Product Development Case Study

Getting Ready for Clinical Trials

A mid-size pharmaceutical company with a promising active pharmaceutical ingredient (API) was ready to move into clinical trials. However, the company needed to outsource manufacturing to a contract provider with the equipment to scale its formula for 5 kg development batches into 80 kg trial batches.

Rottendorf Pharma was selected as the contract manufacturer because of its ability to adapt from lab-scale equipment to larger batch sizes, while optimizing the process not just for clinical trial batches, but with commercial distribution in mind.

"The customer's true aim is not to have clinical trial manufacturing, but to arrive at a manufacturing process for production at the commercial scale," said Kevin Kiehm, Director of Product Development at Rottendorf. "Although the product isn't approved at this stage, we always optimize for the end goal of commercial production."

That commercial mindset helps Rottendorf to create development and manufacturing solutions to quickly and seamlessly carry clients' solid oral formulations to market.

Under a tight timeframe, Rottendorf completed a technical trial batch and adapted the manufacturing process to its equipment and larger batch size. Both the technical batch and GMP clinical batches were manufactured on the same equipment – for a savings in time. The CDMO identified three areas for optimization in scaling from 5 kg to 80 kg. Specifically, Rottendorf determined ways to address issues with:

- Hot melt extrusion
- Milling of extrudate
- Compression

HOT MELT EXTRUSION

The client's polymer API mixture was melting in the feeding zone and blocking it. This forced production to stop every 30 minutes to clear out the feeding zone. Rottendorf's solution was to lower the temperature in the zone and install additional vents that allowed water in the API mixture to evaporate. The process was then performed without interruption and an increase of the extrusion rate was achieved.

MILLING OF EXTRUDATE

A single milling of the extrudate, as performed to the client's specifications, created inconsistent particle size and distribution, therefore, milling had to be repeated to achieve a homogenous blend. Rottendorf reduced the feed rate for milling, resulting in just a single milling step that produced a powder with the desired properties.

COMPRESSION

At the larger scale, cracks were observed on the tablets after compression. Rottendorf increased the dwell time during compression by decreasing compression speed. The company also increased the pre-compression force to ensure a better de-aeration, achieving reduced main compression force.

Rottendorf worked quickly, reviewing documentation and processes at the small-scale level and developing a plan to scale up to 80 kg. The client attended the technical transfer and technical batch manufacturing to ensure Rottendorf had all the information it needed to successfully create the technical batch, since the client had time for just one such batch. That initial process lasted approximately four weeks; GMP manufacturing of the actual trial batches was then completed in less than six weeks.

Next Steps

Pleased with Rottendorf's optimization for the initial clinical trial batches, the client has engaged Rottendorf to scale to 150 kg for the next round of trials.

ABOUT ROTTENDORF

A Top 20 contract development and manufacturing organization (CDMO), Rottendorf Pharma formulates, develops, manufactures, and packages solid oral dosage forms for the global pharmaceutical industry. Clients choose Rottendorf for its broad-ranging expertise, global regulatory capabilities, commitment to quality, state-of-the-art facilities, and exceptional customer service exemplified by Total Process Ownership.

To learn more about Rottendorf and the importance of successful product transfer, in the U.S. please visit our website at www.RottendorfUS.com or call 312.794.7836. Outside the U.S. visit www.Rottendorf.com or call +49 (0) 2524 2680.

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