An Introduction to Structured Product Labeling

Understanding and Preparing for the FDA's New Electronic Labeling Submission Standard

Arbortext

Enterprise Publishing Software

Contents

Overview

This white paper is intended to be used as an educational tool to assist the reader in the following areas:

- Develop a deeper understanding of Structured Product Labeling (SPL)
- Discuss the goals and benefits of SPL
- Understand the impact that SPL will have on your current labeling process
- Identify additional resources for broadening SPL knowledge

There are multiple sources of information (presentations, meetings, web sites, and documents) that address SPL, including the FDA Draft Guidance entitled "Providing Regulatory Submissions in Electronic Format – Content of Labeling," Health Level 7 (HL7) Structured Product Labeling Specification, SPL Implementation Guide, and the FDA web site. These can be accessed from the locations defined in the SPL Resources section of this document. This paper is meant to augment, not replace, existing SPL information and attempts to pull many of the topics from these various sources together into a single, comprehensive document.

Who Should Read This Document

This document provides a comprehensive overview of SPL, covering both business and technical topics. As such, this document is appropriate for the following roles that have responsibility for labeling content within pharmaceutical and biotechnology companies, or other firms impacted by the FDA Guidance on Labeling Content.

- Regulatory Affairs Managers and Directors
- Labeling Managers and Directors
- Information Technology Managers and Directors
- Informatics Resources
- Scientific Writers
- Other roles responsible for creation, management and submission of labeling content to the FDA

Executive Summary

In today's complex, global life sciences marketplace, the ability to manage product information is a daunting task. Many departments across the enterprise use the approved product information for a variety of purposes, including package and labeling, promotional materials, and product web sites. It is common practice for each department to take a copy of the approved content and re-create it for its own use, leading to significant process inefficiencies and potential for inconsistent product information.

Additionally, there are many consumers of this product information including regulatory authorities, academic research centers, health care professionals, and the general public. These people depend and rely on accurate and consistent information about drug products independent of the manner in which they access this information, whether through paper-based, electronic, or other channels.

The ability to ensure greater control over this critical product information has led to the development of a standard for product labeling. This standard, known as Structured Product Labeling, is being adopted by the FDA to assist in greater patient safety and increased usability of product information across its consumer base.

In 2005, the FDA will mandate the use of Extensible Markup Language (XML) that is compliant with the Structured Product Labeling (SPL) standard for electronic submissions. The goals of SPL include:

- Making available timely and accurate product labeling information
- Facilitating review, storage and distribution of labeling content
- Ensuring human readability and machine processing of labeling content

If your company has not begun to think about SPL, now is the time to start. To ensure compliance, you will be required to:

- Convert new and existing labeling content to XML
- Submit to the FDA both the narrative labeling content and drug listing information
- Maintain consistent product information across all package, label, and promotional outputs

Although various options exist for submitting SPL-compliant files, creating and managing labeling content in XML has significant advantages over bolting on an SPL solution on top of traditional authoring approaches. Structured labeling content can help your organization address key business drivers such as:

- Reducing non-compliance risk by eliminating redundant sources of product information and ensuring all documents contain the correct information at all times and adhere to emerging health authority standards

- Improving the quality of product information outputs and reducing the time and cost associated with managing product information by eliminating manual tasks associated with the creation, review, approval and publishing of labeling content for multiple outputs

- Increasing efficiency of labeling content management processes and improving overall time to market

What is SPL?

In February 2004, the FDA issued a Draft Guidance requiring the electronic submission of labeling content to be provided in an XML-based format called Structured Product Labeling (SPL). Upon final approval, SPL will replace the current format in use, Portable Document Format (PDF), and will be used for the process, review and archive of product information. As of September 2004, the FDA is planning for SPL to become mandatory around July 2005.

SPL is an HL7 standard that defines the content and structure of product labeling information that will be required for submission to the FDA. It will improve the integrity of product information through the use of consistent structure and standard terminology. It is intended to be used as the basis for regulatory guidance documents and applications for exchange of product labeling content.

An SPL document, or submission, consists of labeling information traditionally documented in the US Package Insert (USPI), along with additional information to describe the drug listing details of the drug product. Since SPL is in XML format, it is essentially devoid of formatting and layout information, so it contains just the content, similar to viewing an ASCII file in a text editor. Therefore, SPL should not be thought of as analogous to the USPI, but rather as a file containing structured labeling content that can be read by humans and processed by computer systems.

