

INSIGHTS**Top 3 Strategies for Structured Product Labeling Success***Getting the Most from Your SPL Solution*

Actor Dennis Quaid made international headlines in November 2007 when his newborn twins nearly died as a result of a medication mix-up. Originally hospitalized for drug-resistant staph infections, the 10-day-old infants were given 1,000 times the prescribed dosage of the common blood thinner Heparin. Hospital staff blamed the mistake on poor product labeling, saying the adult and pediatric bottles were too similar.

Their claims held weight, as this was not the first time the adult dosage of Heparin had been administered to a child. Just months earlier in Indianapolis, three premature infants died when a nurse made the same mistake. In fact, rather than sue Cedars-Sinai Medical Center, the Quaid family has brought a claim against Baxter Healthcare Corporation, the drug's manufacturer, for failing to adequately address the labeling issue.

High profile cases like that of the Quaid family have served to keep national attention on the topic of product labeling as it relates to patient safety. Meanwhile, the release of alarming statistics has given added credibility to the issue. According to the Institute of Medicine – National Academy of Science, the improper administration of medication is directly related to 10,000 deaths in the United States each year. Furthermore, adverse drug reactions account for about 1.5 million, or 6.7%, of all patients hospitalized annually, at a cost of more than \$3.5 billion.

With so much riding on accurate product labeling, it's not surprising that the industry is taking action in the form of new and stricter labeling requirements. Fortunately, establishing a robust product-labeling program can also provide significant value to your business. Read on to find out how to get the most from your investment.



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An opportunity un-seized

The U.S. Food and Drug Administration's Structured Product Labeling initiative promises greater safety for patients, as well as the ability to help pharmaceutical companies better disseminate critical drug information. However, as the industry pushes toward compliance through third-party "translation" software, many companies are missing the business performance improvement gains that come from implementing a centralized, globally accessible data source—and, perhaps even more detrimental, the related best practice business processes. Failing to seize these opportunities creates inefficiencies resulting in longer lead times, increased errors, higher costs and greater safety risk.

But, for the market leader, a window of opportunity exists to use your structured product-labeling implementation to get ahead of your competition. We will share three strategies to implementing a robust product labeling program that will both increase safety and improve operational efficiencies. They are:

- Build effective document submission and change control business processes;
- Centralize and leverage critical labeling data; and
- Understand the technical and regulatory horizon.

Strategy #1: Build effective document submission and change control business processes

Very simply stated, structured product labeling creates many operational efficiencies system-wide. Indeed, it can drive your entire product information management strategy forward. This is accomplished by building the capability to understand and manage critical documents through a controlled process.

Most apparent are the opportunities for improvement in the document creation and submission process. In addition, the ability to restructure the change control process and the advantages associated with having a centralized data source are significant. Let's look first at document creation and submission.

Document creation and submission

Be proactive in document creation. Through technology solutions, you can collaborate, track versions, maintain templates, and archive and monitor the progress of labeling changes. Content sharing and concurrent editing can also streamline operations.

When it comes to document submission, the process has changed dramatically in recent years. Long gone are the days of manually passing folders from person to person, department to department. In fact, one survey revealed that only 32% of life sciences companies are still using a strictly manual process.

The key here is to take full advantage of today's network-based solutions, which have many practical features, such as common repositories, searchable attributes, electronic routing, life-cycle management and version control. Furthermore, best-of-breed software solutions allow for customized workflow, leading to an effective change control and labeling process.

***Tip:** Think beyond the boundaries of your organization by seeking outside advice on best-in-class methodologies. Outside support also can help you overcome the most common hurdle—resistance to change.*

Change control solutions

Even when appropriate documents are created, efficiency can be compromised. Traditional change control processes are often bogged down by ineffective practices. For example, in many life sciences companies, this process consists of obtaining signatures from executive management throughout the organization. Multiple levels of approval, however, do not necessarily ensure that documents are appropriately reviewed. A better solution is to use management reporting and metrics as mechanisms to inform key personnel.

