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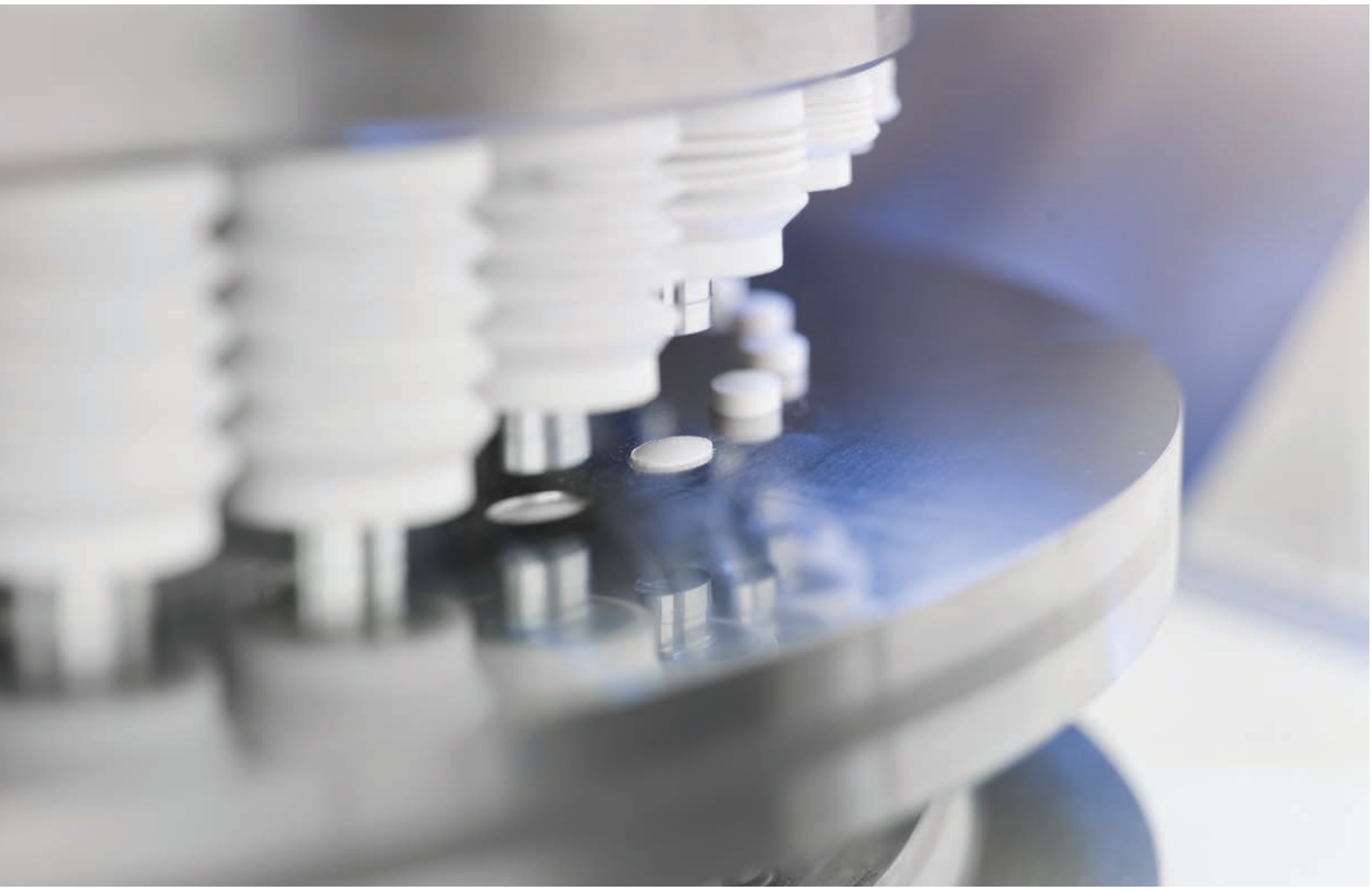

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WHITEPAPER

Continuous or batch: Deciding on the best solution for your oral solid dose product

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Abstract

Chemical process development of an active pharmaceutical ingredient (API) or drug substance and the pharmaceutical development of the final, formulated drug product from this API are frequently treated as independent activities in the overall process of developing a new drug.

