.niehs.nih.gov/) and OECD (http://www.oecd.org) websites at that time.

USA: News from NICEATM and ICCVAM

The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) are pleased to provide this first update to ALTEX on recent and planned activities. ICCVAM consists of representatives from 15 U.S. Federal regulatory and research agencies that use, generate, require, or disseminate toxicological information. In accordance with the ICCVAM Authorization Act (Public Law 106-545, 42 United States Code 285l-3), ICCVAM conducts technical evaluations of new, revised, and alternative toxicological test methods with regulatory applicability, and forwards recommendations on their scientific validity to U.S. Federal agencies. ICCVAM also promotes the scientific validation and regulatory acceptance of test methods that more accurately assess the safety or hazards of chemicals and products while reducing, refining, and/or replacing animal use. NICEATM administers ICCVAM and provides scientific support for ICCVAM-related activities, including the conduct of validation studies. NICEATM and ICCVAM work to achieve national and international harmonization and adoption of appropriately validated test methods. We look forward to providing future updates on a regular basis.

International Cooperation on Alternative Test Methods

Representatives for NICEATM-ICCVAM, the Japanese Center for the Validation of Alternative Methods (JaCVAM), the European Centre for the Validation of Alternative Methods (ECVAM), and Health Canada signed a memorandum of cooperation on April 27 that is expected to expedite the international validation and acceptance of alternative methods that can refine, reduce, and replace animal use for consumer product safety testing worldwide. The agreement will yield globally coordinated scientific recommendations on alternative toxicity testing methods that should speed their adoption in each of these countries and by international organizations such as OECD.

The agreement covers three critical areas of test method evaluation: validation studies, independent scientific peer review meetings and reports, and development of harmonized test method

recommendations for regulatory consideration. The International Cooperation on Alternative Test Methods (ICATM) will promote enhanced cooperation and coordination on the scientific validation of alternative toxicity testing methods. Well-designed and conducted international scientific validation studies that adequately determine the usefulness and limitations of alternative test methods for identifying product related health hazards are expected to be more readily accepted by regulatory agencies.

More information about the agreement, and a link to the memorandum of cooperation, can be found on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/about/icatm.htm

Peer Review Panel on New Versions and Applications of the Murine Local Lymph Node Assay

NICEATM and ICCVAM recently convened an international independent scientific peer review panel (Panel) to evaluate new applications and modified versions of the murine local lymph node assay (LLNA). The Panel, which included 15 expert scientists from the United States, Czech Republic, Netherlands, United Kingdom, France, and Japan, met in public session on April 28-29 at the U.S. National Institutes of Health (NIH) headquarters in Bethesda, MD. It was chaired by Dr. Michael Luster, a distinguished scientist who recently retired from the U.S. National Institute of Occupational Safety and Health.

The Panel supported the use of two nonradioactive versions of the LLNA (the LLNA: DA and the LLNA: BrdU-ELISA), with certain limitations, to identify substances as potential skin sensitizers and nonsensitizers. The Panel recommended that the conduct of an interlaboratory study for a third nonradioactive version, the LLNA: BrdU-FC (flow cytometry), should be given a high priority based on the test method's demonstrated accuracy and intralaboratory reproducibility. The Panel also concluded that the LLNA could be used to test any material for allergic contact dermatitis potential unless the substance has properties that might interfere with the assay. These recommendations are expected to broaden the use of the LLNA and therefore further reduce and refine the use of animals for skin sensitization testing.

The materials reviewed by the Panel, and the Panel's full report detailing their conclusions and recommendations, are available on the NICEATM-ICCVAM website (http://iccvam.niehs.nih.sgov/methods/immunotox/llna_PeerPanel.htm). ICCVAM will consider the Panel's report, public comments, and comments from the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) as it prepares final test method recommendations to forward to U.S. Federal agencies.

Peer Review Panel on Alternative Methods for Ocular Safety Assessments

NICEATM and ICCVAM convened an international independent scientific peer review panel (Panel) to evaluate alternative test methods and approaches that may further reduce and refine the use of animals for ocular safety testing. The Panel met on May 19-21 at U.S. Consumer Product Safety Commission Headquarters in Bethesda, MD. The Panel was chaired by Dr. Wallace Hayes of the Harvard School of Public Health, and included 22 scientists from six countries.

