



BIO•PHARMA
S E R V I C E S

THE POWER TO MAKE

ENSURING QUALITY OVERSIGHT IN PLASMID DNA MANUFACTURING



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As the industry continues to focus more attention and effort on small-batch production for novel drugs, securing a CDMO with ample experience in drug development and manufacturing, including pDNA production, will be a crucial component for success in these emerging areas of the market, especially as companies face heightened expectations from regulatory agencies. Partnering with Aji Bio-Pharma gives you access to decades of experience and a global footprint that stretches across multiple continents, ultimately providing the tools you need to ensure consistent and quality production for the life cycle of your product.

THE POWER TO MAKE

The landscape of today's biopharmaceutical industry is changing rapidly with the introduction of novel drug products, such as personalized medicines. However, while this sector of the market is expected to have a major impact on patient care in the coming years, it also presents significant challenges during development and manufacturing. One such area is a gap in GMP-quality plasmid DNA (pDNA) supply, an essential building block for viral vector and even mRNA-based vaccines and therapies — the latter seeing intensified focus since the success of the COVID-19 vaccines. Most notably is the limited number of CDMOs with the capacity and expertise to provide GMP-quality pDNA at the volumes needed to meet clinical and commercial manufacturing demand, leading to long lead times for companies waiting for this critical raw material.

While there is a growing number of CDMOs entering this increasingly competitive market, it is important to understand the challenges associated with manufacturing pDNA, so you can ensure the partner you select is able to provide high-quality materials for the lifetime of your product.

FDA QUALITY OVERSIGHT IN GENE THERAPY MANUFACTURING

A recent surge of investigational new drug applications for cell and gene therapies (CGTs) shows this field is growing at a rapid rate, with the FDA anticipating the approval of 10 to 20 CGT products a year by 2025.¹ Due to the continued growth — and many CGTs qualifying for an accelerated path to market — the FDA must ensure manufacturers can maintain the highest level of safety and quality throughout development

and manufacturing, leading to stringent oversight of CGT processes. This, combined with an influx of investigational new drug applications for CGT products,¹ has some companies seeing delays in FDA response.² Additionally, tighter regulatory standards have led to requests from the agency for more information about production processes, with six cell and gene therapy programs being forced to delay their development timelines until they were able to provide the necessary data.³ One of those companies had to wait as long as six months to resume production.

Securing a CDMO with knowledge in this space and a strict quality oversight team is critical to preventing any issues related to your process and/or product quality that could jeopardize its market entry. This includes, for example, the inability to classify and resolve deviations as well as a lack of understanding about the analytics that must be performed during plasmid production, which companies versed only in research-grade pDNA may not know how to do. Although these suppliers may potentially be able to offer reagents at a lower price, their operators and building controls are likely not held to strict levels needed to manufacture GMP-quality pDNA or execute traceability throughout the manufacturing process. Quality control and verification systems manned by trained operators can help prevent mistakes and ensure consistency in pDNA during scale-up, facilitating approval by global regulators.

A common strategy for some companies when vying for CDMO resources is to bring certain capabilities in-house rather than compete

for a potential partner's time; however, pDNA production calls on unique expertise, equipment, and containment that require considerable time and money to implement internally. Biopharmaceutical manufacturers equipped only for traditional mammalian cell culture protein production would need a separate facility to produce pDNA, in order to avoid contamination. And while so many in the industry have given rise to the adoption of single-use technology, due to the many benefits it offers during biomanufacturing, these systems are not suitable for plasmid manufacturing, as they do not provide the repeatability and in-process control of a stainless-steel system. Finally, the expertise needed for microbial cell culture processing is also significantly different than with mammalian cell culture processing, such as knowledge about host strain selection and optimizing fermentation.

Therefore, with so much at stake, it is important to find a CDMO with not only experience in plasmid production but also a proven record of success in providing sufficient and consistent pDNA supply to the companies that depend on them.