The ability to present the labeling content stored in XML is done through the use of stylesheets. A stylesheet is a file that supplies instructions for how to format an XML document. Multiple stylesheets can be used with one XML file to produce different documents and output types. For example, using a single SPL XML source file and multiple stylesheets, the SPL content can be transformed to produce a USPI as well as promotional materials, product web sites, and package components.

Why a Standard for Labeling Content?

The primary reason for creating the SPL specification was to ensure a uniform approach to developing labeling content. Through the use of a standard, structured format, measurable improvements can be achieved throughout the creation, review, approval and overall management and distribution of labeling content by both industry and health authorities. Many of the potential benefits include:

- Improved patient safety through timely access to accurate and consistent product information.

- Ease of information exchange, allowing content to be created once and made readily available to all necessary consumers and computer systems.

- Promoting the use of standard terminology and coding across labeling content, such as ingredient names, package types, dosage forms, and routes of administration.

- Reducing the manual effort involved with the review and approval of labeling content.

- Reducing the amount of redundant product information provided to health authorities, such as drug listings.

- Reusing SPL content to generate other product information outputs—such as Package Inserts, Brief Summaries and other promotional materials, product web sites, and package components—which reduces the risk of non-compliance by reducing the incidence of inconsistent product information.

Flow of SPL Content

Traditionally, the flow of labeling content was from the life sciences company to the FDA for review and approval. Once approved, the end consumer or health care professional had to get labeling content from a variety of sources, which creates problems such as inconsistent information being used, untimely access to updated information due to paper-based distribution approach, and recreation of labeling content from the paper source to electronic forms used for other output formats or computer systems.

SPL is a structured format which will allow for a more streamlined flow of product information. This enables more timely access to accurate product information, as well as allowing the exchange of labeling content between computer systems while still maintaining human readability of the content.

This new information flow, as shown in Figure 1, will have life sciences companies submit their labeling content to the FDA where it will be stored in the Electronic Labeling Information Processing System (ELIPS). Following the review and approval of labeling content, the FDA will automatically provide the National Library of Medicine (NLM) with labeling updates to populate their DailyMed repository. The NLM will then be responsible for publishing this labeling content in various formats.

Possible outputs include a browser-based view of product information for access by health care practitioners and the general public, as well as formats that will enable computer systems, such as hospital information management systems and electronic prescription systems, to process the labeling content for analysis, aggregation, data mining or other purposes.
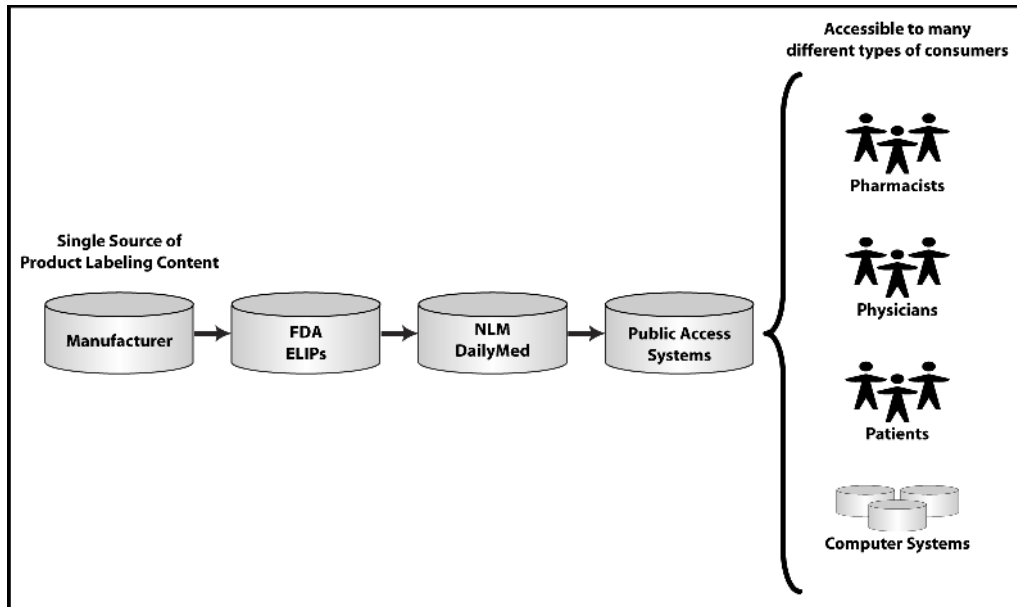
Figure 1: The Vision of SPL

Through the use of SPL, labeling content will flow directly from the manufacturers to end consumers in a timely manner, providing accurate and consistent product information that is accessible to health care professionals, the general public and computer systems.