Highlights of the Panel's conclusions and recommendations include:

- Topical anesthetics and systemic analgesics should routinely be used prior to any *in vivo* ocular irritancy testing. The Panel recommended a protocol of specific pain-relieving drugs and schedule of administration to effectively avoid or minimize discomfort.
- Two *in vitro* test methods for identifying ocular irritants (the bovine corneal opacity and permeability [BCOP] and Cytosensor Microphysiometer® [CM] test methods) could be used in limited circumstances as screening tests to identify some products and substances that would not require hazard labeling for eye irritation.
- Proposed non-animal testing strategies using three *in vitro* test methods (the BCOP, CM, and EpiOcular™ test methods) to assess the eye irritation potential of antimicrobial cleaning products for EPA ocular hazard classification and labeling purposes appear promising. The Panel recommended that studies to further characterize the *in vitro* test methods, and that testing strategies should be designed in coordination with ICCVAM.

The materials reviewed by the Panel and the full report detailing their conclusions and recommendations are available on the NICEATM-ICCVAM website (http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm). ICCVAM will consider the Panel's report and public and SACATM comments as it prepares final test method recommendations to U.S. Federal agencies.

Federal Agencies Accept ICCVAM Recommendations on In Vitro Pyrogenicity Test Methods

U.S. Federal agencies have accepted and endorsed ICCVAM recommendations on five *in vitro* test methods proposed for assessing potential pyrogenicity of pharmaceuticals and other products. These test methods should now be considered prior to conducting *in vivo* pyrogenicity testing, and should be used where determined appropriate for specific testing situations. The availability of these test methods may reduce the number of animals required for pyrogenicity testing. These test methods were also recently adopted by the European Pharmacopeia ("EDQM Accepts Alternative to Rabbit Pyrogen Test", ALTEX, February 2009). ICCVAM agency responses and other information about the test method evaluation are posted on the NICEATM-ICCVAM website at http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm.

NICEATM-ICCVAM Submissions to OECD Test Guidelines Program

NICEATM and ICCVAM actively contribute to the development of guidelines for the testing of chemicals by the Organisation for Economic Co-operation and Development (OECD). Last year, NICEATM and ICCVAM, in collaboration with JaCVAM and ECVAM, developed and submitted draft test guidelines for two ICCVAM-recommended non-animal safety testing methods, the BCOP and isolated chicken eye (ICE) test methods, for use in identification of potential ocular corrosives and severe irritants. The draft test guidelines, which have been designated Test Guidelines 437 (BCOP) and

438 (ICE), were approved by the OECD National Coordinators in March and by the Joint Meeting in June. Following formal adoption by the OECD Council, they will be available on the OECD and NICEATM-ICCVAM websites. The comprehensive ICCVAM evaluation process that included close cooperation with ECVAM, JaCVAM, and the OECD Secretariat contributed significantly to the rapid international consideration and adoption of these test guidelines.

NICEATM and ICCVAM recently forwarded additional submissions to the OECD Test Guidelines Program for the following:

- Skin sensitization testing:
  - A proposed update to Test Guideline 429 for the LLNA to incorporate revisions to the standard protocol, including reducing the number of animals required, guidance on choosing the appropriate test doses, guidance on collection of individual animal data, and guidance on reducing the number of concurrent positive controls.
  - New draft test guidelines for two non-radioactive LLNA test methods (the LLNA: DA and the LLNA: BrdU-ELISA)
- Acute oral systemic toxicity:
  - A draft guidance document on the use of *in vitro* cytotoxicity tests to estimate starting doses for acute oral systemic toxicity tests
- Dermal corrosivity testing:
  - Updates to Test Guidelines 430 and 431 (*in vitro* test methods to identify dermal corrosives) to include performance standards

The draft documents are available on the OECD website, and public comments on the documents are being accepted through early September.

NICEATM and ICCVAM at the Seventh World Congress on Alternatives and Animal Use in the Life Sciences

The Seventh World Congress on Alternatives and Animal Use in the Life Sciences (WC7) has taken place in Rome, Italy, on August 31-September 3. ICCVAM members and NICEATM staff chaired several sessions and made numerous oral and poster presentations. NICEATM-ICCVAM poster presentations are available on the NICEATM-ICCVAM website http://iccvam.niehs.nih.gov/meetings/7thWC/7WCablst.htm.

