Dear readers,

The last page of this last issue of ALTEX for 2019 displays the number 700. ALTEX has almost doubled the number of pages printed per year since I started out as editor in 2011. This is possible thanks to the fivefold increase of submissions in the same time period, from which it is an enjoyable challenge to select the best for publication. Scientists are increasingly comfortable with publishing in and identifying with a journal that carries the name Alternatives to Animal Experimentation. This exemplifies the changing perception of the entire 3Rs field, firmly based on the excellent and innovative scientific work that is being carried out in it. Putting together 700 pages in a year is a big job for a small team, and I am deeply grateful for the enthusiastic cooperation and meticulous work of my colleagues that goes into this publication.

Considering the increasing number of new alternative or nonanimal methods (NAMs), it is now timely to think about how we can best employ them to make decisions on the safety or activity of different classes of substances to minimize the use of animals without compromising on human health and safety. We do not want to use these methods only to prioritize which chemicals are tested first in animal tests and which sometime later. But when do we have enough information to declare that a substance is harmless or decide that it should be dropped from further development owing to possible toxicity? Melvin Andersen and colleagues provide some Food for thought … on these questions.

Without speech communication, we can often not judge whether a fellow human is experiencing pain or feeling unwell, but we do know that individuals deal differently with a painful or distressing experience. Kris Descovich et al. assess the behavior and facial expressions of macaques undergoing biomedical procedures to identify strong indicators of pain or of wellness that show when best to employ analgesics or can be used to refine procedures. In a second refinement article, Jie Mei et al. report that there are different definitions of humane endpoints, i.e. changes in body weight, temperature or sickness scores that trigger euthanasia of the experimental animal to limit its suffering, in the literature. They then use a machine learning approach to optimize the early prediction of a high risk of death for use in different mouse models.

Volatile chemicals may cause sensory irritation. Aiming to replace the mouse sensory irritation assay, Jeanelle Martinez and Thomas Eling develop an adverse outcome pathway (AOP) that describes the process and argue that measuring activation of the TRPA1 receptor *in vitro* can predict a chemical's irritation potency.

We need to know how a new drug works but also how often and how much of it to give a patient to achieve the desired effects without causing toxicity. James Chan et al. develop a simulation model to predict this based on *in vitro* and metabolism data for three different statins and compare the results with biokinetic data obtained from humans to show that such predictions can be made without animal testing.

Thao Tran et al. employ a planarian model, which can regenerate severed body parts, to determine whether iron oxide nanoparticles, used in large amounts for a variety of applications in industry, interfere with stem cell functions required for regeneration or with homeostasis regulation.

Although nonanimal skin sensitization assays have been accepted as OECD test guidelines, none of them are stand-alone-methods and none of them subcategorize skin sensitizers into weak and strong sensitizers. Chantra Eskes and colleagues present a test, based on the coculture of two cell lines, that captures two of the four key events and reliably solves the problem of predicting sensitization subcategory.

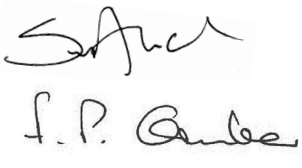
Once a test has been established, optimized and characterized in detail, it is worthwhile considering potential secondary applications. Stefania Serra et al. report on the use of a cell model for carcinogenicity testing to compare samples of airborne particulate matter collected from an urban site during different seasons. They show that the method can be used to assess biological effects of chemical mixtures, in this case environmental samples. Staying on the subject of air, Joelsson et al. present a novel *in vitro* method to study the detrimental effects that mechanical ventilation can have on the human lung. To achieve this, they have designed a device that allows the application of cyclical pressure to bronchial cells cultured at the air-liquid interphase on flexible membranes and investigate the effects on gene and protein level.

The BenchMarks article in this issue by Alice Krebs and colleagues presents a detailed and annotated template designed to assist in reporting non-guideline studies in accordance with OECD GD 211 in a sufficient level of detail to allow regulators to evaluate the data. This can be a valuable contribution towards a higher level of implementation and acceptance of *in vitro* data for regulatory decision-making.

A short communication on a developmental neurotoxicity test based on the elongation of axons in an insect embryo as well as three Meeting Reports and five Corners complete this issue.

In case you missed the EUSAAT Congress in Linz, the Abstract Book is online as an issue of ALTEX Proceedings to document the topics discussed at the meeting. Please consult our website for current news and upcoming events.

A big thank you to all authors, reviewers, subscribers, readers, members and sponsors for supporting ALTEX during 2019.



Sonja von Aulock and the ALTEX Edition Editorial Office
with Franz P. Gruber and the Board of ALTEX Edition