



Dear readers,

The virtual WC11 is behind us, but a new series of congresses focusing on microphysiological systems (MPS) has gained initial funding and sponsors and is shifting into top gear in planning the first MPS World Summit to be held on May 30-June 3, 2022 as a hybrid event in New Orleans, Louisiana. A second, free pre-event focusing on systems engineering of MPS will take place virtually on December 9, 2021. The organizers are now calling for abstracts for the pre-event and for further sponsors of the first summit. Find out more on <https://mpsworldsummit.com>.

The pathogenesis of COVID-19 in animals is different to that in humans, even in genetically modified mice expressing the human ACE2 receptor. This issue's Food for Thought ... contribution by Ian Kang and colleagues argues that human *in vitro* microphysiological systems have already contributed important insights into the disease, for example, on its neuro-pathogenesis, and are suitable and relevant models to answer further pressing open research questions on COVID-19.

Sandra Verstraelen et al. describe a pilot study to assess the acute inhalation toxicity of vapors of petroleum substances and their constituents based on measurement of a selection of endpoints after exposure of an alveolar epithelial cell line at the air-liquid interface. They find that the measured toxicity is consistent with data from previous *in vivo* experiments in animals and humans, indicating that the *in vitro* model can be used to predict *in vivo* toxicity.

Gianluca Selvestrel and colleagues present a software application that can support the safety evaluation assessment of cosmetic products. It can assess the ingredients of a potential cosmetic product based on existing experimental data or on the *in silico* values predicted by its integrated software. Then it considers these in relation to the concentration they will have, the product type they are to be used in, and the resulting expected exposure to determine if the product would pose regulatory concerns.

As adverse outcome pathways (AOPs) for manufactured nanomaterials are still lacking, Sivakumar Murugadoss and colleagues search the literature to identify potential molecular initiating events (MIE) or early key events (KE) of existing AOPs, which were originally developed for chemicals, that appear to also be triggered by nanomaterials. Based on two case studies they demonstrate how *in vitro* strategies can be used to test and verify such potential MIE/KEs to link nanomaterials to AOPs.

Awareness on quality control issues in *in vitro* research is increasing. Julia Tigges et al. show how to put general recommendations on quality control into practice to characterize master cell banks and working cell banks of human induced pluripotent stem cells in an academic research environment. They argue that the moderate investment is worthwhile when considering the implications of discovering that one has been working with a cell line that is not or no longer what it should be.

Pesticide regulation currently requires high numbers of experimental animals although many pesticides fall into groups with structural similarities. Wanda van der Stel et al. present their strategy of using an AOP to determine relevant *in vitro* methods that can feed and support read-across to assess the neurological hazard of the members of pesticide classes. The two case studies they describe may be adapted to guide the assessment of other chemical classes.

Miaoying Shi et al. combine *in vitro* data from electrophysiological assays in cardiomyocytes and transport assays in intestinal cells to predict human *in vivo* cardiotoxicity upon oral exposure to two herbal alkaloids that are used as anti-addiction drugs. They use reverse dosimetry based on physiologically based kinetic modeling to compare their predictions with published human *in vivo* data.

The ban on animal testing for cosmetic ingredients that came into force in the EU in 2013 was celebrated as a breakthrough for the 3Rs and was widely supported by consumers and cosmetics companies. However, this ban conflicts with the REACH regulation, which demands toxicity data for chemicals produced or imported into the EU independent of intended use. Jean Knight and colleagues investigate how many chemicals intended to be used only as cosmetic ingredients have undergone animal testing for REACH purposes since the 2013 ban and call for resolution of the conflict between the two regulations.

The first defined approaches for animal-free skin sensitization testing have recently been published as OECD Test Guideline 497. Andreas Natsch and colleagues use the skin sensitization data collected in the many different assays on many different chemicals to illustrate that the human *in vitro* data predicts the human *in vivo* data from skin patch assays better than the animal *in vivo* data does. They conclude that animal *in vivo* data should not be used as the sole reference data for the validation of *in vitro* assays.

A letter by Paul Locke and colleagues informs on the goals of the Humane Research and Testing Act that was recently introduced in the US House of Representatives. The Corners bring you up to date with recent international developments in 3Rs organizations. Take a look at our online events calendar at www.altex.org to start planning for 2022.

With this last issue of 2021, we thank this year's authors and reviewers as well as our subscribers, readers, members, and sponsors for supporting ALTEX. We wish you a happy holiday season.

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