



## DPT Thought Leadership Issue 13: 3<sup>rd</sup> in a Series

# QbD BASED PROCESS DEVELOPMENT SERVICE — THE DPT LABS APPROACH

### INTRODUCTION

This paper describes the approach and benefits of using DPT Labs' QbD Process Development service and follows the second paper in our Thought Leadership Series, "QbD Based Formulation Services – The DPT Approach."

In that paper, we emphasized the importance of DPT's approach to formulation, in particular the manner in which it establishes a robust baseline from which to advance the drug development process. The key components of DPT's Formulation service – a pre-formulation study, formulation and analytical method development, and informal stability study – combine to set up a solid foundation that minimizes the risk of future unanticipated events.

Like the Formulation service, DPT Labs' QbD Process Development service leads a customer through the steps necessary to manufacture drug product, consistently, at a scale beyond laboratory production. Beginning with a risk assessment of both raw materials and process steps, this service builds on the rigor of the formulation service and examines materials and processes to further minimize risks to development success.

If a customer worked with us during the formulation stage, it is an easy transition to the QbD Process Development service. Some customers, however, come to us for the first time at this critical point in the drug development process. In either case, DPT provides a dedicated, experienced, and talented group of scientists, state-of-the-art equipment and facilities in which to perform the work necessary to prepare the drug product for clinical scale production. The goal is the same – to produce drug product in a reliable, consistent, and repeatable way. Simply finding a stable formulation is only the first step in a development process. Building a documented capability to manufacture drug product the same way, every time, is a critical step on the road to approval. We work with major pharmaceutical companies as well as smaller drug development customers – and both benefit from our vast experience and knowledge of the FDA's expectations regarding process, methods, and documentation.





## QUALITY BY DESIGN FOR PROCESS DEVELOPMENT

As described in our first paper, “What Is Quality by Design (QbD) – And Why Should You Care?” there are numerous benefits to the modern, scientific approach that formalizes product design and streamlines troubleshooting. The QbD approach provides a thorough understanding of the compatibility of a finished product to all of the components and processes and provides insights upstream in the development process. As a result, a quality issue can be efficiently analyzed and its root cause quickly identified.

Once a stable formulation has been identified, the next step in developing this understanding occurs in the Process Development stage where critical material attributes (CMAs) and critical process parameters (CPPs) are examined. This examination measures the extent to which any variation can impact the quality of the finished product. The more information generated on the impact – or lack of impact – of a component or process on a product’s quality, safety or efficacy, the more business flexibility Quality by Design can provide.

DPT Labs works with each customer to understand their needs to support clinical trials with drug product. Through a series of risk assessments, we refine the requirements of the raw materials and processes necessary for the drug product manufacture. Analysis of the feasibility batches helps drive a more thorough understanding of the process, isolating and identifying risks. This detailed understanding helps minimize surprises throughout the remainder of the development process and prepares the customer for commercial scale manufacturing.

## RISK ASSESSMENT

The DPT approach to Process Development involves a series of activities to eliminate or significantly reduce risks associated with manufacturing drug product. At this stage, a customer has likely produced a stable formulation

of their product in lab scale quantities. If the customer used DPT’s Formulation service, detailed documentation exists, deepening the understanding of how to proceed with Process Development. If a customer created the formulation independently, our scientists will use the documentation available to manufacture the drug product in DPT’s facilities.

The first step is a risk assessment of both raw materials and process steps. The mix of material attributes and process steps are examined to define the boundary and limitations associated with each material and the process. The result of this risk assessment yields the critical process parameters, in particular identifying the most controlled steps in the process. The combined understanding of the critical material attributes (CMAs) and critical process parameters (CPPs) contribute to meeting the critical quality attributes (CQAs).

