

ALTEX

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Food for thought ...

Miriam N. Jacobs, Rosemary J. Versteegen, Carol Treasure and Jennifer Murray

Addressing potential ethical issues regarding the supply of human-derived products or reagents in *in vitro* OECD Test Guidelines

Review Article

Elena Dellambra, Teresa Odorisio, Daniela D'Arcangelo et al.

Non-animal models in dermatological research

Research Article

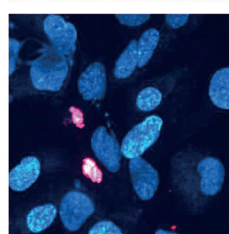
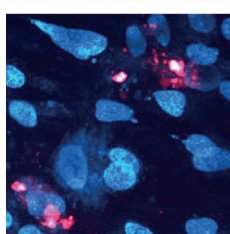
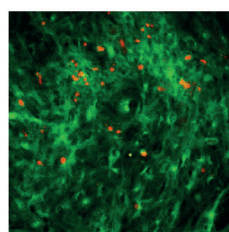
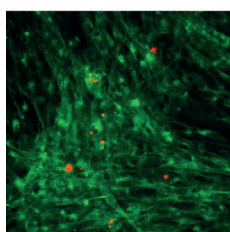
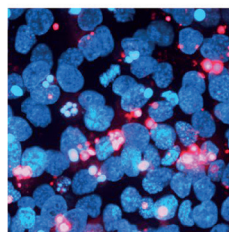
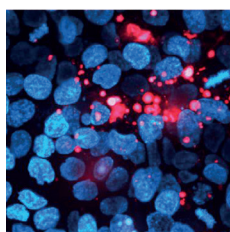
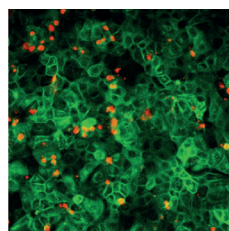
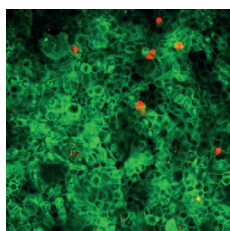
Marcia Boderio, Toine F. H. Bovee, Liza Portier and Peter J. M. Hendriksen

Detection and profiling of diarrheic marine biotoxins in shellfish by mRNA analysis of exposed Caco-2 cells using qRT-PCR and multiplex magnetic bead-based assays

Research Article

Melissa Van Bossuyt, Els Van Hoeck, Tamara Vanhaecke et al.

Prioritizing substances of genotoxic concern for in-depth safety evaluation using non-animal approaches: The example of food contact materials



Research Article

Stefanie Hofer, Marlies Stonig, Verena Wally et al.

Contradictory effects of chemical filters in UV/ROS-stressed human keratinocyte and fibroblast cells

Research Article

Lenny Kamelia, Sylvia Brugman, Laura de Haan et al.

Prenatal developmental toxicity testing of petroleum substances using the zebrafish embryotoxicity test

Research Article

Richard S. Judson, Russell S. Thomas, Nancy Baker et al.

Workflow for defining reference chemicals for assessing performance of *in vitro* assays

Research Article

Miriam Pons, Georg Nagel, Yanira Zeyn et al.

Human platelet lysate as validated replacement for animal serum to assess chemosensitivity

t4 Workshop Report

Mario Beilmann, Harrie Boonen, Andreas Czich et al.

Optimizing drug discovery by investigative toxicology: Current and future trends

Letter

Meeting reports

Corners



**Dear readers,**

The replacement of fetal bovine serum (FBS) in cell culture use is gaining traction. As with the acceptance of alternative methods in general, pity for the animals involved (here the unborn calves) and the development of the necessary tools (here human serum and derivatives thereof used as medium supplements, or chemically defined media), have not been sufficient to achieve wide-spread change. But now, new technologies are creating a greater demand for FBS-free media, i.e., technologies aiming at growing tissues that can be transplanted to humans, OECD has accepted an FBS-free variation of a guideline test, and the arguments for change are focusing more on the benefits of being able to more closely model human physiology and thus better predict human responses.

The Food for Thought ... contribution in this issue shows that alternatives to FBS have gained the attention of the OECD. In a thought-starter ahead of an expert meeting on the subject, Miriam Jacobs and colleagues explore questions surrounding the use of human serum and derived products, such as who and where are the suppliers, what regulations do the products underly in different countries, how can it be assured that a larger scale demand for such products does not compete with the need for human blood products for transfusion purposes, what safety measures are required to protect laboratory workers, and are there cultural aspects that may affect use?

Also on the subject of FBS alternatives, Miriam Pons and colleagues demonstrate the practical application of human platelet lysate derived from outdated platelet concentrates by directly comparing the growth of and sensitivity to chemotherapeutics of different cancer cells grown in medium supplemented with either FBS or human platelet lysate. They show that all parameters measured are the same in both media, further supporting that switching to such a xenofree supplement is feasible.

A review by Elena Dellambra et al. provides an overview of models of the human skin, including currently used animal models and the limitations they have owing to the differences between human and animal skin, the different variants of *in vitro* skin models that have been developed, as well as *in silico* models and *in vitro* models of human skin diseases.

