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WHITE PAPER

Choosing the Right API CDMO

EXECUTIVE SUMMARY

Custom API development and manufacturing requires a CDMO partner who can promise timely, expert delivery and the adaptability to support fluctuating requirements

COVID-19 has put unprecedented demands on API manufacturers, exemplified by the dramatically increased need for drugs used to manage critical respiratory care patients being placed on mechanical ventilation. In turn, this sudden requirement to significantly boost production has emphasized the importance of adaptability for API CDMOs to maintain drug supply, with some organizations proving better able than others to handle the pressures of rapid scale up.

Common Challenges of Scale Up

Scaling up drug production is a notoriously challenging exercise. A multitude of factors can affect product quality and yield, meaning that transitioning from lab-scale production to a scale suitable for commercial supply is by no means a 1:1 operation. Even something as seemingly trivial as altering the geometry of a vessel or the design of a mixing impeller can have serious adverse effects on reaction dynamics and product properties, making comprehensive process design essential.

The primary aim of proper process design is to develop an in-depth knowledge of the critical parameters in each of the manufacturing process steps. This forms a Quality by Design basis to understanding the potential impact of any changes, greatly increasing the likelihood that scale up will be successful the first time. When performed properly, process design can expedite troubleshooting should any unexpected challenges be encountered and can support increased production capacity at a later date.

Scaling up drug production also requires having the right equipment to do the job. This not only involves identifying equipment that is fit for purpose, but also installing it and subsequently qualifying and validating its performance prior to use. The COVID-19 pandemic has often necessitated that additional technologies be purchased to increase capacity, leading many API CDMOs to face a bottleneck while new equipment is assessed for compatibility with existing workflows. Staying ahead of the game means maintaining a current working knowledge of both existing and new technologies to streamline selection and integration of equipment as required.

Another major challenge of scale up relates to the supply chain since continuous drug manufacturing can be jeopardized should a supplier suddenly become subject to restrictions or experience unforeseen delays in acquiring raw materials. To prevent such a situation from arising, it is vital that API CDMOs communicate openly with providers to ensure the measures they have implemented to secure their own supply chains will assure consistent delivery of quality product. Transparency is vital to understand rolling forecasts and retain sufficient stock levels of starting material for API production.

Attributes to look for in a reliable API CDMO partner

- An exceptional track record in quality and regulatory compliance
- Unrivaled adaptability to fluctuating demand
- Continuous investment in supply chain assurance
- Proven experience in delivering on worldwide launch and commercialization goals

Practical Measures to Support Increased Demand

An experienced API CDMO will benefit from an unparalleled knowledge of the factors underlying successful scale up, having spent many years developing both their own, and partner, programs. Leveraging this vast multidisciplinary know-how allows timelines to be compressed by ensuring that scale up goes according to plan the first time.

During process characterization, an experienced API CDMO will quickly be able to identify and troubleshoot any gaps in a provided technology package. Moreover, having encountered many similar problems before, an expert team will be well-practiced in problem-solving within a short time frame, allowing any missing data to be generated before moving to scale.

An API CDMO will also have the internal capability to react quickly to an issue or support a sudden need for increased production, ensuring that projects are kept on track. Anticipating possible issues ahead of time allows for rapid implementation of improvements to existing processes, or the purchase, installation, and validation of new equipment without incurring unnecessary delays.

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Continuous investment in back integration of strategic products is also fundamental in achieving scale up to time. Wavelength's approach of developing additional synthetic steps for manufacturing strategic products from simpler, more readily available starting materials has already seen proven utility across many different projects. Having the option to implement these steps in-house has demonstrated its worth during the COVID-19 crisis.

Another way of expediting the transition to increased scale is to have a shared commonality across equipment and processes used for small-scale and large-scale production. Ensuring consistency at the equipment level as production increases helps to minimize the risk of introducing additional factors that can impact key product parameters related to quality and yield.

Company size can also be highly relevant when it comes to moving quickly on complex projects with challenging timelines. Typically, a smaller API CDMO can respond more dynamically to changing customer needs as a result of senior management being more accessible and involved for rapid decision-making.

