To meet the international requirements for the security of electronic records, Novartis Pharma SAS, Huningue, has chosen Cegelec, one of our longstanding integrators, for certain developments in its production plant in Alsace, France.

Novartis, the pharmaceutical giant, has a production site in Alsace and more precisely in Huningue (Haut Rhin). This site is specialized in the production of medicines in liquid form (such as syrups, nasal sprays, suspensions, etc.). The automated plant is controlled by a control system organized around a programmable logic controller (PLC) and a Wonderware supervision package including a Batch processing software.

This “turnkey” formulation solution, which has already been in service for a number of years, is equipped with InTouch and InBatch for the management of its formulations and Batch traceability.

The facility comprises:
- Formulation tanks;
- Storage tanks;
- A blending unit.

The facility is connected to the filling lines, and is supplemented by a Cleaning-In-Place unit, the current reference in terms of cleaning, disinfection and operating safety.

Meeting the requirements of Directive 21 CFR Part 11

In addition to the many health and safety standards, the pharmaceutical companies that export to the USA must satisfy the requirements of the FDA (Food and Drug Administration) in terms of access and electronic data security.
Directive 21 CFR Part 11 concerns more specifically the traceability of process information and operations, and the protection of access to electronic data via electronic signatures.

To meet the requirements of Directive 21 CFR Part 11 even more optimally, Novartis Pharma Huningue has launched a project to improve its liquids shop instrumentation and control system that is to take the following aspects into account:

- Maintaining of the basic functions;
- Maintaining of the PLC;
- Improving access security and traceability.

In addition to this, a serious challenge had to be taken up, namely the project completion time. The overall time from the specification phase through to qualification was just three months.

The expertise of Cegelec Pharmacy division

To carry out its project, Novartis Pharma Huningue firstly called upon its IT (Information Technology) Department, the guarantor of computer system protection (taking into account the means and risks associated with computer systems). On the advice of FACTORY systemes, Novartis then chose its integrator: Cegelec. The pharmacy division of Cegelec was picked out for its expertise in the pharmaceutical domain and its experience with Wonderware products. And in addition to its expertise in products such as InTouch, InBatch, IndustrialSQL Server and its mastery of the requirements of the pharmaceutical industry, Cegelec had a further advantage brought by its geographical proximity.

Based near Mulhouse, the Cegelec design office specialized in Pharmaceutical industrial control is located just some twenty kilometers from the Huningue site.

Wonderware at the heart of the system

Apart from updating the existing systems, reflection on how to protect the production formulations was necessary. InBatch provided this protection by limiting modification access rights to authorized persons only. The operators thus have easy access to the system thanks to a biometric mouse. The users, who wear gloves in the production areas, can always authenticate themselves in the standard manner (user name and password).

Another objective was to have the possibility of outputting a file of batches directly from the production records. IndustrialSQL Server was chosen for this purpose in order to manage all the records (production and processes) and prevent any modification of the recorded data (in accordance with directive 21 CFR Part 11). IndustrialSQL Server even manages an audit trail of modification of record parameters (e.g. change of the recorded data acquisition frequency). Local supervision with InTouch has also been provided to the operators so that they can acknowledge operations beside the production tanks, while at the same time complying with the requirements of 21 CFR Part 11.

The IT departments of Novartis Pharma Huningue were also obliged to take into account some new “corporate” recommendations. Thus the computer protection of the application is based on domain controllers. Novartis has the identification of each person and their user rights, which means that at supervision level there is no longer any need to manage the operators, simply to apply the group’s security strategy and have a single and unique operator base (e.g. if an operator identifies him/herself incorrectly, the account can be blocked at the domain controller).

Another problem to be considered was what to do in the event of a server failure. How could the number of servers on this application be limited (to facilitate maintenance and the means implemented in the network infrastructure, administration, etc.) in spite of the need for redundancy? System availability had to be very close to 100%. To achieve this, a Stratus fault-tolerant server was installed. This system, which is entirely hardware redundant, limits the costs of development and of licenses (just one server machine = just one license) and its maintenance requirements are simplified to the extreme. This Stratus server solution gives a system availability of 99.999%, one of the highest levels on the market and representing less than 5 minutes downtime per year.
An application combining flexibility and security

Based on the existing elements, the chosen application enables management to run the workshop with great flexibility, while at the same time ensuring access and data security in accordance with the requirements of directive 21 CFR Part 11. Consequently, the system has gained the following functions with respect to the initial application:

- User management;
- System access management;
- Electronic signature;
- Data consulting;
- Automated data archival.

In addition to the requirements of directive 21 CFR Part 11, the production report has been optimized to evolve towards an electronic batch file (in addition to the conventional paper file):

- Addition of alarms and operator actions for each phase;
- Graphic representation of the main critical variable integrated automatically into the report.

Praise for responsiveness

In accordance with Cegelec’s quality procedures, an end-of-project meeting was held to assess the results. The Novartis team appreciated the competence and fast response of the Cegelec Mulhouse team. The time factor was a big challenge, but it was met: the pre-qualification phase began at the end of May 2004 and the system switch was made in August 2004.

Novartis Pharma also underlined the efficiency of Cegelec and the attention paid to its specific needs. The geographical proximity was a real advantage, and still is today, as the Cegelec technicians can intervene on the site without delay.