1. PURPOSE

1.1 This document describes steps to be taken to ensure successful transfer of assay technology between laboratories.

2. SCOPE

2.1 The scope of this document is limited to the Technology Transfer (TT) of a bioanalytical, cell-based assay, or immunological assay method. When performing a TT, there is a Sending Unit (SU) laboratory and Receiving Unit (RU) laboratory, each with defined roles.

3. GUIDANCE

3.1 The state of the assay needs to be identified as developed, qualified, or validated. If the assay has been validated by the SU, then the RU will be required to perform a partial validation. However, if the assay has not been fully validated by the SU, the RU will need to fully validate. If more than one laboratory will be performing the assay within a single study than cross validation must be performed.

3.2 A TT generally follows seven steps: (i) Transfer Preparation, (ii) Feasibility Testing, (iii) Gap Assessment, (iv) Technology Transfer Protocol, including validation plans, (v) Technology Transfer Execution, (vi) Technology Transfer Report, and (vii) Assay Maintenance.

3.3 Transfer Preparation

3.3.1 Pre-Method Transfer Considerations: Prior to performing a method TT, it is critical to assess the level of method development completed by the SU and ultimately the intended use of the assay by the RU. Acquisition of documents (method, SOPs, reports, forms), reagents, equipment, and software take place prior to formal testing and is driven by mutual communication between the SU and RU. Both the SU and the RU are responsible for sharing details of the method, and open communication so that method transfer can succeed. Assumptions should not be made. SU and RU should share all relevant procedures. In addition, training takes place during this time. If the SU has qualified and/or validated the assay, the RU should request from the SU the items below.

1. Method and SOPs - The assay SOP is required, and other supportive SOPs should be provided as well. Supportive SOPs might include reagent qualification, use of a liquid handler, cell culture, etc.

2. Reports (method development, qualification, and/or validation reports) - Reports help illustrate the performance outcomes of the assay. Development reports are very helpful, because they define the assay parameters and inform RU of critical parameters by including aspects of development that failed, e.g. robustness testing.

3. Laboratory forms - Well-constructed forms help the RU track key assay attributes, which in turn helps monitor assay performance and troubleshoot problems in case the transfer experiences failure.

4. List of specific equipment required - The RU should attempt to use identical equipment as used by the SU. Critical equipment as identified by the SU should not be substituted, and the RU must acquire identical instrumentation (manufacturer and model) for a successful transfer (e.g. a specific type of plate reader). If new equipment is required, a full IQ/OQ/PQ is required to ensure proper equipment functionality. If the equipment is used to generate raw data, and intended to support a GLP study, then the equipment must be validated. If identical equipment is not used, then, prior to the validation, an assessment should be performed to demonstrate the assay performance is not affected.

5. Reagents - Critical reagents (reference standard, quality controls, capture antigen, antibodies, etc.) must be provided in sufficient quantities to perform *(i)* feasibility testing *(ii)* technology transfer testing, *(iii)* *and* bridge in new material after the transferred assay is established. Identify reagents that the RU will be responsible for generating when performing the assay after the transfer is complete. Any reagent that is to be purchased commercially should include vendor information, catalog numbers, and reagent grades.

6. Samples – Mock samples may also be generated for training and technology transfer. The SU may generate a blinded panel of samples for the RU to conduct performance testing.

7. Incurred samples (IS) – IS are clinical samples in the same matrix from subjects that were dosed and are required for assay validation. Generally, IS should be from the same dose and regiment to be evaluated in future studies. IS should not be pooled unless sufficient volumes are not available. A minimum of 20 IS are generally required.

8. Data analysis software and/or custom programs – If any custom data analysis, equations, statistics, or programming script (e.g. SAS, R, Excel) were used by the SU to interpolate results, the custom software must be provided. The RU must obtain the necessary computer programs or software licenses for the software versions needed to run the data analysis algorithms provided by the SU. The SU should provide mock raw data for the RU to practice analysis, particularly if the SOP allows for data refined with outlier tests and data masking. This is particularly helpful in ensuring that the RU understands how to follow the SOP's data analysis procedures.