Once the CQAs of the formulation – and how they are affected by the process – are understood, the team observes how the overall process shapes the outcome. In simple terms, we look where these attributes are affected by the process and evaluate their corresponding levels of sensitivity. Based on the risk assessment, we test each likely scenario to determine how each ingredient, or “input,” will affect an output. For instance, one phase of the process may require a longer mixing time of particular ingredients to reach an optimal viscosity. Too little or too much mixing time might change the viscosity and adversely affect the product outcome. We evaluate every combination, taking careful note of the effect of each step of the process to produce a successful batch.

Occasionally, a particular combination of ingredients may result in highly complex interactions. The intent of a QbD approach is to reduce complexity and variation in the drug development process. If we observe such a complex interaction between materials, our team may respond by conducting a variation of a multi-factor Design of Experiments (DOE) study that facilitates planning for a desired outcome. This may be completed with a simple DOE of standard size batches in the lab. The number of batches



will depend upon how many factors and inputs are involved, together with any time and resource constraints. The goal of these batches is to mimic what happens at the commercial scale. These batches would likely be made in either 1 kg or 3 kg laboratory vessels which mimic the commercial-scale equipment.

The DPT team has extensive experience with a wide variety of the materials used in many formulations for drug products. This helps to more quickly evaluate and understand the interactions between materials and processes. It is important to note that if we come across an unfamiliar material, we don't ever guess about its properties. That would be taking a shortcut and contrary to a QbD approach – and potentially devastating to your project.

We invest the time and effort to research and fully understand each raw material. If we aren't completely confident, we consult experts and trusted sources. For example, we might contact a raw material supplier to investigate if a material is heat sensitive, and if so, understand the optimal temperature range to target when adding the ingredient to the vessel. Not only does this new knowledge increase understanding of the overall process, it provides the added benefit of not wasting valuable materials or time conducting unnecessary “trial and error” tests to determine what an expert already knows. Once we have an understanding of the optimal order of addition for ingredients along with appropriate temperatures, mixing times, etc., we can proceed with the process.

Our meticulous approach to risk assessment in the Process Development service allows us to make definitive determinations about each process and material we examine. Our team's vast experience and knowledge of material attributes allows us to operate quickly, consistently providing our customers with the confidence necessary to move ahead with their drug development project. The risk assessment typically takes four to six weeks depending on the number of issues that arise at the laboratory scale.

We understand that many drug development projects are under pressure from strict timelines and constrained budgets. The temptation to take shortcuts can be intense. However, success comes at a cost. In most cases, the cost of discovering potential problems early is far less than discovering them later. As we've said in our other QbD papers, the question customers must ask themselves is if they prefer to “pay now, or pay later.”

## FEASIBILITY BATCHES

Once the risk assessment is complete, the team gathers data accumulated from each test. The work now begins to develop an understanding of how the formulation reacts in a commercial environment (versus a laboratory environment). The team authors “compounding modules,” which are based on the records of all the experiments conducted along with the corresponding data/information from each test. These become the batching instructions that will be used to manufacture the batch(es) in the commercial manufacturing environment, referred to as “feasibility batches.”

These relatively larger-scale batches (feasibility batch sizes can typically range from 20 kg to 200 kg) initially use data from the risk assessment. Depending on the outcome of the first attempt, the team makes modifications as needed. Feasibility batches can be conducted in one of two ways:

1. Execute one proven successful process from the initial findings and modify as needed. Essentially commit to one particular study and design a process based on the laboratory work. Then, fine-tune subsequent batches based on what is discovered.
2. Conduct additional Design of Experiments (DoE) studies and execute in the manufacturing facility. Use different process designs to acquire all the input needed to create a final batch process.





For either option, three to four batches will be produced. Once these batches are made, the team examines the data to determine if the process performed as intended. If so, the team creates another batch or batches at the same size to determine if they are identical to the initial round. The stability and consistency of these batches is monitored and documented. Once the feasibility batches produce consistent results that meet CQAs, it is time to move to the Scale Up stage.

