Validation, Regulatory Acceptance & International Harmonization

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National and international authorities have established regulations and guidelines for the safe marketing, labeling, and (in some cases) transportation of chemicals, pesticides, pharmaceuticals, and consumer products. Many of the provisions require manufacturers to conduct testing to identify potential hazards to human and animal health and to the environment, and to submit the test data to regulatory authorities. Most of the toxicity tests for hazard assessment are animal tests that were developed decades ago. There are many advantages, including scientific, ethical, and economic ones, for replacing these animal toxicity tests with non-animal (*in vitro* and *in silico*) test systems. *Alternative test methods* include any method that reduces, refines, or replaces an animal test. *Non-animal test methods* are *in vitro* or *in silico* methods and are sometimes called replacement alternatives.

To facilitate the replacement of old tests with new ones, national and international authorities have developed processes and criteria for evaluating new toxicity test methods to determine whether they can replace an existing method. The major hurdles include test method *validation* and *regulatory acceptance*. Since most existing toxicity test methods are animal tests, having a new non-animal method *validated* and *accepted* by regulatory authorities for use in place of an existing animal test is of utmost importance to progress in replacing animals in toxicity testing.

The major steps for replacing an existing regulatory test with a new method are:

- Test development (possibly preceded by basic research)
- Prevalidation/optimization
- Validation
- Peer review/independent assessment
- Regulatory acceptance

Government and international authorities have also established processes for promoting the *international harmonization* of validation criteria, regulatory testing requirements, and test protocols, so that different countries and regions require and accep the same types of data for regulatory decisions.

International regulatory acceptance **of a non-animal test method is the ultimate goal, which when achieved has a significant impact on reducing animal use in regulatory assessments.**

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