Continuous manufacturing enables the development of a more diverse pipeline of drug products by greater quality assurance, reduced API usage, and timeline efficiencies. It also reduces scale-up activities as a product increases in volume in the clinical phase through commercial. With that comes the benefits of reduced API usage, and therefore costs. Additional benefits include timeline efficiencies as well as a reduction of technical risks, as continuous manufacturing systems are designed with integrated solutions that allow for real-time analysis and control. The key quality driver with continuous manufacturing is that you understand what the process is doing on a second-by-second basis and judge your material as it is produced rather than in its entirety at the end. Improving quality oversight and thereby reducing rejections also lessens handling and timelines in manufacturing, which helps lower the total cost of ownership. Continuous manufacturing is one node in a more flexible supply chain where production quantities can be flexed based on demand while still maintaining the same assurance of product quality.

As a result of these benefits, we have seen an increase in FDA approvals of oral solid dose drugs produced using continuous manufacturing as well as investments in technology within the pharma industry. Nevertheless, the pace of its adoption still lags when compared to the growing demand for new drug products and the drive to reduce total cost of supply. This delay is not uncommon in an industry averse to change; however, it could also be related to a lack of understanding about the application of continuous manufacturing in both development and commercial manufacturing and/or education about its implementation. Therefore, by gaining a better understanding of continuous manufacturing and its fitness for your oral solid dose product, you could potentially secure more control over the quality and safety of your product and, ultimately, the future of its success.

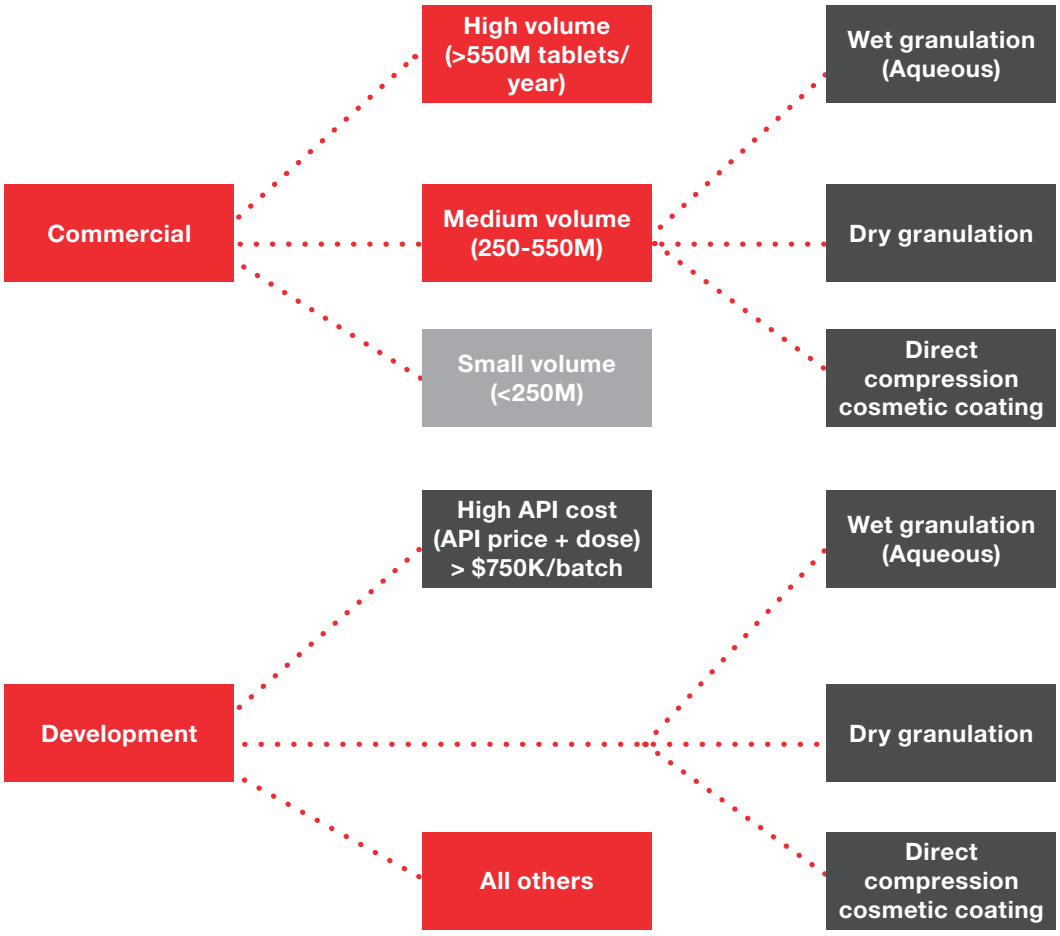
Is your oral solid dose product a fit for continuous manufacturing?

