

## Trebing & Himstedt Case Study: Akzo Nobel Organon

### Advanced Electronic Batch Recording in Biotech API Production

#### The Customer



The Netherlands-based Akzo Nobel group is active throughout the world in three business areas: Pharma, Coatings and Chemicals. With its approximately 64,000 employees in more than 80 countries, sales in 2004 were EUR 12.7 billion. Manufacturing products for both the human and animal healthcare market, Akzo Nobel's Pharma group accounts for EUR 3.2 billion of this turnover. Products developed by these Pharma businesses include, among others, oral contraceptives and antidepressants. The group comprises two innovative, R&D-driven healthcare businesses. *Organon* is a leading international player in several key areas of human pharmaceuticals, particularly prescription medicines. *Intervet*, supplying customers with animal vaccines and pharmaceutical products, is one of the world's largest animal healthcare

companies. Their activities serve customers around the globe.

*Diosynth*, as part of *Organon*, plays a prominent global role in the production of complex active pharmaceutical ingredients (APIs). As an API manufacturer, Diosynth's extensive expertise is chemical synthesis, cell culture, fermentation and chromatographic purification including HPLC.

More than 100 products are provided to pharmaceutical companies all over the world, among them insulin and heparin, steroids or synthetic peptides. In the process of development and manufacturing, advanced and sophisticated technologies, applied while strictly complying with the highest cGMP and HSE standards, form the basis for Diosynth's high levels of quality and reliability.

#### The Plant



Besides traditional production of heparin and insulin from animal tissues, biopharmaceutical APIs are manufactured in state-of-the-art fermentation facilities at Diosynth's headquarters in Oss, Netherlands. From a manufacturing perspective, two stages can be distinguished in the production of biopharmaceutical active ingredients. In the first phase, upstream processing, genetically modified micro-organisms and cells are replicated in fermenters or cell culture reactors. The micro-organisms or cells produce the required biopharmaceutical or a precursor. Depending on the organism or cell type, the crude product is recovered from the cells or the culture medium.

## The Application



In November 2000, Akzo Nobel announced its investment into a new cell culturing and fermentation unit to be used for biotech API production at the Oss site.

Within the scope of the project, fermenters with net working volumes of up to 10,000 liters have been installed in controlled condition rooms and according to cGMP standards. Batch cell culture reactors in suites with controlled conditions allow for capacities up to 18,000 liters working volume in serum-free and protein-free cultures. With these capacities, the project has one of Europe's largest animal cell culture facility. The total amount of EUR 47 million was invested in the project. The facility was validated and commissioned at the end of 2003. FDA IQ approval for the installation was received by Akzo Nobel Diosynth in 2004.

Implementation of RAPID-Pharma began in March 2003 after a thorough evaluation process. After potential suppliers had been limited to three systems, the products had to undergo system tests to prove their suitability. RAPID-Pharma emerged as the only product meeting the project team's complex requirements such as manufacturer-independent connectivity, support of standard interfaces, S88-based reporting and 21 CFR Part 11 compliance.

Besides a speedy solution to FDA compliance and safe data handling, RAPID-Pharma offers many technical benefits and ease of use. Due to these assets, it is easy to train, and broadly embraced and accepted by its users.

RAPID-Pharma is at the heart of the Production-Information-Warehouse system, where all real-time data, batch data, alarms and events of the Unix-based Invensys process control system as well as data from the iFIX facility management system are stored. RAPID-Pharma is responsible for all data capture and the generation of the Electronic Batch Reports. All process and plant information necessary for reporting and analysis are derived from this system. It operates 24/7 and records batches with a runtime ranging from several days to a number of weeks. Batch data, continuous data, alarms and events as well as the respective room monitoring data can be analyzed collectively.

Following system implementation and qualification, the former project manager avidly promotes RAPID-Pharma, in particular the straightforward handling its users enjoy. "Only now are we beginning to realize the system's full potential. We will expand it step by step. Extremely important for us is especially the system's ability to provide access to all data in a database at any one time, and to allow generation of new ad-hoc queries without programming knowledge." For Paul Jansen, RAPID-Pharma is a valuable tool for continuous process improvement and speedy scaling-up upon implementation of new manufacturing processes.

The information captured by RAPID-Pharma is required and used daily by several departments as manufacturing and technical support. The number of recorded data collection points and users has already been increased several times.

## Going Forward

Due to this positive experience the implementation of RAPID-Pharma into other Akzo Nobel production facilities and future projects within the Akzo group can be definitely imagined. "With a system such as RAPID-Pharma, we are in a much better position to speed up commissioning and optimize our facilities during operation", says Paul Jansen.