

# Points to Consider when Moving Towards Acceptance



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# Defining Acceptance

## Regulatory Acceptance

- The method must reduce or replace animals required for regulatory testing purposes
- Formal validation is often – but not always - a prerequisite
- Before a validation authority will consider conducting a validation, they must be convinced that the method has reached a certain level of assay development

# Defining Acceptance

## Scientific or Industry Acceptance

- Method could be useful for a variety of endpoints including efficacy, product development and safety
- It does not have to replace animals
- Companies will often conduct their own evaluation or validation study – especially when using the method for safety decisions
- Companies will move forward much faster if they are shown that the method has reached a certain level of assay development



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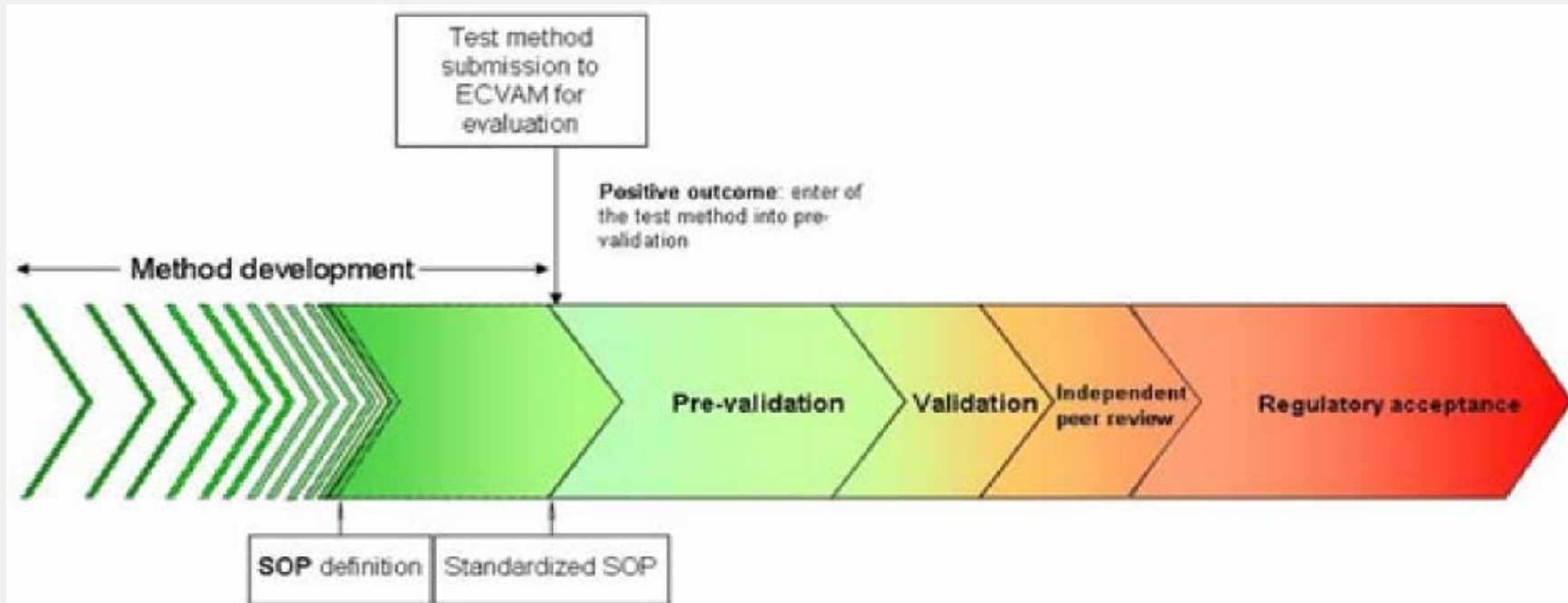
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# Burden of Proof

What package of information does the manufacturer need to supply in order to move forward with validation and acceptance ?

# Pathway to Acceptance



**Figure 1**

*Schematic representation of the evolution of new test methods from development to regulatory acceptance.*

Sens-It-iv Newsletter (No. 23, December 2008)



# Meeting Criteria for a Prevalidation Study

Demonstrating that a method is ready to be considered for a prevalidation study is a key step to both types of acceptance

In addition, a method that meets the criteria for prevalidation may be considered a “suitable” method and therefore be able to be used for testing under REACH



# What is Prevalidation?

- Prevalidation is a small scale inter-laboratory study to ensure that the protocol of a test method is sufficiently optimized and standardized. It gives a preliminary assessment of relevance and reliability.
- 3 Phases: Protocol Development, Protocol Transfer, and Protocol Performance
- Involves testing a limited number of coded substances in at least 3 laboratories

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# Assay Development

- Two references to help define the criteria for prevalidation:
- *Curren et. al, The Role of Prevalidation in the Development, Validation and Acceptance of Alternative Methods, ATLA, 1995 23, p. 211-217*
- ECVAM Submission Guidelines

# Assay Development

## Required Information:

- A summary of how the method was derived and the biological basis for its relevance
- Data derived from the test using an appropriate set of test materials
- Availability of a Standard Operating Procedure (SOP)
  - Sufficiently detailed and clear to allow the transfer of the method to another laboratory
  - Contain a list and description of the materials and instruments needed
  - A step-wise description of the procedure (Protocol)

# Assay Development

- An explanation of how raw data are transformed and analyzed, as well as the description of the preliminary prediction model (PM)
- Additional supporting evidence such as in-house reports, published papers and presentations, etc.



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# Other Considerations during Development

- The method should be time and cost effective
- Proprietary information should be kept as minimal as possible
- Applicability and limitations should be defined

# Considerations in Development

- Production issues must be anticipated
  - Meeting increased/fluctuating demand
  - Training of new staff
  - Adherence to GMP or GLP principles
- Documents must be written in an unambiguous way so that labs in different countries can follow them
- Materials used should be available internationally
- Any preliminary studies should be designed to show that the data are reproducible within and among laboratories



# Special Considerations for Regulatory Acceptance

Various working groups from ECVAM, EPAA and others recommend:

- After determining the regulatory endpoint to be replaced, all supporting data should be developed with the regulators' viewpoint in mind.

→ This implies communication with regulators early in the process





# Navigating the Process

A developer may not have staff experienced in all of these areas. In this case a partner can help.

Look for expertise in:

- Optimizing methods
- Writing SOP's
- Implementing GLP's
- Conducting validation programs
- Communicating with regulators

# Final Thought

- Industry acceptance currently accounts for the majority of testing utilizing alternative methods
- Cosmetic and personal care products which are not registered
  - Pharmaceutical development
  - Efficacy...

*If regulatory acceptance is not achievable there is still a good market for a useful method*



# Thank You for Your Attention



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