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Cycle time reduction in manufacturing using a scientific data management system

ABSTRACT

E-manufacturing enables immediate communication between the various islands of shop floors, corporate business systems and laboratory information management systems so that the entire enterprise can react together to solve problems. Going paperless in manufacturing can allow one to manage the master data across the enterprise's physical boundaries. What is needed is an application-independent, non-invasive data management system for the lab, the plant and beyond.

INTRODUCTION

The life sciences industry today is challenged to maintain product quality, productivity, return-on-investment (ROI) and compliance while at the same time producing a 10-15% growth for their shareholders. This effectively means that biopharmaceutical companies must double the number of new lead candidates entering the Clinical Trial phases of the drug approval process, shorten overall time to market, and decrease the costs of R&D, clinical trials and production. The entire product life cycle must be streamlined, including investigational new drug (IND) and new drug application (NDA) approvals, as well as validation of the production process.

Huge amounts of data are being generated across the entire enterprise in support of faster throughput. However, there are a number of barriers to process streamlining – including globalization, physical boundaries of knowledge transfer and the ubiquitous use of paper systems. Complying with FDA regulations is a special burden for the life sciences industry. Forty percent of overall costs are incurred as a result of compliance issues (1).

REDUCING MANUFACTURING CYCLE

The Regulatory Challenge

21 CFR Part 11 has emerged as among the most demanding regulations for the pharmaceutical and

biotech industries. Regulations like Part 11, which affect the creation, maintenance, transmission, storage and modification of electronic records, have recently added new priorities for the life science industry. 21 CFR Part 11, in conjunction with existing GxP inspections, promises to transform the management of electronic data in the regulated arena. Every system that generates electronic records required by a predicate rule (GxP regulations) must be examined to determine its current ability to comply with Part 11 (2). Potentially, hundreds of systems within a pharmaceutical or biotech company can be affected. This includes analytical instruments and techniques, Microsoft Excel and Word documents, laboratory information management systems (LIMS), supervisory control and data acquisition (SCADA), and manufacturing execution systems (MES). From the lab to the enterprise and beyond, Part 11 significantly impacts current good electronic record management practices.

E-manufacturing to the Rescue

E-manufacturing (paperless, electronic manufacturing) has recently received some attention as a possible solution to the challenges just discussed. E-manufacturing enables immediate communication between the various islands of shop floors, corporate business systems and laboratory information management systems, so that the entire enterprise can act together to solve problems. It is imperative to be able to close the gap between an organization's islands of data and the information in an Enterprise Resource Planning (ERP) system, and systems used in production. Going paperless in manufacturing can also allow one to manage the master data across the enterprise's physical boundaries. The first step in achieving an e-manufacturing environment is to electronically record data (e.g., batch records, lab data, training records, etc.). The next step is to enable all of these disparate data types to be able to interact and work together. Neither of these are easy tasks. What is needed is an application-independent, non-invasive data management system for the lab, the plant and beyond. Once accomplished, e-manufacturing can generate reports that display deviations at a glance, monitor the entire shop floor on a real time basis, reduce validation problems, streamline most communications with existing

environments and provide company-wide transparency to any process bottlenecks. You can also ensure that the right material and the exact quantity are being used at every stage of the manufacturing process. Additionally, you can create pre-configured and validated interfaces for plugging into external systems. For compliance, e-records can be maintained throughout their required retention period in a safe, retrievable environment complete with audit rails to protect record integrity.

Impact of Reduced Cycle Time

Manufacturing choices often are made as a consequence of R&D and marketing choices rather than in harmony with them. The fact that manufacturing is viewed as a cost rather than a profit center may prevent an organization from taking a larger view of manufacturing's performance. However, cycle time reduction in manufacturing represents a very large opportunity for overall cost-savings. Using evidence gathered at fifteen companies through MIT's 'Program on the Pharmaceutical Industry' (POPI) project to benchmark best practices in pharmaceutical manufacturing, a team looked at existing and potential opportunities for cost savings. Key results of this study include:

- Preliminary evidence indicates that more than 95 percent of the cycle time is spent on activities that add no value;
- If a typical pharma company reduced its cost of goods by about 20 percent (assuming that number over the lifecycle of the product) the cost savings could total as much \$ 300 million. If three to six months can be saved in time to market, (assuming an industry-standard \$ 1 million per day in sales for a major drug) this could translate into as much as \$ 200 million in additional savings.

