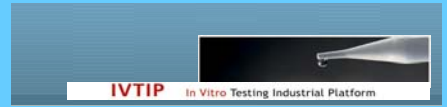


THE APPLICABILITY OF NON-ANIMAL SAFETY ASSESSMENTS: EXPERIENCES OF THE *IN VITRO* TESTING INDUSTRIAL PLATFORM IVTIP

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WHO OR WHAT IS IVTIP ?

The *In Vitro* Testing Industrial Platform (IVTIP) is an association composed of European companies with an active interest in *in vitro* testing, not only to be used in regulatory safety testing but also for compound discovery and product development. Member companies represent the pharmaceutical, chemical and cosmetic sector, as well as independent contract research organizations. The members of IVTIP are all active in supporting and applying the principle of the 3Rs (Replacement, Reduction and Refinement of animal testing), and in promoting the adoption of the fourth R (Responsibility in research promoted by industry). IVTIP is a science-driven organization existing for and by the members.

WHAT IS IVTIP DOING ?

The representatives in IVTIP are scientists who are active in the area of *in vitro* and/or *in silico* methods. IVTIP provides advice to European Union (EU) institutions about industrial activities and needs for research, development and application of alternatives to animal testing. *Vice versa*, they inform industry about upcoming EU activities and new regulations involving *in vitro* testing. IVTIP is an active group of scientists, who discuss new opportunities, inform each other about promising developments and participate in EU projects. The liaison with academic groups is very important to stimulate the applicability of techniques and methods for industrial use, thereby ensuring effective dissemination through transfer of both technology and knowledge.

The Three Rs : Replacement, Reduction, Refinement & the Fourth R: Responsibility

The Four Cs : Communication, Consultation, Collaboration & Coordination

WHAT ARE THE REQUIREMENTS OF INDUSTRY REGARDING *IN VITRO* / *IN SILICO* TESTING ?

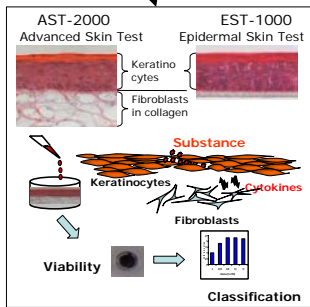
- Results obtained with *in vitro* methods are relevant and predictive to *humans*;
- Results should be reliable, reproducible, unequivocal, relatively simple, robust and cost effective;
- Demonstrated validity and applicability of the assay;
- Regulatory acceptances.

WHEN ARE *IN VITRO* / *IN SILICO* TESTS USED BY THE INDUSTRY ?

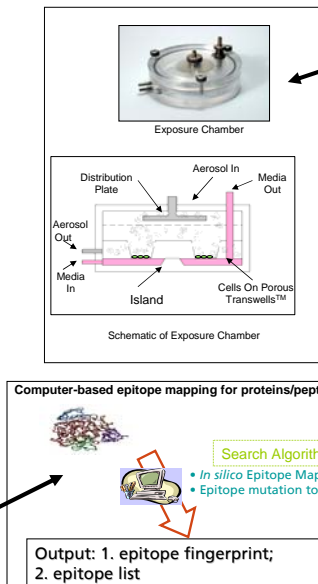
- Safety assessment;
- Discovery and development of new compounds and products;
- To assess biological activity, structural alerts, working mechanisms;
- For making go/no-go decisions regarding further development or maintenance of compounds.

Not only internationally validated and regulatory accepted assays (for authorities) are used, but also many other smaller-scale in-house developed and validated assays are used to investigate different end points (sometimes industry specific) using different combinations of cells, tissues and compounds.

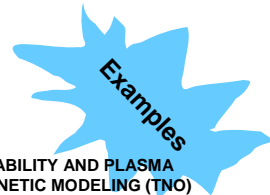
SKIN MODELS FOR THE CLASSIFICATION OF CHEMICALS *IN VITRO* (CellSystems)



NEW TOOLS FOR IMMUNOTOXICOLOGY (NOVOZYMES A/S)



NEW AEROSOL EXPOSURE SYSTEM (BAT)



PREDICTION OF BIOAVAILABILITY AND PLASMA CONCENTRATIONS USING KINETIC MODELING (TNO)



What will the challenges be for the future ?

Dissemination & Technology Transfer

of 3 Rs

The quality of *in vitro* / *in silico* data should be improved (reduction in false negatives and positives) by using human tissue or target organ specific models.

The *in silico*, *in vitro*, *in vivo* and human data should be integrated to increase the predictivity and improve the extrapolation to the human situation. Integrated testing will be challenging because of its complexity, but seems the way to go. Single replacement is usually not possible.

The regulatory bodies should be involved in early development of new methods to increase the possibilities for successful implementation and acceptance. In the light of the new EU legislation, such as REACH and 7th Amendment of the Cosmetic Directive, development and specifically validation and acceptance of alternative methods should be faster to meet the requirements of these new regulations.

The integrated *in vitro* / *in silico* data have to be translated into an *in vivo* message useful for risk assessment and risk management. A major challenge is the definition of no effect levels (NOAELs) using *in vitro* / *in silico* data.

New ways of risk evaluation are needed, including risk communication, risk management and risk perception of the general public.

with Responsibility