Another challenge is that any department in the company can initiate labeling change controls, and each department usually has its own procedures. Often these procedures do not harmonize until late in the approval process. With a structured labeling program, you can create both consistency and a single point of entry. The resulting benefit is a more streamlined and efficient process that has less room for error.

As with any quality initiative, when implementing a change control solution it's important to concentrate on identifying opportunities to streamline processes, shorten time-to-market, and exert greater control and consistency. The result will be a truly integrated and multipurpose labeling strategy that incorporates technologies across key areas managed by research and development, packaging, labeling, regulatory, quality and supply chain.

Strategy #2: Centralize and leverage critical labeling data

Think for a moment about how your organization would benefit from having a single source of data that's accurate, up-to-date and globally accessible. Would you be able to reduce the time and cost associated with new product launches or product and labeling changes? When combined with streamlined processes, would you experience increased operational efficiencies by decreasing lead times and reducing errors?

The answers to these questions make it clear why the next key to successfully implementing a structured product labeling solution is to build a centralized data source. If done properly, this process does not require a significant investment, and the benefits can be far-reaching.

Underscoring the point, recent research by Gartner found that 90% of all unstructured data goes unmanaged. On the other hand, by embracing structured technology, you can eliminate the black hole of data that exists from maintaining proprietary files in formats like PDF and Microsoft Word. When you begin to effectively manage critical information, you speed commercial development while reducing both time-to-market and regulatory concerns.

Keep in mind that your centralized data source should not only include the labeling information provided to regulatory bodies, but also to physicians, hospitals, pharmacies and, ultimately, patients. It's also critical to incorporate each department's requirements into your initial business process design sessions because many departments rely on this data other than regulatory affairs and labeling. For example, labeling information is leveraged for promotional materials, product websites and packaging.

A centralized structured data source also provides greater control and visibility through reporting, consistency and the ability to leverage existing validated work. Organizations that have achieved the highest return on investment minimize data sources and the number of required data conversions by consolidating both systems and processes. Doing so accomplishes two things. First, it reduces the risk of non-compliance by ensuring that all product-labeling materials contain the latest approved information. Second, it provides visibility into all labeling metadata.

It can also have a significant financial impact. A few years ago, Wyeth Pharmaceuticals reported to the Drug Information Association that efforts around its integrated electronic case report form saved the company millions of dollars and reduced the average study duration time from 38 to 20 months.

Using what you've got

An additional advantage of a centralized data structure is the ability to leverage existing work. Companies often find each department taking an approved version of a labeling document and recreating it to meet their own requirements. Through the use of style sheets you maintain one approved source document accessible by all departments.

The use of style sheets—technical documents that allow you to display the same structured data in different formats—minimizes the need to design and approve from multiple sources, and it eliminates the need to create multiple documents based on language, dosage or point of use warnings. This can be especially important for European efforts around Product Information Management (PIM), where the combination of multiple languages, form, strength and packaging can lead to thousands of pages of regulatory documents being exchanged.

Although the technology to help organizations combine programs for labeling is still maturing, your company can continue to move toward a single source of approved data. This is done by creating customized and automated presentations of labeling data, the results of which are greater accuracy, less processing time, reduced costs, improved patient experience and, most importantly, reduced medical errors.

The importance of this last statement can't be overestimated. Any life science investment in compliance must result in a quantifiable reduction in risk exposure and greater control of the business process. As your organization continues to face mounting pressure to provide more information to physicians and regulatory agencies—and to minimize time-to-market—creating a centralized data strategy offers an effective solution.

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In addition, elimination of repetitive document preparation minimizes the time and errors associated with manual work. In the case of regulatory interaction, the ability to demonstrate consistent and repeatable processes improves with better audit trail capabilities. Indeed, the very survival of life sciences companies depends upon compliance with regulatory requirements, so this final area must be taken into consideration when designing a structured product labeling system.

