

Breaking Ground

When building a biotech manufacturing facility and a QC lab, which scenario do you choose — build manufacturing first, build the QC lab first, or build both facilities simultaneously?

Here's a challenge: You are a small, virtual company, and you outsource your clinical manufacturing and quality control (QC). You plan to start up your own manufacturing plant and QC lab, and you need to do that while the product is in clinical trials.

The question is simple. You have three options: You can set up manufacturing first, QC first, or both at the same time. Which option is best for you, and why? Let's look at the possibilities:

Building QC and Manufacturing

This is the most challenging of the scenarios. You have to manage two complex projects and ensure that both succeed simultaneously.

Any new facility (and its staff) has to iron out initial hiccups to work properly. If you start up your plant and your lab at the same time, you can expect to see shortfalls in quality or errors from both facilities. But which facility was responsible for which problems? That can be difficult to figure out. You'll have to investigate both possibilities — a process that can set you back by weeks and even months.

If a problem in the lab makes it appear as if your product has changed upon transfer to the

new manufacturing plant, the consequences will be costly to you and risky to your regulatory strategy. You may have to add additional specifications, testing, process validations, or studies to prove comparability between the "new" and "old" products.

Other aspects to consider when you embark on the simultaneous strategy include the following.

Objectivity. If the readiness of your new QC lab is standing in the way of opening a new plant that costs hundreds of millions of dollars, you'll face great pressure to say that your lab is "good enough," whether it is or isn't.

Compliance. Your contract manufacturer (and its QC lab) is probably at a high level of compliance, or you would not have chosen it in the first place. It has experience handling your product. When you move your product into a new lab with new people, it is reasonable to expect compliance to dip initially — right at a point in the development cycle when FDA expects compliance to be getting better.

Companies need to face this risk directly. "Compliance has to be there, so it will be," is one response. But gritting your teeth won't make a new lab or plant operate perfectly. Instead, you need to factor the dip into your regulatory strategy and find ways to compensate for the extra testing, training, auditing, or time. This is the place to conduct detailed contingency planning!

Resources. In the simultaneous scenario, QC competes directly with manufacturing for money, validation engineers, software, and attention — and it's the little kid in the

family. If the budget shrinks, QC may be hit disproportionately.

Competition for resources can have long-range consequences. For a small company, the process of opening a manufacturing plant is pivotal in developing a corporate culture. A year or two of battling for resources may go a long way toward establishing an adversarial culture in your QC and manufacturing units.

Expertise. For many small companies, the scarcest resource is expertise. And the simultaneous scenario robs you of flexibility in using your best people. If one of your manufacturing people is strong in microbiology, it would be desirable to have her help design your microbiology lab. But that won't happen if all her time is taken up with the manufacturing facility. If you build your facilities sequentially, you have more opportunity to move people between projects — which also helps in team building.

Building the Manufacturing Plant First

If opening the plant and lab simultaneously presents too many risks and problems, how about opening the plant first, and waiting six months to bring the QC lab on line?

Technically, this should work fine. But as a business proposition, it has problems. To realize the advantages of opening the lab after the plant, you need to keep your QC testing at the lab in which it has been done all along. And that may not make sense for the contract manufacturing organization (CMO) you've been working with — the CMO that has just lost your business.



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QC isn't a major revenue stream for a CMO. Whereas manufacturing might start at \$500,000 per batch, release testing is closer to \$20,000 per batch. Your CMO certainly isn't going to be excited about doing your QC work. Worse, the capacity of your CMO's QC lab may be closely linked to its manufacturing capacity; the company may not have the resources to provide you with QC at all. At the very least, you'll pay more than you want to for QC work. At the worst, you'll be in the situation that you hoped to avoid — testing the output of a new plant with QC performed at a new lab. And you will be paying a contract laboratory big bucks to support the mountain of validation testing needed to start up your manufacturing plant and its utilities.

Building the QC Lab First

At first glance, building your QC lab first doesn't seem to offer much advantage. The point of building a new plant is to cut costs and to build the value of your company. Bringing QC in-house will save you some money and build some infrastructure — but not much.

But when you look at a QC lab as part of a *process* — a process that culminates in a new manufacturing facility — you start to see some substantial advantages to building a QC lab before a manufacturing plant.

- You can qualify the lab before changing the facility in which the product is made, which makes comparability issues much easier to navigate.
- You can develop a team that will be able to validate the manufacturing facility, saving money and time.
- You can begin to create a culture in which QC is a core activity, not an add-on.
- You avoid the risks of the other scenarios. In particular, you don't take on the difficult, high-risk task of validating manufacturing and QC simultaneously.
- Finally, because you continue to outsource your most expensive process until everything else is ready, you maximize your economic clout with your CMO.

The Unintended Choice

Any of the three scenarios can be made to work. But for ease and security, building your QC lab first is hard to beat. It even fits well within the timelines of building new facilities: If you start work on a new plant and a new lab at the same time, the

laboratory will be done six months to a year before the plant, which is just about perfect.

In practice, many companies still find themselves trying to get plant and lab up simultaneously. Why? It happens for several reasons. I've seen companies that were pushed into the simultaneous scenario by delays or problems with finance. I've seen companies that had plants under construction before anyone realized that they'd *need* a QC lab.

But the most common reason, I suppose, has to do with the way some companies plan big projects. They create interlocking teams, and send people off to work with their own resources and their own budgets. The

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manufacturing team says, "OK, the plant is going to make its first batch of product in January. QC, you need to be ready." QC calculates a timeline based on the idea that it will analyze its first batch in January, and before you know it, the company is committed to the simultaneous scenario.

When you watch from outside, it's obvious that QC has to be factored in from the start and be coupled to the regulatory strategy — that the plant launch should be modeled as a hand-off from the CMO. The key to planning is maintaining an unbroken chain of validated manufacturing and QC. But the complexity of the tasks makes that a challenge to bring off. Having access to people experienced in start-up projects is one of the biggest keys to success.

Making It Work

Whichever scenario you choose, identify the risks and invest resources in dealing with those risks.

In the simultaneous scenario, perhaps the greatest risk is the immense pressure to say that the lab is working and the product is "good enough" to send to market — when there's not really enough evidence to tell. It's important to insulate the person who has to make that judgment. Consider using a neutral outsider. If you use an insider, do what you can to eliminate conflicts of interest. Try to give the lab a cushion of time and resources.

Have a dedicated team available to solve problems. If you have even five people who go wherever it's "hot," they can shuttle between manufacturing and QC, keeping both in sync. Not only will this help keep the project on track, but it will combat the silo mentality that can develop during big projects.

Strategies like this will help, but the real solution is one you can't implement if you wait until you've broken ground on your new plant. It's something you need to do when you first negotiate a contract and quality agreement with your CMO. Before you sign, say, "Someday we're going to be leaving you. At that time, we want an option to have your QC lab go on testing our product while we qualify our lab." Write that into the contract up front, when the CMO is still eager for your business. You may never exercise the option. But at least you have the choice.

These tips are potentially useful. But the best tip of all is one you've heard before: Start your planning early. By the time your product is ready to go into clinical trials, you should be developing a plan for how you will get that product to market — including your best thinking on how you will manage the crucial hand-offs of manufacturing and QC. It probably sounds like a lot of work — especially when so many products fail before reaching the market. But by picturing the whole chain of events that gets a product to market, you'll spot the opportunities — like the contract option discussed above — that will smooth the road for your product. There are simple solutions for many of the problems you'll encounter along the way if you anticipate and have a plan in place. And be sure that the quality unit has a seat at the table. **BPI**