Upcoming NICEATM-ICCVAM Public Meetings

An international validation study, coordinated by NICEATM and conducted in collaboration with JaCVAM and ECVAM, of an *in vitro* stably-transfected estrogen receptor (ER) transcriptional activation assay (STTA) for screening chemicals for potential endocrine disruptor activity is currently nearing completion. The assay, LUMI-CELL ER, uses a human cell line transfected with the human estrogen receptor, and is being evaluated with 78 coded chemicals previously recommended for the validation of ER and androgen receptor *in vitro* methods. The test method and proposed performance standards for STTA ER assays will be reviewed by an independent scientific peer review panel tentatively scheduled to meet in May 2010. Information on the validation study is available on the NICEATM-ICCVAM website at http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm. Information about the peer review panel meeting and draft documents for review by the Panel will be posted on this webpage.

NICEATM and ICCVAM in conjuction with ECVAM and JaCVAM are organizing an international workshop on alternative methods to reduce, refine, and replace the use of animals in vaccine potency and safety testing. The workshop is scheduled for September 14-16, 2010, at the William H. Natcher Conference Center on the main campus of the NIH in Bethesda, MD. More information about the workshop will be posted at http://iccvam.niehs.nih.gov/methods/biologics/biologics.htm as it is available.

For More Information

Questions about NICEATM and ICCVAM activities are welcomed and can be directed to:
Dr. William S. Stokes, Director,
NICEATM, at niceatm@niehs.nih.gov;
phone 919-541-2384;
fax 919-541-0947.
Copies of documents mentioned in this update can also be obtained by contacting NICEATM.

Information on availability of NICEATM and ICCVAM draft documents, requests for nominations of experts to participate at workshops and on peer review panels, and specific information about NICEATM-ICCVAM meetings is communicated via the ICCVAM-all email list and in notices posted in the U.S. Federal Register.

Subscribers to the ICCVAM-all email list are notified directly of NICEATM-ICCVAM activities. Subscribers receive email notification of publication of NICEATM-ICCVAM Federal Register notices, availability of NICEATM-ICCVAM reports, notices of upcoming meetings, requests for public comments or data, and other events of interest to our stakeholders. If you would like to subscribe to the ICCVAM-all list, or for more information, please visit the NICEATM-ICCVAM website at **http://iccvam.niehs.nih.gov/contact/ni_list.htm.**

USA: IIVS News

Located in the US (Gaithersburg, Maryland), the Institute for In Vitro Sciences, Inc. (IIVS) is a non-profit organization wholly dedicated to the advancement of alternative (*in vitro*) testing methods. To achieve our mission we have created a framework based upon three integrated centers of excellence: Science, Education, and Outreach. This foundation provides a unique forum in which our customers, contributors, regulatory agencies and animal protection organizations can work collaboratively to advance science and animal welfare.

Science, to apply the technology
Rigorous science is the foundation for all IIVS activities. Using innovative technologies, IIVS scientists design efficient testing strategies that help predict product safety and effectiveness for makers of cosmetics, personal care, and household products. Our laboratory also functions as a center for international validation studies and training seminars.

Education, to broaden the use
As a leader in *in vitro* testing, IIVS recognizes the value of sharing knowledge. IIVS scientists share their unique perspective and expertise regarding the use and application of *in vitro* methods. Our scientists host workshops, publish manuscripts, and speak at scientific conferences giving others the tools they need to implement programs and advance the field.

Outreach, to increase acceptance
Outreach is the culmination of our scientific and educational efforts. IIVS utilizes highly focused interactions with government agencies, industry and animal protection groups to increase acceptance of *in vitro* testing.

We appreciate and look forward to sharing our activities with ALTEX readers through this IIVS News section in upcoming issues.

To learn more about our programs and activities please visit www.iivs.org

Alternatives Highlights – 1st Half 2009

In the fall 2008 issue of the IIVS newsletter, I suggested that 2009 would be a pivotal year for activities in the alternatives arena. Therefore I'm very pleased that already one significant event has occurred that seems to justify my optimism: the encouraging decision of the US EPA to begin a pilot program for registering anti-microbial cleaning products (AMCP) with the use of non-animal (*in vitro*) eye irritation data.

EPA's decision provides an exciting step forward, not only for IIVS and the limited number of companies and individuals that directly participated in the project, but also for the many other anti-microbial cleaning product companies that may utilize the proposed *in vitro* testing strategy. Although several years elapsed between the initial suggestion for the project from the EPA's Office of Pesticide Programs (OPP) Pesticide Program Dialogue Committee (PPDC) and the announcement of the pilot program on June 2nd of this year, all the participants feel that their efforts were well worth the time and that even more successes may lie ahead. Thanks go not only to the companies listed in the following paragraph but also to Pat Quinn of the Accord Group who had significant input on the strategy of the group and to Troy Seidel of PETA (now consultant to HSUS) who originally encouraged the PPDC to support the initiation of such a program.

