6.1 Analytical Method Transfer (AMT)

Although an AMT may occur at any point in the method and product lifecycle, analytical methods are often co-transferred with the manufacturing process during product development and /or after commercial licensure.

The stages of an AMT include a preliminary evaluation and preparation of the new laboratory to receive the test method, development of an approved method transfer protocol, and application of suitable statistical tools to analyze the results. the outcome is documented in a method transfer report.

For all AMTs, the responsibilities of the SU's and RU's laboratories should be established. The quality and / or service agreement(s) should clarify all conditions and responsibilities. In addition to the preparation and sharing of samples, critical reagents, and standards to be used during the AMT studies, some continuous post-AMT testing (monitoring) should be considered (4,12). Table 6.1-1 lists the suggested responsibilities for each laboratory and provides some examples of how tasks and responsibilities could be shared by both laboratories during AMT.

Table 6.1-1 Suggested AMT Responsibility Matrix

Laboratory	Suggested Responsibilities
SU laboratory	• Assess feasibility/readiness • Compile QC/process data • Organize training, if required • Establish the transfer package • Write transfer protocol based on requirements of both laboratories and knowledge of methods prior to transfer • Establish protocol acceptance criteria • Allocate resources for training and transfer study • Provide critical reagents and samples • Provide troubleshooting support • Approve the transfer report
RU laboratory	• Review the transfer package • Define the transfer process, including training requirements • Inform the donor laboratory of potential issues identified (such as different suppliers of critical equipment) • Allocate resources for training and transfer study • Analyze transfer data • Write the transfer report • Inform the donor laboratory of the outcome of the transfer • Approve the transfer report

6.1.1 General AMT Strategy

The strategy used for an individual method to be transferred and / or to support a product transfer can vary depending on the exact circumstances. Options for strategies are illustrated in USP < 1224> Transfer of Analytical Procedures (10). A comparative study model is further described below.

6.1.2 Design of Comparative AMT Test Studies

The AMT protocol should include a study design specifying method parameters to compare, samples to test, justified acceptance criteria，and the statistical methodology to evaluate the results (see Table 6. 1.2-1).

Table 6.1.2-1 General AMT Design Parameters and Considerations

AMT Design Parameter	Considerations
How many representative batches? - Matrix approach (number of different sample types and/or batches to be evaluated)	· Two or three batches bracketing the expected active protein concentration ranges could be used. The selected materials should be representative of routine samples. · Retain samples, reference standards, samples at the extremes of acceptance limits, stability samples, and/or spiked samples should be used, depending on the situation. · For impurity tests, samples may be spiked or degraded so that the level of the impurity is below and/or above the acceptable quality limit (AQL) (and/or specification limit). If samples with a measurable impurity level are not available, it might be necessary to prepare spiked samples to evaluate the accuracy and precision of measurable amounts of impurity/degradation levels during the AMT studies. · If there are differences in the formulation, the range of formulation differences should be tested. The rationale for the selection of representative AMT samples should be documented in the AMT protocol.
How many replicates per sample and laboratory? (Number of independent runs)	· The number of replicates depends on the repeatability and intermediate precision performance of the method to be transferred and the desired confidence level(s) for meeting product specifications. The AMV report and other related data sources (for example, routine test results) should be reviewed.
How many Intermediate precision variability factors are used?	· At least two critical factors should be selected based on prior knowledge of which factor(s) may have the greatest expected impact on variations in test results.

6.1.3 Selecting AMT Performance Characteristics

The intended purpose of the method should be used to justify the rationale of the study design and acceptance criteria for each method transfer. Table 6.1.3-1 provides an example of performance characteristics to be compared between laboratories for different types of methods. Other performance characteristics covered during the validation studies may also be considered.

Table 6.1.3-1 Examples of Method Types and AMT Performance Characteristics

Type of Method	Sample AMT Performance Characteristics
Identity tests	· System suitability, specificity, and qualitative comparison (if applicable)
Process and/ or product related	· System suitability, precision, and accuracy · Consider several concentration levels: minimum reportable quantity and/or

impurities (quantitative)	quantitation limit(s) and 120% of the product specification · Stability samples may need to be included to assess stability-indicating capabilities when relevant
Impurities (qualitative, limit)	· System suitability, and detection limit(s)
Assay - content and potency	· System suitability, precision, accuracy, range, and stability samples may need to be included to assess stability-indicating capabilities, as relevant

6.1.4 AMT Documents

AMT processes are documented through AMT protocols and AMT reports. The AMT protocol typically consists of the sections listed in Table 6.1.4-1.

Table 6.1.4-1 Typical AMT Protocol Sections

Section No.	Section Title	Subsections
NA	Protocol approval	Protocol title and signatures with job titles and responsibilities
NA	List of protocol sections	Table of contents, list of figures (if applicable) and list of tables
1	Introduction	Intended use and sample(s) description
2	Method and product/process	Brief description and (target) specifications
3	Samples, materials，equipment，and instruments	Sample preparation and storage, materials, equipment, instruments, and personnel
4	Historical assay performance	Summary of historical data for assay control, s ample, process capabilities, design space limits (if available, and prior analytical platform technology method performance (if applicable)
5	AMT characteristics and design	AMT characteristics, statistics, acceptance criteria, and justification(s)
6	AMT execution matrix	Visualized execution process map(s) and/or execution matrix tables
7	Data analysis	Calculation samples and proposed statistical tests
8	Procedures, references, and guidelines	SOP(s), AMV protocol / report(s) and other references

The AMT report describes the results of implementation of the protocol, compares these results to the acceptance criteria, and draws a conclusion regarding the acceptability of the transfer.

Reference: PDA TR 65