Within the context of the cost-of-quality framework, the pharmaceutical manufacturing organization is mainly focused on minimizing external failure costs through inspection. Yet there is a significant opportunity to move the focus from external to internal failure costs and from inspection to prevention.

Data Management Issues

Large pharmaceutical companies are discovering innovative products and developing new indications for existing products as a result of their continuing commitment to reduce cycle time (3). Firms are also building creative sales, marketing and education techniques; establishing joint ventures, licensing arrangements and health care partnerships with large managed care organizations; and demonstrating to providers the cost-effectiveness of their products. Additionally, achieving continuing productivity gains has become a permanent strategy. Productivity initiatives at the manufacturing level include optimizing plant utilization, implementing lowest-cost processes, improving technology transfer between research and manufacturing as well as throughout the firms, reducing the cost of purchased materials and services, re-engineering core and administrative processes, and streamlining the organization. Companies expect that productivity gains at the manufacturing level will continue to substantially offset inflation. One way to maximize productivity, manage collaborations and enable smooth knowledge transfer throughout the enterprise is through effective, compliant data management.

The NuGenesis® Scientific Data Management System (SDMS) is a process-streamlining tool that is currently deployed throughout scientific laboratories associated with the pharmaceutical manufacturing process.

NuGenesis SDMS can have a significant impact on the reduction of cycle time for the release of raw materials to manufacturing and the release of products to the marketplace. In addition, NuGenesis SDMS will improve overall data quality and enhance cGMP and Part 11 compliance.

Typical Manufacturing Process

Today there are several bottlenecks within a global pharmaceutical company's manufacturing process. The Pharmaceutical Raw Materials Lab and the Pharmaceutical Testing Lab (PTL) contribute to these bottlenecks. The Raw Materials Lab is responsible for testing all raw materials used in the manufacturing of products, including excipients, chemicals, binders, etc. The PTL is responsible for testing all finished products that are waiting to be shipped to market. Currently all other manufacturing processes are at or close to a 95% efficiency rating, including shipping and receiving, packaging and labeling. However, both of the aforementioned labs are performing below the 95% efficiency rating and 30-day turn around time. Chemists working in both labs spend an average of three hours per day manually entering data into Microsoft® Excel spreadsheets and one hour per day reviewing the data. The paper-based data packet is then sent over to the Data Review Group for a second chemist to review. On average, one hour is spent double-checking the data. The data packet is then sent to Quality Assurance (QA) for final review, and if passed, a Certificate of Analysis is issued and then the lot is released for shipment. The delays in both labs can be attributed two factors. Non-value added administrative time, and Test Failure Investigations (TFIs). Last year, one company reported that there were 350 projects conducted by eight to ten chemists in PTL for TFIs across manufacturing. On average, it takes ten days to discover the cause of the failure. Failure may be attributed to lab testing, data management, or other manufacturing functions. If failure is found early – before day 20 of the cycle – it normally does not impact cycle time release. However, if TFI is discovered and requested after day 20, cycle time will be increased. If a failure is discovered on day 28, release is pushed out even further. Average cycle time for most big pharma manufacturing is 34.8 days (goal is 95% 30 day turn-around time).

Manufacturing Data Management Benefits

Implementing a reliable data management system to handle electronic records from manufacturing and the laboratory can significantly reduce overall cycle time for new blockbuster product launches, and reduce cycle time for the release of lots for raw materials. Some products take so long to develop that by the time they are approved their patent expires two years later. Implementing NuGenesis SDMS at manufacturing locations where a company is racing against competitors can also provide a strategic competitive advantage. By reducing data transcription errors, one can reduce the shortage of high demand products that are suffering shortage due to manufacturing difficulties. Cycle times for annual product reviews can also be reduced. Additionally, you can more accurately predict release of lots for scheduling and ordering of raw materials. Better data management can also significantly improve data quality, ultimately decrease the amount of analytical staff and greatly reduce cycle time for instrument maintenance by automating, for example, preventative maintenance forms. Storing regulated records and data in a safe, compliant environment can significantly improve

compliance with cGMP and 21 CFR Part 11 requirements (4).

