Maximizing injectables production to support consistent supply

Introduction

One of the most significant trends today in our industry is the enormous growth of the injectable market. Injectables are becoming the single largest driver of the pharma/biotech market and offer tremendous opportunity.

However, bringing an injectable to market is no small feat. Staying competitive once in the market can be just as challenging. Market and regulatory requirements regarding safety and quality are constantly increasing. Thus, an experienced partner who understands how to navigate the hurdles of clinical and commercial production in order to support your market supply can provide valuable strategic support and customized solutions.

VETTER

Answers that work

Ensuring supply in a challenging market

Breakthroughs in medical research have ushered in a new era of innovative therapies, many of them sensitive, complex biologics that require injectable delivery. Add to that the growing demand from patients for simple, self-administered medications, and the rationale for the rapidly growing injectables market becomes clear.

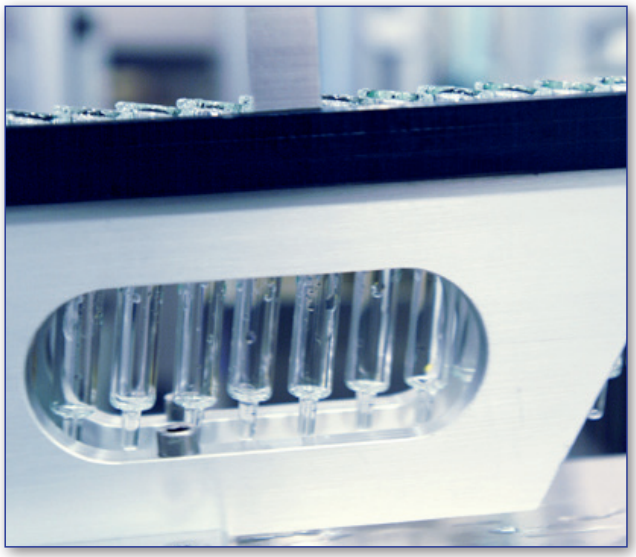
In order to stay competitive on the market, companies have to develop strategies to secure market supply and also reduce risk and costs. Outsourcing is one common strategy. The main identified reasons to outsource with a strategic partner are:

- Temporary lack of capacity
- Lack of technology
- Lifecycle management
- Need to focus on core competencies

The role of the CDMO

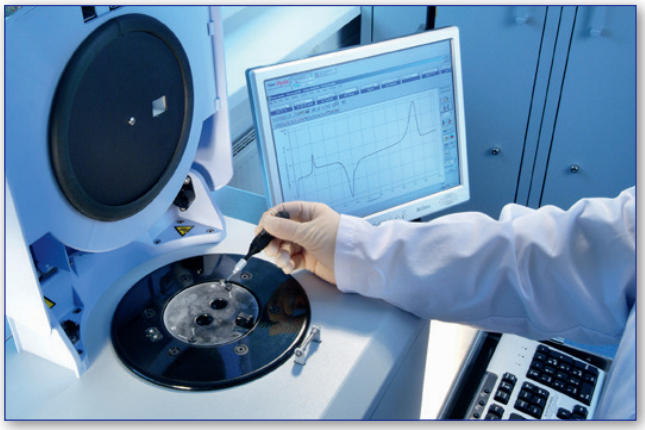
As companies bring new, innovative compounds to market, the need for reliable supply and business continuity is critical. While certain industry developments and regulatory requirements are beyond a manufacturer's control, production management is one area that can be maximized to help high-quality products get to market on time.

The right partner can play a crucial part in this process. As the market reliance on outsourced manufacturing grows, CDMOs become an option since they invest in technology, capacity, and processes that may help drug marketers achieve their goals. And in the face of a challenging market, they can also offer advantages and customized processes to help marketers overcome obstacles.



Vetter, an independent and world leading Contract Development Manufacturing Organisation (CDMO) of aseptically filled drug delivery systems offers the quality, capacity and flexibility, that is needed for individual customer requirements.

Reliability to meet long-term supply needs



The ability to produce consistent, high-quality products is a CDMO's greatest value to a pharma or biotech company. Having a reliable partner allows pharma companies to remain confident that they able to continue to meet their market's needs even in the face of many challenges. Experienced and well-established contract manufacturers that continuously invest in both production systems and processes are best positioned as partners in today's environment.

