Customer Story

LONZA

Challenge

Manufacturers are under intense pressure to speed development of novel bio-manufacturing processes to help products reach the market on short timescales.

At Lonza, institutional analytics speed manufacturing process innovation

A customized design of experiments approach optimizes yield in bioreactors

As vaccine discovery efforts ramp up worldwide in the midst of the COVID-19 pandemic, the global supply chain has been thrown into hyperdrive with technology transfer in many cases running simultaneously with vaccine candidate trials. Few times in modern history has time-to-market been so vital, with the value of quick and innovative manufacturing processes coming under a new spotlight.

Swiss integrated health care solutions provider Lonza uses a wealth of global manufacturing expertise to accelerate batch production of everything from vaccines, monoclonal antibodies and other biologics to drug conjugates, peptides and molecules that require a parenteral dosage form. No stranger to rapid scaling, the company has for years offered its partners state-of-the-art methodologies that optimize processes, deliver on product quality and safety, and increase yields. Lonza's real innovation lies in its expertise in applying statistical approaches that Process Expert Andreas Trautmann says "optimize the optimization."

Optimizing the optimization

In the bioprocess engineering space, optimization is achieved by increasing the concentration of product inside a cell culture bioreactor, thereby improving overall yield while maintaining product robustness. Even incremental improvements can be highly valuable and offer both time and cost savings to the customer. By using similar processes to manufacture different products, Lonza has grown these efficiencies over time into deep process knowledge, the benefits of which are transferred to every new product line the company develops.

As Process Expert for Upstream Processing in Manufacturing Science and Technology at Lonza in Visp, Switzerland, Trautmann supports the effort to bring products from the lab to the marketplace. Part of the scaling process is built on existing process knowledge – "The more projects we're working on, and the more we use these statistical tools with the same or similar organisms and processes, the more we improve our experimental knowledge," Trautmann notes – but some processes must be designed from scratch.

In a particularly interesting recent project, Trautmann and his team were tasked to design a new manufacturing process that went beyond Lonza's standard bioreactor – and do so under demanding timeline constraints. A highly strategic approach to experimental design was crucial in fast-tracking this process while maintaining quality.

"As you can imagine," he says, "the DOE tools provided by JMP in particular were very helpful [in this case] and are often used in this R&D group since a lot of parameters are unknown for the processes we're investigating."

A customized DOE in JMP® results in a near doubling of yield

Design of experiments, or DOE, enables practitioners to reduce the number of experiments needed to produce a desired result by setting the conditions of experimentation with a statistical model. The Custom Design platform in JMP offers users the ability to specify which effects are necessary to estimate and which are desirable to estimate, given the number of runs. It is also possible to specify a number of runs to fit within budgetary constraints.

Instead of testing one factor at a time, Trautmann explains, JMP provided the team with a way to quickly generate a streamlined, strategic approach. "JMP is most helpful because it's much more efficient to investigate several factors at a time instead of investigating only one by one. It saves a lot of time to use statistical methods like this."

jmp
Statistical Discovery™ From SAS

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>
> Andreas Trautmann, Process Expert

In the case of the new process the team developed for a small-scale reactor, Trautmann says they used DOE to increase the product concentration – or overall yield – by almost a factor of two, a stunning outcome considering scientists are sometimes unable to increase yield at all in similar scenarios. "The customer was really happy, and we were really happy as well," he says.

In addition to improvement in yield, the project also achieved significant time savings milestones. With 24 runs in the team's experiment, saving time on each run amounted to significant time savings overall. "Without using the Custom Design tool, we would have needed at least double the amount of time to investigate these factors. Instead of two weeks, probably four weeks at least," Trautmann explains.

In addition to being flexible, the model generated via Custom Design was more efficient: It was able to accurately predict the output variable within the characterized range, despite three out of the 24 experimental runs not succeeding. Although there are other options, Trautmann and his team prefer Custom Design in JMP "because it's more flexible than the standard designs, for example adding or removing some experiments." This flexibility allows them to adapt to ongoing observations and tailor experiments accordingly.

"We used JMP for designing, planning and evaluating the experiments from the very beginning in small-scale bioreactors," he explains. "Then, we continued the work in medium-scale bioreactors, and by the end of this year it will be transferred to a production scale. It doesn't happen so often that very new processes from lab-scale reactors will end up in manufacturing. So it was a very nice success story."

Data visualization and exploration, an important part of any DOE

DOE is not the only JMP application Trautmann says he finds useful in process optimization. Data exploration and graphical functions have also proven effective, revealing some interactions in the data that could have otherwise been missed. "Data exploration is an important tool in JMP, because very often you're able to reveal some interactions which you wouldn't have realized without the explorative data evaluation," he says. "With the human eye, it's very hard to see the differences or the impacts [from a data table alone].

"You can, for example, generate data clouds to see if there's an interaction between the factors, or you can make a histogram to see how just a few data points are spread in the rest of your data set." Data visualization enables a fast evaluation of data quality, which can contribute to enhancing any DOE model.

Building institutional statistical expertise with STIPS, an online learning resource

Like most companies, Lonza uses a variety of training formats to bring scientists and engineers up to speed on statistical methods. But given positive outcomes with JMP, many employees at Lonza are enrolling in Statistical Thinking for Industrial Problem Solving (STIPS), a free online course created by JMP for both industry and academia. STIPS is divided into six modules covering various statistical and data analysis areas with specific industrial applications. It's been popular among Trautmann's team; colleagues with no prior statistical background or experience with JMP were able to integrate statistical methods into their work.

"STIPS is a very good course," Trautmann says. "I was happy to have one online course concentrating a lot of important information in an easy, understandable level." Even as a relatively longtime user of JMP, he adds, the course deepened his understanding of quality methods – things like control charts and process capability – that he is now using more intensively.

Solution

Scientists at Lonza have implemented statistical approaches to process optimization and R&D. JMP allows them to deploy complex design of experiments (DOE) strategies with its Custom Design platform and interactive data visualization features.

Results

In one example, a team at Lonza was able to increase overall yield by nearly a factor of two – an impressive result for a process in which scientists are often unable to make meaningful advances so quickly. "The customer was really happy, and we were really happy as well," says Process Expert Andreas Trautmann.

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