Dear readers,

Safety testing of cosmetic ingredients may no longer be performed on animals for products that are to enter the European market. Although no full replacements for the five more complex toxicity tests are currently available, the European Commission decided not to pull the emergency brake and postpone the deadline or to allow exceptions on a case-by-case basis but to let the final marketing ban enter into force on March 11, 2013. It appears that the minimalistic response of many Member States to the impact assessment survey on the consequences of the ban, the public pressure culminating in the collection of a quarter of a million signatures supporting the ban by the European Coalition to End Animal Experiments (ECEAE), and the commitment of new Commissioner Tonio Borg led to this purely political precedent that will add further drive to the development of alternative methods in this and other sectors.

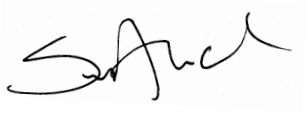
This decision appears very timely in light of a report published in *PNAS* (*110*, 3507-12) which is currently commanding much attention: Seok et al. show that gene regulation in response to inflammatory stresses of different etiology is highly uniform in humans but correlates poorly with that of mice, which is also more variable depending on the type of stress. They state "*Among genes changed significantly in humans, the murine orthologs are close to random in matching their human counterparts*." This article could turn out to be the game-changer, calling into question the relevance of any animal experiments for predicting human conditions and responses because, as Marcel Leist and Thomas Hartung argue in a comment on this article, there are no grounds to think this result would be different for any other disease.

In the Food for Thought column, Thomas Hartung and colleagues explore the challenges of validating new *in vitro* tests on the basis of their mechanism, i.e., how to prove that a change in a cellular mediator is the central mechanism behind the toxicity of a substance and therefore suitable as the basis of a test that will predict this form of toxicity. A second Food for Thought contribution by Martin Paparella et al. deals with describing and quantifying the uncertainly of testing methods. They argue that knowing more about the uncertainty of current, especially *in vivo*, testing methods will help to improve hazard assessment and aid the development of new methods.

In this issue's main articles Si Wang et al. introduce an *in vitro* coregulator binding assay for (anti-)estrogenicity testing and challenge it with a range of reference compounds and Simonetta Ferruzza and colleagues identify suitable serum-reduced and serum-free media for differentiation of Caco-2 cells which can replace the use of fetal bovine serum. In a t^4 article, Nina Hasiwa and colleagues compile the evidence that the monocyte activation test, currently validated as an alternative to the Limulus Amebocyte Lysate assay for pyrogenicity testing, also detects all human-relevant non-endotoxin pyrogens and should therefore be considered a full replacement of the rabbit pyrogen test.

A t^4 workshop report by Ramirez et al. shares the results of an expert workshop on metabolomics and its application in toxicology and preclinical research and a conference report on the Sens-it-iv End Congress summarizes the results of 5 years of work of this large consortium. Further workshop reports, corners, and the news round off the issue.

We hope you enjoy this bumper issue of ALTEX,



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