Customer Story

Mitsubishi Tanabe Pharma

Challenge

Gain insights into overall formulation design that will help to optimize multiple pharmaceutical quality characteristics.

Data-driven Quality by Design boosts drug development

Mitsubishi Tanabe Pharma improves processes for bringing new drugs to market

From basic research through nonclinical testing, clinical trials, approval and production, it takes anywhere from nine to 17 years to bring a new drug to market. And that's only if the drug makes the cut. In fact, only about one in 5,000 new drugs ever makes it to a pharmacy.

Odds like those can drive drug prices sky high, making them costly for cash-strapped consumers whose health depends on access to essential pharmaceutical therapies. And keeping prices down can be tricky. So the Mitsubishi Tanabe Pharma Corporation (MTPC) seeks to optimize quality at all stages of the production process. By increasing quality and efficiency, MTPC can offer state-of-the-art drugs that aren't cost-prohibitive.

Fortunately for MTPC, they're ahead of the game in systematizing process improvement decisions thanks to their analytics-driven approach.

The limited nature of spreadsheets left analysts wanting a higher-power solution

MTPC is a Japanese pharmaceutical company known for the arthritis remedy Remicade and the allergosis treatment Talion. These drugs, along with all of MTPC's products, were the outcome of a lengthy research and development process.

"We study overall formulation design, including pharmaceutical formulations and production methods, and conduct research to optimize multiple quality characteristics such as the hardness, disintegration properties and dissolution properties of tablets," says Keisuke Takagaki, formerly of MTPC's Pharmaceutical Research Labs.

Since the company's early days, however, MTPC's Pharmaceutical Research Labs have redesigned their approach to research. In the past, MTPC labs made minor changes to standard pharmaceutical formulations and production methods using observed, empirical judgments in order to optimize them for the desired quality characteristics.

"We were studying the process parameters and formulation factors affecting pharmaceutical quality based on experimental design," Takagaki explains. "We recognized that there were many analytical operations that could help us to optimize these factors."

The tool they used for this task? Spreadsheets. "Unfortunately spreadsheets were very limited in what they could offer. That's why we started looking to introduce a new statistical analysis tool." And most importantly, notes Takagaki, that tool had to be easily operated by researchers otherwise unfamiliar with statistics and programming. So the MTPC Pharmaceutical Research Labs turned to JMP®.

Analysis helps pinpoint the factors that most affect product quality

The Pharmaceutical Research Labs now use JMP to design more streamlined systems capable of developing and producing pharmaceuticals that meet MTPC's high quality standards. In recent years,

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> We look to JMP to help guide us through experimental design and, from the data we acquire, we use JMP to derive values for each processing parameter, thereby optimizing variations in quality characteristics.
>
> Keisuke Takagaki,
> Formerly of Pharmaceutical Research Laboratories, CMC Division,
> Mitsubishi Tanabe Pharma Corporation

formulation designs that correlate with effectiveness and safety – in addition to formulations and production processes that can stand up to fluctuations in ingredients and process parameters – are a major focus for MTPC.

Equipped with a new tool, Takagaki's team faced their first task: to investigate how the dissolution rates of MTPC's current product offering might be improved. JMP helped researchers to search for the cause of trend abnormalities occurring in tablet dissolution rates, an important quality characteristic for all medications. With univariate analysis, researchers isolated the factors affecting drug dissolution rates and investigated the multivariate correlation between variables. All told, four factors were identified as affecting dissolution rate.

"Through multiple linear regression analysis, we determined that there was an especially strong correlation between the granules' mean particle diameter and tableting pressure," says Takagaki. Due to government regulations and standard tablet hardness and thickness specifications, however, it is difficult for researchers to make modifications to tableting pressure.

"Instead," Takagaki says, "we focused on the granules' mean particle diameter and, after using JMP to analyze the dissolution rate and relationship between factors, reworked our production methods to decrease the number of coarse particles and increase the number of fine ones, thereby improving the dissolution rate overall."

Taking action to advance quality and reliability

Researchers have recently implemented pharmaceutical development and quality risk management strategies based on concepts proposed in the ICH Q8, Q9 and Q10 guidelines, including Quality by Design (QbD) and Design Space (DS).

"For us here in the lab, QbD means we're setting each production parameter for the mixing and tableting processes involved in producing an orally disintegrating tablet," says Takagaki. "We look to JMP to help guide us through experimental design and, from the data we acquire, we use JMP to derive values for each processing parameter, thereby optimizing variations in quality characteristics."

Takagaki and his team have also studied the DS settings for the dissolution rate of a new drug they're developing – a conventional tablet. Specifically, they used an initial risk assessment and analysis of variance to narrow down the major factors affecting dissolution rate. Finally, they've also designed a response surface plan for two selected factors, the drug substance particle diameter and the granule particle diameter, and measured dissolution rates.

Going forward, MTPC's Pharmaceutical Research Labs will continue to use statistical methods to deepen the company's problem-solving abilities. "In the future, a statistical approach to pharmaceutical development and research will be essential," says Takagaki.

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Solution

MTPC researchers used JMP outputs to make pharmaceutical development processes more efficient and reliable.

Results

By using JMP to calculate processing parameters, MTPC was able to both optimize variations in quality characteristics and study design space settings for the dissolution rate of a new drug based on QbD.

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