Reference Project

werum
SOFTWARE & SYSTEMS

genzyme

Founded in Boston in 1981, Genzyme has grown from a small start-up to a globally based, diversified enterprise with annual revenues exceeding $3 billion and more than 9,000 employees.

The company is a leader in the effort to develop and apply advanced technologies in the life sciences. The company's products and services are focused on rare inherited disorders, kidney disease, orthopaedics, transplant, cancer, and diagnostic testing. Genzyme's commitment to innovation continues with a substantial research and development programme focused on these fields.

www.genzyme.com

Werum helps Genzyme production go paperless

Irish plant sets new corporate standard for MES systems

Genzyme needed an MES (Manufacturing Execution System) that could reduce the amount of paperwork on site as they faced a major expansion of production volumes. Werum's PAS-X provided the ideal solution.

Genzyme's Waterford facility manufactures solid dosage pharmaceuticals and biopharmaceuticals, such as the Renagel tablet, a phosphate binder used by patients on hemodialysis. In July 2005, it expanded the site to support Renagel clinical trials, manufacturing its capsule and liquid formulations, and in September of that year, it opened a new facility there for biological fill/finish operations, to make it the major European production and distribution centre for therapies such as Thymoglobulin, an immunosuppressive polyclonal antibody used to treat acute kidney rejection, and enzyme replacement therapies like Cerezyme for Type 1 Gaucher disease.

Waterford Expansion

The Waterford location was established in 2002, and is one of three facilities that Genzyme has built from the ground up. Currently employing more than 350 people, as production of new therapies ramps up, the site is expected to grow to around 450 over the next two years. The development of the facility started three years ago with the transformation of a 12,500 m2 building into a state-of-the-art pharmaceutical facility. In parallel with the implementation, Genzyme has started to build a further expansion of the pharmaceutical site. The Renal Expansion building is occupying 7,500 m2 and will provide Genzyme Ireland with a 100% increase in tabletting capacity

by implementing the latest state-of-the-art tablet manufacturing process. The plant serves as its major European production and distribution centre for large volume runs of its range of products.

Eamonn O'Mathuna

As Eamonn O'Mathuna, Genzyme's MES owner, said: "There is aggressive growth coming, with capacity significantly increasing in the near future, and we needed to develop strategies whereby we could implement a high level of automation."

