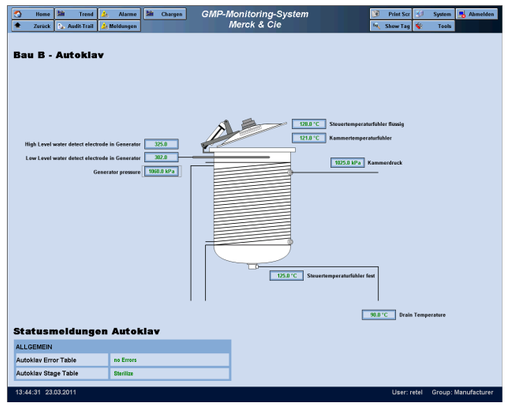

Figure 4: Autoclave chamber and generator pressures, as well as lid, chamber and drain temperatures are clearly displayed. An imported graphic provides an unmistakable understanding of the process.

firewall with the office network.

The Result

Due to a strong background using InduSoft Web Studio, Retel Neuhausen AG was able to develop a quality SCADA application and GMP monitoring system for Merck & Cie. As a general contractor, Retel Neuhausen AG led the project from planning to completion. Through this turnkey solution, interfaces have been reduced to a minimum, allowing an economic monitoring system that is highly effective, reliable, secure, and easy to use.

This GMP monitoring system spans the entire facility, and offers some definite advantages to both the system owner and production managers. The interface is simple to use, and very intuitive, which reduces training time considerably, and helps control human error. Clear limits for values and carefully planned guidelines give operators clear information for quality assurance, and historical data and trends are easy to view and analyze. Off-site facility monitoring reduces response time, and access to the system via existing hardware off the plant floor requires a smaller investment in equipment.

The project manager benefits from the use of a reliable, stable system with low maintenance requirements, and optimized "Life Cycle Costs ". The system is easily upgradable and scalable as well. This means that as new technology is introduced or the processes grow, it is easy to integrate new data into the system and connect to new hardware. This makes it very cost effective to grow the system as technology changes in the future. Interfaces used in the system are standardized for easy use, from fonts, to colors and graphics. Retel Neuhausen AG provides Merck & Cie with an experienced monitoring partner, and InduSoft provides extensive support on all products, allowing Retel Neuhausen AG flexibility in future supports of this system.

Representatives of the FDA and EU Annex will easily be able to audit and verify data captured with this GMP monitoring system. Transparent system architecture with clearly defined interfaces allows easy use and monitoring of data. The system was developed according to GAMP 5 and FDA 21 CFR Part 11, and maintains Design Qualification - DQ, Installation Qualification - IQ, and Operational Qualification – OQ verification.

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Retel Neuhausen AG Helps Merck & Cie Meeting New, Tight Standards

Retel Neuhausen AG uses InduSoft Web Studio to create comprehensive software solutions for pharmaceutical manufacturing

- InduSoft Web Studio was used to create GMP monitoring systems that are FDA 21 CFR Part 11 and EU Annex 11 compliant
- A scalable solution was created by utilizing the built-in features of IWS including: historical alarming, historical trending, database connectivity, web publishing, eSignatures, security, PLC drivers and many other SCADA software features
- Remote monitoring facilitates reduced response times and achieved a reduction in overall equipment costs

Figure 1: Environmental conditions are monitored across rooms, storage and production facilities and superimposed on building layout diagrams

Background

In the pharmaceutical industry, the chemical integrity of the compounds may rely on the strict control of hundreds of variables, from air humidity and freezer temperatures to mixing times. Active Pharmaceutical Ingredients (APIs) may be used in anything from prescription drugs to cough drops. Other high-purity substances rely on strict environmental control for production. Because these controlled substances and pharmaceutical compounds must be perfectly consistent across each batch, records of every aspect of the process must be maintained, from storage to mixing and processing, to transport and delivery.

Merck & Cie operates within the strict guidelines of FDA 21 CFR Part 11 and EU Annex 11 in the development and production of active pharmaceutical ingredients and high-purity substances for active substance transport, and drug transportation and delivery. Merck & Cie is an international company, located in Schaffhausen, Switzerland and is a subsidiary of Merck KGaA in Darmstadt. Merck is the world's oldest pharmaceutical and chemical company – its roots date back to 1668.

Merck & Cie enlisted the aid of Retel Neuhausen AG in developing a GMP Monitoring System (Good Manufacturing Practices), which is required by the FDA and EU in the production of pharmaceutical ingredients and products. Retel Neuhausen AG was able to create a complex FDA compliant system for Merck & Cie using the InduSoft Web Studio SCADA software solution.