Although many of the readers of the IIVS Update are aware of the AMCP project, I believe it is useful to review several important points. First, this program illustrates the advantages gained when companies work together toward a common goal. In this case seven companies – The Clorox Company, Colgate-Palmolive Company, The Dial Corporation, EcoLabs, JohnsonDiversey, Inc., S.C. Johnson & Son, Inc. and The Procter & Gamble Company – pooled data from historical *in vivo* studies and past (plus newly commissioned) *in vitro* studies to create a strong data base covering all major types of AMCP. Second, the object was to find a non-animal testing strategy for a small, restricted class of materials – AMCP. By keeping the target small and not attempting to prove the effectiveness of an ocular replacement for the universe of chemicals, our proposed strategy became much easier to substantiate. Third, frequent positive interactions with the EPA during the course of the project kept both sides well-informed of the thought process of the other.

As a result, the EPA's Office of Pesticide Programs (OPP) has agreed to an eighteen-month pilot program (http://www.epa.gov/oppad001) that will review the effectiveness of the proposed non-animal testing strategy. This pilot program "will involve determining the effectiveness of the decision tree, as well as whether submitted assays were conducted according to the published guidance and are acceptable. Initially, packages submitted to the EPA under the pilot will be reviewed by the workgroup. One member of the workgroup will perform the primary review, while a secondary review will be performed by one or more of the remaining workgroup members. Any issues which arise during this initial phase of the pilot will be discussed by the workgroup as a whole. Toxicity reviewers from the Antimicrobials Division (AD), who will ultimately be responsible for assessing these packages, will participate in these discussions."

"During this pilot phase, labeling decisions will be made using data acquired from these non-animal tests, as long as the testing methods and testing results are deemed by EPA to be adequate and appropriate to support labeling decisions. To ensure accuracy, the pilot will be conducted by a knowledgeable OPP team, experienced in the evaluation of these non-animal studies."

Some of the information received during this pilot program will likely

be shared with ICCVAM which has recently reviewed the supporting data. ICCVAM has given a more limited acceptance of the strategy by supporting its use for EPA I and EPA IV hazard categories and has suggested that additional data be generated. Look for more information on this program in future issues.

Rodger Curren, President IIVS

Meeting report – Forinvitox: from innovation to market success

The Forinvitox meeting was designed as a marketplace to facilitate communication between *in vitro* method developers and users of the models, including scientists from industry and regulatory agencies. Held at the prestigious Karolinska Institute in Stockholm, Sweden on May 12-14, the meeting drew 70 participants representing researchers, end users, producers, and regulators from the US and Europe. A total of 30 different methods with commercial potential for *in vitro* testing were presented as posters. Seventeen of these methods were presented orally and received feedback from participants who have experience in validating or incorporating *in vitro* methods into testing schemes. A vital part of the conference was the generously scheduled "market time" where participants could discuss the use of the methods informally. These sessions provided a very positive environment in which scientists from industry learned detailed information about methods and offered their advice on how such methods might be marketed to industry.

Rodger Curren and Erin Hill of IIVS gave two oral presentations regarding the use of reconstituted skin models and led a discussion about points to consider as developers move toward acceptance. The event was supported jointly by the EU projects Forinvitox and Invitopharma and was organized by Silverdal Science Park of Stockholm, Sweden. For more information on the meeting please contact Erica Toft at Erica.toft@silverdal.se.

Practical Methods for *In Vitro* Toxicology Workshop 2009

IIVS held its 12th annual Practical Methods for In Vitro Toxicology Workshop last month (June 9-11). It was encouraging that several international participants were able to join us this year, including two toxicologists from the Shanghai Municipal Center for Disease Control and Prevention (SCDC) in China. This indicates the growing international awareness of non-animal testing methods. As always, the course featured several outside speakers, including Helena Kandarova of MatTek and Stephen Ferguson of Lifetech. The highlight of the workshop was the in-laboratory, hands-on instruction training provided by the IIVS biologists. If you are interested in attending the course next year, please contact Amanda Ulrey for additional information at aulrey@iivs.org. Tentative dates have been set for June 15-17, 2010.

