MODERNIZING AUTOMATION SOLUTIONS

Digital Transformation Optimizes Pharmaceutical Manufacturer's Production, Quality, and Compliance

Case Study

NEW, HIGHLY AUTOMATED MANUFACTURING FACILITY

Honeywell's experience in executing automation projects based on strict pharmaceutical and life sciences industry standards allowed for timely and efficient implementation of Fermion's new automation solutions.

Honeywell

OVERVIEW

The pharmaceutical and life sciences industry places a high value on innovation. New therapies are constantly being developed that treat a wide range of diseases. However, innovation in manufacturing solutions has often lagged behind in this industry.

Pharma producers seeking to adopt innovative approaches to production assume certain risks but do have the potential to reap significant rewards.

Advanced process control, safety and security technologies, seamlessly integrated on a common system platform, have proven to be an enabler of improved operational and business performance in the competitive pharmaceutical manufacturing sector.

Today's Operating Challenges

The role of active pharmaceutical ingredient (API) manufacturers in the pharmaceutical industry supply chain is evolving in response to emerging market demands and growing pressures from global competitors. API producers are seeking to invest in both technology and scale to help their customers bring new medicines to patients faster.

The increasing trend of highly potent active pharmaceutical ingredients (HPAPI) being used in new drug development has created a need for expanded production capabilities. The shift toward HPAPIs is not only driving more effective medicines, but also posing new manufacturing challenges.

Large-scale production of highly potent APIs at desired levels of quality consistency requires highly specialized process development and manufacturing capabilities, as well as a broad mix of associated advanced technologies. Innovations such as single use production and batch culture fermentation for separating molecules will offer opportunities for contract manufacturers in coming years.

IMPORTANCE OF AUTOMATION

At pharmaceutical plants, including those utilized for the production of APIs, automation of manufacturing processes must be implemented while maintaining the highest safety standards required by regulatory agencies.

Effective process automation solutions can improve the quality of products, increase operating productivity and add flexibility. The goal is more cost-effective and efficient manufacturing systems that allow safer drugs to reach the market in less time.

However, process automation isn't the only aspect of the manufacturing optimization being pursued in the pharmaceutical industry. Batch and recipe management, facility automation, collaborative production management, and process analytical technology are the other crucial elements of highly automated production facilities.

Effective automation solutions can reduce the number of operators required to run a given pharma plant process. They can also minimize operator interactions, and as a result, lessen opportunities for human error and increase worker safety. Processes run under optimum conditions provide higher-quality product more consistently, often in higher yields. They also consume less energy, produce less waste and fewer emissions, and minimize problems that require shutdown.

The digital aspects of automation provide additional benefits, particularly if control systems are linked with other aspects of plant operation via the Industrial Internet of Things (IIoT). Data from processes in multi-step synthesis of pharmaceutical intermediates and APIs can be linked to enable greater efficiency. New solutions can also help operators identify and respond faster to process excursions and digitally record data for easier management and analysis of trends.

ONE COMPANY'S STRATEGY

Formed in 1970 as a joint venture between Rikkihappo Oy (now Kemira Oy) and Orion, Fermion produces generic APIs, intermediates and active ingredients for both Orion and external customers at its facilities in Finland. The company serves as a strategic partner to innovative pharmaceutical firms and focuses on providing synthesis, process development and lifecycle management solutions. To date, it has commercialized more than a dozen innovative APIs.

Fermion develops, manufactures and markets APIs to customers in the global generic pharmaceutical market as well as under exclusive contracts to firms focusing on new chemical entities (NCEs). The company is a fully integrated contract development and manufacturing organization (CDMO) and offers services covering both drug substances and drug products.

Fermion has systematically invested and expanded its capabilities in the production of various HPAPIs. Its manufacturing operations are based on current Good Manufacturing Practice (cGMP) guidelines and apply the highest environmental, health and safety and other sustainability standards. The facilities are regularly inspected by relevant authorities, including the U.S. Food and Drug Administration (FDA).

In the mid-1980s, Fermion began the holistic use of automation at its production facilities in Hanko, Finland. This strategy included deployment of the Honeywell Alcont 1 system for process control and a history database for plant process data collection and manipulation. A decade later, TotalPlant Alcont was put into use and with the new Millennium, the control solutions were enhanced to meet the requirements of the FDA's Code of Federal Regulations (CFR) Part 11.

At the heart of the process management system were electronic recipes, batch records and a database for collecting historical process information, which could be easily accessed, searched and analysed. Because historical information maintained in the database was traceable, it could be used for process optimization, troubleshooting and deviation investigation. The process management system was integrated with SAP R/3 enterprise resource planning (ERP) software for production planning and inventory management.