What gets measured gets done

Because creating accountability is key to performance, the ability to measure and track a process effectively ultimately determines its success. By embracing technology, including the implementation of a centralized data source, you can develop consistent, automated metrics. The result is global access to such information as:

- Costs associated with labeling changes
- Cycle time and bottlenecks
- Sources of labeling changes
- Reasons for labeling changes
- Effective audit trail and timely responses

Additionally, strong reporting capabilities and usable dashboards will allow you to define, analyze, design and control critical path issues. A best practice is to establish effective dashboards based on historic and quantifiable data reported at set intervals.

Leading-edge software companies now offer labeling software that manages content in an agency-neutral XML format capable of meeting multiple submission standards. Glemser Technologies, for example, is leading the way with the release of its xmLabeling package that leverages an intermediate XML format and can render HTML, Word, PDF, SPL or PIM files as needed. The software supports a phased implementation approach and offers a high degree of configurability to support local requirements.

Take note, however, that large life sciences firms face tremendous challenges in process harmonization if they are truly going to leverage the potential benefits from this kind of solution.

Strategy #3: Understand what's on the regulatory and technical horizon

Before you embark on your structured labeling initiative, it's crucial to understand the emerging trends in the IT and regulatory environments. However, this is perhaps the most difficult step because it involves attempting to predict the future.

Electronic document transformation

Closely tied to structured product labeling is electronic document transformation, which is already well underway in the life sciences industry. The opportunities presented by e-documentation are broad and unprecedented and include the ability to electronically cross reference patient and product history, including adverse effects and clinical testing. Not only will this facilitate an immediate analysis of possible side effects, it has the potential to eliminate human error and the distribution of misinformation.

When it comes to implementing your e-document strategy, we recommend looking at your organization as a whole rather than conducting a series of individual departmental studies. This is important in order to create consistency in the strategy. Ultimately, when combined with your structured product labeling solution, e-documents will allow for greater consistency and a better-informed health care industry.

The XML standard

Another important emerging trend is the use of XML as a standard and its growing role in future interaction with regulatory agencies. Although it is currently not universal, the use of XML can be found in many areas, including labeling submission, research and development, drug submissions, privacy standards and other key life science functions. In fact, Gartner predicts there's an 80% probability that by 2010 all enterprise content management will be supported by XML-aware database management technology.

The message here is don't be shy about pushing the XML envelope. While managing the different standards may be challenging in the short term, developing technology solutions around XML content will ultimately be a sound investment.

***Tip:** When considering software, look for solutions that have the potential to merge one-off standards into a one-stop ERP-style electronic data solution.*

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Ever-changing regulatory environment