BCOP and ICE Test Guidelines

Proposed OECD Test Guidelines for the Bovine Cornea Opacity and Permeability (BCOP) and Isolated Chicken Eye (ICE) assays for identifying corrosive or severe eye irritants were approved the last week of March 2009 at the 21st meeting of the OECD Working Group of National Coordinators of the Test Guideline Program. The Test Guidelines must be approved at the joint meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology before final approval by Council. It is hoped that these final steps will be completed by late summer 2009. ICCVAM/NICEATM led the effort to create the proposed Test Guideline, and IIVS staff played a significant role in the process.

OECD Draft Guideline for Skin Irritation

On June 14-17, 2009 the OECD held an expert meeting in Washington D.C. on a proposed *in vitro* skin irritation Test Guideline (TG). This Draft TG had originally been outlined based on the ability of the three *in vitro* models to predict European Union hazard categories defined by the appropriate risk phrase, e.g. R38, irritating to skin. However, it became clear that in the future most countries would be using the Globally Harmonized System (GHS), and so it would be more useful to have the final TG address the prediction of GHS hazard categories. This in fact has now been done, and the experts at the meeting reached agreement on most aspects of the proposed TG. Particularly important is that at least three reconstructed skin models will be referenced in the TG – EpiSkin, SkinEthic RHE and EpiDerm. However, different exposure protocols will be necessary for each tissue model in order to reach the same predictions. Hopefully, this TG will move forward with the same rapidity as the recent TG for ocular irritation, allowing the world to have an accepted OECD *in vitro* skin irritation TG sometime next year.

Recent IIVS Presentations:

2009 Society of In Vitro Biology Meeting

June 6 – 10 Charleston, SC, USA

Hans Raabe presented "3-Dimensional Tissue Models in Contract Research: Points to Consider for Efficacy, Product Development, or Regulatory Testing Programs"

10th Contact Dermatitis Meeting
July 9-11, Hershey, PA
Hans Raabe presented "In Vitro Methods for Evaluating Skin Irritation of Ingredients and Formulations"

CAAT Information Day on 7th Amendment to the Cosmetics Directive
July 8, Baltimore, MD, USA
Rodger Curren presented "Developing non-animal testing strategies for the cosmetics industry."

World Congress on Alternatives & Animal Use in the Life Sciences
Aug. 30-Sept. 3, 2009, Rome, Italy
Industry Activities
R. Curren presented "Providing Solutions for Industry, Regulators and the Animal Protection Community"
Skin and Eye Toxicity 1
Rodger Curren chaired session and presented "Current Regulatory Status of in vitro Dermal Toxicity Assays"
IIVS was also present with 7 posters throughout the congress.

5th International Workshop on Genotoxicity Testing
Aug. 17 -19, 2009, Basel, Switzerland
Rodger Curren presented "Performance Characteristics of the Reconstructed Skin Micronucleus Assay"

Chinese Society of Toxicology
Aug. 10-13, 2009 Guiyang, Guizhou Province, China. Hans Raabe gave a poster presentation "Use of Histopathology to Improve Predictive Capacity of the Bovine Corneal Opacity and Permeability Assay".

Upcoming Events
Eurotox
September 13-16, Dresden, Germany
Please visit the IIVS booth.

Personal Care Products Council Science Symposium
Oct. 27-29, 2009, Newark, NJ, USA
Please visit the IIVS booth.

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USA: Pfizer and US EPA enter into agreement to exchange data

In a groundbreaking development, the pharmaceutical giant Pfizer, Inc. has agreed to provide the U.S. Environmental Protection Agency (EPA) with human data on the toxicity of 100 chemicals, which will then be compared to the output of the high-throughput (HTP) tests of the agency's ToxCast program. The agreement was announced by Robert Kavlock, director of the EPA's National Center for Computational Toxicology, during the National Academy of Sciences recent conference on "Toxicity Pathway-based Risk Assessment: Preparing for a Paradigm Change", and reported in the Bureau of National Affairs' *Chemical Regulation Reporter* on May 18th.

Pfizer had been developing these chemicals as potential new drugs but the candidates proved to be too toxic to humans. The company will be providing the chemicals as well as data on doses, blood levels, and effects to EPA. Under the agreement, the first of its kind, the EPA will screen the chemicals, compare its HTP data to the human data, and provide the information to the company.

