What is test method validation (TMV) and what can it do for me?

What is test method validation?
Test method validation is the documented process of ensuring a test method is suitable for its intended use. It involves establishing the performance characteristics and limitations of a method and the identification of influences which may change those characteristics. The experimental results are subjected to statistical analysis and a series of pre-defined acceptance criteria are applied to the results. Establishing that a test method consistently produces reliable results is a critical element of assuring product quality and safety.

Why should TMV be performed?
TMV is an important element of quality control. Without validation there can be no assurance that the test results will be reliable and fit for the purpose. In some fields, validation of methods is a regulatory requirement. Generally, any method used to produce data in support of regulatory (e.g., FDA) filings or the manufacture of devices for human use should be validated.

What types of methods require validation?
Test methods can be *destructive* or *non-destructive*, based on the disposition of the test samples. The methods can measure *attribute data* (qualitative) or *variable data* (quantitative). All are candidates for validation, though the process for each can vary. Most test methods exist as validated standards, methods developed by technical standard organizations (ANSI, ASTM, ISO…) to establish uniform methods and procedures for testing. But standard methods do not always fit the requirements of the tests to be performed. These test methods may require validation:

- standard (verifying lab version of standard is acceptable) - the lab specific version of a method must meet or exceed results of the standard
- standard methods outside normal scope - when using an established standard for testing outside the original scope of the standard
- amplified/modified standard methods - validation of a version of a standard, with modifications
- laboratory designed/developed - validation of a method developed specifically for the test lab, to cover a requirement not sufficiently met by a standard

When should methods be validated?
TMV is a risk based activity. The extent of the activity is often dictated by the potential level of patient harm weighed against the business risk of not performing the activities. The device *risk index* or *harm classification* dictates the minimum level of statistical confidence required. Higher risk requires more rigorous testing. In most cases, TMV is not mandated in the medical device industry (ISO 11607 testing is one exception). But demonstrating the safety and effectiveness of a device is difficult to do if the methods for establishing these parameters are not shown to be appropriate and reliable. Conditions when TMV may be required:

- new method is developed
- revision of established methods
- when established methods are used in (or transferred to) different test facilities
- for comparison of methods

Are there different types of TMV?

The type/extent of testing for a given method is driven by its intended purpose. A test for appearance will not require the same validation experiments and supporting data as a test to determine the rated burst pressure of a balloon catheter. A *full validation* is needed for new methods or when major changes to an existing method affect the scope. *Partial validation* is performed on previously validated methods that have undergone minor modifications. Generally, fewer tests are needed and are based on the potential effects of the modifications. *Cross-validation* can be used as a means of assessing inter-laboratory execution of the same method.

Validation activities can be performed using several methods, though the most common include crossed or nested Gage R&R and Attribute Agreement Analysis.

What does method validation entail?

Method validation involves conducting a variety of experiments that focus on performance elements of the method to be validated. Generally, a test method validation goes through the following phases:

- determination of test specifics and protocol development (sampling plan, acceptance criteria…)
- performing testing per protocol
- results analysis
- refining the test protocol and procedure if initial testing does not meet pre-determined acceptance criteria. This would be followed by execution of the new protocol.

The level of activity in each phase is dictated by the customer requirements of each particular method and validation.

Validation characteristics that should be considered include but are not limited to:

- Accuracy: a generic concept of exactness related to the closeness of agreement between the average of one or more test results and an accepted reference value.
- Precision: the closeness of agreement among test results obtained under prescribed conditions.
- Repeatability: closeness of the agreement between the results of successive measurements of the same measurand carried out under the same conditions of measurement.
- Reproducibility: closeness of the agreement between the results of measurements of the same measurand carried out under changed conditions of measurement.
- Linearity: Indicates that gage response increases in equal increments to equal increments of stimulus
- Range: The values within which a measuring instrument is capable of measuring or which a generating instrument is capable of generating.

What are the benefits of TMV?

Proper validation of a method provides documented evidence of method performance and prescribes on-going measures to ensure quality monitoring for the life of the method. Well documented validation facilitates internal QC/QA review. Customer and regulatory audits can be executed more smoothly because detailed documentation provides a clear links between a validated method and the systems, facilities, and procedures upon which the method is founded.

Test method validation of some kind is a must in any industry that collects data. If a company cannot objectively justify its test method(s) for a particular inspection/measurement, then resulting data is suspect, making the related product validation and verification suspect and challengeable. FDA observations that test methods are inadequate or that the company does not have appropriate data that demonstrates the method performs as intended, rank high on the list of observations in the medical device industry.

For more information about test method validation, please contact Jim McGovern, TMV Consultant, DDL at jim.mcgovern@testedandproven.com or 952-283-2002.