Although there has been considerable growth in the biologics market over the last decade, oral solid dose products continue to make up a large part of the pharmaceutical market. And while some require large-scale production, many drugs administered in oral solid dose form are manufactured in relatively small batches.

This, combined with the common misconception that continuous manufacturing is only a good fit for large-volume products, may be one of the biggest reasons the oral solid dose industry has been slow to adopt this modernized approach to pharmaceutical manufacturing. Yet, any program that faces scalability risks, regardless of the volume, can benefit from continuous manufacturing.

In terms of scale-up, batch manufacturing typically involves moving to commercial production after the supply of clinical batches. This change in scale is often large (between 3x and 10x), and the size of the final batch makes it impractical to fully characterize the effect of the scale-up, so a limited number of technical batches are run due to cost.

Rather than using this approach, which makes it difficult to find out how a formulation will behave at a commercial scale, continuous manufacturing scales up by running the same small-scale process for commercial scale but for a longer period of time.



This eliminates any potential errors that can occur when scaling up powders from tens of kilograms to hundreds or even thousands and also reduces time and API usage. As a result, oral solid dose programs in the development phase with an API that is high value or has limited availability and/or one that faces an aggressive clinical timeline are great fit for continuous manufacturing.

Where you are in your timeline will determine how you evaluate if continuous manufacturing is the best fit for you. For example, is this a situation where you want to optimize speed to market and costs in development, or is the focus on reducing total costs of supply and optimizing your supply chain for something that will be commercially produced?

The traditional mind-set of testing quality at the end of a batch must change to one that is focusing on whether a product can remain within specifications while meeting quality requirements at a faster pace.

Another factor slowing the adoption of continuous manufacturing may be the challenges associated with the transition. Specific expertise, experience, and capacity are required. All three are relatively limited in the industry today.

Most challenging, though, may be the cultural shift that must occur within your organization to successfully execute continuous manufacturing as well as a change in the skills needed within your quality organization, such as a deeper technical grasp of the process, which is often overlooked.

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Making the switch to continuous manufacturing

The first step to implementing continuous manufacturing for your oral solid dose product is determining your manufacturing strategy. Do you want to build the continuous manufacturing capabilities internally, or do you want to work with a CDMO with experience and existing capacity? This may depend on whether you are in development or looking for commercial launch. If you choose to take your manufacturing in-house, begin with a calculated approach toward a reasonable end goal.

Consult with or build an internal team that includes technical, quality, and regulatory knowledge to fully understand how this technology is going to interface with your existing process or, if you are establishing a new line, how to build this technology from the ground up. It is important to understand the full strategy of a continuous manufacturing program prior to investment in capacity. Will the line need to run just one product or multiple? What level of containment is necessary? Will the line do development and commercial work?

All of this is important to understand before making an equipment order. If you choose to work with a CDMO, make sure you understand the capability of their manufacturing suite. How ready is it? How many programs have been executed by their team? What other supply chain services are available? You want to ensure they have the flexibility and knowledge to not only develop an effective process for your product but also react quickly and be able to tweak the process if necessary.

With one of the benefits of continuous manufacturing being the ability to produce a large amount of material quickly, the CDMO you partner with must have the ability to package, ship, and store the expected volume as well as the ability to deliver raw API to the process at a frequency commensurate with the manufacturing process. A history of product development and commercial manufacturing and their quality culture is also critical.

Thermo Fisher Scientific, a market leader in both development and commercial manufacturing, has had continuous manufacturing since 2017 and has experience with multiple products. Their experience with continuous manufacturing is coupled with expertise in logistics and distribution as well as packaging and storage, making them a strategic partner that has the capabilities necessary to overcome the challenges of continuous manufacturing.

About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. As a leading pharma services provider, we deliver unrivaled quality, reliability and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

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As the Senior Director and General Manager of Continuous Manufacturing at Thermo Fisher Scientific, Jessica is responsible for the operations, strategy and commercial growth of the continuous manufacturing businesses which is centered around a novel processing technology for the pharmaceutical industry. Jessica joined Thermo Fisher in 2013 and has served in several roles including Strategy, Innovation and Marketing. Prior to her roles at Thermo Fisher, Jessica worked as a consultant through the Center for Innovation Management Studies at North Carolina State University focusing on the application of big data analytics in the biopharmaceutical industry. She earned a Master of Business Administration and Master of Microbial Biotechnology from North Carolina State University and holds a Bachelor of Science in Biotechnology from Rochester Institute of Technology. Jessica also serves on the Board of Trustees with the Pharma Biopharma Outsourcing Association.

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