A model using human skin cells to test the antioxidative capacity of chemical UV filters used in sunscreens is described by Stefanie Hofer and colleagues. They found that although some UV filter substances protected the cells from UV damage, others instead displayed undesirable pro-oxidative properties, which should be further investigated.

Seafood for human consumption must be free of marine biotoxins, which are produced by algae under certain conditions. Although the animal test has now been mostly replaced by chemical-analytical methods that detect the presence of the toxins, these tests can only detect known structures, not new variants. Marcia Boderó et al. propose a tiered testing strategy that includes measuring the expression of selected genes in a human cell line that point to the presence of a marine biotoxin signature to investigate samples that are positive in a previous *in vitro* screening assay but cannot be confirmed by chemical-analytical assessment.

Most food comes into direct contact with packaging materials, from which components may transfer to the food items and be consumed. Melissa Van Bossuyt et al. asked how much we know about whether printed paper and board materials used for this purpose can cause cancer. As they found little clear evidence either way for most of the relevant substances, they combined the existing data with computer-aided predictions and results of an *in vitro* test to prioritize the substances of further testing. This strategy could also be useful for other applications, as it aims to both increase human safety and reduce the number of substances tested in animals.

The zebrafish embryotoxicity test (ZET) was used to assess the potential effects of petroleum substances on prenatal development by Lenny Kamelia and colleagues. This test is considered an alternative assay as it uses early stage fish embryos that have not yet developed a functional nervous system and are thus unable to experience pain. Although the results produced by this test for this class of compound did not correspond as well with existing *in vivo* data as results produced with a different *in vitro* assay, the authors conclude that testing substances in a battery of *in vitro* assays including the ZET is preferable to relying on a single *in vitro* assay for this complex endpoint.

In developing and validating a new *in vitro* test, the availability of reference chemicals, for which there is clear evidence that they either do or do not have the property of interest, is essential so as to demonstrate that the test specifically detects the desired property. Judson et al. present a semi-automated process to develop reference chemical lists for *in vitro* tests by extracting information from public data sources.

Industry has become a major driving force in the field of alternatives to animal experiments, in some cases owing to outside forces, e.g., the ban on animal testing for cosmetics ingredients, but often also because of its drive to take up innovative technology and to make processes more efficient. Mario Beilmann introduces the Investigative Toxicology Leaders Forum, a group of European-based leaders from different pharmaceutical companies, who have joined forces to improve the precision of safety decisions early on in the drug development process by adopting new, human-relevant technologies that investigate the underlying toxicity mechanisms. Together, they hope to improve the accuracy of predicting which potential new drug will have a low risk of toxicity in humans.

In their letter, Katy Taylor and Laura Rego Alvarez report on animal use in European countries during 2016 compared to 2014, both with regard to the quality of each country's reporting and the changes in animal use. Four meeting reports and the Corners update you on recent activities in the field. Please note that the EUSAAT Congress has been moved to October 10-13, 2019.

Best wishes,

Sonja von Aulock

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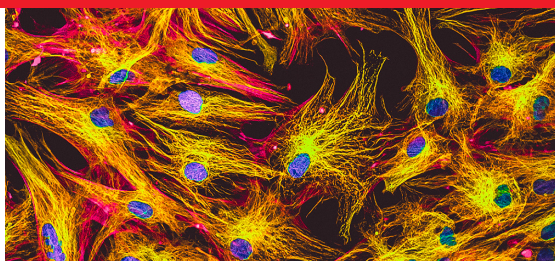
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www.eusaat-congress.eu

**NEW
DATE!**

10 – 13 October 2019 – University of Linz, Austria



Call for abstracts

Topics/tentative sessions

- Refinement: best practice approaches, animal welfare, avoidance of severe suffering, culture of care
- Reduction: transparency, reproducibility and translational aspects (species differences)
- Replacement: advanced technologies for implementing the 3Rs
- 3Rs in education and academia
- 3R Centers in Europe & international
- International progress in 3Rs research
- 3D Models & multi-organ-chips (MOC), human-organ-chips (HOC)
- Biological barriers
- In Silico Models: toxicology & efficacy of drugs, chemicals & cosmetics, new approaches for biomedical research
- Disease models using HUMAN cells, tissues and organs
- Efficacy and safety testing of drugs, medical devices & biopharmaceutics
- REACH
- Advanced safety testing of cosmetics and consumer products
- Alternatives to animal testing in food safety, nutrition and efficacy
- Specific Endpoints of Toxicity
- Neurotoxicology & Developmental Neurotoxicology (DNT)
- Ecotoxicology
- Stem cell models and technology
- Implementing EU Dir 63/2010
- Ethical & legal issues
- Advanced GMO models – CRISPR/Cas in vivo & in vitro
- Initiative for implementing Serum Free Culture Media
- Publication policies with regard to animal experiments and the 3Rs principles
- An integrated interdisciplinary approach to animal-free nanomaterial and chemical safety assessment: Results of the in3 project
- Vaccines & the 3Rs
- „Young Scientists“ session
- Free communications

Deadlines for the submission of abstracts:

for oral presentations: **14 June 2019**

for posters: **14 June 2019**

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