NEW, HIGHLY AUTOMATED MANUFACTURING FACILITY

Fermion recently constructed a Greenfield production unit at the Hanko plant to expand its HPAPI manufacturing capacity. The EUR 35 million project focused on deploying modern manufacturing systems, improving regulatory compliance, ensuring a high level of quality and delivery reliability for contract manufactured products, and meeting increased customer demand.

The new manufacturing unit is used to produce final APIs, crude APIs and some advanced intermediates. The total reactor capacity is 75 m^3, including 25 m^3 capacity for OEB5-level compounds. Two modules of empty space can be used to reach the total capacity of 100m^3 in the future.

As part of the plant expansion, Fermion decided to acquire a new automation system from Honeywell and integrate it into an existing automation network. The company sought to deploy an integrated control and safety system that could be developed, documented and tested in accordance with GAMP5 requirements, which address risk management for automated and computerized systems used in pharmaceutical manufacturing operations. The GAMP5 reference standards focus on validation and control methods for identifying the functions and processes that pose the most risk for pharmaceutical products.

Fermion worked with Honeywell to configure a turnkey automation solution for the Hanko plant encompassing process control, utilities, recipe management, batch control, and product and raw material tracking. Honeywell has extensive global pharmaceutical industry project implementation experience but can also focus its capabilities to execute projects at the site level using qualified local resources.

To protect people and the process, the upgrades included a new safety instrumented system (SIS). The new control system was connected to the plant's legacy automation network and ERP system. The scope of delivery also included a digital video system that was tied to the facility's building automation system.

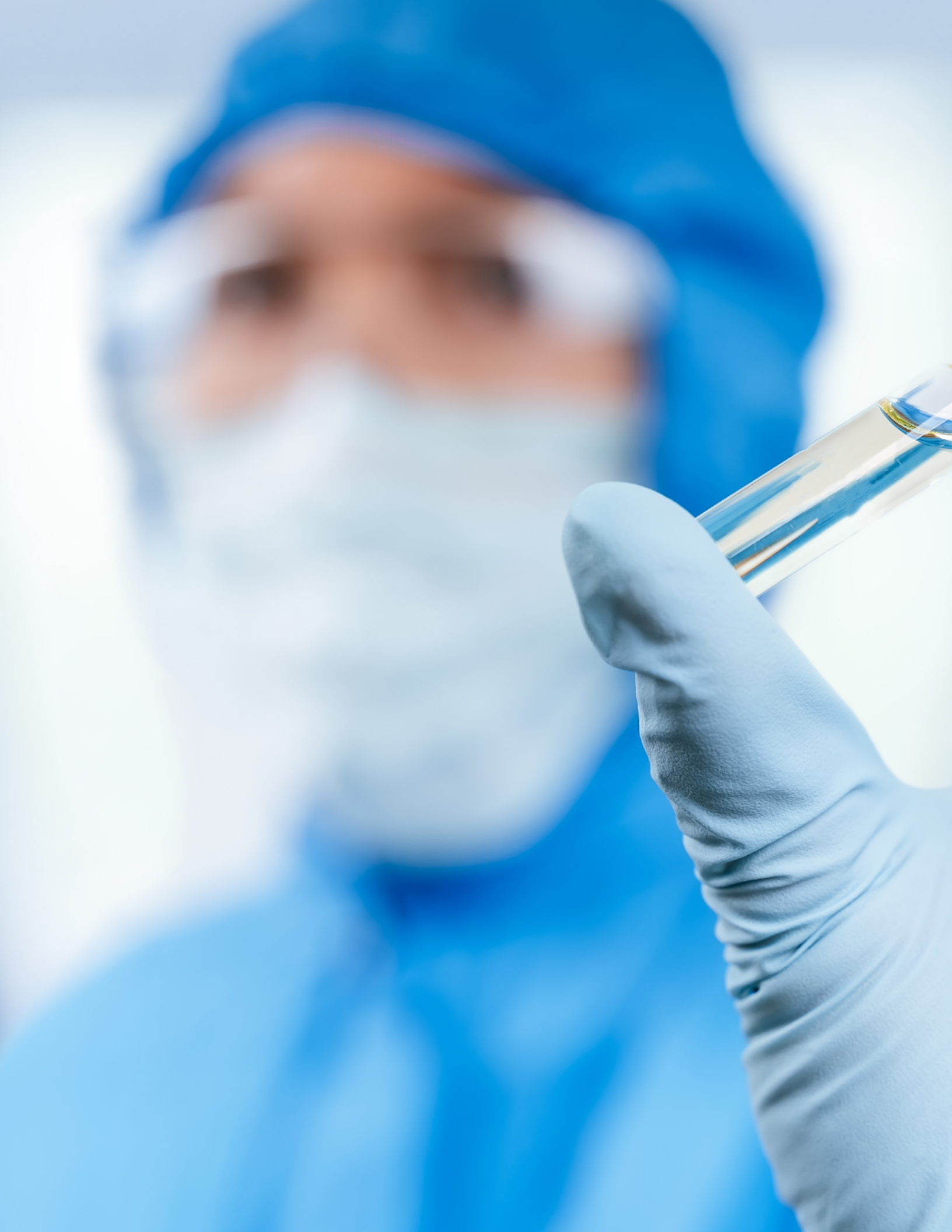
Key to the controls project was ensuring validation efforts were minimized during commissioning and all work was completed on time and within budget.