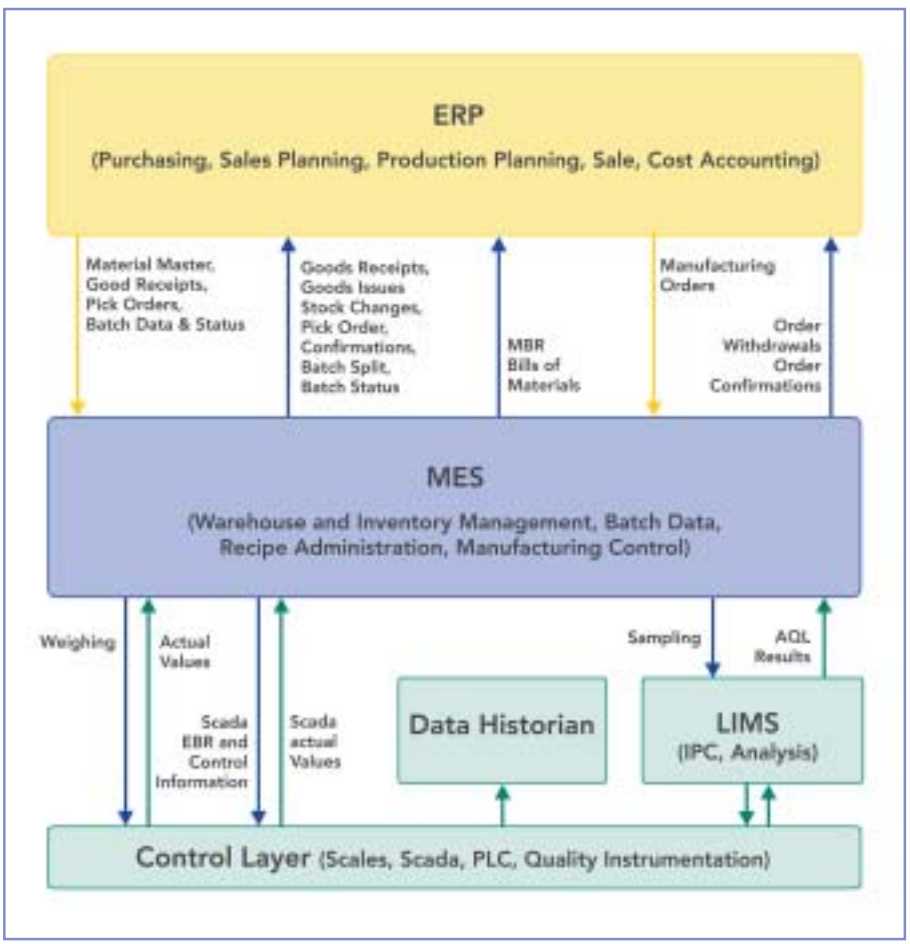
Genzyme Waterford Automation Program

To manage this growth in, and diversification of, production, and to promote Genzyme's right-first-time and real-time-release strategy in manufacturing, the company decided to introduce a number of „visions": One was to increase the level of automation in the Waterford facility to achieve a paperless manufacturing supply in various areas of the facility including the Warehouse, Oral Dose, Packaging, Quality Control, and Fill Finish, initially by introducing paperless EBR (electronic batch recording). Called gWAP (genzyme Waterford Automation Program), its scope was to implement a MES, a DHS (Data Historian System), and a PDMS/LIMS (Product Data Management System). Its implementation, principally in the tabletting and packaging areas, provides an integrated system, which created EBR's supported by bar-coding technology, MES to ERP integration, and MES to LIMS integration.

Following an exhaustive tendering programme, which involved looking at 11 vendors initially, and then inviting three to site to answer specific questions about how they would develop software to meet Genzyme's needs at Waterford, the company decided to use PAS-X MES from software specialist Werum Software & Systems.

MES Functionality

While PAS-X is a standard off-the-shelf product specifically designed for the pharmaceutical and biopharmaceutical industries, Genzyme's use of the software modules from the PAS-X portfolio enabled it to cover a broad spectrum of functionality. The core functions used include recipe creation (MBR), weigh and dispensing (WD), electronic batch recording (EBR), warehouse management (WMS), material tracking (MT), and deviation management (DM). The PAS-X system is a central building block in the IT & Automation infrastructure of the facility and links the enterprise business system (ERP) with the equipment level. It exchanges data with the business level through an ERP interface and also integrates the shop floor equipment.



IT and Automation Infrastructure

PAS-X helps in streamlining manufacturing processes, improving product quality, decreasing product cycle times, increasing equipment efficiency and assuring compliance within GMP- and FDA-regulated production and packaging environments.

As an example of PAS-X's effectiveness in streamlining the manufacturing process, O'Mathuna highlighted the problems associated with a five-fold increase in SKUs. "We saw huge complexity in trying to manage these multi-product, high volume systems - indeed it was estimated the number of SKUs would increase from 50 to about 250 - and PAS-X would aid in better control of the inventory and its real-time monitoring, through its various equipment and material tracking functions. It would also eliminate the paperwork involved, which was another part of the vision. If you consider that we estimated there are about 1.000 signatures on each batch sheet, and we are looking at a five-fold increase in the number of SKUs, you can see the increase in resources that would be needed, in Manufacturing & QA to support this increase. The fact that PAS-X gathers the electronic signatures means we significantly improve right-first-time metrics, and so don't see a dramatic increase in the need for rechecking."

