Sterile Barrier Association

GUIDANCE DOCUMENT
TEST METHOD VALIDATION

ISO 11607 part 1 section 4.4.1 requires test methods used to show compliance with the standard to be validated and documented. The standard defines validation as applicable to test methods as:

'Confirmation by examination and provision of objective evidence that the particular requirement for a specific intended use can be consistently fulfilled.'

Fitness for purpose is the key principle in validation and includes as assessment of the technological possibilities, the risks and the costs involved. If the fitness for purpose principle is maintained then validation may be carried out at a reasonable cost but with a higher degree of uncertainty.

ISO11607 part 1 section 4.4.2 requires the validation of a test method to demonstrate the **suitability or representativeness, repeatability, reproducibility** of the method plus the **sensitivity** for integrity tests. Sensitivity can be considered as the lowest amount that can be measured with reasonable statistical certainty.

Unavoidable systematic and random errors are inherent in any test procedure. This lack of perfection is often described as uncertainty. There are many factors, apart from sample variations, which may contribute to the variability in the application of a test method including human, equipment, technical and environmental factors.

The aim of validation of test methods is to demonstrate that the method is fit for its intended purpose and the results have an acceptable uncertainty.

How suitable or representative a test method is for the application and intended range for which it has been designed depends upon its ability to produce results that correlate to the performance characteristics of the product in use.

When interpreting test results, the inherent variability of a test method must be taken into account in order to assess whether single result or batch to batch differences from a specified value are within the expected variation due to unavoidable random factors or are a true deviation from it. The closeness of test results to the accepted reference value is known as the accuracy of the test method. The accuracy of the method can be defined in terms of it precision and bias.

Precision is the closeness of agreement among test results obtained under stipulated conditions and **Bias** is a consistent or systematic difference between a set of results and an accepted reference value.

Precision can be expressed in terms of repeatability and reproducibility.

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Repeatability refers to the variability between independent test results gathered from a single or intra-laboratory testing.

Reproducibility refers to the variability among single test results gathered from different or inter-laboratory testing.

Repeatability is a measure of how well a single laboratory can control the variability factors and characterises the minimum variability of results whilst reproducibility demonstrates the precision between different highly controlled laboratories and characterises the maximum variability of results.

It should be born in mind that a test method may prove to be accurate and stable without necessarily being a *suitable* method for the product and it's use under test.

Once a new test method is being used more extensively, exploration of the effect of changes to the test parameters can be initiated to show how **robust or rugged** the method is.

A range of different validation techniques are available and their effectiveness and how applicable they are depends on the type of test method. It is necessary to specify the method being used in any particular instance.

Examples of useful documents are listed below:

ISO 5725:-	Precision of test methods - Determination of repeatability and reproducibility for a standard test method by inter-laboratory tests.
ASTM E 2282:-	Standard guide for defining the test result of a test method
ASTM E 1488:-	Standard guide for statistical procedures to use in developing and applying test methods
ASTM E 456:-	Standard terminology relating to quality and statistics
ASTM E177:-	Standard Practice for use of terms precision and bias in ASTM test methods
ASTM E 1169:-	Standard guide for conducting ruggedness tests
ASTM E691:-	Standard practice for conducting an inter-laboratory study to determine the precision of a test method.

This list is not exclusive and is not a recommendation by the SBA and is offered for educational purposes only.

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