The Modernized System

Providing seamless integration of process control, safety access and security solutions, the modernized system is comprised of:

- **Experion PMD system for distributed control and process visualization**
- **Data historian tested and validated to 21 CFR Part 11**
- **SIL 3 Safety Manager system integrated with sequence controls**
- **Closed system architecture with controlled access for data integrity**
- **Integrated batch execution control and electronic recordkeeping**
- **Batch and recipe management**
- **Advanced process control (APC) for reactor and dryer temperatures**
- **Product and raw material tracking with wireless bar code readers**
- **Embedded 21 CFR Part 11 electronic signatures**
- **Integrated Experion backup and restore**
- **Real-time process and batch data exchange with the ERP system**
- **Digital Video Manager (DVM) integrated with building management**
- **Industrial cybersecurity solutions**
- **Heating, ventilation and air conditioning (HVAC) solutions as part of the Honeywell Enterprise Buildings Integrator (EBI) system**
- **Marshalling cabinets with Profibus I/O and ATEX barriers**

The Honeywell Experion PMD system is specifically designed for critical pharmaceutical and life sciences manufacturing operations, integrating alarm management, process historian, wireless network, and digital video solutions, among others. The system employs a single, consistent set of engineering tools to reduce validation and testing as required in the pharmaceutical industry.



Honeywell assisted Fermion with developing the automation solution during the pre-design phase. Working together, the best possible solution was found. The Honeywell engineering team designed the system structure and hardware. Software functionality was engineered in collaboration with Fermion's automation, process and quality assurance professionals. Operators for the new plant were also involved in the design process from the very beginning. The primary task was to combine the requirements of the process, product and authorities to arrive at a robust, safe, effective, and user-friendly solution. Designed functionality was programmed into the system and the sample solutions were reviewed and tested prior to plant-wide deployment and integration with the delivery system. The system was carefully tested in the Honeywell Integration Center according to procedures engineered by Honeywell. When the tests were approved, the system was delivered and installed at the Hanko site. Fermion personnel took care of the commissioning procedures, but Honeywell engineers were still closely involved in the testing and tuning.

Honeywell's experience in executing automation projects based on strict pharmaceutical and life sciences industry standards allowed for timely and efficient implementation of Fermion's new automation solutions. Its proven know-how in managing global-scale projects was particularly helpful in this case.

LEVERAGING NEW TECHNOLOGY

As a leading manufacturer of generic APIs, intermediates and active ingredients for the pharmaceutical industry, Fermion has taken effective steps to modernize production capabilities at its Hanko plant and prepare the site to meet tightening regulatory requirements, stricter quality standards and increasing product demand.

For example, the recent project at the facility will guarantee the ability to deliver active ingredients for customers' current and new proprietary products, including a number of essential medicines.

In addition to significant cost and labor savings, increased productivity and worker safety, and minimization of waste, the implementation of modern automation solutions will allow Fermion to improve its process optimization, troubleshooting and deviation investigation capabilities—all of which will provide the company with key business benefits.

Due to the ability to improve production efficiency and optimize raw material usage on a continuous basis, the Hanko facility can now manufacture highly potent APIs with large batch sizes.

The robust tools included in Honeywell's Experion PMD system helped to streamline validation and testing to meet stringent pharmaceutical industry standards, while the amount of manual, paper-based documentation has decreased by 70 percent compared to earlier projects.

Overall, the Hanko plant is realizing important advantages from reduced database maintenance, easier training, increased access to diagnostic information, single alarm and event logging, and faster control responses.

CONCLUSION

Pharmaceutical and life sciences companies need innovative manufacturing solutions to keep pace with drug development initiatives and market requirements for new medicinal substances and products.

Experience has shown that modern automation and safety system technologies, deployed holistically on a common, plantwide system platform, are the answer to meeting evolving operational and business demands on producers of highly potent active pharmaceutical ingredients and other crucial biopharma materials.

For More Information

To learn more about Honeywell's Advanced Automation Solutions, visit www.honeywellprocess.com or contact your Honeywell account manager.

Honeywell Process Solutions
2101 CityWest Blvd. Houston, TX 77042
Honeywell House, Arlington Business Park
Bracknell, Berkshire, England RG12 1EB UK
Shanghai City Centre, 100 Zunyi Road
Shanghai, China 200051
www.honeywellprocess.com

SS-20-5 ENG I 04/20

THE FUTURE IS WHAT WE MAKE IT

Honeywell