Customer Story

Tillotts Pharma

Challenge

Ensure pharmaceutical drugs adhere to the highest quality standards.

When trending means much more than popularity

Analysts at Tillotts Pharma use JMP® statistical discovery software from SAS to explore drug stability data

Pius Dahinden is concerned with what's trending, but it has nothing to do with social media. Rather, Dahinden spends his days looking at trend analyses in compliance with whatever new regulatory guidelines are "trending" in the world of pharmaceutical manufacturing.

As Analytical Science Manager at Tillotts Pharma, Dahinden is responsible for helping ensure the quality and reliability of pharmaceutical drugs at various points in the product pipeline. And while a lot of attention has been paid in recent years to the increasing availability of substandard drugs on the market, international regulatory bodies like the European Medicines Agency are cracking down on noncompliant products by applying ever greater scrutiny to quality control in production.

A subsidiary of the Japanese corporation Zeria Group, Tillotts Pharma is a specialty pharmaceutical company headquartered in Rheinfelden, Switzerland, that focuses on pharmaceutical treatment solutions for gastrointestinal diseases like ulcerative colitis, Crohn's disease and irritable bowel syndrome, among others. With a portfolio of GI therapies – innovative drugs resulting from years of development activities and collaborations – Tillotts is especially vigilant when it comes to quality control and monitoring. In Tillotts' view, quality is not only an essential legal requirement; it's also a commitment the company makes to the tens of thousands of people in over 65 countries who use Tillotts' products to manage their gastrointestinal health.

Customized scripts are a real advantage in the ever-changing world of compliance

In October 2014, the European Union introduced a new Good Manufacturing Practices (GMP) Guideline on quality control. Under this new measure, the trend analysis of drug product stability data has become a quality control requirement for pharmaceutical manufacturers like Tillotts. The regression control chart procedure – a popular tool for GMP compliance in the industry – looks at historical data as a comparative reference for current data points. Since the publication of the new EU GMP guideline, the European Compliance Academy has proposed as a best practice the application of a simplified random coefficient regression method, given the inherent uncertainty in historical data.

While others saw in the academy's recommended methodology a sea of new methodological hurdles, however, Dahinden saw an opportunity – an opportunity to think outside the box and create innovative, tailor-made scripts to simplify the process.

JMP statistical discovery software from SAS was a natural choice. With the robust JMP Scripting Language (JSL), Dahinden says, he has customized the already advanced analytic features of the software to develop new functionality and integrate core capabilities. "Quite a bit of data comes in and, before we had JMP, we had to do [data entry and analysis] by hand," he says. "And when you do it by hand, errors can easily occur." Data management processes automated with Dahinden's custom JSL add-ons dramatically reduce the prevalence of simple errors that previously had to be eliminated by a time-intensive, manual data-checking process ensuring the integrity of the data and

jmp® Statistical Discovery.™ From SAS.

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>
> Pius Dahinden, Analytical Science Manager

analysis. And they make it easy for Dahinden's colleagues to reproduce and repeat trend analyses, whether or not they're statistics pros.

Among other things, Dahinden's script simplifies the identification of important out-of-expectation and out-of-trend points in the stability data and conveniently packages all the information required by regulatory oversight bodies into a visual output that conveys results cleanly and clearly. "JMP allows us to gather our data much more quickly, and then presents it in a format that makes it so easy to explore," he says. The depth of analysis that JMP customization affords and the ease with which it presents review-ready outputs allow Dahinden to not only more firmly substantiate a determined shelf life but to potentially recommend extensions, thereby saving Tillotts both money and resources.

JMP Graph Builder: An analyst's blank canvas

Since the regulatory environment for pharmaceuticals is constantly evolving – requiring more extensive testing – Dahinden and his colleagues have to remain at the ready to analyze ever larger, more complex data sets. Scripting aside, JMP offers powerful statistical analysis capabilities linked with interactive graphics. In fact, Dahinden says that his group's initial attraction to JMP was its ease of use – even for those with little statistical background. While statistical software can often be intimidating to the novice, he says, "JMP is so accessible. Our people have been very satisfied with the user experience. JMP has quite a good interface for the import of data from different sources. This is a real advantage."

The JMP platform Dahinden turns to most frequently is Graph Builder. It operates like a blank canvas. Graph Builder's interactive interface allows him to create and modify graphs in an efficient manner – to experiment with different variables in different places. Dahinden can change the graph type with the click of a button. He can sample a variety of graphs until he finds the best fit. Graph options include bar charts, pie charts, histograms, maps, contour plots and more, and Dahinden says he takes full advantage of the option to place several plots in one canvas.

Linking dynamic graphics with powerful statistics, JMP assists the Tillotts team in constructing a narrative and interactively sharing findings in ways colleagues and decision makers can readily understand and act upon. Analyses unfold, driven by what the data reveals at each step, allowing users to explore their data without leaving the analysis flow or having to rerun commands as new questions arise – all of which allows Dahinden and his colleagues to work considerably more efficiently.

The scientific underpinning of assurance

Dahinden says his team also regularly turns to the JMP Degradation platform to estimate shelf life on the basis of stability data in accordance with the International Council for Harmonization guidelines. For the purpose of shelf life estimation, three linear degradation models are fit. Of these three, the best model is selected at the significance level of 0.25 and is used to estimate the expiration date. Dahinden's script for the identification of out-of-expectation and out-of-trend points in stability data uses the regression control chart procedure based on the simplified random coefficient regression method. "We do the trending, and we also have prediction and tolerance intervals," Dahinden explains, "and then we check to see if all data points of a new batch are in the prediction range. And if one point is outside of this interval, then this is an out-of-expectation result, and you have to check why this has occurred."

In sum, heightened assurance of stability is what's trending at Tillotts – a very healthy trend indeed.

Solution

Tillotts' analysts use JMP on a daily basis. The JMP Graph Builder and Degradation platforms provide valuable support to their work in addition to custom scripts for trend analysis.

Results

Analysts can now make a more confident assertion of the shelf life of their products.

To contact your local JMP office, please visit: jmp.com/offices