



BOEHRINGER INGELHEIM AND THE QUEST FOR THE GOLDEN BATCH

The story of pharmaceutical production is often a quest for the golden batch: a repeatable process that consistently optimizes yield and quality. Recently an animal health subsidiary of Boehringer Ingelheim — a top international pharmaceutical company — began collaborating with Sartorius Stedim Data Analytics, a long time OSIsoft partner, on a project that uses multivariate data analysis techniques (MVDA) to create golden batch trajectories based on historic data. These golden batch trajectories can then be used for real-time monitoring and prescriptive process control for higher potency batches.

Compliance is always a chief concern for biopharmaceuticals. Results must fall within a narrow framework or Proven Acceptable Range (PAR) of acceptable variability. “It’s about demonstrating that your batch is under control. That’s the compliance aspect of this,” Will A. Penland, Principal Data Scientist, at Boehringer Ingelheim, Animal Health said recently at the OSIsoft’s PI World 2018 San Francisco. “The government takes that very seriously. You need to demonstrate that your process is under control and that you are capable of meeting the specification limits.”

Minimizing batch variation and understanding the causes of variability is a crucial but difficult task. As Penland explained, “When you are dependent on biological processes for the creation of your product, there is a lot of inherent variability that you have to contend with. [...] With a bio-fermentation process, you can put

the same thing in and if you have production variances you can get something quite different day by day.”

The problem is that variation can arise at many points in the process. Part of the mystery is always what process attributes or conditions are responsible for the greatest degree of variation. The sheer number of different potential sources of variation makes this a critical but difficult question to answer when pursuing the golden batch.

WHAT IF?

Penland and his team began by asking themselves a simple question: “what if?” What if they could reduce production variation? What if they could identify crucial process attributes? And then what if they could target those key process components to reduce production variance, generate greater batch potency, reduce batch destruction, and increase yield?

CHALLENGE:

Understanding variation in biological batch processes.

SOLUTION:

Use PI System to facilitate MVDA of process and attribute data.

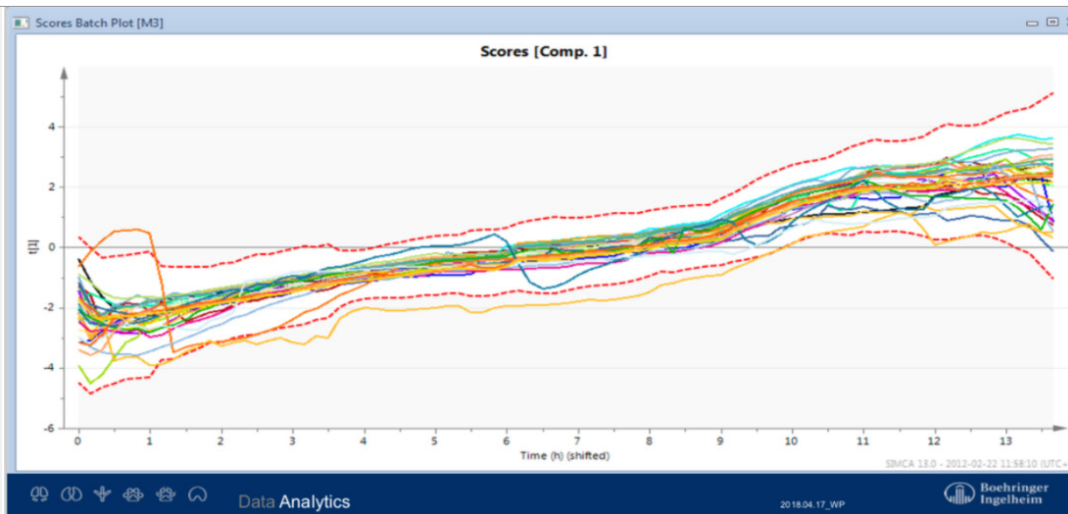
BENEFIT:

Reduce production variance, generate greater batch potency, reduce batch destruction, and increase yield.

BATCH EVOLUTION MODEL

Each Line = 1 Batch:
Multivariate Control Chart

Multivariate data analysis and batch evolution modeling enable Boehringer Ingelheim to gain insight into their fermentation process.



The answer seemed to lie with using MVDA and advanced statistical modeling techniques like Principle Component Analysis (PCA) and Partial Least Squares (PLS). But implementing MVDA presented another set of obstacles. Gaining a better understanding of process variability meant monitoring their process at many different levels. This complex monitoring generates many different kinds of data. In order to use their data-analytic software, SIMCA, they needed a way to first aggregate and contextualize all the data from all these potential sources of variation.

MANAGING THE DATA IS THE HARD PART

“80 to 95% of the work is managing your data,” Penland explained. This is where the PI System came to their rescue. Using Asset Framework, they created data tags of different classes for different types of data streams related to the fermentation process. The PI System allowed them to bring their diverse data streams together, aligning their SCADA, LIMS, process control, and attribute data, with their time-resolved spectroscopic data.

They also triggered process steps within their programmable logic controller and used a step numbering system to create Event Frames. They now use a parent-child event frame model to keep a close eye on the various stages of the fermentation process, particularly the growth phase. The parent event represents the batch

and the child events are the various steps within the fermentation process.

Templates enable them to ensure consistent configuration of their process stages. Templates are crucial for a large international company like Boehringer Ingelheim. “The analytics is one thing but the challenge these days is to make these things scalable, reproducible, and easy to template to move across platforms,” Chris McCready, Lead Data Scientist at Sartorius Stedim Data Analytics said. “If we come to a customer and they have PI with a good configuration then we can have a monitoring process, advanced analytics, the whole thing up and running in a matter of days. And if they have Asset Framework then we can take what we did in New York and we can apply it in Singapore. It’s very cut and paste.”

With the PI System enabling their advanced data analytics and batch evolution modeling, Boehringer is becoming more data driven and predictive, and proactive. They can now see things as they are happening or before they happen with each batch. “We have a data driven mindset now. We are asking ‘how do we interpret this and what is the data telling us’ rather than having a more reactive knee jerk response, fighting fires all the time,” Penland said.

For more information about Boehringer Ingelheim and the PI System, watch the full presentation [here](#).

PARTNER: SARTORIUS STEDIM DATA ANALYTICS

PI System Components Used:

PI Server

- Asset Framework
- Data Archive
- Event Frames
- Asset Analytics



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— Chris McCready
Lead Data Scientist,
Sartorius Stedim
Data Analytics

Penland, Will and McCready, Chris. “A Case Study in Biopharmaceutical Data Analytics: Using Asset Framework and Event Frames for MVDA”
<https://www.osisoft.com/Presentations/A-Case-Study-in-Biopharmaceutical-Data-Analytics--Using-Asset-Framework-and-Event-Frames-for-MVDA/>