Background of SPL

Development of SPL Specification

The initial developments around SPL began with members of the HL7 Regulated Clinical Research Information Management Technical Committee. This team was comprised of industry, FDA, and HL7 representatives with expertise in the technical as well as business aspects related to product labeling. The approach was to develop a standard for exchange of labeling content that will serve the needs of global health authorities, not any one individually.

As part of the development of the SPL specification, analysis was performed on existing labeling content, such as USPIs, and existing and evolving regulations related to labeling content. Submission requirements were also taken into consideration to ensure that the standard could accommodate such things as:

- Modular updates of labeling content
- Identification of inserted or deleted content from previous submissions
- Creators and reviewers of labeling content

This team produced an HL7 ballot package consisting of a set of schemas, which define the rules for creating various types of documents, along with an SPL Specification that details the schema and rationale for SPL, and sample files. This began the formal balloting process to bring forth SPL as an ANSI standard.

Adoption of SPL by FDA

SPL has been architected as an open, flexible standard capable of being used by global health authorities for their management of labeling content. This flexibility allows an individual health authority the ability to put additional constraints or requirements on their labeling content submissions. In February 2004, the FDA announced its plans to adopt SPL as its standard for electronic submission of labeling content, as identified in the Draft Guidance "Providing Regulatory Submissions in Electronic Format – Content of Labeling."

As an example of how the FDA has placed additional constraints on the HL7 standard, the SPL schema identifies certain information about drug products, such as trade name, generic name, lists of active and inactive ingredients, and dosage forms. These may be defined as optional data elements in the schema, but the FDA can choose to make this information mandatory for SPL submissions of products marketed in the U.S.

As more formal plans were being made for the adoption of SPL by the FDA, the need for additional involvement from a larger audience was recognized.

SPL Working Group

In January 2004, the SPL Working Group—consisting of representatives from FDA, HL7, life sciences companies, and software vendors—was formed to continue the work of the initial team and help foster an awareness, understanding and application of SPL throughout the industry. Its primary deliverables included:

- **Educational Sessions** – Most industry representatives were not aware of SPL or XML and its impact on their labeling content management processes. Various approaches were identified to share ongoing information related to SPL, including seminars, web-based presentations and web sites.

- **Common Stylesheet** – The FDA will provide a single stylesheet for displaying an SPL document in a standard browser. This stylesheet, developed by the SPL Working Group, will be used by industry and agency to ensure a consistent presentation of labeling content during the review and approval process.

- **Implementation Guide** – This document will provide useful information to individuals responsible for creating SPL documents, and will augment the HL7 Structured Product Labeling Specification. Best practices and examples will assist with the understanding of SPL.

- **Testing Phase** – Following the development of the above items, sample SPL documents will be put through various use cases to ensure the validity of the SPL standard, which will allow the industry and the FDA to understand the impact of creating, reviewing, and updating labeling content in the SPL format.

Ownership of SPL Standard

Since the FDA is the first to adopt the use of the SPL standard, it is a common misconception that the FDA owns the standard, when in reality it is owned by HL7. As noted above, individual health authorities can use the standard as a basis for their electronic labeling content submission requirements. HL7 will accept recommendations for updates to SPL, which then go through a formal investigation, review and balloting process.

Who is HL7?

As stated on the HL7 web site (www.hl7.org), Health Level Seven is an ANSI-accredited Standards Developing Organization operating in the healthcare arena, focused primarily on producing standards in the clinical and administrative domain. It is a volunteer organization consisting of members from industry, government agencies, vendors and others wanting to advance standards in this domain.

Its mission is: *"To provide standards for the exchange, management and integration of data that support clinical patient care and the management, delivery and evaluation of healthcare services. Specifically, to create flexible, cost effective approaches, standards, guidelines, methodologies, and related services for interoperability between healthcare information systems."*

Structured Labeling Content

SPL, along with additional requirements imposed by the FDA, defines the content and structure of product labeling information required for submission to the FDA. The format of an SPL document is XML. There are three components, or files, that comprise an XML document:

- **Data Model** – Defines the rules by which the structure of the document will be enforced. This type of file is known as a Document Type Definition (DTD) or Schema. The SPL uses schemas to ensure the validity of the content being created.

