



Dear readers,

We are thrilled to celebrate the 40th birthday of ALTEX in 2024. The journal has come a long way since its humble beginnings as a German biannual booklet first published by the *Fonds für versuchstierfreie Forschung* (FFVFF, Zurich, now Animalfree Research, Berne, Switzerland) in 1984. Our success and international recognition have flourished thanks to the continuous support of the scientific community as authors, reviewers and readers, as well as the financial support and guidance of the members and sponsors of our society ALTEX Edition, and the excellent work of our editorial team.

Starting with this issue, each article now includes a plain language summary describing its scientific and 3R relevance to make it more accessible to a broader audience. Working on the first summaries with the authors has confirmed how hard we as scientists often find it to communicate research concepts in plain terms. Improving this by making a conscious effort and asking our listeners for feedback could be an realistic and rewarding New Year's resolution.

This issue's main articles start off with Food for thought ... by Alexandra Maertens and colleagues on green toxicology and how it can align with overarching policies and bridge differences between environmental protection and animal welfare goals. The idea of green toxicology is to enable the design of safer chemicals by using new approach methodologies already at the design stage to avoid developing or producing harmful substances.

Véronique de Bruijn and colleagues combine *in vitro* and mathematical modeling to capture how a model drug can inhibit bile acid uptake in the gut. The approach could be used to predict this detrimental side effect in other chemicals without animal testing.

Hsing-Chieh Lin et al. combine *in vitro* and *in silico* methods to predict which pollutants may affect the rhythm of the human heart. Human heart cells derived from five healthy donors showed the best performance in predicting drugs with known effects on the heart rhythm. The model was then used to assess 900 pollutants, of which 150 were predicted to have potential to affect heart rhythm. Combining these results with exposure predictions flagged seven of these pollutants as unsafe.

Clemens Wittwehr et al. make their case that adverse outcome pathways need to be documented following the FAIR guidelines – findable, accessible, interoperable and re-usable. This will allow them to become more visible and create trust, allowing them to be exploited to their full potential.

A novel non-animal method to assess the quality of different diphtheria vaccine products is introduced and tested by Laura Hassall and colleagues. The method detects different amounts of diphtheria toxoid as well as any degradation by heat exposure or oxidative stress and can be successfully transferred to other labora-

tories. Regulatory approval would enable the replacement of the animal test currently used for this purpose.

To benchmark the activities of research institutes in the implementation of animal-free methods, enable them to learn from each other, and encourage further improvement, Cyrille Krul and colleagues introduce the Beyond Animal Testing Index (BATI). The paper describes the tool as well as a successful field-test with three Dutch research institutes.

Nanomaterials share the activation of adverse outcome pathways relating to the dysfunction of mitochondria with some chemicals. Sivakumar Murugadoss and colleagues investigate this overlap and its implications for the risk assessment of nanomaterial exposure without using animal testing.

Yvonne Staal et al. review different designs of *in vitro* experiments intended to model human health impacts of airborne pollutants. They distill the important parameters that need to be considered to design relevant and robust experiments.

Some chemicals are difficult to test using non-animal methods owing to their physicochemical characteristics. Allison Greminger et al. assess all available data on skin sensitization from different methods for four such chemicals and compare the resulting patterns with those of many known skin sensitizers using computational analysis. This comparison can deliver a rationale for a classification without performing the traditional animal tests.

Richard Currie and colleagues explore what it will take for a company to register a new pesticide without the use of animals. They develop the concept of compiling two parallel submissions for the same pesticide, one based on traditional methods and the other based on new approach methodologies. Gaps or deficiencies in the latter will indicate where more work is still needed, and discussion of the data with regulators will build confidence in working with the methods without endangering the registration of the new active ingredient.

The BenchMarks contribution by Eike Cöllen et al. provides an overview of the essential elements and the development process of complete toxicological test methods and explains how they differ from mere data generation.

The Meeting Reports and Corners as well as our online Events Calendar will bring you up to speed with recent and planned activities in the field.

Wishing all our readers a successful and healthy 2024,

Sonja von Aulock
Editor-in-chief