Statistical Discovery.™ From SAS.

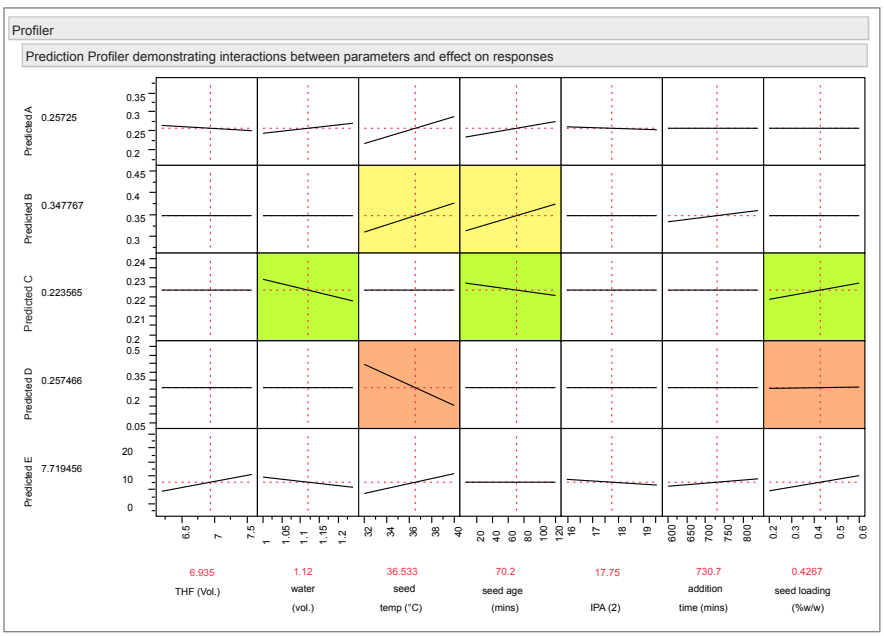
It's Quality by Design at GlaxoSmithKline

Scientists and engineers improve production processes using modeling and data visualization

Martin Owen is a proponent of Quality by Design – a scientific and proactive approach to pharmaceutical development – and he's ever in search of improvement.

As an Innovation Leader at GlaxoSmithKline, Owen is always looking for more effective and efficient ways to generate and visualize data to support risk assessments and to control manufacturing processes. He seeks out evidence-based, innovative solutions to take Quality by Design from an abstract concept to a day-to-day reality.

Owen's objective is to ensure that processes optimized in the lab will become robust manufacturing methods that enable continuous improvement throughout the process life cycle.



The Profiler shows the relationship between factors and responses (here factors included in interactions are highlighted by color).

JMP® statistical discovery software from SAS has helped Owen make considerable progress in this effort. The reward is a stream of new insights that translate to peak-performance processes – all by design.

The desktop software combines dynamic statistical analysis and rich data visualization capabilities. Used by scientists, engineers and data explorers across industries, its modeling functions include extensive design of experiment (DOE) methods that are essential to optimizing manufacturing processes in the fewest possible runs, thereby saving time and reducing costs.

Owen says JMP makes his data come alive. "The thing that's really impressive is that you can interact with the data; you can look at the what-ifs."

In one package

Fundamental to Quality by Design is understanding the relationships between the process parameters and the ways materials that go into a product affect materials at the intermediate stages of manufacturing and in the finished product itself. This requires knowledge of complex relationships across numerous unit operations – information that is continually evolving throughout the development and early manufacturing stages.

Understanding the process is essential to ensuring that the root causes of manufacturing problems are quickly corrected. The pharmaceutical industry is heavily regulated, and regulators stress that a vigilant and nimble approach to problem correction is an essential element of consumer protection.

"This is truly a case where a picture tells a thousand words. You've done the experimental design work, and now you're visualizing the impact."

Martin Owen

Ensuring product quality requires understanding the control strategy. For example, the material that results from a chemical reaction often contains minor impurities. "For each impurity, we need to know whether it's already present in the starting materials or whether it's formed in the process, and how effectively we can remove it," Owen explains.

Suppressing one impurity may cause others to increase. The key is to select the best combination of control-strategy options to achieve optimized, robust processes.

JMP offered the combination of modeling and visual discovery tools Owen was seeking.

"I became interested in design of experiments as a way of improving processes, and what was important to me in a statistical analytics package was that it simply did that," Owen says.

"But as I began to look at the bigger picture, it became increasingly important to me that we have an analytics package that also provides data visualization and has the technology to arrange the output. We also need to examine and integrate other types of modeling, such as kinetics and principal components analysis, to build our understanding.

"That's exactly what JMP has provided," Owen says.

