

The Move to XML in Manufacturing

Improving the Management of Batch Records

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The authors describe how XML-based technology can be used to manage the creation and approval of batch records. By taking advantage of the single sourcing of information, the use of XML and an intelligent content-management system can streamline processes, increase control, and reduce costs.

In today's environment of increasing regulatory vigilance, pharmaceutical manufacturing organizations face the challenge of maintaining compliance while introducing new manufacturing systems and keeping costs under control. Manufacturing processes must be accurately documented and up-to-date, all with an eye toward cost and time. Firms rely on information systems to manage complex processes, and more recently have adopted XML as an integral part of their approach.

XML, a recommendation of the World Wide Web Consortium (www.w3c.org), is a set of rules that provide the ability to create self-defining documents. XML is the basis for many industry standards that are used for the free flow of information among partners, suppliers, professionals, consumers, and regulatory agencies.

Until now, the use of XML in the pharmaceutical industry has been focused on the area of regulatory submissions and clinical data. However, XML has proven to be an area of tremendous opportunity in manufacturing as well. Documents used in the manufacturing organization tend to be data-centric and contain redundant information. In addition, the intensive processes by which these documents are created, managed, and published result in a high-risk of noncompliance.

How XML works

At a high level, XML allows a component to be written and approved once and then to be linked to many documents—a marked difference from traditional authoring practices that consist of cutting and pasting. When combined with an intelligent content-management system, XML also allows multiple authors to work on the same document concurrently. The benefits to an XML-based approach include

- **Quality.** Reusable XML content components reduce duplicate effort and therefore reduce opportunities for errors. XML also enforces consistency and overall quality, which results in high-quality regulatory submissions and a minimized risk of compliance issues.
- **Time-to-market.** Collaborative authoring and reusable components shorten the time needed to produce final content and more importantly, reduce the number of updates to existing content. These time savings, combined with improved content quality and consistency, can lead to shortened agency review time and result in improved time-to-market and time-

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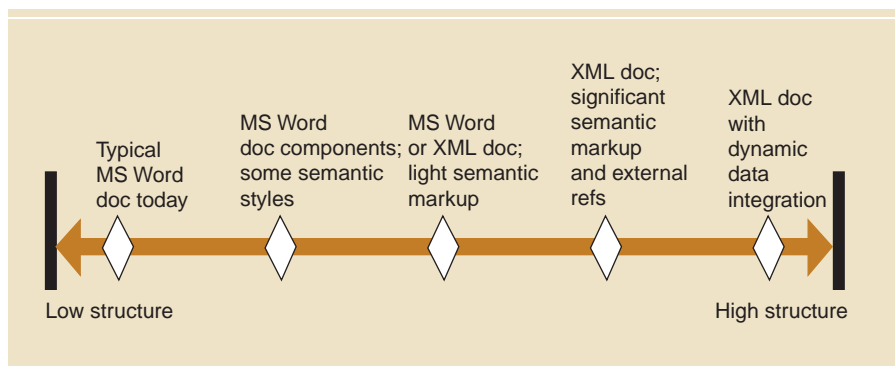


Figure 1: Examples of different levels of structured content.

clear benefit is that MBRs can be created, modified, and approved in a fraction of the time required without an XML-based system.

To understand the benefits of XML, let's look at how batch records typically are created and used. Companies typically maintain a library of MBRs that encompass all manufacturing processes related to the production of a product "batch." An MBR comprises many individual component documents such as specifications, formulations, instructions, and bills of materials. To complicate mat-

to-peak-sales for new products and new indications.

- **Interoperability.** With the growing number of partnerships bringing drugs to market, and a significant percentage of clinical trial and other drug development activities being outsourced, there is a growing need to exchange information easily.
- **Repurposing.** XML separates the content from presentation. By applying different stylesheets, the user can produce multiple output formats (e.g., print, Web, wireless, or CD) from a single source of XML content.

Variations in XML-based solutions

A drive toward structured content often means authoring XML content. However, the delivery of XML does not require authoring. Content can be authored in a variety of formats and with varying amounts of structure. The level of structure applied should match the current and planned business needs for that content (see Figure 1).

XML in manufacturing

Content-management systems. Before XML can be applied to manufacturing, an intelligent content-management system must be in place. A content-management system provides core functionality such as content check-out, check-in, versioning, security, and workflow. Most organizations that have moved forward with content-management solutions in the manufacturing and quality areas have started by tackling problems relating to the control of forms and standard operating procedures (SOPs). A common approach is to choose a content-management solution and then use it to manage specifications, methods, quality documents, and occasionally production control or batch records. This implementation approach has proven to be a sound, low-risk method for introducing content-management. A content-management system provides compliance benefits such as ensuring that a particular production line has access only to the latest approved version of an SOP.