The Challenge

The biggest challenge in creating any GMP-compliant process control is adhering to the long list of federal and international regulations for record keeping and control. There are standards employed in the United

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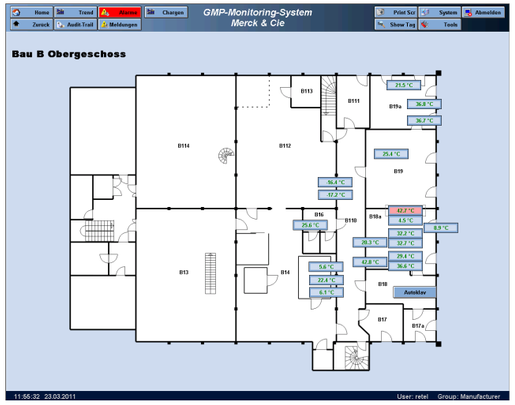

Figure 2: Detailed floor plans of every building show realtime data on environmental conditions.

States, such as FDA 21 CFR Part 11, and the EU Annex 11 standard used in EU countries. FDA 21 CFR Part 11 details a set of guidelines for data management, and the use of Electronic Signatures (eSignatures).

The EU Annex 11 standards address computer-based systems, which must also adhere to GAMP (Good Automated Manufacturing Practice) guidelines. They specify, for example, that user access should be traceable, and that each user should be tracked and logged. The GMP regulations also play an important role at the international level. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was created to standardize the guidelines used by the European Commission, and by U.S. agencies such as the FDA (Food and Drug Administration) and Ministry of Medicine.

Under these internationally sanctioned guidelines, not only must process data be recorded, but environmental conditions of rooms and storage and production facilities must be monitored as well. In addition, security is required that will allow record-keeping of user access to equipment and materials. This requires traceability features, such as individual user access with protected usernames and passwords, and the verification of eSignatures.

This left Retel Neuhausen AG with the difficult challenge of designing a stable, safe, and compliant GMP Monitoring system for Merck & Cie that would meet the needs of an international pharmaceutical company, deliver reliable and accurate data, and hold up to the rigorous international guidelines.

Main objectives of this project included installing a central GMP monitoring system that combines monitoring of the facility, locks, freezers/refrigerators, and the linking of all product lines into one system for overall management.

The challenge was to bring together diverse requirements and technologies into one overall system, and increase reliability in the different departments. For this purpose, Retel Neuhausen AG decided to use the InduSoft Web Studio SCADA solution to meet their goals of creating a powerful GMP system for Merck & Cie.

The Solution

The GMP-monitoring system was developed by Retel Neuhausen AG using Indusoft Web Studio, and has standard interfaces to connect to any measurable data from sensors across a variety of hardware. With the help of distributed data nodes that communicate over Ethernet with the SCADA application, the readings from the sensors are monitored and recorded. Thanks to multiple redundant data acquisition mechanisms, it is possible to guarantee a system that will remain operational at all times.

The central system is a SCADA system, which is installed in a virtual machine on an ESXi server. The measured values are digitized by decentralized installed data nodes from the server via Ethernet. The decentralized placement of data nodes helps reduce installation costs considerably.

Thanks to over 240 drivers native to InduSoft Web Studio, Retel Neuhausen AG was able to integrate external systems, such as autoclaves, production lines, and reactors with the GMP-monitoring system easily. With the integration of the GMP-Monitoring-System in the existing computer network of the plant, operators can access Web thin clients on remote computers while away from the plant floor.

Data is logged and monitored in real time. If values exceed accepted levels, the user is informed via an alarm. The first step of the alarm involves locally mounted alarm lights. In the second step, an alarm signal is given by alarm server and transmitted to mobile phone using SMS and a land-line phone. Values are archived, and can be represented graphically as historical trends. Using a historian, recorded data is sent to an online SQL database using InduSoft's patented database connectivity. The archival of the data reduces the load on the GMP-monitoring system, and allows consistent and reliable performance from the server.

The convenient user interface displays building and floor layouts for a quick overview of facility floor plans. Thanks to the intuitive user interface, the system needs only a short introduction to allow employees to make use of it. The web thin client allows the user to access the GMP monitoring system from any office computer. This increases the efficiency of even the maintenance staff, who can perform analysis off-site.

The security system ensures that only authorized users can make changes to system parameters. In addition, InduSoft Web Studio provides tools to split users up as individuals or groups, and restrict access to different aspects of the system, depending on user credentials. This helps ensure that all user actions are recorded for traceability reasons, and eSignatures can be verified. InduSoft Web Studio can connect to Microsoft Active Directory using the LDAP protocol to allow advanced SCADA security capabilities.

Custom modules were developed to allow evaluation by the "Statistics Report," which can display trends over the course of several weeks or months. These trends include features such as: The number of times value thresholds were exceeded, minimum, maximum and average values. Production processes and sterilization cycles can be evaluated automatically with the module "reference book". On the basis of a defined value set point, each process is subsequently evaluated based on the template qualification laid out in the reference book. An evaluation report is then generated for release along with the finished product. The GMP-Monitoring-System created by Retel Neuhausen AG using InduSoft Web Studio is integrated into a GMP-network specially built for this system. The GMP-network is connected via a

> "Through this turnkey solution, interfaces have been reduced to a minimum, allowing an economic monitoring system that is highly effective, reliable, secure, and easy to use."

Figure 3: Going back weeks or months to view how values compared to high or low set points was easily implemented by using InduSoft Web Studio's included historical trending features.