The EPA has relied primarily on animal data when assessing the HTP data generated in ToxCast and the related Tox21 initiative, which are designed to prioritize chemicals for testing. If other pharmaceutical companies share their human data with the EPA, then the HTP data can increasingly be interpreted and evaluated by comparison with data from the species of interest - humans.

Chemical Regulation Reporter,
May 18th 2009

USA: Russell and Burch Award 2009 for Thomas Hartung

The Humane Society of the United States (HSUS) bestowed its 2009 Russell & Burch Award to Thomas Hartung for advancing the development and implementation of non-animal methods in toxicity testing.

The HSUS presented the award at the 7th World Congress on Alternatives and Animal Use in the Life Sciences. Hartung is a co-organizer of the meeting. The award recognizes scientists who have made outstanding contributions toward the advancement of alternative methods in the areas of biomedical research, testing or higher education. Alternative methods are those that accomplish one or more of the "Three Rs" devised by William Russell and Rex Burch in 1959. The Three Rs are: Replacing or Reducing animal use in experiments and Refining methods so that animals experience less pain and distress.

Hartung was head of the European Centre for the Validation of Alternative Methods (ECVAM) from 2002 to 2008. He was recently appointed to two positions at Johns Hopkins University in Baltimore, Md.: director of the Center for Alternatives to Animal Testing (CAAT), and the inaugural Doerenkamp-Zbinden Chair for Evidence-Based Toxicology in the Department of Environmental Health Sciences at the Bloomberg School of Public Health. In addition, Hartung is honorary full professor at the University of Konstanz in Germany, an active affiliation he has maintained since teaching there.

"Thomas Hartung is recognized as the world's foremost authority on alternative methods of toxicity testing," said Martin Stephens, Ph.D., The HSUS' vice president for animal research issues. "In addition to being a scientist, administrator, author, and a sought-after speaker, Thomas is also an excellent magician, and he is slowly but surely helping to make many animal-based tests disappear."

As head of ECVAM, Hartung was responsible for coordinating the independent evaluation of non-animal tests, as well as organizing efforts to promote their scientific and regulatory acceptance. Hartung accelerated the process of validating alternative methods. The test strategies developed at ECVAM will change the way safety assessments for chemicals are carried out in Europe and elsewhere.

Hartung has also helped strengthen international cooperation and coordination among national and regional validation centers.

The Russell & Burch Award is a $5,000 prize and trophy. The 2009 Award comes on the 50th anniversary of the publication of William Russell and Rex Burch's pioneering book, The Principles of Humane Experimental Technique, detailing the Three Rs approach. The first Award was given in 1991 to Alan Goldberg, Hartung's predecessor as director of CAAT.

Press release HSUS

USA: National Academy of Sciences wins 2009 CAAT Recognition Award

The National Academy of Sciences (NAS) and the authors of the groundbreaking report, *Toxicity Testing in the 21st Century: A Vision and a Strategy*, were selected to receive the CAAT Recognition Award for 2009. The award was presented September 3 in Rome at the 7th World Congress on Alternatives and Animal Use in the Life Sciences.

This award, presented at every World Congress, honors an individual or organization that has made an outstanding contribution to the development of alternative methods or the field of *in vitro* science. The NAS and the report authors were a clear choice for this year's award. This visionary publication has done nothing less than launch a paradigm shift in toxicology, changing the way toxicology will be conducted in the future.

The NAS report advocates sweeping and transformative changes in regulatory toxicity testing. The report outlines a new approach that will rely less heavily on animal studies and instead focus on *in vitro* methods that evaluate chemicals' effects on biological processes using cells, cell lines, or cellular components, preferably of human origin. This new approach is expected to generate more robust data and expand capabilities to test chemicals more efficiently. It also promises to improve animal welfare and substantially reduce (and ultimately eliminate) the use of whole animals in toxicity testing.

This "toxicity testing of the 21st Century" should demonstrate more clearly than ever that the most humane science is also the best science.

Previous recipients of the CAAT Recognition Award include: Robert A. Scala, Herman B. W. M. Koëter, Andrew N. Rowan, Gerhard Zbinden, Per Ottar Seglen, Procter & Gamble Co., Avon Products Inc., Zeneca, Michael F. W. Festing, Julia H. Fentem, and Horst Spielmann.

