



UNIVA UD

# GLAXOSMITHKLINE: Implementing Breakthrough Technology for Clinical Development Modeling and Simulation

Univa UD Case Study  
Life Sciences: **Clinical Development**



## SOLUTION OVERVIEW

<b>CUSTOMER CHALLENGE</b>	GlaxoSmithKline is a top research-based pharmaceutical company and a drug development innovator. When faced with the challenge of improving efficiency in modeling and simulation, the Research, Modeling and Simulation team at GSK's clinical development organization set out to develop new, faster methods of establishing and running models for a drug's effects on the body.
<b>SOLUTION</b>	The Research, Modeling and Simulation team first automated the process of model selection through an algorithmic approach. The team leveraged GSK's installed grid infrastructure to assess hundreds of models in parallel. Using the selection algorithm to pick better models faster – and then running more models at a time using the grid – has allowed the Research, Modeling and Simulation team to achieve significant productivity gains.
<b>BENEFITS</b>	The GSK team found that by combining their algorithmic approach to model selection with a grid solution for processing, they achieved: <ul style="list-style-type: none"><li>• Project timeframe reductions</li><li>• Reduced cost of analysis</li><li>• Improved development decision capability</li></ul> GSK's investment in grid technologies has helped the company realize savings of over US \$1,000,000 while streamlining the modeling process to help the company accelerate clinical development for life-saving new drugs.
<b>TECHNOLOGY</b>	Univa UD Grid MP' for PCs, clusters and workstations

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## BUSINESS CHALLENGES FOR A DRUG DEVELOPMENT LEADER

One of the top 5 Pharmaceutical firms in the world, GlaxoSmithKline (GSK) is a Fortune Global 200 company with over 106,000 employees worldwide. A leader in genomics/genetics and new drug discovery technologies, GSK spends billions of dollars annually on research and development at its 24 R&D sites worldwide. To support this investment, GSK is exploring breakthrough ways to speed the lengthy process of bringing drug candidates to trial – a process which can take 10-12 years according to the FDA.

One of the methodologies GSK considers critical to efficient development is modeling and simulation. Traditional approaches to developing valid models of drug effects are, while valuable, extremely time-consuming and labor-intensive. To address this problem, the Research, Modeling and Simulation team within GSK's clinical development organization set out to develop new, faster methods of establishing and running models for a drug's effects on the body. At stake were project timelines, modeling accuracy, and labor time and expense.

**“In this approach, we first define a search space for our candidate models and then let the algorithm do the searching and selecting. Our algorithm generates hundreds of models at a time, picks those that are most useful and then learns from this selection to go back and generate better models. The result is a much larger set of much better models to use in PK/PD analysis and a better chance of finding a better model.”**

**Mark Sale**  
Global Director of Research  
Modeling and Simulation, Glaxosmithkline

## CLINICAL DEVELOPMENT MODELING: SPEED VS. SCOPE

In the clinical development process, pharmacokinetic and pharmacodynamic (PK/PD) computer models are increasingly used to simulate the actions of drugs and to support informed decisions about development based on those

actions. These models describe the time course and drug concentrations in the body (pharmacokinetic) and the physical effects of drugs (pharmacodynamic). The result of such modeling is “a mathematical description of a drug's fate in the body, for an individual. Population modeling involves the analysis of data from a group (population) of individuals, with all their data analyzed simultaneously to provide information about the variability of the model's parameters.”<sup>1</sup>

**“With the algorithmic approach, we have essentially substituted a very computationally intensive method of selecting the optimal model for a labor intensive method. The grid computing environment provides the computational power to make this approach feasible.”**

**Mark Sale**  
Global Director of Research  
Modeling and Simulation, Glaxosmithkline

However, the establishment of these models is frequently extremely labor intensive and time consuming. Scientists must select the demographic factors to be considered and then select those models which are most likely to accurately describe the drug's effects. There are far more models possible to build than can be run, and scientists need ways to intelligently (and quickly) select and then run models to enhance the development process.

“Modeling and simulation is used in drug development to project the effect of drugs on disease populations prior to actually giving the drug in those populations. The most time-consuming part of this two step process is the modeling,” explains Mark Sale, Global Director of Research Modeling and Simulation for GSK. “Clinical development teams are eager to explore and adopt new technologies and approaches to this process in order to help them deliver a drug to trials that has the highest probability of successful performance. The challenge is making this happen in a reduced timeframe without compromising the quality of the information – the last thing we want is to quickly deliver a drug to trials that has a less-than-optimal shot at success.”

## A Unique Approach To Model Selection

Unfortunately, no methodologies or tools exist commercially to speed the process of model selection & analysis,

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## A UNIQUE APPROACH TO MODEL SELECTION

Unfortunately, no methodologies or tools exist commercially to speed the process of model selection & analysis, and it is costly to spend the weeks or months doing this the traditional way (with scientists painstakingly selecting models and then running them one by one on high-powered hardware). So the Research Modeling and Simulation group at GSK set out to develop faster methods of establishing PK/PD models for analysis. An automated method for model selection was developed using a machine learning algorithmic approach based on a Genetic algorithm – this method was able to examine far more candidate models that a single team of scientists could do.

## BETTER MODELS FASTER – FOR LESS

Ultimately, the Research Modeling and Simulation group's approach delivered higher quality models while reducing the effort required to produce them. The machine learning algorithm reduced the person-hours required in model selection by several fold. In one case, a job that used to take 2 months with over 200 person-hours of labor time was completed in under a week with only 15-20 person-hours of time. This approach also raised the quality of models selected for analysis by increasing the scope of models considered.

In addition to efficiency benefits, GSK has seen a reduced cost of analysis from this approach – since analyses can be done in house with no extended timeframes or need for outsourcing.