Perhaps most importantly of all, assuring reliable delivery of the finished product means having a robust supply chain in place. A knowledgeable API CDMO will select suppliers based on their quality processes and regulatory track record, and will always qualify at least two suppliers from different geographies for key starting materials to ensure a back-up is available in crisis situations such as that presented by COVID-19.

The COVID-19 pandemic has emphasized the need for all pharmaceutical manufacturers to continuously enhance their supply chain for strategic products. This includes prioritizing suppliers with a spotless track record of regulatory compliance and an uncompromising quality culture, who are investing in improving and strengthening their own supply chain to assure uninterrupted drug production.

Finally, a close working relationship between the API CDMO and any suppliers is pivotal. By working together to plan ahead, ideally on a rolling 12-month basis and with supplies coming in continuously over that time, an API CDMO can guarantee that sufficient starting material will always be available to avoid shortages.

SCALE UP SUCCESS DEPENDS ON SEVERAL KEY FACTORS

- Acknowledging the challenges of scale up
- Performing rigorous process design to ensure a complete data package is in place before moving to scale
- Implementing measures that allow for rapid resolution of any issues and that are supportive of a sudden demand for increased production
- Continually investing in back integration of strategic products
- Using the same or similar equipment and methods at both development and commercial scale
- Reacting dynamically to changing requirements
- Building a robust supply chain
- Maintaining transparency with suppliers

Key attributes of an API CDMO capable of scaling up efficiently

- Performs comprehensive process design
- Maintains an up-to-date working knowledge of new and existing technologies
- Engages in frequent communication across the supply chain
- Understands the importance of fostering transparency with providers to secure rolling forecasts and retain sufficient stock levels

Selecting an API CDMO Partner

An API CDMO is an invaluable partner for drug development and manufacturing, offering a vast array of services designed to expedite the route to market. But irrespective of whether the partnership is intended to support the ongoing manufacture of an existing drug, to scale up drug production, or to develop and manufacture an entirely new drug product, several key attributes of the API CDMO are critical to the success of the relationship.

First, it is essential that the API CDMO demonstrates a comprehensive range of technical capabilities, backed by expert knowhow and a proven track record of consistent quality and regulatory compliance. It is also vital that best-in-class supply chain management practices are in place to assure reliable, uninterrupted drug production.

Other important qualities of a trusted API CDMO include robust project management practices, open communication, and full transparency with customers; a track record of executing on time, every time, in full and with all the required documentation; a highly experienced and accessible management team that puts customers first; and a proven ability to problem-solve through complexities and challenges to maintain momentum and meet project timelines.

Additionally, with the COVID-19 pandemic continuing to evolve, it is prudent to look ahead. An API CDMO with the capacity to significantly expand supply at short notice represents a sound future investment, especially with the likelihood that many new drugs will soon require scale up. Moreover, with novel drugs often requiring unique starting materials, an API CDMO partner able to carefully select potential vendors will be well placed to support changing demands as projects reach fruition.

CHALLENGES OF DEVELOPING A NEW DRUG

A new drug may require unique starting materials. As a result, fewer potential sources may be available, meaning that due diligence is vital when selecting a supplier.

Starting material specifications often have a significant impact on product yield and purity, and a chosen supplier must be able to consistently deliver the required quality, on time, and at a cost that is viable for scaling up to commercial production. Through collaboration, an API CDMO and a supplier can establish the required specifications as process development and optimization progresses.

Typically, with a new drug, raw materials are ordered less frequently and have longer lead times compared to existing commercial existing products. Consequently, frequent production planning is essential. It is good practice to order raw materials based on a 12-month rolling forecast and to maintain some safety stocks to address any sudden changes in demand.

PROVEN SUCCESS IN MEETING COVID-19 DEMAND

Midazolam, Cisatracurium, and Rocuronium are all drugs that have experienced massively increased demand as a result of the COVID-19 pandemic. Used as a first-line approach in the management of COVID-19 patients being placed on mechanical ventilation, their availability became a major concern early on.

