

Bridging the gaps between inventors and final users

Testing needs and expectations: the importance of **industrial applicability**

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IVTIP

IVTIP In Vitro Testing Industrial Platform

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Introduction : what is IVTIP & how does it work?

IVTIP is an informal platform of 35 companies with an *active interest in in vitro testing* with very specific key activities, including:

- providing EC institutions **feedback** regarding implemented EC initiatives
- active **participation** in EU funded framework programs as Board members
- **monitoring** promising test methods for their **industrial applicability**
- **dissemination** and technology transfer towards successful implementation

<http://www.ivtip.org>

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Powerful drivers for new test method development

Regulatory drivers: eg. cosmetic directive, REACH, EU legislation and new visions and strategies

Non-regulatory drivers: screening methods for

- pre-clinical toxicology/ pharmacology/ efficacy
- occupational testing/ workers safety/exposure
- quality control testing/batch release

Regardless where the method will eventually be developed for, **industrial applicability is mandatory**

Industrial applicability of test methods: a possible definition

Google for 'industrial applicability':



A newly developed **industrially applicable testing method** should at least comply with a set of **criteria**:

- capturing key events of the *in vivo* mechanism of action (MOA)
- be relevant to the human exposure
- reproducible and reliable
- readily available
- user and implementation friendly
- '*validated*' for a specific purpose
- economically viable
- cost effective

C1: Capturing key events of the *in vivo* mechanism of action (MOA)

- How do I define the characteristics of the developed method biochemically/morphologically?
 - What are the tools used to mimic the *in vivo* MOA? (cytotox vs gene arrays)
 - Did I prove/demonstrate well the rationale of the test method?

Successes: ultimately cells/tissues identical with *in vivo* counterparts; realistically, *in vivo*-like cells

Failures: cells lacking relevant functionality (plant-based assays)

C2: Relevance to the human exposure

- What are the exposure regimen used compared to the human situation (acute vs chronic)?
- What is the domain of applicability (limitations)?
- Does my method mimic the human bioavailability?
- Are the cell types, tissue, organism used relevant?

Successes: 3D modeling of human epithelial models using primary cells (AST1000, EpiDerm, MucilAir, ...), organotypic models, reconstituted organs

Failures: most animal based models, cell-based models based upon animal specific functionalities

C3: Reproducible and reliable

- How reproducible is my method over time?
- Is acute vs chronic, or simple vs multiple application testing possible?
- Can it be easily transferred to other labs?
- Is transportation an issue?
- Was batch-to-batch variability checked?
- What is the (intrinsic) level of variability of the model?
- Is GMP/GLP or ISO certification an added value?

Successes: OECD accepted methods

Failures: some previous validation exercises (monolayers cultures)

C4: Readily available

- How can I ensure easy availability of the method?
- Can it be ordered on a regular and flexible basis?
- What are the distribution challenges?
- How is technical back-up organized?

Successes: commercial available reconstituted skin/epithelial models

Failures: academic models?

C5: User and implementation friendly

- How easy can the method/model be implemented?
- What is the required level of technical competence?
- Does it require special infrastructure?
- How easy is data analysis?
- Can I overcome some technical hurdles by working with a CRO?
- Is patent protection a roadblock for implementation?

Successes: 3D tissue models, BCOP, ICE...

Failures: Microphysiometer, patented technologies?

C6: 'Validated' for a specific purpose

-What is the purpose of my method? 'Validation' has a variety of definitions!

- Will the method used in regulatory test environment or for pre-clinical screening?
- What will the method eventually replace/reduce?
- How does my method compare to other existing ones?
- Should I perform benchmark validation?
- Can it be used as stand-alone test or as part of a strategy?
- Does it cope with the validation performance criteria?
- Did I choose the right validation partners (industrial/regulatory)?

Successes: ESAC endorsed methods

Failures: Home Office Study (Brampton et al, TIV, 1997)

C7: Economically viable

- How expensive is the production/commercial development cost?
- Can I make a profit when marketing my method (ROI)?
- Is the timing for marketing right?
- Will I reach a break-even in a reasonable time frame?
- Do I have the right business partners for successful marketing?
- Will I require active lobbying to become successful?
- Are all the 'P's' in place?
- Are there any juridical hurdles related to the use of the model?

Successes: SkinEthic IPO

Failures: ATS Skin² /LSE models (early 90')

C8: Cost effective

- What is the cost-benefit relation once implemented?
- How much time is gained/ replaced by the method?
- Does it require expensive equipment?
- Will the test decrease the product development cycle?
- How many products can be tested simultaneously (HTS)?

Successes: pre-clinical in vitro screening methods

Failures: FT-skin model for corrosion testing

Conclusion and recommendations

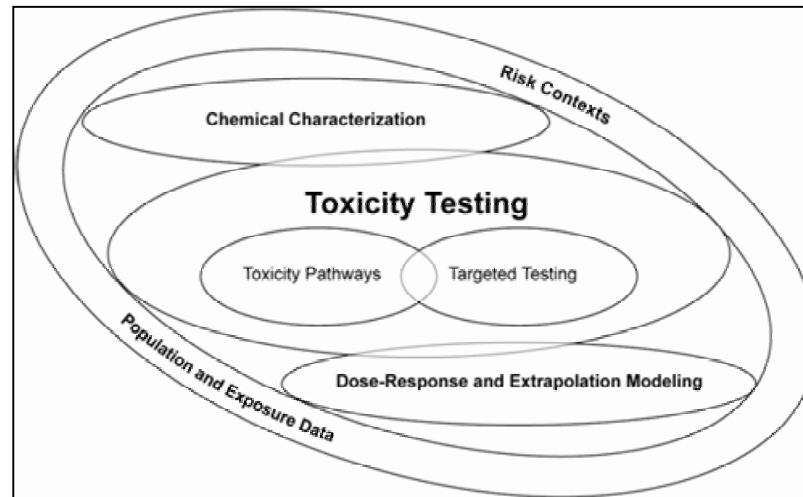
All issues/questions presented need to be carefully evaluated and answered

- a commercial business needs professional expertise/guidance
- the inventor/developer may not be the best commercial agent
- 'separation is an illusion': multiple stakeholders are be involved!

Industrial applicability should be discussed **early on** in the development of new testing methods and strategies

Challenges for the future

“Toxicity testing in the 21st century: a vision and a strategy” ©2008 Melvin Andersen, Daniel Krewski, Ellen Mantus, and Laren Zeise



IVTIP Fall meeting: Nov-Dec 2009, CARDAM, Belgium

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You never fail until you stop trying...

Thank you for your attention