Dear readers,

In June, the *European Pharmacopoeia* announced the complete removal of the rabbit pyrogen test as a requirement for pyrogenicity testing. This important safety test for parenteral medicines will in future be done solely using *in vitro* tests. The implementation of the revision on July 1, 2025 comes into force 30 years after publication of the first article on the "Detection of pyrogens using human whole blood" by Thomas Hartung and Albrecht Wendel in ALTEX. This invention led to a successful international validation study followed by the stepwise acceptance of monocyte activation tests. The number of rabbits used for pyrogen testing, which was around 160,000 in Europe in 2008, will now finally drop to zero without compromising patient safety.

The Food for thought… contribution by Fenna Sillé et al. in this issue introduces CAAT's new IMPACT initiative, which aims to set up a public-private partnership to drive forward an ambitious *Human Exposome Project*. This project aims to comprehensively assess how environmental exposures impact human health to identify causes of disease and guide prevention strategies. The authors are calling on interested stakeholders to join a forum to be held in May 2025.

PFAS, i.e., per- and polyfluoroalkyl substances, are persistent chemicals that may be harmful to humans and the environment. As there are thousands of PFAS, a testing strategy is needed to determine which are most problematic. Han-Hsuan Doris Tsai and colleagues test the effects of 26 PFAS from 8 structural groups on cell functions and gene expression in human cell-based liver and heart models. They do not find clear structure-based similarities among the PFAS and suggest that instead of testing representatives of the structural groups in animals, the chemicals should all be tested in human cell-based models of different organs to prioritize them for further testing.

Monica Vaccari and colleagues also test prototypical PFAS, but in a cell-based cancer model, the cell transformation assay, which is currently under consideration for inclusion in an integrated approach to testing and assessment. They observe concentration-dependent malignant transformation caused by one of the two tested substances, which have both been linked with cancer in some epidemiological and animal studies, indicating that they differ in their modes of action.

Non-technical summaries are synopses of approved research projects that use animals published by the countries of the European Union to inform the public. Katy Taylor and colleagues reassess the information content of non-technical summaries six years after their first review. While they find some improvements in reporting, many summaries still do not adequately describe the harm that animals will experience and therefore do not fulfil their intended purpose.

Although the validation of methods to assess chemical safety is a lengthy and costly process, the benefits of achieving validation as OECD Test Guidelines include their acceptance in all OECD member countries. Anne Gourmelon and colleagues discuss the challenges of validating methods and suggest how the process can be improved to make it more efficient and more attractive for stakeholders to complete.

Susan Debad et al. compile the results of a webinar series and workshop held at the National Institutes of Health on how to integrate non-animal methods for gastrointestinal toxicity into the risk assessment of drugs, food additives, dietary supplements, pesticides, and industrial chemicals. These approaches aim to reduce and replace animal-based testing.

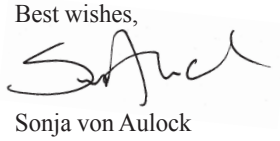
Colleen M. Pike and colleagues work with a gastrointestinal model based on primary human stem cells. The aim of their study is to identify sources of its variability and improve its physiological relevance by comparing cells from multiple human donors, cell lots, and passage numbers. Their results can improve their study design and also inform the design of other primary cell-derived systems.

Nathalie Alépée and Els Adriaens describe and assess the accuracy of a defined approach to assess the eye hazard of solid chemicals using two *in vitro* methods. This approach complements the defined approaches for liquid chemicals and has just been adopted for inclusion into OECD TG 467.

The review article by Pelin L. Candarlioglu discusses how microphysiological systems (MPS) can be used to study cell therapies. MPS lend themselves to the study of these "living drugs" as they allow longer-term studies, mimic complex biological functions, and are based on human cells. The authors discuss the opportunities and remaining challenges.

Meeting Reports on 3D bioprinting, micro-replace systems, and alternatives to higher animals in science as well as the Corners round off this issue. In case you could not attend the MPS World Summit in Seattle, you can access the Abstract Book at doi:10.58847/ap.2401. ALTEX Proceedings will also be publishing the Abstract Book for the EUSAAT Congress 2024 in September on https://proceedings.altex.org/.

Best wishes,



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