By being closely aligned with this need, Wavelength Pharmaceuticals was able to rapidly triple and quadruple API production for all three drugs, thereby meeting the requirements of global customers and providing a lifeline for patients ventilated in critical care.

Increased throughput was achieved via a combination of scale ups, process improvements, and greater operational efficiencies. For example, by increasing reactor size from 250 L to 1000 L, installing an additional double-size drier, and shortening the drying cycle from 60 hours to 35 hours, monthly yields were increased from 20 kg to 75 kg. Additionally, using a quadruple-size drier on a different product increased monthly yields from 100 kg to 400 kg.

Wavelength also implemented personnel-related changes to assure continuity of operations and supply during the COVID-19 pandemic, including altered shift patterns to allow for 24/7 manufacturing while maintaining social distancing in fixed 'capsules'; implementing e-meetings; and introducing additional PPE measures to ensure the safety of personnel.

The time and effort invested by Wavelength in supply chain assurance over more than 30 years was pivotal in allowing for rapid expansion of the company's manufacturing capacity, providing urgently-needed support to pharmaceutical manufacturers, public health and government agencies, and group purchasing organizations (GPOs) for hospitals across multiple geographies.

In combination, Wavelength's scale up expertise and ongoing efforts to improve manufacturing processes remain key to support current efforts toward tackling the pandemic, as well as ensuring readiness for additional waves of COVID-19 infection.

Best-in-class supply chain management practices ensure reliable, consistent, and even significantly expanded supply.

Wavelength — Your API CDMO Partner of Choice

With an exceptional track record in quality and regulatory compliance, Wavelength is globally recognized as a leading API CDMO. Routinely manufacturing commercial batch sizes ranging from hundreds of grams to many hundreds of kilograms, including production on practically dedicated lines 24/7 throughout the year to meet annual demand, Wavelength's extensive A to Z capabilities include complex developments, tech transfers, cGMP scale ups, commercial supply, and much more. These competences are backed by over 30 years' experience in delivering on worldwide launch and commercialization goals and underpinned by best-in-class supply chain management practices that ensure reliable, consistent, and even significantly expanded supply, as demonstrated during the current COVID-19 global crisis.

Some API CDMOs are better able than others to handle the pressures of rapid scale up.

Building on an established reputation as an API CDMO able to manage new requests and solve unforeseen challenges, Wavelength maintains an ongoing focus on investing in the future. This includes making continual improvements to process design, safeguarding an up-to-date knowledge of both new and existing technologies, and working to ensure transparency and open communication with providers remains a priority. In combination, these measures aimed at assuring uninterrupted drug supply make Wavelength your API CDMO partner of choice to accommodate diverse market requirements. As demand for existing drugs fluctuates and new drugs designed to tackle COVID-19 begin to enter development, Wavelength's expertise, flexibility, and forward-thinking approach will be paramount — not only in driving global efforts to resolve the pandemic but also in continuing to support the treatment of many other health conditions.

ALIGNED WITH YOUR PROJECT

We have all the required capabilities to bring your drug to market, backed by the flexibility to accommodate growth and fluctuating demand. Contact us at ***marketing@wavelengthpharma.com*** to discuss how aligning with Wavelength can help your next project succeed.

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Wavelength is a world-class developer and manufacturer of Active Pharmaceutical Ingredients (APIs). It is the independent company of choice for pharmaceutical industry leaders that require advanced API solutions to gain sustainable competitive advantage. The company is on the same wavelength as its customers — a partner in tune with the results required to better support their needs. Founded in Israel in 1987, with more than 250 customers in 50 countries, Wavelength employs a highly skilled team with all the expertise required to advance products to market. Its cGMP-compliant facility is a first-class operation recognized for excellence in safety and environmental stewardship. Wavelength has achieved an exceptional track record for more than 30 years with all leading global regulatory authorities, including USFDA, EU-EMA, PMDA, TGA, KFDA, ANVISA and COFEPRIS. The company includes experts in complex chemistry, innovative process development, crystalline forms and particle design, and offers customized solutions to meet individual customer requirements including full spectrum API CDMO services from pre-clinical grams to multi-ton commercial scale.

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