Food for thought ...
Thomas Hartung

The human whole blood pyrogen test - lessons learned in twenty years

Research Article
Jorid B. Sørli, Jitka S. Hansen, Asger W. Nørgaard, Marcus Levin and Søren T. Larsen
An in vitro method for predicting inhalation toxicity of impregnation spray products

Concept Article
Mounir Bouhifd, Melvin E. Andersen, Christina Baghdikian, Kim Boekelheide, Kevin M. Crofton, Albert J. Fornace Jr., Andre Kleensang, Henghong Li, Carolina Livi, Alexandra Maertens, Patrick D. McMullen, Michael Rosenberg, Russell Thomas, Marguerite Vantangoli, James D. Yager, Liang Zhao and Thomas Hartung
The Human Toxome Project

Research Article
Outi Huttala, Hanna Vuorenpää, Tarja Toimela, Jukka Uotila, Hannu Kuokkanen, Timo Ylikomi, Jertia-Riina Sarkanen and Tuula Heinonen
Human vascular model with defined stimulation medium – a characterization study

Review Article
Heike A. Behrensdorf-Nicol, Karin Weisser and Beate Krämer
“BINACLE” assay for in vitro detection of active tetanus neurotoxin in toxoids

Short Communication
Ewa Aleksandrowicz and Ingrid Herr
Ethical euthanasia and short-term anesthesia of the chick embryo

Workshop Reports
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Corners
News
Dear readers,

After many years of publishing mainly research articles on *in vitro* work, ALTEX recently has been receiving more articles including work in animals, either in the context of refining animal experiments or comparing newly developed *in vitro* assays with *in vivo* data. As stated in our instructions for authors, ALTEX requires authors to report animal experiments in line with the ARRIVE or the GSPC guidelines.

Although the guidelines received much attention at the last World Congress in Prague and although one would expect scientists involved in 3R research to be particularly sensitized to the importance of comprehensively reporting animal experiments, we have often found a number of points that have not been fully documented according to the guidelines. It is encouraging that the authors until now always have been able to provide the information upon request. It is to be hoped that the value of the guidelines will be embraced more fully to improve the quality of reporting and avoid unnecessary duplication.

Twenty years ago, the first paper on the human whole blood pyrogen test was published in ALTEX. It is shocking to read in Thomas Hartung’s Food for Thought … that the use of rabbits for pyrogen testing nonetheless increased in the last reporting period in Europe although the *in vitro* test is able to detect pyrogens in all types of samples investigated to date. Thomas Hartung shares the lessons he has learnt from driving this test from an idea to a validated alternative method which, considering the hundreds of thousands of rabbit tests that could be replaced each year, might have been the flagship of alternative methods and might have led to the 3Rs field receiving more international recognition and investment to drive forward other tests.

In their research article, Jorid Sørli and colleagues present the use of an *in vitro* biomechanical test for the assessment of the potential of impregnation spray products to cause acute lung toxicity. This elegant method managed to detect all products that were toxic in the mouse inhalation experiment, suggesting that it could reduce animal numbers used for this purpose and guide the formulation of new products.

Mounir Bouhifd et al. provide an overview and an update on the Human Toxome Project. The project aims to determine how to define pathways of toxicity, what (quality) criteria must be met to prove a pathway of toxicity, and how to collect the information and make it publicly accessible. The concept is that response patterns induced by known toxicants, e.g., the pattern of up- and downregulation of numerous genes, can be used to identify unknown toxicants that induce the same patterns.

Outi Huttala and colleagues report on the optimization of a defined culture medium that supports the development of vascular networks in cultures of two human cell types, i.e., adipose stromal cells and umbilical vein endothelial cells. They find that the defined medium, not containing fetal calf serum, yields excellent results as illustrated on the cover picture and shown by staining for respective markers. This test has application opportunities in embryotoxicity testing, drug testing and for tissue engineering.

Heike Behrensford-Nicol et al. from the Paul-Ehrlich-Institute explain the principle of a test they have developed which determines *in vitro* whether a tetanus vaccine batch is safe for use. The test combines two assays for different activities of the tetanus toxoid to verify that it has been efficiently inactivated. If implemented into the European Pharmacopoeia the test could replace the respective *in vivo* assay.

Ewa Aleksandrowicz and Ingrid Herr remind us that although experiments on chicken eggs and embryos are considered alternative methods, chicken embryos have functional brains by day 13 of incubation and can feel pain days before that. They should therefore be anesthetized or euthanized by a humane method. Although in the UK avian embryos are protected from the mid-point of the incubation period, Directive 2010/63/EU did not introduce the protection of avian embryos for Europe and so humane euthanasia will remain a personal choice of the informed experimenter outside the UK.

In the News we report on two cases of alleged unethical treatment of animals in research facilities that have recently gained widespread media attention. The successes of a number of alternative methods in attaining validation and implementation as well as political developments in the field of animal experimentation and alternative methods will be of interest. Calls for applications and prizes are also included. Notably, EUSAAT has announced that the Linz Congress will take place on September 20-23, 2015; abstract submission is now open.

The ALTEX staff congratulates Irène Hagmann, our former language editor, on her 90th birthday.

Hoping you enjoy this issue of ALTEX,

Sonja von Aulock
Editor in chief, ALTEX
Call for papers

Topics/tentative sessions

- New technologies: systems biology, -omics technologies, stem cells, 3D models & human-on-a-chip
- International progress in 3Rs’ research
- Global cooperation on implementing the 3Rs
- Replacement – new approaches
- Predictive toxicology & risk assessment bases on the AOP concept
- Specific toxicological endpoints: oral & repeated-dose toxicity, inhalation toxicity, sensitization, reprotox
- Nanotoxicology
- Bio-barriers
- Efficacy and safety testing of drugs, biological and vaccines
- Disease models
- Ethical and legal issues & EU Dir 63/2010 update
- Refinement & welfare, culture of care, best practice approaches, avoidance of severe suffering
- 3Rs in education and academia
- „Young scientists“ session
- Free communications

Deadlines for the submission of abstracts for:
- oral presentations: 15th May 2015
- posters: 31st May 2015

Congress fees
before 21st August 2015 - early bird fees
- members of EUSAAT: EUR 175.–
- general registration fee: EUR 270.–
- students: EUR 95.–

after 21st August 2015
- members of EUSAAT: EUR 217.–
- general registration fee: EUR 334.–
- students: EUR 106.–

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