

How to Select a CMO:

What Should You Look For in an R&D Team?

Part 2

Choosing the best CMO to prepare an API for manufacturing requires that you ask the right questions.

Our continuing series on how to evaluate and select a Contract Manufacturing Organization (CMO) covers the key differentiators – R&D, manufacturing, analytical capabilities, technology transfer, and quality assurance.

This article continues our focus on how to evaluate a CMO's R&D team, which is crucial to timely completion of projects and subsequent regulatory submission. In [Part 1](#) we cautioned that you should not be star-struck by a well-designed website, gleaming glassware and good salesmanship. Instead, focus your attention on the people who will be involved in the technical aspects of your project, the R&D team, their equipment and capabilities.

There are the six key R&D team attributes to look for:

1. Low turnover → **People**
2. Proven ability to innovate and think outside the box → **People**
3. Well equipped with a wide array of capabilities → **Equipment**
4. Readily available analytic support → **Support**
5. Scale-up capabilities → **People** - **Equipment**
6. Technology transfer capabilities → **People** - **Equipment**

In Part 1 of “how to select a CMO,” we covered what questions to ask to determine whether there is a productive, well integrated, experienced R&D team with reasonably low turnover and proven ability to innovate and problem-solve. We also discussed how management can impact job performance.

In this article, we will now turn to assessing how the equipment and analytical capabilities the R&D team can impact your project.

If an unanticipated technical challenge arises, as it likely will in creating new process chemistry, you will want the team to be able to respond and solve the problem quickly. The solution to the problem may involve an alternative method, reaction, reagent or manipulation, which in turn could require the use of equipment or instruments other than what was originally used to develop the process. Consequently, it is important that the CMO's labs are well equipped. The R&D team should have a wide array of different capabilities, and a good amount of experience using that equipment.

But even if they don't have the specific equipment, have they faced and solved such problems previously? If so, it's a big plus in their favor.

So ask these questions: **Can you give an example of a project where you ran into a problem but were able to come up with an alternative solution even if you didn't have the exact equipment you would have liked?**

Also, **Does the equipment you have in the R&D lab help you handle process research problems that arise? How?**

Specific Capabilities Your CMO Should Have

In particular, look for and ask about the following capabilities:

- Experience developing robust crystallization procedures for intermediates and final products.
- Salt selection and polymorph screening.
- Rapid screening of reactions conditions by utilizing parallel equipment.
- Critical process parameter assessment.
- Development of continuous flow processes.
- Jacketed glass reactors for process research.
- Large-scale hydrogenation capabilities.
- Synthesis at extremely low or high temperature (-100 °C to 200 °C).
- Ability to work under high-pressure reactions (> 100 psi).
- Large-scale chromatography purification equipment.

Readily Available Analytical Support

You can't get to where you want to go if you can't see where you are going. Never is that more true than in process development. It's mission-critical that the CMO's R&D team has readily available and timely access to strong analytical support. At PCI Synthesis, that means having:

- **High-performance liquid chromatography (HPLC)**, used to separate, identify, and quantify each component in a mixture.
- **Gas chromatography (GC)**, used for separating and analyzing compounds that can be vaporized without decomposition, for testing a compound's purity or separating components of a compound.
- **Liquid chromatography–mass spectrometry (LCMS)** combines the physical separation capabilities of liquid chromatography (HPLC) with the mass analysis capabilities of mass spectrometry (MS). The two combined synergistically enhances the individual capabilities of each technique.
- **Gas chromatography–mass spectrometry (GCMS)** combines the features of gas-chromatography and mass spectrometry to identify different substances within a test sample, detecting even trace amounts of a substance.

- **Nuclear magnetic resonance spectroscopy (NMR)** exploits the magnetic properties of certain atomic nuclei and is used for determining the physical and chemical properties of atoms or the molecules in which they are contained.

In order for the R&D team to be productive, the majority of this capability needs to be on site and within the direct control and access of the lead scientist on the project. Otherwise, the R&D team will be waiting for data and then deciding what changes are needed. Because process development is such an iterative process, it is very important that the lead scientist in charge has the ability to access analytical data quickly and easily. Otherwise, progress can slow to a crawl.

Throughout the drug development program, it's essential to develop reliable methods for in-process testing as well as analysis of intermediates and APIs. It is also important that the technical team be able to perform real-time reaction monitoring to generate detailed reaction/impurity profiles. For that, they will need that array of instruments you'll be looking for, without which it would be impossible to optimize reaction conditions. Optimization reduces cost and maximizes throughput by classical methods or statistical design of experiments (DOE).

Speak with the technical team of your prospective CMO. It should become fairly obvious where they stand in terms of their internal analytical support for their R&D function. Anything less than consistent and reliable access to strong analytical capabilities should not be acceptable.

For more about scale-up, check out other articles on our blog, [ranging from "10 Factors to Consider When Picking a Partner for Commercial Scale API Manufacturing,"](#) and technology transfer (we have two articles, including a [checklist](#) and a [list of do's and don'ts](#)) capabilities. Or call us at 978-462-5555.