'A picture tells a thousand words'

GlaxoSmithKline scientists, engineers and analysts work with two types of data: experimental and observed.

CHALLENGE

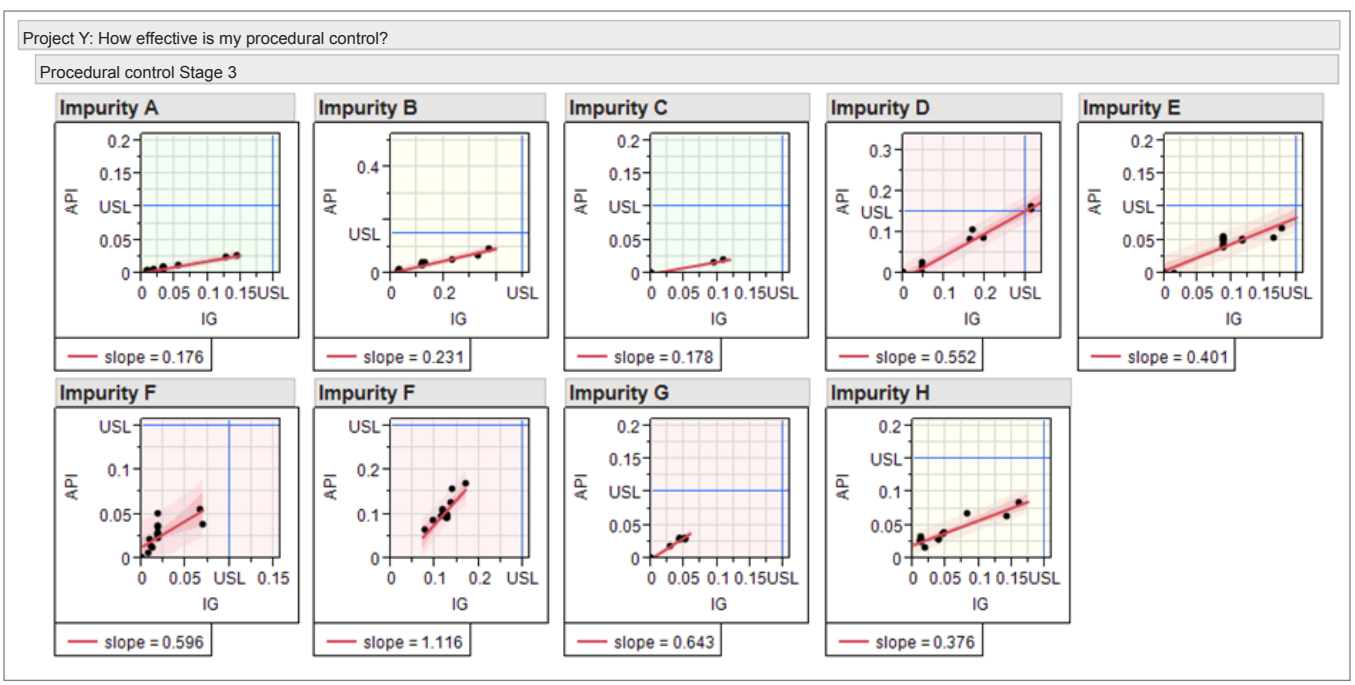
To make evidence-based decisions that ensure robust drug-production processes.

SOLUTION

GlaxoSmithKline scientists assess risk and develop process-control strategies using unique experiment design features and other capabilities in JMP statistical discovery software from SAS.

RESULTS

World-class design of experiment methods help scientists optimize manufacturing processes quickly, thereby reducing costs. JMP journals and customizable dashboards allow analysis results to be structured, shared and interactively interrogated. The software makes it easier to identify gaps, highlight important control features and demonstrate control.



Data-derived information (models and visualization) is structured by project and stage using the Journal functionality. Here, the impact of the crystallization stage on different impurities is shown.

Typically, data is generated under experimental conditions in the lab and is used to optimize a process. The goal then becomes to make that process robust and reliable. Observed data is gathered in the production process and is monitored to demonstrate that processes can be kept in control during manufacturing.