- **Content** – The information being created, without any formatting. XML is a non-proprietary, open standard and is viewable in ordinary text editors. The content file for SPL will include product information such as warnings, precautions, overdosage, and drug interactions. This content will be created in conjunction with the data model, resulting in a structured document according to the specific business rules.

- **Presentation** – Once you have created your content free of any formatting, you can re-use the content for multiple outputs. The presentation of XML content is done using stylesheets. For SPL, the FDA will provide a stylesheet that will enable any SPL-compliant document to be viewed in a web browser. Using different stylesheets, the same SPL content file could be used to produce outputs such as a PDF of a USPI, a PDF of the Prescribing Information, HTML output for product web sites, and outputs for other package and label components.

Structured vs. Non-structured Documents

Figure 2 represents one of the contrasts between traditional word processing and XML authoring: the difference between marking up text based on how it should look, and marking it based on what it is. For example, in a traditional word processing tool, the Indications and Usage section of a USPI is marked as "Body Text, 10pt. Book Antiqua" while in XML, this content is identified as a "paragraph" inside a "section" titled "Indications and Usage."

Since XML separates the content from the formatting, you can use the same information automatically in multiple documents and multiple output formats. You can maintain this product information in a single source format and use it for many output purposes such as a package insert, promotional materials, product web sites, and product cartons. Therefore, if content related to indications required a change, an author could make an update to the content in one place and have the change automatically proliferate to all appropriate outputs.

This can produce significant process improvements throughout the enterprise, including:

- Streamlined content creation and review processes

- Reduced risks of product recalls or delays in product to market due to inconsistent product information across various output channels

Arbortext

- Lower overall costs to produce all the product information outputs
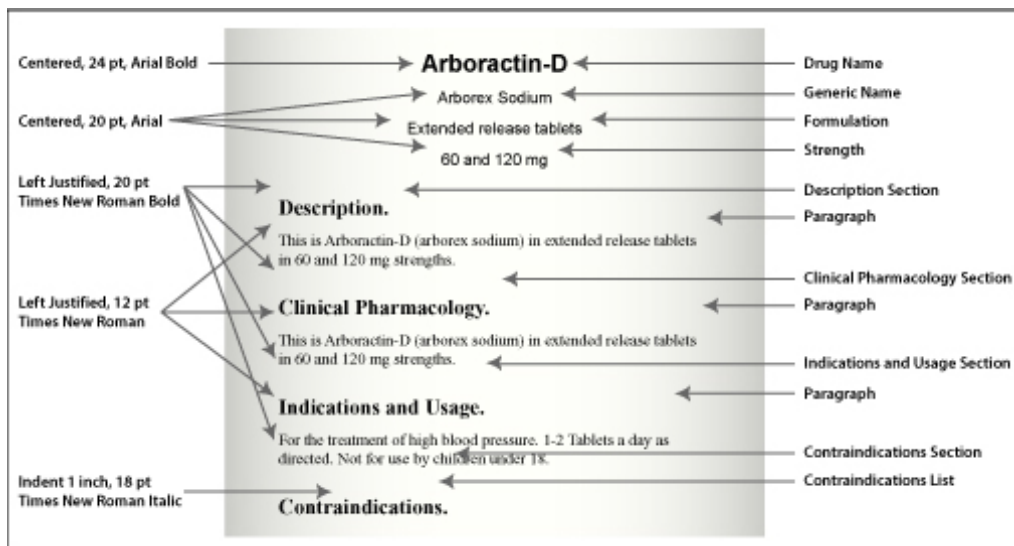
- Improved time to market

Figure 2: Unstructured vs. Structured Content

Structured content provides significant advantages over unstructured information, such as ensuring consistent and accurate information through content reuse, dynamic assembly and publishing, and automatic output to both print and electronic media.

Benefits of XML in Life Sciences

In addition to the specific benefits regarding XML-based labeling content, there are other advantages to creating structured documents:

- XML defines the overall structure of the document explicitly. So if documents across your organization identify product ingredients using XML, such as <ingredient> lactose </ingredient>, your organization has the ability to perform context-related searches to find all information related to products containing lactose. Without this information stored in XML, companies are left to do full text searches or manual searches, resulting in lower productivity.