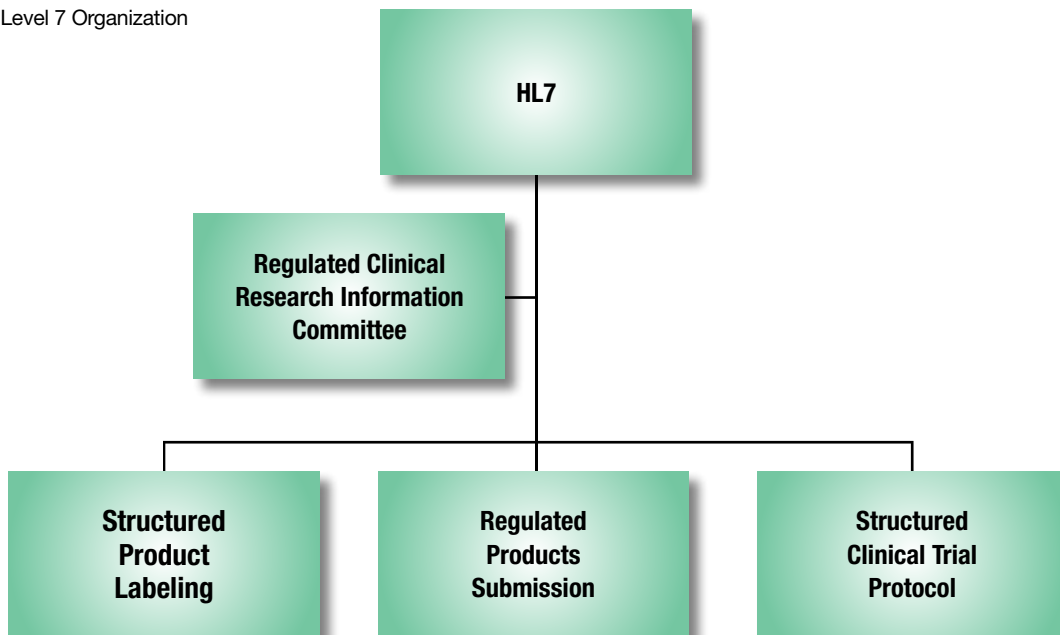
While there are a number of important regulatory players to consider when developing your product label implementation process, two of particular importance are the Health Level 7 (HL7) organization and the U.S. Food and Drug Administration (FDA). HL7 (figure 1) is important because it's ultimately responsible for developing the standards for labeling submissions. Within HL7 is the Regulated Clinical Research Information Committee (RCRIM), which oversees many of the current technical committees. These include Structured Product Labeling, Regulated Products Submissions (RPS), and the Structured Clinical Trial Protocol (SCTP).

The Regulated Product Submissions (RPS) group should be closely monitored in particular because its goal is to create standards for submitting products to all regulatory agencies.

The idea is to create a form that includes the application, as well as key information needed to process the application. This procedure eliminates the need to repeatedly submit the same data during the development process, from investigation through marketing applications. The standard has already been approved as a draft and some initial pilots are being launched. It's expected that the FDA will quickly adopt this standard following an HL7 endorsement. This development will no doubt have a profound impact on your organization's electronic document strategy.

HL7 also works in collaboration with two other groups worth noting—the Clinical Data Interchange Standards Consortium (CDISC) and the International Conference on Harmonization (ICH). Monitoring the activities of these key organizations will help you predict shifts in FDA submission standards.

Figure 1: Health Level 7 Organization



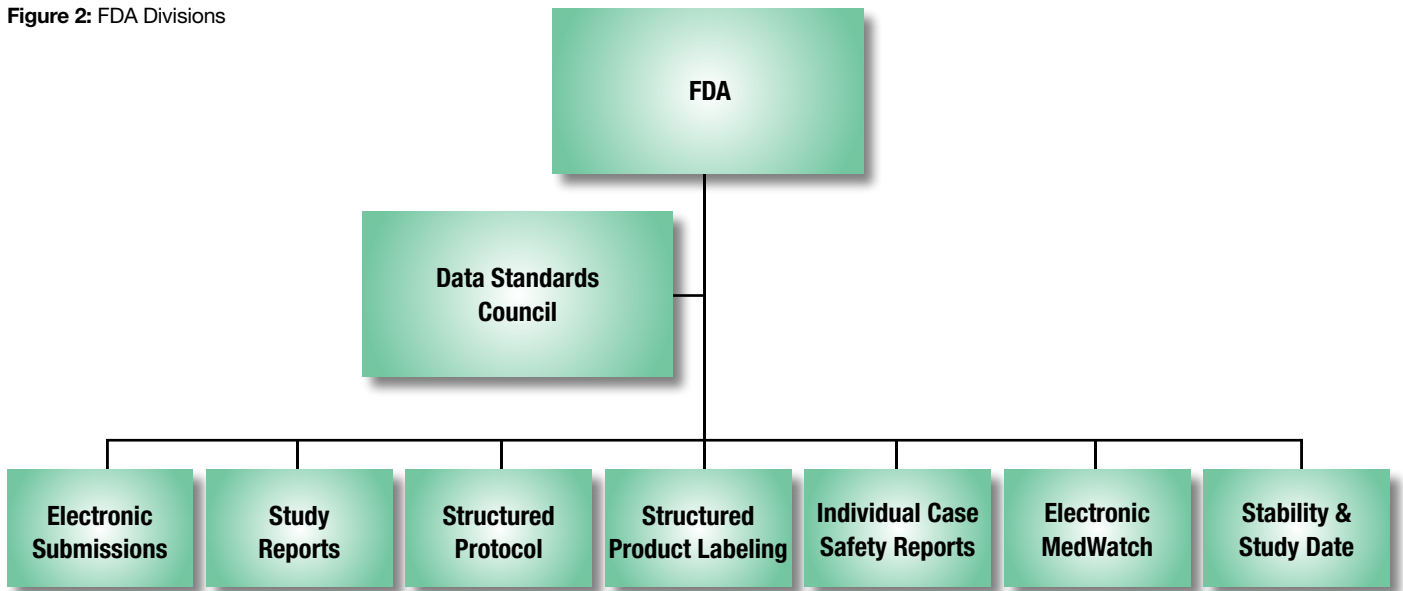
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Within the FDA, the Data Standards Council acts as the medium for organizations to develop universal requirements across key areas, including:

