

CONTRACT FERMENTATION LANDSCAPE

Facility Selection in an Environment of Limited Options

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Funding for early stage advanced biotechnology is ramping up and companies commercializing fermentation-based technologies are faced with the decision to either build their own demonstration-scale facility or utilize existing contract manufacturing organizations (CMOs). There are clear benefits of using CMOs, however conducting a successful CMO search is much like preparing for a difficult hike, the most important factor going in is having the right mental perspective to understand the challenge that lies ahead.

It is important to understand what a CMO is and is not. In the world of biotechnology, a CMO is a manufacturing facility with aseptic fermentation and downstream recovery to make a range of products from microbes. Implied in the name is that these are primarily manufacturing facilities that have long term agreements to make products (primarily pharmaceuticals) from processes with an operational history and have successfully been scaled-up. By contrast, most emerging biotechnology companies looking to do scale-up work, are seeking shorter term arrangements (as low as just a few fermentation runs) to prove their technology and produce samples for potential clients. While CMOs can successfully support scale-up work, it is usually a small subset of the CMO world and finding the right partner is a complicated and time-consuming journey. Some lessons-learned based perspective is as follows:

Don't be a "5" looking for a "10" – sounds like advice you might get from a buddy in high school, but also applicable most CMO searches. Many early stage biotechnology startup ventures often believe their scale-up project is much more attractive to the CMO world than the CMO world views the work. They get funding and expect a line to form of CMO's wanting to do their scale-up work, but are surprised when they not only don't have a line, but find it difficult to get calls back when they start their search. Pharmaceutical production is strong and the world the CMOs has continued to diminish, making the effort longer and more costly than often expected. Scaling-up through CMOs is still a valid approach, but understanding the market conditions can streamline the process.

Clearly define your goals – scale-up has many facets, including getting data on fermentation and unit operations at larger scale, generating sample product for potential clients and in the case of novel foods, producing representative materials to be used in regulatory (GRAS) testing. All of these are goals are important, however they often conflict. The client and regulatory product samples are an example. In the case of client samples, the largest amount of product practical is usually the goal, while in the case of regulatory samples, there is often a need for the material to come from a series of batches, not just one large batch. This dictates a need for more runs in smaller fermenters than the product runs. These factors will have an impact on selection of a CMO site and needs to be understood up front.

Start at the end and work backwards – building on the goals discussion, it is important to start with the goals as an end point and work back to understand what is required. What type of fermenter is required? How much downstream recovery? Is a spray dryer required? Does the product need to be produced to food standards? These are just an example of common and critical early stage questions that will reduce a theoretical starting list of 20 or 30 sites down to just a few very quickly. As time and money are usually in short supply for biotechnology ventures, this triage at the front end of the process will save significant time and effort.

Commercial Structure – another key issue to understand up front. There are typically different structures used for scale-up work at contract manufacturing facilities, generally broken into fee for service and hybrid with some form of equity. While traditional CMOs are typically fee for service, they are not always open to shorter duration scale-up activities. The facilities that are often best suited for scale-up work, are often interested in “a piece of the action” in the form of equity. Neither is right or wrong, but experience has proven any deal involving equity, will be much more complicated and have a much longer timeline.

Get a passport – often a surprise to many doing a first time CMO search is the limited number of options within the United States, especially when looking for larger scale operations (10,000 liters or greater) open to supporting scale-up work. Sites in Europe and Mexico are the most often used, with options in eastern Europe becoming more common.

Downstream recovery, where the wheels can come off – as advanced biotechnology is typically driven by aseptic fermentation, this can receive a disproportionate amount of attention during the initial search efforts, but the requirements to make a final product dictate that the CMO have (or be able to assemble) the required downstream recovery. This is commonly a major obstacle in the selection process. While the CMO may have some key equipment, it is uncommon for a CMO to have all required equipment. The most common approach is to bring in skid-mounted rental unit operations where possible. Most CMOs are set to accept process skids and this is generally the cleanest approach. In the case where this does not work, it is possible to ferment at one site and do downstream recovery at another, but the risks involved in packaging and shipping fermentation broth make this a less desirable option.

For additional details on the advantages and challenges, check out my previous publication [Scaling-up Through Contract Manufacturing](#).

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