A FOCUS ON QUALITY

With more than 40 years of CDMO experience, Ajinomoto Bio-Pharma Services understands the importance of a robust quality control system during all areas of biomanufacturing, including pDNA production. That is why its facilities are equipped with the infrastructure needed to consistently produce high-quality pDNA for its wide range of customers. For example, Aji Bio-Pharma's San Diego site includes a microbial production facility that specializes in producing

biologics from E. coli and yeast. It has a drug substance business segment with dedicated suites capable of multi-campaign production activities. Each suite has internally plumbed USP-grade water, WFI, oxygen, clean compressed air, plant steam, chilled water, and nitrogen and is ISO-7 and ISO-8 rated and sanitized on a weekly basis. A high level of cleanliness and state of control is maintained by Aji Bio-Pharma's quality control team through weekly environmental monitoring of the suites and utilities.

Using its drug substance, drug product filling, and high-potency antibody drug conjugate services, Aji Bio-Pharma's team of experts employs their expertise in upstream and downstream development as well as in-house tools to complete cell banking and plasmid production for a full, quality-assured batch release within 45 days. This includes the use of proprietary development platforms, such as its CORYNEX® Protein Expression System. The CORYNEX system, which relies on *Corynebacterium glutamicum*, simplifies downstream processing, reduces cost, and shortens a product's time to market through a direct secretion of biologically active, properly folded recombinant proteins. Aji Bio-Pharma also developed a proprietary plasmid platform, including culture media, that allows for fermentation at high cell density. **Case studies** highlighting the know-how of the Aji Bio-Pharma team demonstrate its ability to optimize yield for each of its clients' plasmid needs, with a focus on quality and repeatability, resulting in a transition from being one company's second plasmid supplier to its primary provider of this vital raw material.

As the industry continues to focus more attention and effort on small-batch production for novel drugs, securing a CDMO with ample experience in drug development and manufacturing, including pDNA production, will be a crucial component for success in these emerging areas of the market, especially as companies face heightened expectations from regulatory agencies. Partnering with Aji Bio-Pharma gives you access to decades of experience and a global footprint that stretches across multiple continents, ultimately providing the tools you need to ensure consistent and quality production for the life cycle of your product.

ABOUT THE AUTHORS



Katya McLane, Ph.D. is the Director of the Process Science Department at Ajinomoto Bio-Pharma Services, which includes functional subgroups in Upstream and Downstream

Process Development, Scale-up and Technology Transfer of Drug Substance unit operations. During her past six years at Aji Bio-Pharma, she has been responsible for implementing all of the protein and plasmid DNA Drug Substance projects and developing the company's proprietary plasmid manufacturing platform. She has over 25 years of experience in the biotechnology industry.



Ron Chantung is the Director of Drug Substance for Ajinomoto Bio-Pharma Services. Since joining Aji Bio-Pharma in June 2015, he has worked alongside a team of individuals dedicated

to manufacturing protein and plasmid DNA drug substances to produce life-saving drugs. Ron has over 20 years of R&D and clinical and commercial manufacturing experience in the biotechnology industry. He holds a degree in Biomedical Engineering from the University of Southern California. When he is not working, he enjoys spending time with his family and surfing at his favorite reef break in Encinitas, California.

ABOUT AJINOMOTO BIO-PHARMA SERVICES

Ajinomoto Bio-Pharma Services is a fully integrated contract development and manufacturing organization, with sites in Belgium, the United States, Japan, and India, providing comprehensive process development services, cGMP manufacturing, and drug product fill finish services of small molecule and large molecule APIs and intermediates. Ajinomoto Bio-Pharma Services offers a broad range of innovative platforms and capabilities to rapidly scale from clinical and pilot programs to commercial quantities, including: CORYNEX technologies, oligonucleotide synthesis, antibody drug conjugations (ADCs), high potency APIs (HPAPIs), biocatalysis, continuous flow manufacturing, and more. Ajinomoto Bio-Pharma Services is dedicated to providing a high level of quality and service to meet our clients' needs.

REFERENCES

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