9. Training – When travel is feasible, the RU should send a technical representative to observe the method in practice at the SU's laboratory. However, if travel is not feasible, then technology should be employed such as creating training videos, video calls, or other means where critical aspects of the method can be observed.

3.4 Feasibility Testing

3.4.1 Once TT preparation and planning is complete, (documents have been received and reviewed by the RU, reagents and equipment are in place, and training has been completed), the RU lab will execute feasibility testing of the assay per the SU SOP. The data generated during these preliminary runs should be documented however auditing by the quality assurance unit is not a requirement, nor should it contribute toward acceptance or rejection of the official method transfer. Rather, this training data is merely needed to evaluate preliminary technical proficiency and provide a basis for the Gap Assessment in Section 3.5.

1. The RU should perform assay feasibility with at least 1-2 test operators following the SU SOP and provided reagents, and if possible, utilize the SU laboratory forms.

2. The SU sends a technical representative to the RU's laboratory to observe the RU performing the assay. If the SU technical representative cannot observe in-person, then video monitoring is helpful, particularly if troubleshooting is needed.

3. Upon completion of the feasibility testing, the RU reviews the data and procedures to identify areas of success and necessary adjustments (e.g. change in equipment or detection systems, extensions of the assay range).

3.5 Gap Assessment

3.5.1 A gap assessment is a review the status of the systems, procedures and protocols that are already in place to determine what needs to be done to fill in the gaps in order to ensure that a validated method from the SU can be successfully performed at the RU's laboratory.

1. The gap assessment begins with formal team review of the SU's existing practices (SOPs, forms, acceptance criteria, reagent supply, equipment functionality, etc.) against requirements for qualification or validation, and an evaluation of whether the requirements can be met by the RU.

2. RU identifies areas of concern in the process or barriers to meeting upcoming validation criteria. Risks and weaknesses are highlighted.

3. The gap assessment should result in a precise checklist of action items that need to be implemented for the RU to meet the requirements of the TT.

3.6 Technology Transfer Protocol

3.6.1 Prior to the initiation of the formal TT, the RU will prepare laboratory specific assay SOP, and other supportive SOPs and laboratory forms based on those provided by the SU. The RU SOPs will clearly define the system suitability and assay acceptance criteria that were previously established by the SU.

3.6.2 The RU lab will then prepare a formal TT protocol captured under a controlled number (e.g. study number, validation number) to identify all aspects of the TT within the RU's quality system. The TT protocol should include (but is not limited to) the following elements:

1. Protocol elements - All TT testing requirements should be described in the TT protocol. The test requirements include identity and lot numbers of specific materials and reagents with expiry dates, instrument/equipment model and serial numbers used, number of required test operators, test days, and specific test sample material or preparation (if prepared by the RU rather than supplied by the SU). Protocol must specify the number of allowable repeats for invalid and failed individual assays and/or system suitability criteria failures. Retention requirements of all data obtained from the TT should be defined.

2. Test plan – Full or partial validation will be performed based on the method status as determined by the SU. A developed or qualified assay requires a full validation. A fully validated assay requires the RU to perform partial validation of specific parameters. The specific parameters required include precision, linearity, ULOQ and LLOQ. The RU TT protocol must describe test plan for evaluating the reference standard; quality control sample(s); and mock test and incurred samples (provided by the SU, if possible) representing the lower limit of quantitation (LLOQ); and low, mid, high, and upper limit of quantitation (ULOQ) targets of the analytical range. It is recommended that testing be performed by at least two test operators over 3-day period to generate data that supports the various validation parameters.

3. Statistics - The testing requirements should also include details for data analysis and statistical evaluations. The extent of the TT testing, data analysis, and statistical analyses should be sufficient to confirm that the results obtained by the RU are comparable to results obtained by the SU. Equivalence testing should be performed if the RU performs the same level of testing as the SU during validation where the data sets may be compared statistically.

4. Reportable value review - The TT protocol should describe which results (either raw data, final reportable values, or both) the RU will provide to the SU for review. The TT protocol may also specify a time frame for providing data to the SU for review.