- As mentioned earlier, XML separates the content from the instructions that control the formatting of the content. This separation enables reuse of information in multiple formats and multiple document types across the enterprise, as well as the ability to support automated publishing of multichannel outputs (both print and electronic).

- XML is becoming prominent in the life sciences industry because global health authorities continue to develop XML-based regulatory standards. Some of them, other than SPL, include:

  Electronic Common Technical Document (eCTD) – an XML backbone used for submitting documentation to health authorities (U.S., EU, Japan)

Product Information Management (PIM) – European Union's XML-based standards for submitting product information/labeling content

E2B – XML-based standard for submitting adverse event reports to health authorities

Clinical Data Interchange Standards Consortium (CDISC) – XML standards for the collection, reporting, submission, and archive of clinical trial data

Stability reports – the FDA is moving toward the use of XML for submission of drug stability reports

Structured Clinical Trial Protocol (SCTP) – the FDA is working with HL7 and industry representatives on the use of XML for submission of clinical protocol documents

Components of an SPL Document

An SPL document is a structured document in accordance with the SPL schema. There are essentially three components to an SPL document: header, narrative and structured data elements. While this white paper provides an overview of an SPL document, additional details can be found in the HL7 SPL Specification and FDA SPL Implementation Guide, available from http://www.fda.gov/oc/datacouncil/SPL_schema.html and http://www.fda.gov/oc/datacouncil/spl.html, respectively.

SPL Header

The header of an SPL document identifies and classifies the document. It is analogous to the envelope for a letter: it can contain information such as company name, address, responsible persons, and a title of the document. In the case of SPL, the title usually contains the trade name, generic name, and dosage forms of the drug product for which the SPL document references.

A sample of a document header is shown in Figure 3.

```
<Document xmlns="urn:hl7-org:v3" xmlns:voc="urn:hl7-org:v3/voc"
xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
xsi:schemaLocation="urn:hl7-org:v3 PORR_MT050016.xsd">
  <id root="2.16.840.1.113883.3.933"/>
  <code code="34391-3" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"
  displayName="Human prescription drug label"></code>
  <title>Arbortec (Arborizine hydrochloride) 500 mg Tablets</title>
  <effectiveTime value="200212"></effectiveTime>
  <availabilityTime value="200212"/>
  <languageCode code="eng"/>
  <author>
    <assignedEntity>
      <id root="f20f60af-fded-11d8-ae89-15c8e06e3daa"/>
      <representedOrganization>
        <name>Arbortext, Inc.</name>
        <addr>Ann Arbor, MI 48108, USA</addr>
      </representedOrganization>
    </assignedEntity>
  </author>
```

Figure 3: Sample Document Header

A sample document header captures information regarding the document being submitted. The combination of machine readable information, such as the company name and address (emphasized in bold), is presented along with other information, such as LOINC codes and language identification, that can be processed by computer systems (shown in lighter emphasis).

SPL Narrative

The narrative section of an SPL document contains the human-readable product information, which includes most of the content traditionally found in a Package Insert or Summary of Product Characteristics. Along with the narrative text, the SPL schema allows for inclusion of images such as molecular structures, tables and graphs.

The SPL narrative is conceptually broken into sections, each of which can contain additional nested sections of content. The FDA has identified its primary sections based on those identified in 21 CFR 201.56 and 21 CFR 201.57. Additional sections and subsections can be defined as necessary to represent labeling content accurately and unambiguously.

```
<component>
  <section>
    <id root="2.16.840.1.113883.3.933"/>
    <code code="34070-3" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"
    displayName="CONTRAINDICATIONS SECTION"></code>
    <title>CONTRAINDICATIONS</title>
    <text><paragraph>ARBORTEC (Arborizine hydrochloride) is contraindicated in
    persons with a history of hypersensitivity to Arborizine hydrochloride or
    any member of the cephaloporin class of antimicrobial agents.</paragraph></text>
  </section>
</component>
<component>
  <section>
    <id root="2.16.840.1.113883.3.933"/>
    <code code="34071-1" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"
    displayName="WARNINGS SECTION"></code>
    <title>WARNINGS</title>
    <text>
      <paragraph><content emphasis="bold">Pregnant Women:  THE SAFETY AND
      EFFECTIVENESS OF ARBORTEC IN PREGNANT AND LACTATING WOMEN HAVE NOT
      BEEN ESTABLISHED.</content>  (See PRECAUTIONS: Pregnancy,and Nursing Mothers
      subsections.) </paragraph>
      <paragraph>Pediatrics: Arborizine hydrochloride should be used in pediatric
      patients (less than 18 years of age) only for infections listed in the
      INDICATIONS AND USAGE section. An increased incidence of adverse events
      compared to controls, including events related to joints and/or surrounding
      tissues, has been observed. (See ADVERSE REACTIONS.)</paragraph>
    </text>
  </section>
</component>
```

