Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
This document provides guidance for setting experimental testing patterns and acceptance criteria for Analytical Method Transfer Exercises (ATME).

This document provides guidance to GLP sites in identifying lots and number of samples for testing, setting appropriate acceptance criteria for conducting transfers.

The extent of AMTE testing should be commensurate with the method capability and its intended use. The specification levels, validation data and historical performance for each method should be reviewed (where available) to determine the appropriate transfer criteria/limits. Based on the intended use of the method, appropriate acceptance criteria may include evaluation of inter laboratory differences, system suitability, reproducibility, selectivity, sensitivity, recovery and/or comparison to the appropriate specification or method requirements (e.g. spectroscopic or chromatographic identification).

Appendices I and II provide decision trees for conducting assay and impurity method transfers.

Identification of Lots to be used for Transfer
When an API or a single strength of a drug product is being transferred, a minimum of one lot may be used for the AMTE. If a single lot is to be used, it is recommended that the testing pattern include multiple analysts, multiple days and /or multiple instruments to assess the Receiving Laboratory's (RL) ability to generate consistent, reproducible results. Where multiple lots or batches are used for the transfer, the

Transferring Laboratory (TL) should evaluate the necessity for including multiple analysts, multiple days and /or multiple instruments in the transfer testing pattern.

If multiple drug product strengths are manufactured from a common or similar blend, only the highest and lowest bracketing strengths need to be included in the AMTE.

Successful transfer of the high and low dosage strengths will qualify the RL to test all of the strengths within the bracketed range, provided that the sample preparations for the different strengths are similar.

When identifying the materials to be used for the transfer, the TL will determine if historical data will be used or if comparative data will be generated specifically for the transfer. Historical data is defined as data generated by a qualified laboratory outside the transfer process. Some sources of historical data are stability, certificate of analysis, and validation data. If commercial lots are used for the transfer, it is recommended to avoid using lots whose most recent results lie near the specification limit. This is not a concern for expired, purposely degraded, or development lots.

set the criteria at 1/4th of the recovery range (e.g. ≤ 20% High -Low for a recovery range of 140% -60%).

For the transfer of TLC methods, there is no intra-laboratory precision requirement. When conducting an inter-laboratory comparison, the criteria should be set such that the reported level of each impurity is consistent with the historical TL result. If a spiking experiment is to be conducted for a drug product, the impurity should be spiked at a level below and above the specification limit. For Active Pharmaceutical Ingredients, it may be possible to qualify a RL based on its ability to observe the lowest level standard band. It is also important to obtain a copy of the RL's TLC plate for verification of the reported result.

Replicate and Criteria Setting When Transferring Residual Solvent Methods
Even when lots are available with residual solvent levels at or above the QL, it is recommended that a spiking experiment be conducted to accurately assess the RL's ability to perform the testing. When conducting the experiment, a minimum of one solvent needs to be assessed to qualify the RL. Ideally, the solvent with the lowest specification limit should be used. If the historical data show levels of that solvent in the lot identified for the transfer, then it is recommended that the experimental plan
includes a requirement to perform multiple analyses (e.g. 3) of an un-spiked sample from the same lot and then use the average results from the un-spiked sample in the recovery calculations to correct for the presence of the solvent in the sample.

1. Replicates
At a minimum, three spiked samples should be analysed when transferring a residual solvent method. 2. Inter-and Intra-Laboratory Acceptance Criteria The following guidance, in conjunction with available validation data, may be used to establish recovery ranges and precision requirements. For spiking levels between 0.1% and 1.0%, the recommended mean recovery should be 100% ±
25%. Typically, precision should be set accordingly using either %RSD or the absolute difference between the highest and lowest recovery results. Where the difference between the highest and lowest recovery results is used, set the criteria at 1/4th of the recovery range (e.g. ≤ 20% High-Low for a recovery range of 140-60%).

Replicate and Criteria Setting When Transferring Identification Methods
1. When transferring an identity method, a single sample preparation may be used for the assessment; however, it is also possible to include multiple samples, including those that would fail the test. Typically, identification methods have acceptance criteria within the method itself; therefore, it is acceptable to qualify the RL by meeting this requirement. No inter-or intra-laboratory acceptance criteria are required; however, if the identity method involves an intricate technique (e.g. proteolytic map identities) it may be advisable to include an intra-laboratory criteria to ensure the RL can perform the test consistently.

Replicate and Criteria Setting When Transferring Dissolution Methods
1. Replicates
At a minimum, 12 units/lot are required to transfer a dissolution method. If review of historical data for the lots to be used in the transfer, as well as other lots, show product variability > 10%

Table 2. Suggested Transfer Acceptance Criteria for Impurities

If the specification is between two limits in the table, the wider criteria of the two should be used. The maximum allowable difference between labs should be set based on method precision, product variability and any historical data available. If the criteria to be used are different than those supplied in Table 1, then appropriate justification should be included in the transfer plan. **Reminder:** If commercial lots are used for the transfer, it is recommended to avoid using lots whose most recent results lie near the specification limit..

How to Use This Table: In instances where the amount of an impurity is less than the specification limit, calculate the interlaboratory criteria using the table below. For example, if a lot of material to be used in the transfer has an impurity present at a level of 1.2% and the specification limit is ≤2.0%, then the interlaboratory agreement may be set at ±0.4% (20% of 2.0%). This criterion should be evaluated against any historical and/or validation data available to ensure it is appropriate.

Product Specification	Maximum Allowable Inter-Laboratory Difference† (Absolute)	Within Lab Precision Requirements
≤10.0%	± 13% of the expected result	RSD ≤ 5.0%
≤5.0%	± 16% of the expected result	
≤3.0%	± 20% of the expected result	
≤1.0%	± 25% of the expected result	RSD ≤ 10%
≤0.1%	± 40% of the expected result	

† The number of significant figures assigned for the acceptance criteria should be equivalent to the number of significant figures required by the test's specification.

