

> TEST METHOD VALIDATION (TMV)

Maetrics employs consultants and engineers with an average of more than 15 years of relevant experience including former managers, directors and vice presidents representing a wide variety of industries. Their business and project management expertise covers every level of validation planning, execution and reporting for the pharmaceutical, biotechnology and medical device industries. These areas include but are not limited to:

- Site Validation Master Plans (SVMP)
- Master Validation Plans (MVP)
- Design Validation Master Plans (DVMP)
- Test Method Validation (TMV)

The U.S. FDA defines method validation as: "the process of demonstrating that analytical procedures are suitable for their intended use." Maetrics recommends the use of a risk-based approach using the USP (Chapters <1225> & <1226>) and International Conference on Harmonization (ICH) guidelines (Q2 & Q3) for Pharmaceutical method validations and verifications. These include Specificity, Accuracy, Precision (Repeatability & Reproducibility), Ruggedness, Detection Limit, Quantitation Limit, Linearity, Range, Robustness and Stress Studies. Additionally, limits for Residual Solvents and Impurities may need to be identified. These methods are also consistent with ISO 14971.

Bioanalytical method validation includes all of the procedures that demonstrate a particular method used for quantitative measurement of analytes in a given biological matrix - such as blood, plasma, serum or urine- is reliable and reproducible for the intended use. The fundamental parameters for this validation include accuracy, precision, selectivity, sensitivity, reproducibility and stability.

For Medical Devices, characteristics identified through the Risk Assessments and Specifications are tested as either attributes or variable data, and may utilize metrics such as alpha, beta, GR&R or P/T ratios.

Not only can our staff prepare the plans and protocols, they can also coordinate the resources assigned to execute the activities and prepare the summary reports.

> EXAMPLE CASE STUDY #1

Initial State

A pharmaceutical manufacturer was testing finished products using methods that had not been properly validated. Several large batches of product were about to be rejected using these test methods.

Objective

The primary objective was to develop and validate the test methods for the finished product analysis.

Maetrics Engagement

The following items and tasks led to the development of several new test methods and validation of existing methods for finished product testing:

- Developed solvent residue test methods for a solid dosage steroid product to monitor for methylene chloride, methanol, ethanol and acetone residues.
- Validated finished product test methods for solid dosage hormone products according to USP Chapter <1225>.
- Performed Minimum Detectable Limit (MDL) studies for 23 analytes.

Results

All requested test methods were validated, and supported the release of current and successive batches.

> EXAMPLE CASE STUDY #2

Initial State

While performing process and design reviews at several sites across the country for a global manufacturer, it was determined that several of the test methods required to test the products either did not exist or were not validated. Many items listed in the product specification and risk analysis had never been tested.

Objective

The primary objective was to develop and validate test methods required for the process and design validation/verification testing of a variety of products. This was to include visual inspection, attribute data and variable data methods.

Maetrics Engagement

The following items and tasks led to the development and verification of test methods for compendial methods, as well as the development and validation of attribute and variable data test methods for all applicable products:

- Created matrix of test requirements for EN 1707, EN 20594-1, EN ISO 10555-1, EN ISO 10555-2, ISO 594-1, ISO 594-2, and client requirements to ensure that test methods and validations encompassed the full range of all applicable variations of luer and catheter testing.
- Verified corrosion resistance test method for compliance to EN ISO 11070 for guide wires using the criteria delineated in EN ISO 8044 as guidance.

- Developed visual standards to support surface and appearance testing requirements for compendial and client methods. Commissioned, purchased and ensured proper calibration of magnifiers used for visual inspections.
- Ensured all operators successfully passed qualification requirements to accurately identify known good and known bad products for all identified visual failure modes prior to performing product release testing.
- Improved processes by delivering TM and TMV protocols and reports for stents, catheters and dilators including Graphic Operator Interface documents for medical device manufacturing.
- Created and validated variable data test methods including dimensional tests such as ID and OD and performance characteristics such as tensile and kink resistance.
- Established process nominal tolerances and control plan, process parameter limits and demonstrated performance using validated statistical techniques: sampling plan analysis based on FMEA risk index, DOE, TMV [attribute (visual) and analytical].
- Developed comparative standards for Radiopacity attribute test methods for guide wires.

Results

Process and design testing was completed using the validated test methods and standards generated. Existing products were recertified and subsequent products were able to leverage test methods and validations during development.