

CHAMPIONING CHANGE: OPTIMIZING PLASMID PRODUCTION STRATEGIES

Identifying the right plasmid supplier to help manufacture your biologic is a critical decision that can help ensure reliable timelines and reduce risk. There are several key factors to consider, including a contract development and manufacturing organization's (CDMO's) product quality and analytical testing offerings, their ability to maintain timelines, and whether they offer a pressure tested quality system for good manufacturing practice (GMP) production. In a recent webinar hosted by Ajinomoto Bio-Pharma Services, Erika Morris, Director of Business Intelligence and Business Development, offered her insight into how to avoid common plasmid production pitfalls and identify an experienced, capable plasmid supplier. In the post-webinar Q&A session, Erika tackled questions on best practices for dealing with inconsistent yields and implementing risk mitigation throughout plasmid production. Read her insights below:

Q: Our plasmid supplier has produced two batches, but the yield is not consistent, which is impacting our product deliverables. How would you deal with inconsistent yields?

Erika Morris: It really depends on where the inconsistency is coming from. Is the CDMO working with you to determine the source of the inconsistency, and do they have a structured program? For example, if this was occurring at Ajinomoto Bio-Pharma, we have regular in-process checks through fermentation, processing, and purification. As we are setting those benchmarks, we could quickly identify where the problem occurred so that we could address it. But again, without those regular analytical checks, it would be a bit more challenging to figure out the source of that inconsistency.

Q: What are your typical timelines?

Morris: It is going to depend on where a client is starting. Are we generating the whole plasmid for them as well as a master cell bank, or is the client sending us a master cell bank that we can put through the quality

control checks and release into the tech transfer process? Overall, it is most important that the CDMO and the client discuss timelines to make sure that their thoughts align, based on where the project is.

Q: We would like to work with a more experienced plasmid provider, but we're struggling to justify the cost. What makes it worthwhile to spend more initially?

Morris: Sometimes it is a hard sell to spend a little more up front, particularly if you are in that startup space. You might think about the cost benefit or risk ratio that you are willing to tolerate. If you work with a lower cost provider, they may not have a GMP system in place. Consider if they are going to have to build the GMP quality system while you are working toward a GMP release. What are the risks of working with a non-GMP provider? Are you willing to have a potential delay in the release of the product? Sometimes it is worth spending a little more to make sure you have the GMP experience to address any issues and avoid surprises at the end of production.

Q: What testing do you perform?

Morris: We have a suite of standard testing that we complete for clients, but we're also open to working with testing that a client may need. Typical testing could include residual host cell protein, which is very important as you're producing a plasmid. We're also going to look at purity. It is sometimes important to have highly supercoiled plasmid. Typically, we are seeing greater than 85% supercoiled plasmid being produced. You need to confirm that the plasmid produced is correct at the end, so a simple restriction digest for confirmatory ID is important. We will also look at bioburden, endotoxin, and pDNA concentration. There are a variety of other assessments we could do, including pH, conductivity, osmolality, and anything that the client feels is important. We have a full analytical lab and can work with clients' specific needs for those analytical tests.

Q: What if we don't need GMP at this stage? Can you still support us?

Morris: Yes, we can absolutely work with a client that doesn't need GMP at their current stage. The good news is that when a client is ready to go to the GMP process, we are willing and able to quickly make that transition due to our robust system.

Q: How consistent are yields between different plasmids? Are they consistent enough to know the number of batches necessary for a given quantity?

Morris: Since we are using platform technology at Aji Bio-Pharma, we typically see consistent yields. It is most important to understand how each plasmid is going to perform via early small-scale studies. In those early small-scale studies, we are going to know exactly how much plasmid will be consistently recoverable. If you are a client that knows you have some issues with your plasmid – perhaps it is larger and harder to produce in high amounts – we will determine in our process science lab how to optimize it. From there, we will make sure that we are getting the most out of it when we go to scaled-up production.

Q: Do we need preliminary small-scale studies?

Morris: I would always recommend them. There is a risk if you jump right into GMP large-scale production; it might save you on the timeline and you might get lucky. However, how much experience do you have with that plasmid in terms of production and purification? If you skip right to large-scale 1,000 L production without doing a small-scale 5 L tech transfer, it could add to your timeline in terms of materials and costs. Personally, I wouldn't skip it. There is value in taking that pause. I prefer the slow and steady path to ensure we deliver on what we have promised.

To watch the complete webinar and Q&A session on plasmid production strategies, [click here](#).

About Ajinomoto Bio-Pharma Services

Ajinomoto Bio-Pharma Services is a fully integrated CDMO with sites in the US, Belgium, Japan, and India, providing comprehensive development, cGMP manufacturing, and aseptic fill finish services for small to large molecule APIs and intermediates. Our San Diego site was founded on plasmid manufacturing and offers over 25 years of experience, 17 independent suites, and GMP production scale-up from 100 L and 1,000 L fermentation vessels. We are dedicated to quality in our drug substance and drug product platforms and provide a high level of service to meet our clients' needs. To learn more, visit our website: <http://www.ajibio-pharma.com/>.