- Electronic submissions
- Study reports
- Structured protocols
- Structured product labeling
- Individual case safety reports
- Electronic Med Watch

The FDA also announced another development that demonstrates the intersection of technology standards. During a recent subcommittee standards briefing, it revealed proposed changes to the Drug Listing Regulations. If implemented, these changes will make the FDA the central authority for the National Drug Code (NDC) and will, in turn, accomplish two things. First, it will move the drug registration and listing process from a manual, paper-based process to an automated electronic process. Second, all of this information ultimately will be distributed through the DailyMed website. These moves will both simplify the process and make a structured labeling system even more crucial. To be sure, active structured product labeling is the only way to reap the rewards of this initiative.

Figure 2: FDA Divisions



Major e-document initiatives

The ways in which XML will be used within the life sciences industry are constantly evolving. To understand XML's future, it's imperative to understand the key initiatives that are currently underway. Here are the most significant:

- **Adverse Events Reporting System** – an initiative of the International Committee on Harmonization, it was one of the first to utilize XML and electronic submissions when reporting individual case safety reports
- **Regulated Product Submissions Standard** – HL7's attempt to create standards for new product applications and related information submissions
- **Study Data Tabulation Model** – a standard developed by the Clinical Data Interchange Standards Consortium (CDISC) and adopted by the FDA to support electronic exchange of human clinical drug trials
- **The Electronic Common Technical Document (eCTD)** – expected to be the data standard for FDA drug applications; guidance has already been provided suggesting this as the preferred method of submission
- **Electronic Health Record** – a repository of a patient's health and healthcare experiences maintained over their lifetime; currently HL7 is addressing the electronic standards supporting this initiative

Conclusion

Regulatory requirements and the desire to ensure patient safety may be the initial catalysts for implementing a structured product labeling solution. However, it's the opportunity for business performance improvement—including greater efficiencies, lower costs and improved access to business intelligence—that will provide a significant return on your investment.

Begin the structured product labeling journey by developing a centralized data structure, an effective electronic document workflow, and a consistent change process. Select a technology provider that has the resources to facilitate the harmonization of your technology solutions with your business processes. Understand the technical solutions available, as well as the key industry players and initiatives that are underway. And, finally, take a proactive approach to the dynamic regulatory landscape in order to position your company to influence future regulatory standards. Together, these strategies will enable your company to provide critical product information, reduce exposure to litigation and regulatory audits and reach the ultimate goal: increased patient safety.

For more information, visit: www.clarkstonconsulting.com

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