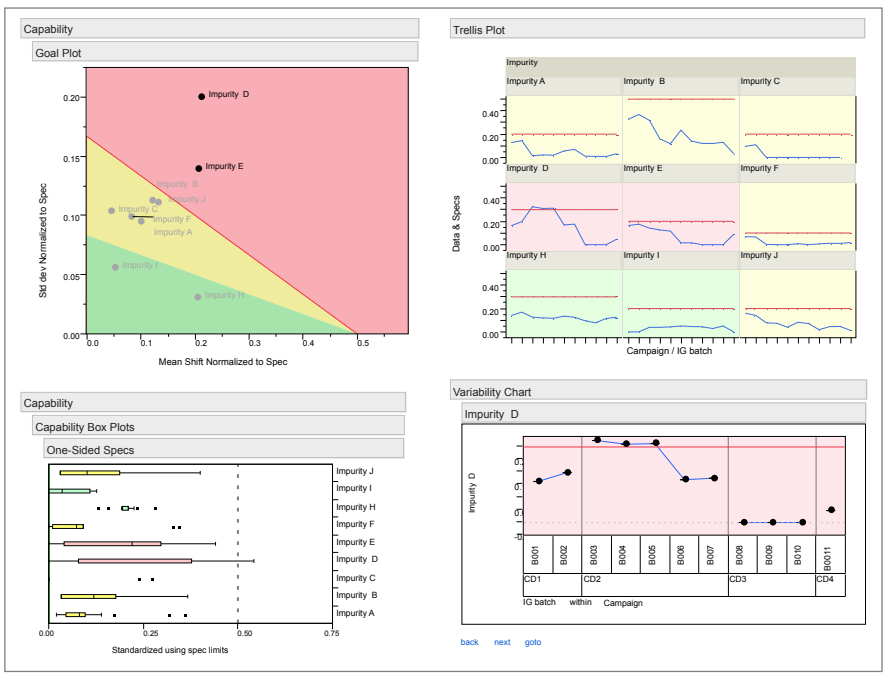
Owen must come to a comprehensive understanding of the process, but he also must minimize the time and cost of investigation. That's where the Quality by Design concept calls for design of experiments – a structured way to investigate the multivariate relationships between parameters and attributes.

"Through experimental design, a great deal of information can be obtained using relatively few resources, as compared with one-factor-at-a-time approaches," Owen explains.

DOE requires first asking some important questions about the process ahead:

- What are my goals?
- What attributes am I going to measure?
- How well can the attributes be measured or categorized?
- What parameters am I going to experiment on?
- What do I keep constant?

"When we're in product development, we identify the attributes that are critical to quality and then we set about looking at the relationships between the parameters and the attributes and seeing how we can optimize those and produce a robust process," Owen says.



The dashboard allows the viewer to look at the overview and drill down into more detail for specific responses.

First you must explore all the factors, he says, then optimize them, then narrow the ranges to control the process.

"Then you implement those conditions in production mode, and what you want to do is show the improvements you made in the design of experiment as you transfer them into practice."

Using the JMP Profiler, for example, Owen can shift parameters and see the effect immediately.

"This is truly a case where a picture tells a thousand words," Owen says. "You've done the experimental design work, and now you're visualizing the impact."

A unified perspective

Historically, investigators have relied on text and PowerPoint presentations to try to explain what's going on in a process. "But that brings all sorts of problems," Owen says. "It's difficult to hold all that information in your head, and you're at the mercy of whatever the presenter or author has chosen to focus on." Most significantly, "you can't explore the data dynamically."

Owen introduced JMP journals to his colleagues. They now drag and drop and arrange their data and reports in ways that make it easier to follow processes and determine how and where quality attributes will be controlled.

"The journal functionality offers a huge advantage," he says. "You can access,

navigate and retrieve different models and different visualizations very quickly."

The next step was to create diagnostic dashboards to communicate important information at a glance.

The dashboards are designed to support optimal organization of information to overcome the limitations of short-term memory and to direct the focus to where it matters most. Owen says that because processes and products vary from one to the next, he and his colleagues need the flexibility to create "adaptive dashboards" rapidly.

In the past, they used a variety of statistical and modeling packages, but Owen says that created a silo mentality. He and his co-workers now use the adaptive dashboards in JMP to break down those silos.

"Quite often, there are several ways in which we control the quality," he says, "and JMP provides a means of bringing these different types of procedural controls, attribute controls and parametric controls together to present them in a coherent story.

"If you bring together people from diverse perspectives and enter their data into the same package, you can see the synergies between different types of models," he says.

Some of Owen's colleagues have statistical backgrounds and some don't, "so we needed the flexibility to look at the big picture or drill down into the detail to check the assumptions that underpin the models." A core capability of JMP is integration of interactive graphs and comprehensive statistics.

Owen says he regularly discovers new features in JMP.

"I continue to gain new insights with JMP," he says, "and our processes continue to improve."

Owen emphasized that he and his colleagues are not applying dashboard methodology to all products or all aspects of drug development. "We are still in the incubation stage, progressing new applications and continuing to simplify and refine, to work toward long-term sustainable implementation," he said.

ONLINE

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