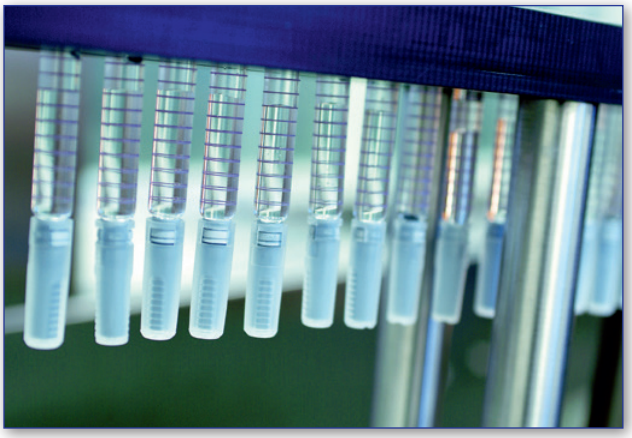
The importance of a robust infrastructure

Multiple self-sufficient production sites allow for backup capabilities in the event of an emergency that could force production to cease. Also, having redundant, independent power supplies at each facility is critical to maintain production in the case of a power loss. In addition to innovative technology, a reliable partner, also has the processes and people in place to maintain it properly so problems can be avoided in the first place. Vetter has its own technical department with well trained experts, that are familiar with all facilities equipment. The team can act to immediately correct technology issues rather than having to stop production while waiting for an outside technician to be brought in.

Vetter offers three fully equipped and independent production facilities

Regulatory expertise and support along the way

An outsourcing partner with experience in regulatory affairs can be of vital support for its pharmaceutical and biotech customers. It is´ important that a CDMO has an excellent track record with key international agencies, having recently passed site audits and inspections. Understanding the specific inspection and process requirements of different countries and their regulatory agencies respectively help to prevent problems from arising during site audits. Standard documentation that is already in place can also smooth the submission process for customers.



Regulatory support after a product's approval and throughout its lifecycle is also critical. A supportive partner should also have staff ready to provide support on a variety of issues, from change announcements, to variation documentation, or to annual product reviews with key agencies. They should be able to continually monitor the regulatory environment and be able to respond quickly to issues and new regulations.

During product development phases, experts from Quality Control, Quality Assurance and Regulatory Affairs/Quality Compliance should be available to help address regulatory questions throughout the entire submission or registration process.

Country	Authority
USA	Food and Drug Administration (FDA)
Europe	European Medicines Agency (EMA)
Japan	Pharmaceutical and Medical Devices Agency (PMDA)
Germany	RP Tübingen
Brazil	National Health Surveillance Agency (ANVISA)
Mexico	Ministry of Health (MoH)
Taiwan	Bureau of Food and Drug Analysis (BFDA)
South Korea	Korean Food and Drug Administration (KFDA)
Iran	Ministry of Health (MoH)
Gulf States	Gulf Central Committee for Drug Registration (GCC-DR)
Uganda	Ministry of Health (MoH)
Turkey	Ministry of Health (MoH)
Algeria	Ministry of Health (MoH)
Kenya	Ministry of Health (MoH)
Russia	Russian Health Authority

List of international regulatory authorities Vetter worked with successfully in recent years.

Efficiency throughout the production process

For new compounds on their way to market, the stakes are higher than ever given the complicated nature of many of today's therapies. And for drugs that have been on the market for years, the pressure to remain competitive against new entrants is.
No matter which situation pharma or biotech companies find themselves in, efficiencies in all aspects of manufacturing processes are essential to the success of a compound. This also allows them to act quickly with emerging changes during the fill and finish process.

