Customer Story

Menarini

Challenge

Design high-quality experiments that test pharmaceutical products to detect possible degradation through time and environment and potentially identify formulation improvements.

Data visualization can help standardize pharmaceutical quality control

Italian drug manufacturer Menarini relies on JMP to test its existing products and implement continuous improvement measures efficiently and within the mandated regulatory framework

Quality control efficiency in pharmaceutical testing is vastly more intricate than determining active-ingredient efficacy and side effects; drugs must be tested for thermal stability, under varying shipping and storage conditions, and results must be presented covering a period of at least six months. The variables in formulation are endless, and investing in extending the shelf life of products is not just about the manufacturer's bottom line but can be a matter of life and death. The Menarini Group, an Italian pharmaceutical giant, has over 100 years of experience in the creation and manufacture of drugs. And as a market leader, the company has specialized in putting data at the heart of what they do.

"In general, International Council of Harmonization (ICH) guidelines require that a drug product should be evaluated under predefined storage conditions that test its thermal stability. The storage conditions and the lengths of studies chosen should be sufficient to cover storage, shipment and use. The long-term testing should cover a minimum of 12 months' duration at the time of submission, while the intermediate and accelerated condition should cover a minimum of six months," says Paolo Nencioni, a formulation development technician at Menarini, during a presentation at the 2018 JMP Discovery Summit in Frankfurt. "During development phases, more than one formulation may meet the project requirements. How can we choose the best one? Surely, we would like to choose the formulation with the longest shelf life possible."

'With analysis, we can decide the more important and most relevant results later'

Historically, pharmaceutical research and development has always relied on good and abundant data, and as such, expertise in data handling has always been paramount to the job. But as technology evolves, the volume and type of data available has forced companies like Menarini to change their approach to analytics and experimental design. "My approach is to design many tests, many try-outs," Nencioni explains. "I collect all data. With analysis, we can decide afterward what were more important and most relevant results. And also with analysis, we can understand it, not only from an analytical point of view, but also from the process perspective on how we get the data, and the application of technology testing on the line."

Nencioni and his team are primarily concerned with designing experiments for drug formulation. "We use JMP, especially for the design of experiments. We needed to adjust a little to create formulations," he explains. "We perform analyses of the quality of each product – and this is important work because it concerns the drug as a pharmaceutical form and in a bigger way, also the pharmacology of the drug."

Because of Menarini's long history of drug development and manufacturing, the company places a lot of emphasis on both product development and product maintenance; that is, the process of continuous improvement. "For example: during early stability studies, we might have a product compliant with specifications, but we might observe some

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strange behavior in pH, for example, shifting from the natural value to a higher one," explains Nencioni. "We also might observe a yellowing of the solution. We've not been able to relate these behaviors to any other critical quality attributes, so the overall quality of the product is good, but we try to understand better this unexpected behavior. We can improve other factors as well as get a longer shelf life." Nencioni and his team carry out analytical studies into the changing pH, color and shelf life in order to come up with preliminary results that can inform whether formal formulation studies need to be carried out to improve the drug.

'The visualization is impressive, and the flexibility on design is important'

For this, Nencioni relies on the JMP suite of data visualization tools. "It is the most important feature of JMP," he says. "Because every time I have to present a project or if I have designed an experiment, I use JMP because it offers graphic visualization to show my tasks, to show my needs, and I get a better response from my management. It is important to really understand the data and its distribution. Especially when I speak with the colleagues I don't know, or who don't understand the statistics behind it or who aren't familiar with the processes, having that visualization as support is very important. It is much easier to explain statistical tests with JMP."

Nencioni believes that having an effective data visualization tool can be helpful for colleagues with more limited knowledge of statistical analysis, but where JMP really becomes invaluable to his team is in the design of experiments. "I chose JMP many years ago because it has always had a more flexible platform for design of experiments," he says. "It's very [useful] for me to mix up the continued factors and categorical factors. You can drift from design to the lab. I only use custom design [in JMP] because you always have the best solution and get more results. That flexibility on design is so important…. We can mix process parameters and complements."

Reducing modeling time drives efficiency and allows for savings

JMP allows Nencioni and his team to produce efficiencies in their processes, which in the pharmaceutical testing business can be invaluable. In one notable example, by performing accelerated stability studies using a higher temperature than ICH conditions, Nencioni's team could determine the behavior of some formulations in a relatively short time – not more than 30 days – when a typical ICH study takes six months or more to gain useful results. With the JMP Fit Model platform, it was possible to estimate degradation rate in function of the stress factor, arriving at a data-driven decision about the more stable formula. The estimated degradation rates were then used to predict the quality attribute values at time points and storage conditions required by the ICH guidelines. The predicted results have been compared with the actual value of one batch followed using ICH conditions, in order to verify model efficiency. Effectively, the model built using JMP allowed Nencioni and his team to improve the efficacy of drugs, extend their shelf life more rapidly and document adherence to international regulations.

For Nencioni and his team, the experiment would not have worked without JMP, even though he did consider other statistical analysis software. Ultimately, however, "I choose JMP because it is user-friendly and has [unmatched] data visualization features. I think it can have a real business impact because with it, you can quickly make your analysis and even more quickly communicate the results."

Solution

Use JMP® to model experiments that cut testing periods while remaining within regulatory parameters.

Results

Experiments that test for components affecting drugs' shelf life can now be run in 30 days, rather than the previous benchmark of six months.

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