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# Integrated safety assessment (ISA) of food products: flexible strategies are needed

van der Geest, L.; Bouwmeester, H.; Bovee, T.; Hoogenboom, R,; Kok, E. and Peijnenburg, A.

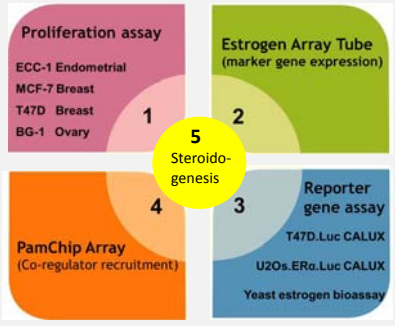

## Abstract

Safety assessment of novel and complex food products or food ingredients remains a complicated task. Classical approaches are debated, alternative approaches not accepted yet. Clearly for chemical mixtures and complex foods, *in vivo* tests are not providing the answers needed to scientifically underpin the safety assessment. An integrated testing strategy (ITS) combining computational toxicology, *in vitro* cell systems, and sensitive adverse outcome pathway analysis is emerging as a promising approach for risk assessment of chemicals.

However, complex food products provide an additional challenge due to the large variety of components present, the majority of which are harmless. By extending the ITS with compositional analysis (analytical profiling using various omics approaches), biotransformation, and effect based identification of hazardous components (bioactivity driven mass spectrometry: bio-MS), we aim to create an integrated safety assessment strategy for complex (food) products.

The resulting platform is flexible and may occasionally also comprise animal feeding trials, but given the advancements in analytical, *in vitro* and *in silico* methodologies, this should be determined case by case rather than being considered obligatory for the approval of novel food products or food ingredients in general.

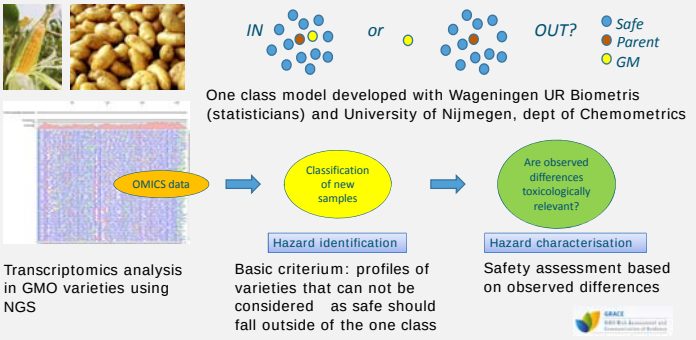

## Examples and cases



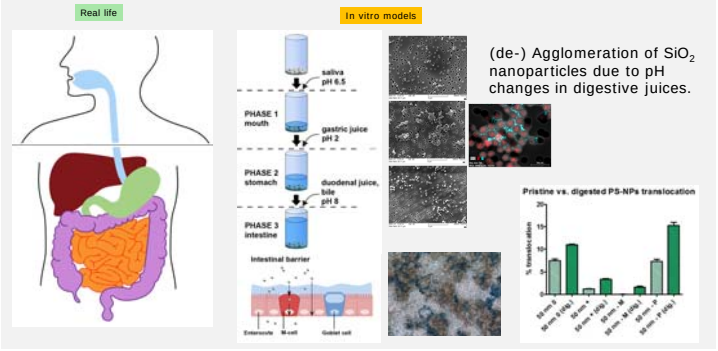

In the standard test for oestrogenic activity, the 'rat/mouse uterus test', young or ovariectomised rats and mice are injected with a test substance, in order to see the effect on uterus weight.
A combination of 5 *in vitro* assays can assess all aspects of oestrogenic activity:

1. Hormone induced cell proliferation
2. Hormone induced gene expression
3. Hormone induced expression of reporter genes in yeast and mammalian cells
4. Hormone dependent recruitment of transcriptional co-activators
5. Hormone induced changes in steroid profiles

**Example 1. In vitro assays for estrogenic activity.**
A combination of 5 *in vitro* assays can assess all aspects of oestrogenic activity, providing a more sensitive and reliable assessment than the standard rat/mouse uterus test.

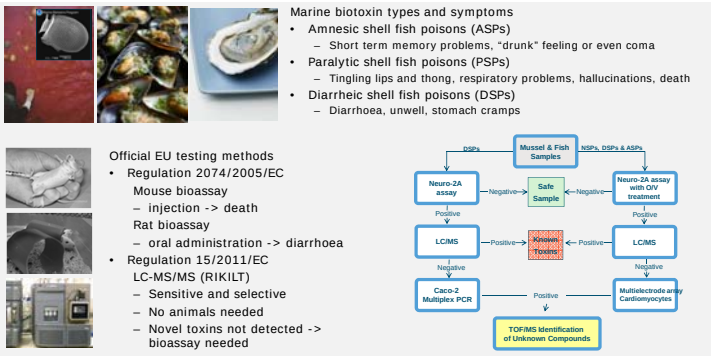



**Example 2. GMO compositional analysis.**
Using advanced analytical omics approaches to identify unintended effects (transcriptomics / metabolomics) instead of animal feeding trials.




(de-) Agglomeration of $SiO_2$ nanoparticles due to pH changes in digestive juices.

**Example 3. In vitro digestion and translocation models.**
Realistic *in vitro* exposure conditions are important to adequately mimic real life processes in the human intestinal tract.




**Example 4. Marine biotoxin detection.**
A testing strategy combining chemical analysis and bioassays that possibly can replace standard mouse testing for marine biotoxins.

## References


Wang, S., et al., (2014). Extending an in vitro panel for estrogenicity testing: the added value of bioassays for measuring antiandrogenic activities and effects on steroidogenesis. Tox Science Doi: 10.1093/toxsci/kfu103.

Kuiper, H.A., et al., (2013). New EU legislation for risk assessment of GM food: no scientific justification for mandatory animal feeding trials. Plant Biotechnology Journal 11: 781–784.

Peters, R., et al., (2012). Presence of Nano-Sized Silica During in Vitro Digestion of Foods Containing Silica as a Food Additive. ACS Nano 6: 2441–2451.

Walczak, A.P., et al., (2014). Translocation of differently sized and charged polystyrene nanoparticles in in vitro intestinal cell models of increasing complexity. Nanotoxicology, in press.

van den Top, H.J., et al (2011). Quantitative determination of marine lipophilic toxins in mussels, oysters and cockles using liquid chromatography-mass spectrometry: inter-laboratory validation study. Food Addit Contam A 28 (12):1745-1757.

Nicolas, J., et al., (2013). Marine neurotoxins: State of the art, bottlenecks, and perspectives for mode of action based methods of detection in seafood. Mol Nutr & Food Res 58: 87–100.



RIKILT Wageningen UR
P.O. Box 123, 6700 AB Wageningen
Contact: Lonneke.vandergeest@wur.nl
T + 31 (0)317 48 04 62
www.wageningenUR.nl/RIKILT