# Developing QC-Friendly Analytical Methods

By Shawn Watson, Head of Research and Development

Analytical method transfers are a natural part of project progression. But transferring a method from one laboratory to another – even within the same company – can face challenges related to sample stability, documentation, procedural ambiguity, and underestimating the importance and complexity of the transfer. An out-of-specification could result in investigations, rework, delays, and regulatory implications.

Often, between-lab transfers can involve instruments from different vendors or with different configurations, adding multiple variables that can affect the method and subsequent results.[1] A primary objective of a contract development and manufacturing organization (CDMO) is to ensure the method being transferred from the sending unit (SU), which is often the analytical R&D lab to a receiving unit (RU), often the Quality Control laboratory, will be “QC friendly” and maintain result consistency.

## Types of Validated Assay Transfers

When undertaking analytical methods transfer, it is imperative to base the approach on the stage of development. The later the stage of product and method development, the more stringent the requirements. Therefore, determine a transfer strategy based on the nature of the method, its validation status, the intended product, and experience of the receiving laboratory, in this case the QC lab.

The USP General Chapter <1224> outlines approaches to methods transfer[1]:

- **Direct Transfer:** This transfer includes a physical demonstration and joint analysis of sample by the sending laboratory (SU) and the receiving laboratory (RU). The SU actually visits the RU site to demonstrate the method by analyzing the sample per the protocol. Then, the RU independently performs the analysis.

- **Comparative Testing:** The most common is comparative testing on homogeneous lots of a target material from standard production batches or samples intentionally prepared for the test. A comparative test requires analysis of a predetermined number of samples of the same lot by both the SU and the RU.

- **Covalidation Between Two or More Laboratories:** In this situation, the complete or partial validation of the analytical method is performed by two laboratories that are qualified to run the procedure. The SU involves the RU in an interlaboratory covalidation, including them as part of

the validation team and, thereby, obtaining data for assessing reproducibility during method validation. This assessment is made using a preapproved transfer or validation protocol that provides the details of the method, the samples to be used, and the predetermined acceptance criteria.

- **Revalidation:** When a change is made to an analytical method (i.e., a change in a piece of equipment or reagent or a change in manufacturing process or formulation), revalidation of all or part of the method must be considered. For example, the SU may use a different brand or model of instrument than the RU. In this case, revalidation may be required to demonstrate that the method is not only transferred, but that it is also validated on the new instrument. Revalidate to ensure the analytical method maintains its critical performance characteristics. The degree of revalidation will depend upon the nature of the change.

- **Transfer Waiver:** Under certain circumstances, the RU is qualified to use the analytical test procedure without comparison or generation of inter-laboratory comparative data. If eligible, the RU must appropriately document the justification for receiving the method without a formal transfer.

# Best Practices in Methods Transfer

Despite the best in due diligence, methods often do not perform as well in the RU as they did in SU. To avoid the common pitfalls of method transfer, it is fundamental to take note of these best practices.

1. **Train receiving personnel**

When appropriate, the sending unit (SU) should train the receiving unit (RU), or RU should consider running the analytical method to identify any issues that may need to be resolved before the transfer takes place. While the SU provides the analytical method, reference standards, validation reports, and other necessary documents, the RU must properly train staff before the transfer to ensure that the facilities and instrumentation are properly calibrated and qualified as needed, as well as verify that systems are in compliance with applicable regulations and general lab procedures. The two labs should compare and discuss data to address necessary corrections or updates.

2. **Keep methods simple**

The receiving unit must be able to run the tests reliably and reasonably quickly from batch to batch. The procedures should be written with sufficient detail and explicit instructions so that a trained analyst can perform it without difficulty. The protocol should be discussed, agreed upon, and documented before the transfer. This document should represent a consensus between The SU and the RU, indicating the intended execution strategy and both departments' requirements and responsibilities. Objective, scope, materials and instruments that will be used, experimental design, and acceptance criteria should all be contained within the protocol. Specific analytical performance characteristics to be evaluated and the analysis used to evaluate acceptable outcomes must be clearly defined.[2]

3. **Think like a QC scientist**

The sending unit (SU) needs to understand the restrictions that RU scientists face and develop an assay that accounts for these restrictions. Prepare a method procedure following good manufacturing practice

(GMP) documentation processes. Recognize that what works best in the SU (often Analytical R&D) is not necessarily going to work in the RU environment (often Quality Control), so it is important to think about that translation from the start of method development. Don't specify any material that can pose a supply or quality consistency problem in the receiving unit. Simplify the sample preparation and data acquisition, and make the method unbiased, where possible, to a specific type or instrument brand.

4. **Communication is key**

Accurate communication between the transferring and receiving laboratories and a clear plan with defined roles and responsibilities are essential. The SU and the RU should regularly communicate early on in the drug-development process to ensure that the analytical method works in a QC environment and provides accurate data on a consistent basis. Understanding the needs of QC will ensure that personnel in AR&D create robust methodologies and transfer them successfully the first time, saving time and money. A successful AMT requires accurate communication between the transferring and receiving laboratories and a clear plan with defined roles and responsibilities.

5. **Develop a risk management strategy around the method transfer**

Asking the right questions prevents analytic method transfer failure. Don't underestimate the benefit of a risk analysis. Such an analysis should consider the experience and knowledge of the RU, the complexity and specifications of the product, and the analytical method itself. The time spent investing in this exercise will inform decisions about the method being transferred, the extent of the transfer activities, and the implementation strategy. Most importantly, this will improve the success of the transfer as it's passed from the SU to the RU.

**Summary**

Analytical method transfer done right is an opportunity to deliver better results. Whether an early concept project or scaling the manufacturing of a drug product, each transfer should result in better validation procedure, improved process, and a more robust analytical procedure.

**References**


1. Getting it right: best practices for analytical method transfer, *Manufacturing Chemist*, June 8, 2020.
2. USP <1224> Validation of Alternative Microbiological Methods.
3. Analytical Procedures and Methods Validation for Drugs and Biologics, Guidance for Industry, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, and Center for Biologics Evaluation and Reseach.


**About Pii**

Pharmaceutics International, Inc. (Pii) is a contract development and manufacturing organization (CDMO) with a passion for solving problems efficiently with the highest quality standards. Pii's Analytical Research & Development scientists pride themselves on their experience and ability to expedite method development and tech transfer in support of complex sterile fill/finish projects.

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**About the Author, Shawn Watson**

Shawn Watson joined Pii in July 2020 and is responsible for all product development, including sterile, non-sterile, oral, and topical dosage forms, as well as analytical methods development.

Shawn has over twenty years of leadership experience in the pharmaceutical industry in specialty, generic and contract development and manufacturing organizations (CDMOs). His wealth of knowledge spans Research and Development, Quality, and Technical Services.

Prior to joining Pii, he served as the Vice President of Quality and Laboratory Operations at Lupin Pharmaceuticals, Vice President of Compliance at Sigmapharm Laboratories, and Supervisor of Analytical R&D at Teva Pharmaceuticals. Additionally, he has held a variety of other key positions including Vice President of Quality, Senior Director of Chemistry & Manufacturing services, and Senior Manager of Analytical Research and Development. Shawn's passion for working in the pharmaceutical industry began with his very first job as a quality control chemist with a CDMO and included work with Pii.

Shawn earned a Masters of Business Administration from the Fox School of Business at Temple University, a Master of Science in Chemistry from Villanova University, and a Bachelor of Science in Chemistry and Biology from Heidelberg University. He also obtained a six sigma green belt from Villanova University.