## RESULTING CHALLENGE: SUPPORTING INCREASED DEMAND

While this automated method proved valuable in its ability to create more, better models for analysis, it also presented a dilemma: How to perform analysis on the hundreds more models created? Scientists were thrilled to have more high-quality models to consider but realized the limitations of their compute resources would weaken the value of this achievement. If the automated algorithms were to positively impact clinical development timelines and costs, then a solution for analyzing more models at once would be needed.

## GRID TECHNOLOGY FOR MODEL ANALYSIS

The Research, Modeling and Simulation team at GSK decided to supplement their automated model selection system with a grid solution for distributed processing. GSK had already deployed Univa UD's Grid MP software to accelerate virtual high-throughput screening applications in the area of drug discovery, and the Research, Modeling and Simulation team decided to leverage the software as

a secure way to increase speed of work without sacrificing scope and quality.

## THOUSANDS MORE MODELS RUN WITH HUNDREDS OF HOURS SAVED

Within days, the team's PK/PD analysis software (NONMEM from GloboMax) was up and running on the 1500-node Windows grid. An internal GSK team grid-enabled the application themselves using Univa UD's flexible APIs for application enablement. GSK can now run thousands of models concurrently, and the grid manages the scheduling of these runs depending on the resources best suited (and available) for the work.

Execution of jobs on the grid is transparent to the user – he/she only knows that a job run is submitted to NONMEM and results come back a great deal faster than before. The Research, Modeling and Simulation team now assess six to eight thousand models per analysis compared to the one to two hundred that were previously possible when analysts wrote the required code one model at a time. What used to take months can now be done in weeks.

Mark Sale explains that “our approach requires a grid technology solution because the algorithm generates so many more models to run. The grid lets us run those models concurrently and manages assignment of jobs to compute resources so my team isn't taxed with this function.”

**“The Grid MP platform keeps track of all the data related to our job runs – where the job was executed, what type of machine, how long it took. So not only does the grid save us time, but in automating this function it allows us to define a validated process for job execution. That goes a long way toward achieving FDA compliance.”**

**Mark Sale**  
**Global Director of Research**  
**Modeling and Simulation, Glaxosmithkline**

## Improving the Decision-Making Process

Prior to this approach, complex drug response models were difficult to implement within the timeline constraints inherent to the modern, competitive drug development

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## COMPLIANCE CAPABILITY IMPROVEMENTS

The clinical development team at GSK is finding other benefits to running PK/PD jobs on a grid – including an opportunity for increased compliance capability via automated tracking and control features.

Unlike other solutions, Grid MP provides a database and tracking mechanisms to automate tracking and manage storage. Scientists submit data and Grid MP manages where it goes, controls the software version, sets environment constraints to insure data quality, and stores result sets. This unique approach greatly increases an organization's ability to be compliant while reducing the person-hours spent on tracking and quality control.

**“GSK’s adoption of grid technology proves they are a leading innovator in the field of drug development. They’ve applied the grid to multiple areas of the business, including discovery and development, and they’ve succeeded in migrating dozens of their internal applications to the platform on their own.”**

**Jikku Venkat**  
Chief Technology Officer, Univa UD

## LESSONS LEARNED

- **Consider new approaches to manual tasks:** Since no commercial solution has emerged as a standard for clinical development teams to use, innovators like GSK's Research, Modeling and Simulation team looked for (and found) ways to automate this process themselves. They continue to seek better, faster ways to do their work effectively.
- **Promote new technologies across the business:** The success of the grid implementation in GSK's drug discovery organization led to this unique application within clinical development. Companies should seek ways to benefit from adopted technologies in multiple areas of business.
- **Put compliance-related functions in place for productivity gains down the road:** The more a drug company can validate its processes for compliance, the stronger its chances of moving quickly through trials. Tools like a Univa UD enterprise grid make the necessary tracking and control easy, taking data and process management off the plates of busy scientists.

## ABOUT GRID MP™ SOLUTIONS

Univa UD's Grid MP™ allows organizations to coordinate and share existing computing, application, data, storage, and network resources across departmental and geographically dispersed organizations. By harnessing the underutilized compute power of its existing resources – including workstations, clusters and data centers – an organization can create a powerful new resource capable of delivering high-performance processing power to run compute-intensive applications in extremely reduced timeframes. As a result, project scope can be increased and new projects tackled without sacrificing speed or quality of work.

Grid MP allows businesses to attack the problem of insufficient compute power in the most efficient and cost-effective way possible – by leveraging the compute resources they've already invested in. Using Grid MP solutions, organizations are able to significantly increase the speed, scope and quality of their analysis projects, resulting in improved productivity and substantial return on invested capital (ROIC). In contrast to more traditional high-performance computing (HPC) solutions, Grid MP solutions increase in power over time (Moore's Law) and never depreciate in value.

This technology delivers high-performance computing power for a fraction of the cost, enabling:

- Dramatically accelerated runtimes for compute-intensive applications
- Increased project scope & accuracy of results
- Significantly reduced IT spending
- Increased ROIC on existing compute resources

## ABOUT UNIVA UD

**Univa UD** is the leading provider of open source products for grid and cluster computing environments. The company's industrial-strength offerings range from departmental and HPC cluster management to enterprise-wide grids, and represent the proven and cost-effective alternative to traditional products that customers have been waiting for. Based on a combination of open source and proprietary components, Univa UD offerings include a downloadable open source product for integrated cluster management, a proprietary cluster product with added functionality and robust analytics, and a comprehensive enterprise grid product based on award winning technology. All Univa UD products are run by Fortune 1000 companies in large-scale, production environments. For more information, contact Univa UD at **1-800-370-5320** or visit us at **[www.univaud.com](http://www.univaud.com)**.

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