## BENEFITS OF DPT'S PROCESS DEVELOPMENT SERVICE

The ultimate deliverable of DPT's Process Development service is documentation for the customer that consists of:

- Raw materials testing and supplier information
- Process development report
- Clinical/registration supplies of formulated product
- Validated analytical methods
- Pathway forward to validation and commercialization

The customer receives various reports that can be included as part of an FDA submission package. For those customers who desire, DPT Labs also offers a service to complete the CMC portion of the submission for you.

At the completion of the Process Development service, DPT Labs offers follow on Scale Up services and cGMP manufacturing capabilities. DPT is one of only a handful of contract development companies that offer complete end-to-end services from Formulation to commercial manufacturing. We offer the unique guarantee of staff continuity, that is, the team and scientists that begin work with you will remain with you throughout the length of our development relationship. This unparalleled continuity assures that DPT Labs has a deep understanding of your drug product, its development and manufacturing processes, and can represent it effectively for FDA submissions.

You can read more about these services in our next Thought Leadership series paper.

## PROCESS DEVELOPMENT – THE IMPORTANCE OF CHOOSING A RELIABLE QbD PARTNER

The challenge of adopting QbD begins shortly after a molecule is discovered. Systematically selecting an initial formulation, well-understood raw materials, and establishing repeatable process steps can be the beginning of a successful journey to launching a valuable drug product. As discussed earlier, many companies have short-term resource and/or time constraints that prevent them from using the thorough approach that QbD demands. This results in a “pay now or pay later” choice that ultimately results in development that spirals out of control.

Given the FDA's commitment to QbD and the incentives they provide for adopting it, companies now have the imperative to find a way to adopt this scientific approach. Many companies have tried and given up in frustration. As the saying goes, “If it were easy, anyone could do it.” How do you give your company the best chance at success with QbD?

One way is to join forces with an experienced, knowledgeable partner who can help your team benefit from QbD with minimal disruption. DPT Labs brings together multiple sources of information, vast experience, and practical insights into your product. Our experienced team has delivered many QbD-based Process Development services to its customers. We can help take the mystery out of QbD and get you moving toward your goal of launching a valuable drug product in the most cost-efficient and robust manner.



## CONCLUSION

This paper describes the approach and benefits of using DPT Labs' QbD Process Development Service and follows the second paper in our Thought Leadership Series, "QbD Based Formulation Services – The DPT Approach."

After reading this paper, you should possess the information to see the benefits of using DPT Labs' QbD-based Process Development service in your operation.

When it comes to drug development, the old saying of "pay now, or pay later" holds true. Overlooking key material attributes or proceeding without full understanding of critical process parameters will only compound problems later and can lead to a never-ending attempt to troubleshoot issues. The perceived savings of time and money in the near term will only haunt your efforts later as the cost of discovery after the fact will surely escalate.

DPT Labs' Process Development service can provide several benefits:

- More efficient use of development time and costs
- Ability to meet FDA submission guidelines and expectations
- Reduced approval times – and fewer queries – from the FDA

Look for the final paper in this Thought Leadership Series that will address QbD Services for Scale Up.

To discuss your Formulation needs and how DPT Labs can help, including gaining timely FDA approval and minimizing the cost of your development project, call 1.866.CALL.DPT or visit [www.DPTLABS.com](http://www.DPTLABS.com).

## ABOUT DPT LABORATORIES:

DPT is a contract development and manufacturing organization (CDMO) providing companies the best solutions to their sterile and non-sterile pharmaceutical development and manufacturing needs through innovation, technology, and service. Specializing in semi-solid and liquid dosage forms, DPT has a reputation for quality, unmatched technical expertise, extensive manufacturing capabilities, and an exemplary regulatory compliance record. With five cGMP facilities in San Antonio, Texas, and Lakewood, New Jersey, DPT offers full-service outsourcing solutions, including stand-alone development, site transfers, state-of-the-art manufacturing, packaging, and worldwide distribution.

## CONTACT:

DPT Laboratories, Ltd.  
1-866-CALL-DPT  
[www.DPTLABS.com/Contact-Us](http://www.DPTLABS.com/Contact-Us)