Figure 4: Sample Narrative Content

A fragment of an SPL document representing the Contraindications and Warnings sections demonstrates how the human readable content, shown in bold, is preserved. The other content shown in this example is used for processing by computer systems.

SPL Structured Data

The structured data section of an SPL document consists of drug listing information such as trade name, generic name, active and inactive ingredients, National Drug Codes, and packaging details. This information will be used primarily for allowing data interchange between computer systems, as well as data mining and analysis.

Arbortext

The FDA has identified one SPL section to contain all of its required structured data elements and recommends that this section be placed before any narrative SPL sections. The SPL schema has been architected to allow for additional data elements to be added, and it is expected the FDA will, over time, continue to add more required structured data to SPL submissions, thus extending the potential uses of labeling content.

```
<component2>
  <section>
    <id root="f20f60af-fded-11d8-ae89-15c8e06e3dac"/>
    <subject>
      <manufacturedProduct>
        <manufacturedLabeledDrug>
          <name>ARBORTEC</name>
          <formCode displayName="TABLET"></formCode>
          <activeIngredient>
            <quantity><numerator unit="mg" value="500"/></quantity>
            <activeIngredientIngredientEntity>
              <name>Arborizine hydrochloride</name>
              <activeMoiety>
                <activeMoiety>
                  <name>Arborizine hydrochloride</name>
                </activeMoiety>
              </activeMoiety>
            </activeIngredientIngredientEntity>
          </activeIngredient>
          <playedDrugWithGeneric><genericGenericDrug>
            <name>Arborizine hydrochloride</name>
          </genericGenericDrug></playedDrugWithGeneric>
          <inactiveIngredient>
            <inactiveIngredientIngredientEntity>
              <name>magnesium stearate</name>
            </inactiveIngredientIngredientEntity>
          </inactiveIngredient>
          <inactiveIngredient>
            <inactiveIngredientIngredientEntity>
              <name>lactose</name>
            </inactiveIngredientIngredientEntity>
          </inactiveIngredient>
          <playedcontainedLabeledDrug>
            <quantity><numerator value="50"/></quantity>
              <containerPackage>
                <code code="BOT" codeSystem="4.3.2.1" codeSystemName="PackageType"
                displayName="BOTTLE"></code>
                <regulator>
                  <code code="9999-1111-50" codeSystem="2.16.840.1.113883.6.69"
                  codeSystemName="NDC"></code>
                </regulator>
              </containerPackage>
          </playedcontainedLabeledDrug>
        </manufacturedLabeledDrug>
        <consumedIn><substanceAdministration>
          <routeCode code="ORAL" displayName="ORAL"></routeCode>
        </substanceAdministration></consumedIn>
      </manufacturedProduct>
    </subject>
  </section>
</component2>
```

Figure 5: Sample Structured Data

A fragment of a sample SPL document shows how structured data elements (displayed in bold) such as the trade name and active and inactive ingredients are coded. Once the FDA has all drug products available in SPL format, the potential for data mining, data exchange, aggregation, and analysis will extend and enhance the use of product information for humans as well as computer systems.

SPL Compliance

The current Guidance regarding SPL will only affect some divisions of the FDA and only some submissions of labeling content. According to the FDA Draft Guidance for SPL, it applies to submissions including "marketing applications for human drug and biologic products, including new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biological license applications (BLAs), except BLAs for Licensed Bloodborne Pathogen Tests for Blood and Blood Components for Transfusion. The content of labeling is the labeling required under 21 CFR 201.100(d)(3) including all text, tables, and figures (commonly referred to as the package insert or professional labeling). This guidance applies to the content of labeling provided with original submissions, supplements, and annual reports. Copies of the formatted label and labeling and specimens of enclosures required elsewhere in the regulations (e.g., 21 CFR 314.50(e)(2)(ii)) must still be submitted either electronically in PDF or on paper."

