Dear readers,

this issue of ALTEX strikes a balance between exciting *in vitro* work towards improving prediction of neurotoxicants, endocrine active substances and eye irritants, and analytical approaches, harnessing the power of existing data to deduce toxicological concerns and inform regulatory decisions.

Thomas Hartung explains the concept of thresholds of toxicological concern in his Food for Thought … contribution. Highly sensitive chemical analytical methods now let us detect the tiniest amounts of chemical contaminants in regulated products. Do we have to test each such contaminant for possible toxicological effects? Where can we draw a line and comfortably state that traces of substances in amounts below this threshold are not going to have effects on people or the environment? And what scenarios can this approach be applied to?

Andrea Gissi and colleagues from ECHA have analyzed data from REACH dossiers following the hypothesis that data from one type of *in vivo* toxicity test, the sub-acute oral toxicity test in mice, can be used to predict the outcome of another toxicity test, i.e., the acute oral toxicity test. They reach the conclusion that this is indeed the case with the immediate consequence that the latter test must now no longer be done for REACH purposes if data for the former test is available and indicates no toxicity at high doses.

The "mini-brain" already has raised much interest in the news. The seminal publication in this issue on the culture and characterization of these brain microphysiological systems reported by David Pamies and collaborators presents beautiful images of 300 nm spheres derived from induced pluripotent stem cells made up of neurons whose axons are wrapped in myelin and that generate electric signals. They promise to provide a kaleidoscope of insights into the effects of toxicants on the nervous system but also on the malfunctions that occur in neurological diseases when the mini-brains are generated using cells from patients.

In vitro experiments are often based on cells derived from a single person. Chiu and colleagues examine how large the response variability will be in a large population based on data derived from about 1000 cell lines from different people. On this basis, they develop a strategy by which to determine population variability to improve the definition of safety factors.

Building on the knowledge that some substances only gain the ability to modulate the human hormonal system through metabolism in the liver, Julie Mollergues et al. have modified *in vitro* assays measuring activation or interference with the estrogen or androgen receptors by adding a metabolizing system. They elegantly show how the activation of some substances by the metabolizing system reveals their potential endocrine activity.

Zhichao Liu and colleagues addressed themselves to the task of extrapolating *in vitro* toxicity results to predicting risk in humans by comparing datasets for chemicals each tested on primary human cells, primary rat cells and live rats. They find a better correlation between the responses of rat cells and live rats than between the liver cells or the two species, suggesting that human liver cells will predict human liver toxicity better than experiments on live rats.

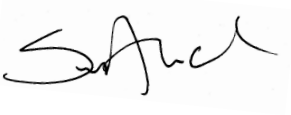
How can we find out how experimental animals are feeling if we cannot ask them? Kris Descovich and colleagues explain how the assessment of facial expression using validated tools can be used not only for pain assessment but also for overall welfare assessment.

In a short communication, Karsten Mewes et al. report on a ring trial of two new variations on *in vitro* eye irritation testing based on bioartificial equivalents of the human cornea.

The current importance of analytical approaches again becomes evident in the news, where the REACH Report on the use of alternative methods demonstrates it is the *in silico* methods, i.e., read-across, weight of evidence and QSAR, which are being used most predominately to avoid animal testing as *in vitro* methods are accepted only for few endpoints and they have still not supplanted the *in vivo* tests.

Recent regulatory development initiatives to ban animal testing for cosmetics in Guatemala and Australia are promising as well as the revision of the US Pharmacopeia to include *in vitro* pyrogen tests which can replace respective tests in rabbits. Also, a bill has been introduced to US Congress that would require the reporting of all animal species and numbers used for toxicity testing conducted or demanded by federal agencies. At last the numbers of laboratory rodents and birds, even if only those used for toxicity testing (probably about 10% of total use), would at least be documented if the bill is passed.

The Tenth World Congress on Alternatives and Animal Use in the Life Sciences will bring together hundreds of eminent and young scientists in Seattle this summer to forge new collaborations and report and give feedback on new approaches. ALTEX joins the organizers in wishing all participants safe travels and a successful, inspiring anniversary meeting.



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