

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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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

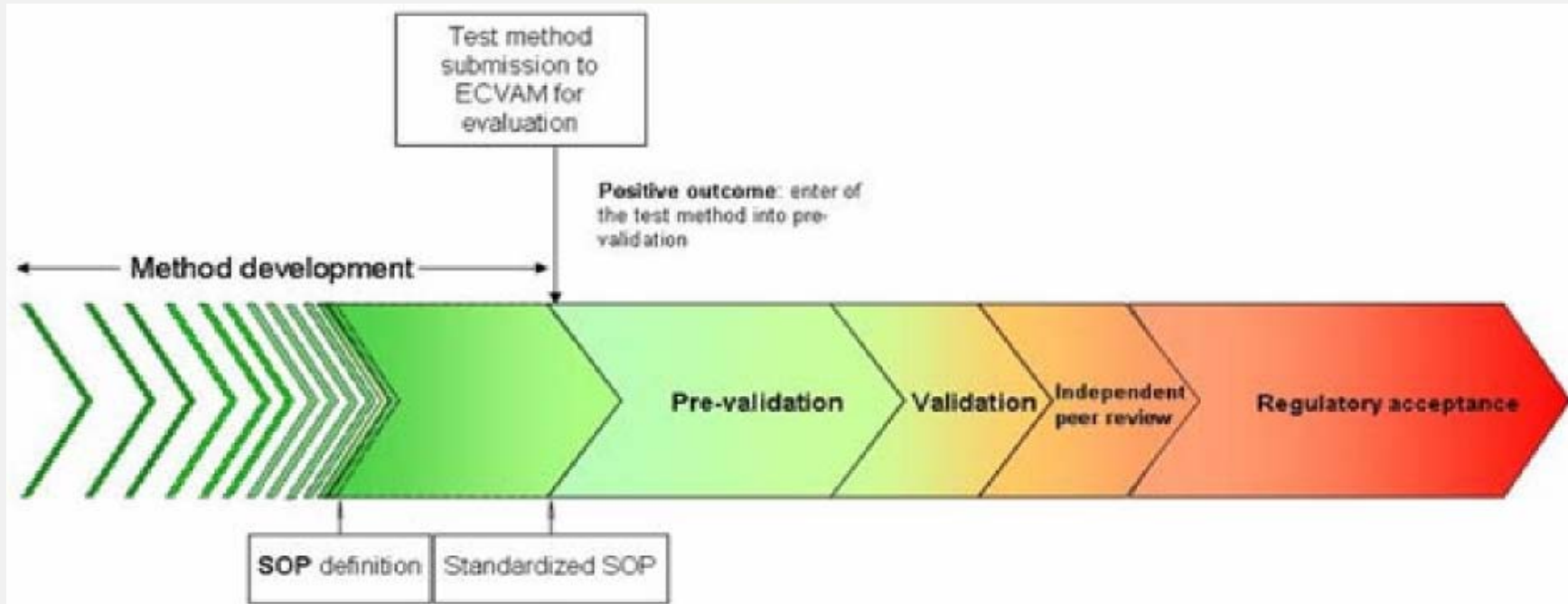


Figure 1

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



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.





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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