JMP® CUSTOMER STORY

Adocia

Scaling up from discovery to GMP

CHALLENGE

Successful and efficient technology transfer requires a continuity of process knowledge only possible through statistical approaches; a fact now recognized in ICH guidelines. Though process data is abundant at the discovery stage of any biotechnology pipeline, too often data streams are siloed beyond the reach of both process development teams and their contract manufacturing partners.

SOLUTION

Adocia's process chemistry group has turned to JMP® statistical discovery software from SAS to resolve data access and management challenges as well as to boost reproducibility via statistical methods like design of experiments and quality by design. The software's wide-ranging functionalities enable optimization and streamline process transfer for Adocia's innovative excipient, BioChaperone®.

RESULTS

Process development chemists at Adocia now use JMP extensively for multivariate analysis and simulation. In one example, scientists running custom designs in JMP were able to optimize a difficult crystallization process leading to the product's successful manufacture at a hundred grams scale without defects.

jmp STATISTICAL DISCOVERY FROM SAS

At clinical-stage biotechnology company Adocia, statistical approaches boost reproducibility and knowledge continuity in process transfer for a groundbreaking excipient.

Statistical approaches today are playing an outsized role in knowledge continuity and process insights that improve technology transfer from R&D to good manufacturing practice (GMP) commercial scale manufacturing. While previously scientists working at this stage in the biotechnology pipeline primarily utilized processes as designed by R&D labs, it was not uncommon for the related data to remain siloed. With the revolution in industrial statistics instigating widespread uptake among life science companies, scientists are increasingly seeing statistical approaches as essential to optimal technology transfer from both a quality and regulatory compliance perspective.

Clinical-stage biotechnology company Adocia has had a strong culture of analytics since its founding in 2005 by organic chemist Gérard Soula and his sons Oliver and Rémi Soula, both polymer scientists. Based in Lyon, France, the company was formed around a proprietary protein formulation platform, BioChaperone®. This innovation, a molecular delivery system for therapeutic proteins, has widespread applications in diabetes and chronic disease.

Adocia's expanding portfolio now includes a variety of formulations customizing BioChaperone technology to form a physical complex with already-approved therapeutic proteins and peptides. The platform's innovation increases safety and efficacy in pipeline therapies through protein stabilization and solubilization. In the diabetes space, Adocia offers five clinical-stage injectable treatments including two ultra-rapid formulations of insulin analog lispro (BioChaperone Lispro U100 and U200), a combination of basal insulin glargine and rapid-acting insulin lispro (BioChaperone Combo), and a combination of prandial insulin with amylin analog pramlintide, M1Pram. The company also produces novel formulations for the treatment of hypoglycemia and other metabolic diseases.

Design of experiments, an increasingly vital method for scaling to GMP

While statistical methods were not privileged in early discovery stages at Adocia, the building out of chemistry, manufacturing and controls and shifting focus to technology transfer motivated the emergence of widespread statistical enablement. "As Adocia's products have matured and as ICH guidelines incite pharmaceutical companies to deeply understand product-process parameter linkages, we are increasingly using statistical approaches like design of experiments in our laboratories," says Head of Process Chemistry Thomas Cochet.

Cochet is by training an organic chemist who now heads Adocia's chemical process design, industrialization and process transfer, focusing on the company's lead innovative excipients. His team, in addition to leading in-house manufacturing for early-stage batches, is tasked to ensure the scalability of chemical processes to industrial (GMP) manufacturing facilities.

As Adocia's technologies have advanced through the development pipeline, Cochet and his team work together with the company's contract manufacturing organization (CMO) partners to scale commercial production. "ICH guidelines strongly incite pharmaceutical companies to use statistical approaches to justify process design and robustness," Cochet explains. It was therefore at this stage that the team responsible for technology transfer realized they would need a more sophisticated software to ensure knowledge continuity between Adocia and its partners.

"We had the increasing feeling that we would need to implement statistical approaches like DOE in our process developments," said Cochet, "and one of our CMO's project leaders recommended JMP."

A tool with which to navigate data access challenges – and boost reproducibility

Cochet's team of highly skilled technicians and PhD-level scientists all come from a background in organic synthesis and, he says, "are highly meticulous when tuning process parameters and determining impurity profiles with extensive laboratory work throughout the journey toward GMP manufacturing." Reproducibility is a key focus in process chemistry, and Cochet soon saw the advantage of a tool like JMP®, a software widely regarded as the industry standard for statistical approaches like design of experiments (DOE) and quality by design that allow practitioners to explore and replicate multifactor opportunity spaces.

In the synthesis process involved in Adocia's BioChaperone excipient, Cochet and his colleagues use a screening plan followed by a response surface plan in JMP to model responses according to key process parameters. Furthermore, they use the platform's simulation tool to determine the extent of each parameter leading to a minimum non-compliance rate. The result is a clear depiction of the design space, a visualization that helps scientists quickly and comprehensively explore interactions between factors. "For process development applications, the Profiler and associated simulation tool in JMP are very helpful," says Cochet.

The team also uses DOE extensively in the laboratory setting to structure experimentation processes in such a way as to optimize insights while minimizing experimentation time and resource inputs. Most of the time, Cochet explains, designs are based on common chemical parameters like temperature, time and stirring speed, among others. With DOE, experiments can be replicated more precisely by external teams like those at CMOs tasked with executing manufacturing at a commercial scale. Control charts and process capability assessments are also key.

JMP® helps solve a process development dilemma

Since its introduction at Adocia, JMP has played an invaluable role in helping scientists to quickly identify solutions to a number of process challenges. Cochet cites the example of a crystallization step in the early development of BioChaperone that was particularly complex and prone to variation. "Depending on the conditions that were implemented, the solid would melt, over time forming a gel," Cochet recalls. "We observed that temperature, stirring rate and volume all had strong effects. A custom design was therefore run in JMP to optimize this step, and the benefits of a multivariate approach were established when we were able to determine many interactions between factors." Once the team defined a set of optimal parameters, they transferred the process to demo-batch scale for clinical study, resulting in successful production at a hundred grams scale.

The team's biggest challenge has since become fine-tuning the balance between model accurateness and process robustness, which varies according to project stage. "Unlike with commercial manufacturing, in early-stage process development the most difficult part is to define when we need to go further in DOE implementation. A risk management-based process design allows us to focus our work on pertinent studies," Cochet says. "We are always aiming for a balance between work efficiency and the precision required for a given situation. For example, how many parameters must be evaluated? Do we need a response surface model?""

Putting JMP into the hands of scientists has helped Adocia optimize the utilization of its domain experts who understand most intimately the mechanisms behind the production of BioChaperone. And, says Cochet, "faced with issues or questions about JMP capabilities, JMP engineers are always available to help."

By enabling chemists to apply statistical approaches independently of dedicated statistical experts, Cochet and his team are able to work smarter – and more quickly on process development. This optimization is now saving time and ultimately accelerating process transfer.

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