Yield optimization

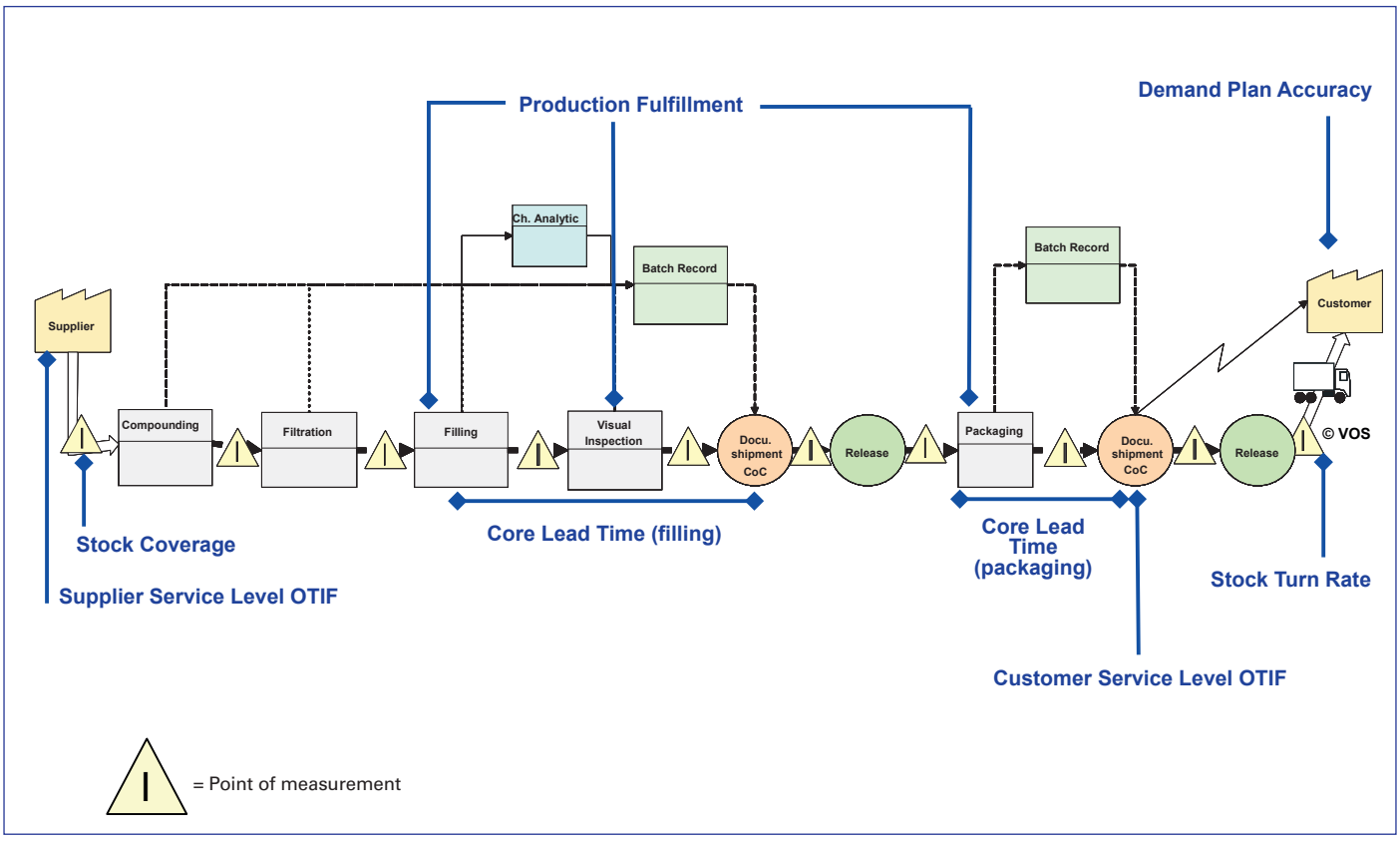
Given the costly nature of today's compounds one of the goals during either clinical or commercial production is to maximize available API. In close co-operation with their clients, CDMOs design processes, from test and sampling runs to full-scale production that make the most of a given volume and minimize API losses during filling. Once a detailed statistical analysis of all manufacturing steps is done and key critical process steps are identified, methods and processes can be implemented and improved to increase yield.