Press release CAAT

USA: 2009 Charles River Laboratories' Excellence in Refinement Award

Paul Flecknell, PhD, widely recognized for his expertise in the identification and management of pain in laboratory animals, is the 2009 recipient of the Charles River Laboratories Excellence in Refinement Award. This award was presented on September 3 at the 7th World Congress on Alternatives and Animal Use in the Life Sciences in Rome, Italy.

Sponsored by Charles River Laboratories, in cooperation with the Johns Hopkins Center for Alternatives to Animal Testing (CAAT), the award honors an individual who has made an outstanding contribution to the development, promotion and/or implementation of refinement alternatives. "Refinement", one of the "3Rs of alternatives", refers to methods aimed at minimizing pain and distress for laboratory animals.

Flecknell was a clear choice for this refinement award, as much of his career has been devoted to making life less painful for laboratory animals. His efforts have greatly enhanced both our understanding of the complex nature of pain in laboratory animals and our ability to provide these animals with effective pain relief. His work is cited in nearly every paper that discusses pain in lab animals.

Flecknell currently is Director of the Comparative Biology Centre at the University of Newcastle (UK) and Professor of Laboratory Animal Science. His main research interests are anesthesia and analgesia of all species of animals and, in particular, the development of methods of pain assessment and alleviation.

The Charles River Laboratories Excellence in Refinement Award, which includes $5,000 to further the recipient's scientific endeavors, was established in 2005. The first award, presented at the 5th World Congress in Berlin, was given jointly to Dr. Bert van Zutphen and Dr. Georgia Mason. Dr. Linda Toth received the 2007 award.

Press release CAAT

WC7: Balls, Goldberg and Spielmann became "Patrons of animal welfare in the life sciences"

The last day of the World congress in Rome was dedicated to the celebration of the 50th anniversary of the publication of Russell and Burch's book on the reduction, refinement and replacement of the use of animals in life sciences. At this occasion the Congress unanimously named **Michael Balls** of FRAME, Nottingham, UK, **Alan Goldberg** of the Johns Hopkins University, Baltimore, USA and **Horst Spielmann** of the Free University of Berlin, Germany as the official Patrons of Animal Welfare in the Life Sciences. In handing the recognition awards to the Patrons, the Co-Chairs of the congress said: "Through their personal endeavour these three experts have achieved what for many years was considered impossible, namely to turn the reduction, refinement and replacement of experimental animals from an ethical issue and marginally scientific hobby into mainstream science, involving leading experts in life sciences around the globe." Co-Chair Prof. Thomas Hartung added: "Your work will not only be remembered in the decades to come, it will be continued at an increasing speed and level: the Johns Hopkins University Center for Alternatives in Animal Testing (CAAT) has already started a trans-Atlantic dialogue of the world's best experts to implement at national and regional levels such strategies for scientific risk assessment as proposed by a US National Academy of Sciences Committee of international experts."

Herman B. W. M. Koëter
and Thomas Hartung
Chairs, 7th World Congress

WC7: Doerenkamp-Zbinden Poster Awards

The following posters were choosen from the DZF poster award commission at the end of the World congress.
Congratulations from the ALTEX Team.

Routine and experimental application of the monocyte activation test (MAT) in the Paul-Ehrlich-Institut (PEI)

I. Spreitzer, B. Loeschner, C. Bache, K. M. Hanschmann, C. K. Schneider and T. Montag
Paul-Ehrlich-Institut, Langen, Germany

Characterization of patho-mechanisms relevant to Alzheimer's disease in a human neuronal model system

D. Scholz and M. Leist
University of Konstanz – Doerenkamp-Zbinden Chair of Alternative In-Vitro Methods, Konstanz, Germany

Human neurospheres can identify neurotoxicants *in vitro*

T. Rockel, J. Abel and E. Fritsche
Institut für umweltmedizinische Forschung (IUF) an der Heinrich-Heine-Universität GmbH, Duesseldorf, Germany

Software controlled artificial animal models for teaching animal experiments

C. Patil[1] and R. Raveendran[2]
[1]R. C. Patel Institute of Pharmaceutical Education and Research – Department of Pharmacology, Shirpur, India; [2]Jawaharlal Institute of Postgraduate Medical Education and Research – Department of Pharmacology, Pondicherry, India

The influence of environmental enrichment on clinical pathology and cardiovascular parameters in rats

