

Case Study:

Company Profile

TEVA USA is a wholly-owned subsidiary of TEVA Pharmaceutical Industries Ltd., Israel's largest pharmaceutical manufacturer operating globally in 30 countries on 5 continents with 2004 sales of US\$4.8 billion. TEVA is among the top 20 pharmaceutical companies and among the largest generic pharmaceutical companies in the world. The company has approximately 14,000 employees worldwide with production facilities in Israel, North America, Europe and Mexico.

TEVA USA has an aggressive Research and Development effort and one of the best overall ANDA approval records in the industry. The company's mission is to play a leading role in the transformation of the U.S. healthcare system through its preeminence in the development, manufacture and marketing of generic pharmaceuticals.

IT Organization

TEVA's IT operations are predominately located in Israel and North America. Primary platforms and development environments in use include Oracle ERP – SQL, JAVA, Windows, and some applications run on the IBM iSeries. Developers in North Wales, Pennsylvania collaborate on projects with developers in Israel, California, and Canada, also working on Oracle ERP – SQL and in JAVA.

Business Issues

As a pharmaceutical company operating in the U.S., TEVA must comply with Food and Drug Administration (FDA) regulations. The FDA requires stringent application development and change control practices surrounding software registration, phlebotomy, component processing, testing, and distribution of applications. A particular compliance challenge is FDA 21 CFR Part 11, concerning electronic records and

electronic signatures. All pharmaceutical companies are subject to audit by the FDA and face scrutiny with respect to their systems and processes, including computer systems.

The FDA has enforced validation of software and computer systems pharmaceutical manufacturing since the mid eighties. Computer validation in the eyes of the FDA means:

"Confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through the software can be consistently fulfilled"

A pharmaceutical company is obligated to follow the basic principles of validation. They must specify intended use and user requirements, of the software; make sure and verify that the software meets the requirements through proper design, implementation and testing and maintain proper use through an on-going performance program.

The goal for TEVA is to reduce the burden and cost associated with compliance to FDA regulations. In parallel, TEVA has experienced significant operational growth. With completely manual, paper-based change processes, the organization's ability to adopt less burdensome and low cost processes was limited. With respect to change controls, the transition from the actual work products implemented, and deployment to production was not a smooth process. As a result, TEVA staff was spending a disproportionate amount of time on change control activity.

TEVA's manual processes also made it difficult for management to conduct root cause analysis, identify potential bottlenecks and anticipate potential problems. The manual Change Control

Request Forms (CCRFs) resulted in an inefficient change control process with disconnects to internal reporting systems, reducing management visibility and control over the status of work in process. This was detrimental to management's ability to efficiently manage and allocate resources.

Inefficient configuration management and security policies around how software assets were versioned further complicated compliance objectives. The problem affected all business critical applications in the distributed client-server environment (Oracle, LIMS, as well as other Java and HTML based applications).

With an ever-increasing rate of change, disconnected tools, and manual processes, the IT organization was challenged to remain efficient and meet compliance requirements.

Initial Steps for Compliance

In 2003 TEVA's IT department identified requirements for a change control process that is more efficient and compliant with Good Manufacturing Processes (GMP). Good Manufacturing Practices are standard guidelines set out by the FDA to ensure drug development is carried out in safe and quality processes, to avoid contamination and ensure repeatability.

In support of this compliance effort, TEVA evaluated change and configuration management solutions. Following a thorough evaluation process, MKS Integrity Manager and MKS Source Integrity Enterprise, key components of the MKS Integrity Suite, were selected for four primary reasons:

- Flexibility – the solution could support any process that TEVA had implemented or would implement
- Ease of development – TEVA recognized that MKS's solution was the easiest to install, administer and use
- Customer support – MKS's

team had a proven track record of providing fast and effective technical support

- Cost – it was determined that MKS’s solution would provide a lower total cost of ownership when compared to the other solutions

Another primary concern for TEVA was finding a solution that could be linked with other technologies in TEVA’s environment, such as Oracle, Microsoft, and Mercury Interactive, just to name a few.

Implementation

The U.S. implementation consisted of six phases: planning, specification, design, construction, testing and operation use (production). An MKS services consultant was brought onsite to provide a process assessment and map appropriate workflows into the tool before the solution was deployed to the first projects. During meetings with various stakeholders of the MKS project, TEVA personnel provided sponsorship of the newly designed workflows by reviewing and suggesting changes to the system. These changes were discussed, and based on a team consensus, were implemented into the workflow.

It was important for TEVA personnel to verify and sponsor changes made to the workflow in order to elicit personal buy-in to the new process. With this sponsorship from all of the team leads and department heads, transition to the new system went smoothly. After initial projects were fully deployed, the MKS Integrity Suite was then rolled out across all application development areas.

Business values realized by TEVA

Since implementing MKS Integrity Suite in 2004, TEVA has achieved:

- Improved operational efficiencies from tighter integration between lines of business, development and IT operations. This has been achieved through process automation and seamlessly linked change control and configuration management processes;
- Greater management visibility, control and metrics with full traceability for software assets promoted into production environments;
- Improved software application quality, accuracy, reproducibility and consistency from enhanced cross-team communication and real-time collaboration; and
- Stronger security for software assets and intellectual property as well as secure and reliable promotions to production.

TEVA has increased compliance through higher software quality. Change control tracking time has been reduced by 75% (1 full-time employee to 0.25) and MKS has brought greater management visibility over the entire distributed development process. TEVA now benefits from a centralized repository of application code that is secure, versioned, and under control, further satisfying compliance requirements and enhancing IT governance.

TEVA now has a working change request management system in place that replaces its existing outdated paper driven system. The Integrity Manager workflow provides better visibility, traceability and audit ability to users and managers wanting to track their change control requests. Users now receive email notifications when a change request is assigned to them. This notification system will shorten wait times on current processes and expedite the life cycle of the change control process.

And, all histories of the new Change Control Requests will be kept in a central repository where any user with proper authority will have the ability to search for historical issues worked on in the past. This is extremely beneficial for internal and external audits that require high visibility of existing and past change controls.

“One of the main measures for success in the implementation of the MKS Integrity Suite was the reduction in the amount of paper and forms that get manually pushed from person to person. By simply automating service request forms and routing them via electronic workflows we have become much more effective, and dramatically reduced our time spent managing projects,” said Tom Loane, Chief Information Officer for TEVA Pharmaceuticals USA.

Future Direction - Systematizing Compliance

In 2005 TEVA plans to systematize the compliance effort specifically in the areas of IT change management and version control. With the MKS Integrity Suite, TEVA will move to a completely paperless change control system. An important feature of this system is support for Electronic Signatures. This feature enables compliance verification of change prior to commitment – a requirement of FDA 21 CFR Part 11.

TEVA continues to identify ways in which the workflow flexibility and lower TCO values of the MKS technology can be applied across not only distributed development as well as IT Operations teams globally, but also how the technology could be leveraged to manage, automate, and enforce business processes in lines of business as well.



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