Paper Elimination

Examples of paper documents removed

- BMR Issuance Checklist
- BPR Issuance Checklist
- BMR Issued Logbook
- BPR Issued Logbook

Manual steps removed/reduced

- BMR Issuance Checklist - prepare (Doc Control)
- BMR Issuance Checklist – review (Doc Control)
- BPR Issuance Checklist – prepare (Doc Control)
- BPR Issuance Checklist – check (2 x QA)
- BMR Issued Logbook (QA)
- BPR Issued Logbook (QA)

Documents Eliminated in Oral Dose production

- BMR
- Room & Equipment logbooks (16)
- Purified water usage logbook (2)
- Yield investigation form
- Compression end of Batch report
- Coating end of Batch report
- Retain material record
- Product change checklist (Compression, Coating & Printing)
- IBC Cleaning & Usage logbook
- Coating solution vessel Cleaning & usage logbook
- LOD Analytical report form

Total Documents eliminated 31

Total Number of paper entries eliminated 1,000 per batch

Table 1 lists in detail where the paper eliminations were made. The impressive system installed by Werum uses electronic batch recording - barcoding - and once up and running a target of better than 93% Right First Time results was achieved.

Often in the processing there was a reduced need for second signatures, with the PAS-X system also completing critical complex calculations, providing real time update of information on inventory and batch status, all of which led to improved equipment and container management and utilisation.

Production Process / Equipment Integration

The MES has been installed in Genzyme's tableting and packaging facilities at Waterford, and one of its first uses was in making the production of Renagel paperless, using wireless, handheld, terminals that allow the operative to complete the batch record on-line. The Renagel process involves wetting and blending the active with excipients in IBCs (Intermediate Batch Containers), and the PAS-X system is used via these wireless terminals, to download such parameters as, the amount of water to add, or the blending time. The operator is then asked for conformations of actions completed from the MES, so these can be logged or captured as electronic signatures. Interactions with the MES and the tablet press and coater involve the downloading of batch numbers and recipe numbers to the local equipment control systems and then recording In Process Controls (IPCs) in PAS-X while the team member operates the machine from the local control systems.

On the packaging side, the PAS-X controls stock movements and transactions in real time, and has made the warehouse paperless. This has meant that there is no requirement for printed pick-lists and has led to an integrated production with only one label needed for the entire life of the batch being produced. Material is consumed on the packing line using scans of the PAS-X labels.

Operator checking the tabletting process

The PAS-X then verifies the materials are acceptable for use in the batch and allows the operator to proceed after the reporting of information to the batch record and depleting the stock in real-time. During the packing operating IPCs are again recorded via PAS-X to the batch record and finished product is added to stock and reconciled via PAS-X, as it is produced on the line. The line clearance and line setup activities between batches have been added to the electronic batch record, resulting in productivity increases on batch turnaround.