The NuGenesis SDMS Impact

NuGenesis Technologies' approach to managing electronic records or data files is to accurately, automatically and completely capture the analytical and manufacturing data and associated files – all the raw, processed, method, and report files that are generated during the "run" or "experiment". Just as important are the result files and any written notes or interpretations used for decision support – NuGenesis SDMS utilizes proprietary "print-to-database" technology that captures these as well, whether in the form of documents, spreadsheets or email. Also unique to NuGenesis SDMS is the ability, when producing decision support material, to include embedded hyperlinks that point directly back to the original data – which can be opened for visualization and review (during an FDA audit, for example) or restored to the source application for additional processing.

Once the data and results are captured, they can be outputted into any format, including XML, using either NuGenesis *Extraction Templates* or the NuGenesis *Software Development Kit*, both of which enable data to be found and extracted from the NuGenesis repository. XML is also used as a means of automatically entering meta-data into the database through our *per file template* technology. In this case an XML file is defined and its contents inserted automatically when a file is archived. If the industry ever adopts a defined standard for analytical data, whether XML or something else, the architecture of NuGenesis SDMS is designed so that output into this new standard will be quickly and easily accomplished. In a typical pharmaceutical firm, in one month it may take 100 Chemists 37 days to release 313 lots of product. A chemist typically spends about four hours a day manually performing administrative tasks such as entering and reviewing data. Conservatively estimating two hours per day for administrative tasks that can be eliminated using the automatic data capture technology of NuGenesis SDMS, cycle time can be reduced by five days per month for release of lots. The calculation goes like this: If a department has 100 chemists who collectively spend 4,000 hours performing data management each month, then 4000 hours divided by 100 chemists equals 40 hours per chemist. Divide 40 hours by 8 hours per day, and this comes to five days per month.

Another way to look at the numbers is: A chemist works 160 hours on average per month, multiplied by 100 chemists in a department, this equals 16,000 hours to release 313 lots. It takes 51.1 hours to release one lot (16000/313). The 4,000 hours saved above could be

applied to releasing 78 additional lots (4000/51.1) 313 plus 78 = 391. In this way, the department may now achieve an efficiency rating of 96%.

NuGenesis SDMS could significantly improve inventory turnover, drive a company's cash conversion cycle lower and ultimately reduce the cost of goods sold.

CONCLUSION

Implementing NuGenesis SDMS across the pharmaceutical enterprise can result in an annual ROI of \$ 30 to \$ 200 million or more. This concept can also be applied across R&D to reduce cycle time while at the same time significantly improving data quality and enhancing compliance, with an ROI three times that in the manufacturing example. The major benefits of utilizing NuGenesis SDMS in terms of impacting ROI are, first, usability – as it relates to the ability to quickly visualize information within the appropriate context. This is essential for easy data reuse, as the more visual the presentation of critical information, the more likely it can be used effectively for better decision-making. Next is scalability – many currently available products are not designed with scalability in mind and have poor visualization from their user interfaces. As visualization plays a bigger role in data and information retrieval and usability, sophisticated data storage and system management functions must be developed in conjunction with a highly visual/graphical/analytical user interface. NuGenesis SDMS allows for enterprise-wide scalability to cover many needs in data accessibility, reuse and visualization. Lastly, at the core of most products used in the Life Sciences there must be the notion of a metadata environment. More than any other discipline, the Life Sciences are predicated on understanding the transition of data throughout the different stages of drug discovery and development. Data must be managed universally across applications and platforms (5). NuGenesis SDMS enhances the 'metadata' core environment for data searching and retrieval.

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