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Ten Things Biologics Contract Manufacturing Organizations Don't Want You to Know

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The biologics contract manufacturing industry is a competitive, low margin business. During their hey-day – approximately 10 years ago – when demand was high, investor's money for biotech companies was easier to get, and capacity was lower, it was relatively easy for CMOs to ask for and get a long term manufacturing capacity commitment. This led to entry of more competitors and additional capacity – which became excess capacity when investor's money became harder to get. To win business CMOs have had to adjust by taking on smaller projects with limited immediate revenue prospects and without long term commitments. Nonetheless, since they negotiate many contracts they are quite good at hiding things they don't want you to know in order to improve their prospects of winning your business. Here are ten things they won't tell you which will help you when you are considering signing a services contract with them.

1. They need your cash now to stay in business

The contract manufacturing sector is a cash flow business. Companies make money by keeping costs as low as possible. While this should not be surprising it is not fully appreciated by biotechnology and pharmaceutical companies which either have money from product sales or have raised large amounts from investors. To keep costs down CMOs keep salaries down, keep aging facilities and equipment in use as long as possible, minimize services provided, and pay vendors (and reimburse employees) as late as possible. The result is high employee turnover, possibly late delivery of materials and components, and the bare minimum provided to the customer.

2. They need a "take or pay" commitment

These days most CMOs will agree to do cell line development and/or process development – whether or not they have the capabilities. They do this for a couple of reasons: Though the absolute amount of money for these stages is not great, the margins are very good because they know for the most part that it is difficult to compare these custom services among multiple CMO proposals. Once you are in the door and your project progresses you are

likely to sign an additional contract for manufacturing. They will take as many of these projects as they can reasonably sign but the reality is that they would greatly prefer that you sign a commitment for manufacturing capacity well in advance of actually needing it. They need these "take or pay" commitments to stay in business. Without them they know that you are free to take your project to a competitor or stop it altogether at any time after the early stages are completed.

3. Excess capacity is always available

CMOs are always scrambling to fill capacity with revenue-producing manufacturing batches. Capacity rarely fills up cleanly as contracts are signed. As a result there will always be "orphan" manufacturing slots which do not coincide with the agreed timelines. The CMOs do not want you to know about these open slots because then you could negotiate a price which includes only a small margin above the variable cost of production. They would of course prefer to sell you this manufacturing slot at their "market" price.

4. They will charge a premium for add-on services

The fact is that no matter how good you think you negotiated the original services contract there will be other services you will need. You will realize this after the project gets started and you receive some results. But even if you don't know that you need anything else, the CMO will be happy to tell you. They do this because they didn't tell you when you negotiated the agreement that you will need additional services in order to get your product ready for the clinic. They can then charge you more – a lot more – because you are now a captive audience and it is more expensive for you to have those services performed elsewhere.

5. They want to make all processes the same

It costs the CMO less money and allows them to more easily schedule the project in their facility if they can use a generic process. By using a standard process less research is needed in the lab, less training is required to transfer the process to the operators in the manufacturing facility, and fewer new batch records need to be written. The timeline from cell line development to GMP manufacturing becomes more predictable. While this can be an advantage to you as you plan your clinical trials, the generic process they develop may not be the optimal process for your product forcing you to pay for changes at a later time.

6. They will want to include their proprietary technology into your process

Let's face it all businesses seek a competitive advantage. For the CMO, this includes patentable technology, trade secrets, know-how, techniques, or other confidential information. By introducing these proprietary components into the process they can generate direct revenue by requiring a user license; or indirect revenue by making it difficult for you to transfer the process to a competitor without their detailed assistance. In extreme cases they will forbid you to transfer the proprietary information to a competitor.

7. They prefer not to improve expression levels (requiring you to pay for more batches)

When you think about it, you realize that there is rarely an incentive for a CMO to improve expression levels – unless you are willing to pay them for improvements. And to be clear the payment would not be performance-based but rather just for putting out the effort. Unless the payment for process improvement is more than the batch manufacturing price they are much better off just having you pay for another manufacturing run. If you have some clinical success and come back for more manufacturing runs they are way better off than if they had improved the process for you in the first place.

8. They do not want to commit to meeting specifications

For a manufacturing run to be categorized as a successful GMP run, two criteria need to be met: A. GMP guidelines were followed; and B. the agreed to specifications were met. There is no way for a CMO to get around the requirement that GMPs be followed. But they have you in a bind with regard to specifications. If you ask them to agree to given specifications before you sign the contract they will argue that they have no in-house at-scale data on which to set the specifications. If you agree to an "engineering" run at-scale before negotiating specifications, the CMO will still insist on specifications which are so broad only incompetence would cause them to fail.

9. They will not agree to produce specific amounts of product

This is often one of the bigger disconnects during a negotiation. It doesn't do you a lot of good if the CMO cannot or will not agree to produce the amount of product you need for a clinical trial. The reality is that unless many batches are performed the manufacturer has little control over the biological process they have developed or transferred in and cannot agree to produce a specified amount of product unless you agree to pay them for however many batches are required to produce that amount. Just don't let them tell you then that the biological process they developed is "in control".

10. Their definition of success is different from yours

CMOs will routinely advertise that their "success rates" are much greater than 90%. It would be difficult to accuse them of false advertising since this is clearly a situation where success rates have different meanings to different organizations. We have seen situations where "success" can variously mean completing batches, meeting timelines, meeting specifications, performing under cGMP, and even starting manufacturing runs. What success should mean is performing a manufacturing batch under cGMP conditions that meets specifications in amounts sufficient to perform a clinical trial and within the agreed timeline. If you ask your CMO you will find that their definition of success is a lot easier to achieve.