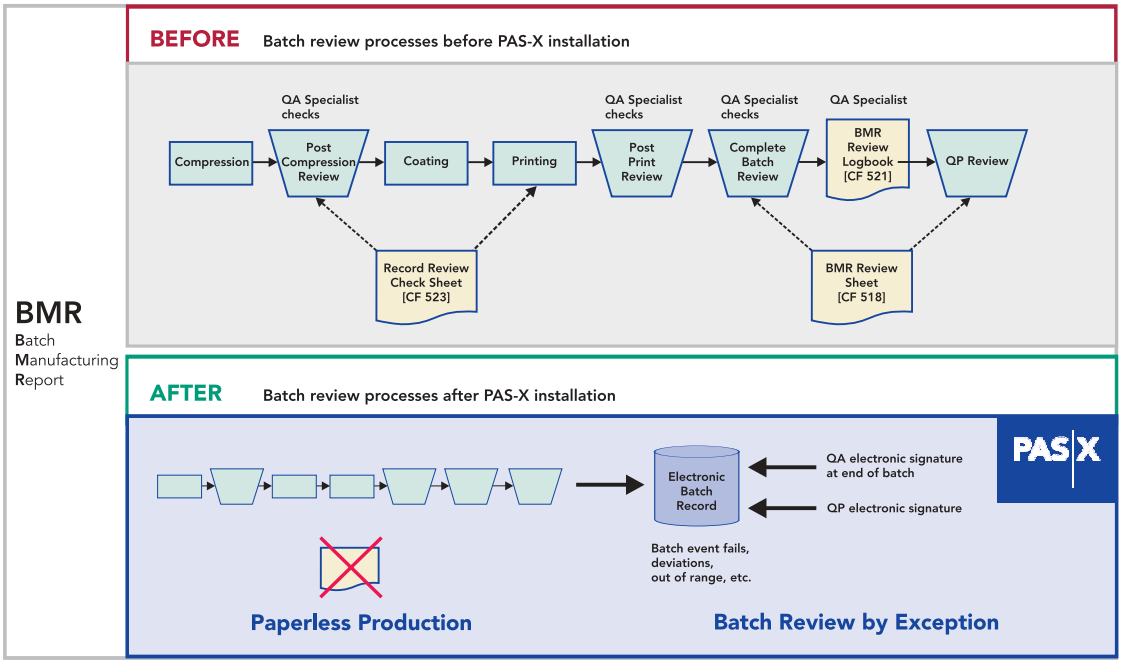
Benefits / Lessons learned

As O'Mathuna quipped, "We expected a short term slowdown in the production rate because of the go-live, but that didn't materialise! Because of the ease of use of the system and the training, the operators virtually maintained full capacity, and we had major headaches with supply of barcoded material from the warehouse. The warehouse was busy barcoding the inventory for the paperless switchover!"

Probably the best example of PAS-X installation is seen in figure 2, which shows batch review process before and after PAS-X installation.

PAS-X deployment in Waterford has been a KI (key investment) in the operational excellence initiative for the site. Its introduction has ensured that Genzyme are better equipped for the challenges of increased complexity as a result of becoming a Multi-product site, while optimising its resource needs. The KI returns have been in the areas of improved efficiencies of batch cycle time and increased inventory accuracy/visibility.

One of the major lessons learned has been the importance of a good vendor selection process. The success of Werum's MES system, together with their willingness to take on board company suggestions and ideas, can be gauged from the fact that Genzyme have selected Werum's PAS-X system as the corporate standard for MES systems.



Project Goals and Achievements

On the packaging side the team set up to implement the installation had set a number of goals. These included:

- Consistency in manufacturing approach. As seen from the figures earlier Right-First-Time/RFT data improved significantly;

- Review of batch record/ reports. More time on line, and the freeing up of documentation personnel, who were moved to more beneficial roles in production or research;

- RFT improvements, which led to 10,000 manual entries on a weekly basis eliminated; and minimal documentation errors;

- Enforcing controls so improving efficiency in production and seeing the development of real time inventory updates. Production output reached new heights of 1.3 batches per 8hr day: the highest output since commencement of tablet production.

Dispensing from a drum

Werum Software & Systems AG

Werum is one of the world-wide leading suppliers of Manufacturing Execution Systems (MES) for the pharmaceutical and biopharmaceutical industry. Thirteen of the world's top 20 pharmaceutical companies and leading biotech companies use Werum's standard product suite PAS-X to run their manufacturing business.

Werum's solutions and services range from software consulting, creation of functional specifications, and software development to turn-key delivery of integrated and validated Manufacturing Execution Systems. A global partner network ensures reliable local support services all over the world.

Founded in 1969, the IT company employs currently more than 300 people in its headquarters in Lueneburg (North Germany), the regional German offices in South West and West Germany, and the subsidiary in Parsippany, New Jersey, USA.

Werum Software & Systems AG
Wulf-Werum-Strasse 3
21337 Lueneburg, Germany
Tel. +49 (0)41 31/89 00 - 0
Fax +49 (0)41 31/89 00 - 20
info@werum.com
www.werum.com

Graphics: Werum
Photos: Genzyme

20.232.38.12.01.E.1