

# Sound Process Optimization Never Really Ends

On the road to drug substance supply and commercialization, one of the most critical stages is Process Optimization since it lays the groundwork for scale-up, when you move into GMP.

By Ed Price, President, [PCI Synthesis](#)

This process is a continuous activity that enables Contract Manufacturing Organizations (CMOs) to get good yields of Active Pharmaceutical Ingredients (APIs), as well as good quality.

As mentioned in an earlier [post](#), the Process Optimization stage fully establishes and tests the process that will form the basis for the whole program. This stage determines what will be required to scale up the molecule and turn a chemical into a drug substance that is free of impurities and meets FDA requirements and ICH guidelines.

During this stage, the scientists need to understand as much as possible about the process. This includes the Critical Process Parameters (CPPs), or the key variables affecting the production process. CPPs are attributes that are monitored to detect deviations in standardized production operations and product quality. Parameters usually include temperature, concentrations, the time involved in a reaction, crystallization, agitation speed, etc.

## Why Process Optimization is Never Done

Once the initial Process Optimization phase is completed, it never ends there. Once a process is successfully optimized for a commercial product, engineers are always fine-tuning it to get cycle times down, improve yields and further reduce costs.

In a common scenario in which Process Optimization is in play, a CMO may expect to produce 760 kilos of a new pharmaceutical in 2,000 gallons, yet when they are finished, it may only yield 740 kilos. While the 20 missing kilos may not be that big of a deal, the engineers would still work backward to determine where the 20 kilos went, pouring through extensive data, since they had to go somewhere, whether they decomposed or were in filtrates. They would determine if it was a plant issue or conditions that they could not have predicted. In this way, new batches in a manufacturing campaign can be improved based on the experiences of the earlier batches.

## Key to Success in Process Optimization: Experienced Scientists

The key to a successful Process Optimization project lies in the expertise of the scientists and engineers doing the investigative work. This phase can often last several months and continuity is crucial to meet timelines and budgets. Experience helps you get it right the first time, which saves money and helps you get to the Kilo lab faster, with the right process.

## The Role of the FDA in Process Optimization

There are no rules regarding Process Optimization when it comes to FDA compliance, other than the requirement that you have a reproducible process in place, and that you are following it each time. In some cases, if there is a significant change, such as using a new solvent or a different piece of machinery, you may have to notify the FDA about that. CMOs should work to avoid major chemical or equipment change, because that may trigger delays and extensive new reporting, which may not really be worth the effort.

## What a CMO Wishes a Sponsor Understood about Process Optimization

While Process Optimization is critical to the quality of the drug substance and the costs of delivering it, many sponsoring organizations don't really understand the process. Many times, Process Optimization can uncover problems that are completely unpredictable and no fault of anyone, yet can necessitate going back to the lab, causing delays in delivery, as well as added costs for the specific batch.

For this reason, it's important for CMOs to educate their partnering companies about the critical role of Process Optimization, which can uncover problems in the short-term, but avoid bigger problems in the future. It can also ensure that future batches are optimized to reduce costs by eliminating process steps, improving yields, shortening cycle times and producing higher-quality product.

While there are different ways CMOs conduct Process Optimization, the ultimate goal is to derive better yields of chemicals and eliminate problems that can impact successful delivery. As an iterative process that brings about constant refinement, it's never really done but the results are worth the effort.

Want to know more about Process Optimization? Contact us at 978-462-5555 or <http://info@pcisynthesis.com>.