Production strategies to optimize yield
■ Design filling machines with features and processes created for efficiency
■ Assemble product lines with exchangeable equipment and parts to address specific product needs
■ Employ disposables that are low cost and easy for staff to handle
■ Plan for multipurpose sampling, using samples for a variety of tests
■ Use technical runs to validate additional issues
■ Continually monitor processes using Quality Control management tools (eg. Six Sigma)
■ Train staff to identify inefficiencies or opportunities for improvement within processes

Key Performance Indicators

Transparency and open communication between a CDMO and its customers is a key contributor to efficiency during production. Regular reviews provide continuous insight for accurate forecasting and planning. Further processes are continually screened and reviewed, and issues can be raised and discussed between the involved parties. These include:

- KPIs which are developed and agreed upon with customers prior to the production process
- Manufacturing processes that are reviewed and evaluated according to the KPIs at key time points or milestones
- Perfomance results that can be shared and discussed as part of business and quality reviews
- Reports that include both quality and supply chain metrics
- Additional KPIs e. g. yield trending, cycle times, and customer service levels that can be analyzed if required



An example for points of measurement along the supply chain

Flexibility in a dynamic market

In today's rapidly innovating market, it's difficult to predict products will be in demand in the future. Services, processes, and technology that can be customized to a particular compound's needs or adapted to meet unanticipated market shifts can help pharmaceutical companies meet the needs of both prescriber and patient.

In addition, advances such as personalized medicine will continue to shift the model from high-volume, standard production of drugs to more individualized products requiring smaller-scale manufacturing. Manufacturers must be ready with flexible, easily scalable production solutions.

Versatile manufacturing processes

Whether it's a sudden increase in demand or decrease in available API, the ability to adapt to the needs of the market is critical. Flexible filling line configurations and modular processes are just two of the ways outsourcing partners can provide the range in capacity needed to fill both large and small batch sizes.

Having a range of automated, validated processes in place, such as end-to-end track-and-trace solutions, in-line weighing systems, or automated in-line control of syringe closures, may help a manufacturer adapt to changes quickly. Should an unexpected event occur, automated processes can reduce the need for new processes or revalidation.

Comprehensive in-house capabilities

A CDMO with a wide variety of services is better able to create solutions that meet both the compound's current needs and remain responsive to changes in the future. Resources such as purified water systems, siliconization technologies, a variety of pump systems, full lyophilization capabilities, and Restricted Access Barrier Systems (RABS) are just a few of the core capabilities drug makers should look for in a contract manufacturer.

Flexible storage capacity, with areas at different temperatures, also allow to meet virtually any requirements for APIs, ingredients and final products.

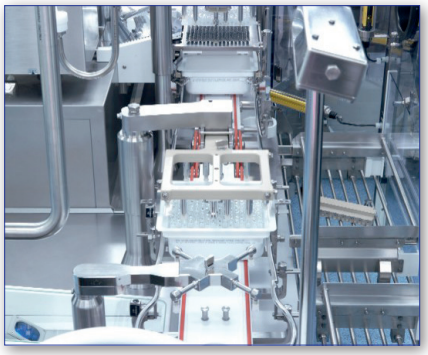
Storage Area	Nomina Value
High-bay storage	+15 to + 25°C
Cold storage	+2 to + 8°C
Walk-in freezer	+8 to -20°C
Chest freezer	-20°C or cooler (product specific)
Hazardous goods storage	+15 to +25°C
Sampling room grade C	+15 to +25°C
Incubator chamber	+15 to +25°C
Incubator chamber	+30 to +35°C

Vetter offers customers a variety of areas for processing and storing their products

The advantages of experience across the production chain

As drugs become increasingly complex and the market increasingly dynamic, there is no substitute for experience in manufacturing. Vetter has decades of experience in identifying and solving the quality and supply issues that often impede or stop the progress of a pharmaceutical company's drug on its path to market. Vetter's highly skilled team of scientific, engineering, and production experts work together to create solutions, and optimize the manufacturing process. industry leader in analytical services, aseptic techniques, supply chain management, and quality control, Vetter helps keep products on track at each step of production. Continuous investments in its technology and facilities, enable Vetter to meet increasing demand from its pharmaceutical and biotech customers for filling capacity, as well as keep pace with evolving regulatory requirements.

The company operates three independent commercial production sites. Complete packaging services and comprehensive logistics support provide customers with the capabilities and infrastructure needed to anable products get to market consistently and reliably.



Vetter provides seamless expertise across the production process

- *Development and analytical services*
- *Engineering/pharmaceutical production*
- *Primary and secondary packaging*
- *Project management*
- *Customer service*
- *Supply chain management*
- *Quality Control and Quality Assurance*
- *Regulatory Support*

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