L. Mikkelsen[1], D. Sørensen[2], T. Krohn[2], B. Lauritzen[1], N. Dragsted[1], A. Hansen[2] and J. Ottesen[1]
[1]Novo Nordisk A/S, Novo Nordisk Park, Maaloev, Denmark, [2]University of Copenhagen, Department of Veterinary Disease Biology, Faculty of Life Sciences, Frederiksberg, Denmark

Influence of modes of action and physicochemical properties on the correlation between *in vitro* and acute fish toxicity data

N. Kramer[1], J. Hermens[1] and K. Schirmer[2]
[1]Doerenkamp-Zbinden Chair, Institute for Risk Assessment Sciences, Utrecht University, The Netherlands; [2]Eawag, Swiss Federal Institute of Aquatic Science and technology, Duebendorf, Switzerland

Zebrafish (*Danio rerio*) as a versatile *in vivo* screening platform

W. Kamphuis, E. Groen, S. Thun-Battersby and E. Ronken
Solvay Pharmaceuticals Research Laboratory, Weesp, The Netherlands

An inter-laboratory study of short time exposure (STE) test for predicting eye irritation potential of cosmetic ingredients and formulations

T. Hayashi[1], Y. Takahashi[2], S. Watanabe[3], M. Koike[2], N. Aisawa[3], S. Ebata[3], H. Sakaguchi[2], T. Nakamura[3], H. Kuwahara[1] and N. Nishiyama[2]
[1]Kanebo Cosmetics Inc., Kanagawa, Japan; [2]Kao Corporation, Tochigi, Japan; [3]Lion Corporation, Kanagawa, Japan

New risk assessment approaches for cancer: assuring safety without animal testing

P. Carmichael, Y. Adeleye, B. Cochrane, M. Dent, J. Fentem, S. Fletcher, J. Li, C. Mackay, S. Malcomber, G. Maxwell, C. Moore, D. Parkin, C. Pease, F. Reynolds, A. Scott, S. Scott, C. Westmoreland, A. White and S. Windebank
Unilever Safety & Environmental Assurance Centre, Sharnbrook, UK

ORCHESTRA: a new EC project to link the research of *in silico* models with users' needs

E. Benfenati[1], G. Gini[2] and I. Malerba[3]
[1]Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy; [2]DEI, Politecnico di Milano, Italy; [3]Centro REACH, Milano, Italy

Validating alternatives to the LLNA: what is the gold standard?

D. Basketter[1], S. Casati[2], I. Kimber[3] and A. Mehling[4]
[1]DABMEB Consultancy Ltd, Sharnbrook, UK; [2]In Vitro toxicology Unit, European Commission, Ispra, Italy; [3]Faculty of Life Sciences, University of Manchester, UK; [4]Cognis GmbH, Duesseldorf, Germany

Transportation as major life event in rats, effect on welfare and limits of adaptation

J. Arts, K. Kramer and F. Ohl
Utrecht University, The Netherlands

Development of an *ex vivo* human gut mucosal challenge model to replace animal testing

J. Drew[1], A. Farquharson[1], E. Moss[2], K. Macdonald[2], S. Lynagh[2] and D. Bunton[2]
[1]Rowett Institute of Nutrition and Health, University of Aberdeen, UK; [2]Biopta Ltd, Glasgow, UK

The use of a long shelf-life *in vitro* cell model of the human airway epithelium (MucilAir™) for inhalation toxicity assessment

S. Constant, S. Huang, M. Caulfuty and L. Wiszniewski
Epithelix Sàrl, Geneva, Switzerland

International acceptance of *in vitro* alternative ocular safety test methods: bovine corneal opacity and permeability (BCOP) assay (draft OECD TG 437)

J. Merrill[1], M. Wind[2], W. Stokes[3], J. Barroso[4], V. Zuang[1], P. Amcoff[5], H. Kojima[6], A. Jacobs[1], D. McCall[7], D. Allen[8] and R. Tice[9]
[1]US FDA, Silver Spring, MD, USA; [2]US CPSC, Bethesda, MD, USA; [3]NICEATM/NTP/NIEHS/NIH/DHHS, Research Triangle Park, NC, USA; [4]ECVAM, JRC, EU, Ispra, Italy; [5]OECD, Environment Directorate, Paris, France; [6]JaCVAM, Tokyo, Japan; [7]US EPA, Washington, DC, USA; [8]ILS, Inc./NICEATM, Research Triangle Park, NC, USA; [9]NTP/NIEHS/NIH/DHHS, Research Triangle Park, NC, USA