5. Acceptance Criteria - The TT acceptance criteria should be described in the TT Protocol. The rationale for the TT acceptance criteria should be based on criteria established by the SU. The TT acceptance criteria must be the same as or more stringent than the criteria that were established by the SU. Only data that meet the acceptance criteria defined in the TT protocol will be used in the evaluation of the TT. These data are used to evaluate the overall success or failure of the TT.

6. Failure - The TT protocol may contain a contingency plan on what to do if the TT acceptance criteria are not met.

7. Communications - Deviations and failures/Out of Specification (OOS) should be reported by the RU to the SU within a predetermined period of time (typically 1 to 3 days) from the identification of the occurrence.

3.7 Technology Transfer Execution

3.7.1 The TT protocol must be approved by all parties, including but not limited to, responsible technical personnel and Quality Assurance Units (QAUs) of both the SU and RU, and the sponsor(s) if applicable. The SU is a signatory on the protocol to verify that the protocol meets mutually agreed upon requirements to complete the TT. Once the TT protocol is signed, the TT assays will be performed by the RU.

1. The RU should provide quality review and oversight of the TT execution.

2. The RU must communicate with the SU per the TT protocol requirements.

3.8 Technology Transfer Report

3.8.1 Upon completing the requirements of the TT protocol (regardless of the success or failure of the TT), a report will be written. The report must be detailed and address all elements of the TT and validation. The report must further address the following:

1. The report must include an executive summary, regulatory compliance statement, location of testing facility, and discussion and conclusions of the overall transfer of the assay.

2. The RU must provide adequately documented evidence that critical aspects of the TT protocol was completed.

3. All individual and compiled results should be included in the TT final report. This includes OOS and failed/invalid results. Failed and invalid results are excluded from the evaluation of the overall TT acceptance criteria for RU to SU comparison, and from the final analysis. However, these must be documented in the final report.

4. The report should include a complete description of any deviations from the TT protocol or SOPs, and include investigational reports.

5. The TT report must be approved by all parties; including but not limited to SU and RU responsible technical personnel and QAU, and sponsor(s) if applicable.

6. A copy of the TT final report should be available at both the SU and RU's sites.

7. All data on the assay should be retained by the RU per the TT protocol.

3.9 Assay Maintenance

3.9.1 Once the TT is complete, the assay then exists as a "living" entity that must be maintained to ensure that the method remains in control and in a validated state over the period of use.

1. Reagent Monitoring: Often times, the SU may only be able to supply a finite amount of critical reagents, and for the RU to support the assay long-term, new critical reagents must be bridged-in. SOPs should be developed by the RU (post-TT) that describe the qualification of new critical reagents that ensure the performance characteristics (as developed and if necessary, validated) do not change.

2. Proficiency Monitoring: Establish a training (and refresher training) course for the method. Ensure that analysts demonstrate proficiency in performance of the assay. Document this training in the analyst's training record. The RU lab should ensure that a training package is in place, as well as a well-developed set of proficiency test samples to ensure that operators are qualified to perform the assay.

3. Modifications: All post-TT updates to the SOP/assay/method should be conveyed to the SU as needed and vice versa if the SU makes changes the procedure on their end. Updates may include changes to reagents, controls/standards, equipment, and software versions.

4. Trending: Assay performance should be continuously at the RU to demonstrate that the performance of the assay remains in control over time. Trend the performance of the assay using the following information (not limited to):
    1. Date of assay
    2. Plate ID
    3. Reference standard curve lot number
    4. Reference standard parameters
    5. Control lot number(s)
    6. Control result(s)
    7. Other important critical reagent lot numbers (e.g., antibody lots, kits, etc.)
    8. Analyst Initials

5. Oversight: QAU oversight (e.g. through audits) should be performed and documented to ensure adequate assay maintenance occurs.

4. REFERENCES

Not applicable

5. ADDITIONAL INFORMATION

5.1 Document Lead: Office of Regulatory Affairs (ORA)

5.2 Posting externally: Yes