Creating master batch records (MBRs) with XML. Some top-tier pharmaceutical companies are considering the development of XML-based solutions to improve the process for the creation and maintenance of MBRs, and to provide a semiautomated process for issuing and publishing batch records from these masters. These documents are highly suited to XML because of their highly structured nature, significant opportunity for reuse, and the need to maintain the documents during the drug's full life cycle. The

same formulation or specification may be used in many different MBRs. In a large organization, the many permutations created by thousands of formulations used in hundreds or thousands of MBRs can quickly become unwieldy. For some companies, these individual components are already managed within a content-management repository. However, even where content-management systems are in use, in most cases, the production of an MBR is accomplished today by a manual copy and paste of components. The content-management solution will then store the MBR as a monolithic document for each permutation.

To respond to these challenges, the industry is pursuing innovative solutions using XML-based technologies. MBRs and their components can be authored in XML and stored in a content-management repository. In the most innovative of solutions, there is no copying and pasting of component content into an MBR. Instead, XML components are linked together in virtual documents. Semantic tags within these components represent links to batch-specific information that resides in external data sources. The batch-specific information can range from simple pieces of information such as the unique batch number, batch size, or manufacturing date to complex tables of information such as the complete bill of material.

When an MBR is used to issue a batch record using XML, several critical processes are executed that are very different from the processes typically used with monolithic documents. Some of these critical processes include

- the assembly of preapproved components that comprise the MBR.
- the semantic tags that represent links to the external data sources, which are resolved by pulling the batch-specific information from the native data source(s) such as the manufacturing resource planning/enterprise resource planning (MRP/ERP) system. This linking allows the issued document to be specific to the batch record without replicating data sets (i.e., single sourcing of information).
- a stylesheet, which is applied to XML to produce the final printable document. Because a stylesheet is used to format the content, every batch record that is issued from a given master will have a standard look.

Managing changes and approvals. When a change occurs in the manufacturing process, MBRs are affected. In systems that use a monolithic document for each permutation, it can take weeks

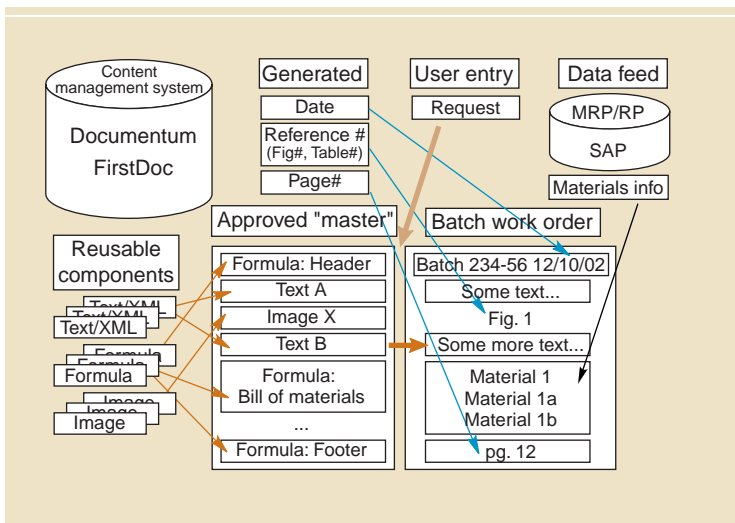


Figure 2: The anatomy of an XML-enabled batch record.

or months to change and approve the hundreds of documents involved. With a system that uses XML components that are linked together as virtual documents, a single change to a component can ripple through hundreds of masters, significantly reducing time and effort. However, this new capability does not come without added responsibility. Given that a single change can affect hundreds of MBRs, an error introduced in a single

component can negatively affect hundreds of related MBRs. This power places much more responsibility on the approver. In the past, review and approval affected only the object being routed. With this new functionality, not only must the content of the individual component be approved, but the context in which the component may be used must be approved as well (see Figure 2). Many of the other challenges of managing XML content are the same as those seen for other types of content. Security, versioning, workflow, and life cycle are examples of content-management services that are required regardless of content format.

Conclusion

The capabilities of XML-based solutions, when combined with an intelligent content-management system, can be beneficial to life sciences manufacturing organizations. XML demonstrates great promise for a broader impact in an area where information technology spending has traditionally been hard to come by. **PT**