The current guidance affects various types of submissions to the CDER and CBER divisions within the FDA. However, depending on the success of this initiative, it could prove useful in other divisions, such as CDRH and Animal Health, to improve the accessibility and sharing of product information.

Timeline for Submission Requirements

As of September 2004, the FDA has a goal of mandating SPL for the submission of prescription drug labeling content starting in July 2005. With Annual Reports included within the scope of the guidance, all approved prescription drugs will have SPL submissions. Then, beginning in July 2006, SPL will be required for submissions of all drug labeling content, including over the counter (OTC) drug products. However, these dates are not finalized since it is likely there are dependencies on other systems, such as the Electronic Labeling Information Processing System (ELIPS), being in place.

Steps Required to Achieve Compliance

To ensure compliance with SPL, you will be required to perform the following steps:

- Convert new and existing labeling content to XML
- Submit both the narrative labeling content and structured drug listing data
- Maintain consistent product information across all outputs

In addition to achieving and maintaining SPL compliance, it is important to look at your labeling content management processes holistically. During this process of addressing the SPL mandate, you may have opportunities to improve other processes related to the use of product information across your enterprise.

Approaches for Producing SPL-Compliant Submissions

Various options exist when considering how to convert existing labeling content to the SPL format. There are software vendors such as Arbortext who provide tools to convert various formats automatically to XML, thus removing the need for significant manual effort. Arbortext products can convert Microsoft Word, FrameMaker, and Interleaf documents to XML. There are also manual approaches, such as hiring consultants, using internal XML-knowledgeable resources, or having conversions done by service bureaus.

The following sections identify three potential approaches, along with their respective benefits and challenges.

Retain Current Processes

This option maintains the existing labeling content creation processes, and then requires the content to be converted to XML for submission to the FDA. Conversion could be done through internal or external resources.

Benefits

- Minimal change management to authoring community
- May be cost-effective depending on number of submissions and updates during review process

Challenges

- Additional time required due to conversion efforts may increase time to market
- Potentially very costly to convert each submission (including multiple conversions during review cycles)
- Does not allow for reuse and repurposing of product information for other uses
- Existing departments across organization still suffer from inefficient labeling content management processes
- Additional quality assurance steps required to compare original content to converted content

Integrate Microsoft Word-based Tools

This approach augments an existing Microsoft Word-based process through the use of Word plug-ins to assist in the creation of SPL-compliant documents.

Benefits

- May require minimal change management to authoring community depending on the tools
- May be cost-effective depending on number of submissions and updates during review process

Challenges

- Authors may require additional training for new authoring environment and processes since the tools may change the standard look and feel, and because styles, formatting or other user actions will need to be performed to ensure proper XML conversion

- Additional time required due to conversion efforts may increase time to market

- Potentially very costly to convert each submission (including those during review cycles)

- Output format may not allow for reuse and repurpose of product information across organization

Migrate to XML Environment

This approach involves converting existing labeling content to XML, and migrating the labeling content creation process to an XML-based authoring and publishing environment.

Benefits

- No additional conversion from native XML authoring format, yielding reduced review cycles

- Enables reuse of labeling content for SPL, Package Inserts, promotional materials, and other product information, reducing content creation and publishing time and costs, and ensuring consistent product information across all outputs

- Automated publishing of labeling content to multiple outputs can improve time to market

Challenges

- Authors will require additional training for new authoring environment and processes

Enterprise Benefits of Structured Product Information

As noted previously, there are various options for creating and submitting SPL-compliant documents to the FDA. Due to this mandate by the FDA, organizations have essentially two paths from which to choose:

1. Focus only on achieving compliance with the new SPL standard by retaining current labeling content creation, review and approval processes and convert to SPL only when ready to submit to the FDA. This will result in additional time and cost to the existing process due to "bolting on" additional process steps.

2. Recognize the opportunity to improve control over the entire labeling content creation, review and approval processes across the enterprise by creating structured product information directly.

In the traditional label content creation process, each group (e.g., Regulatory Affairs, Label Design and Control, Sales, and Marketing) that contributes to the labeling content creation process usually has its own process for creating content, such as using its own document templates and document repository. Each group ends up creating, or re-creating labeling content and reformatting it for its own output needs, as well as performing document clean-up and quality assurance tasks. Each time this task is repeated, it incurs additional time and cost and provides an opportunity to introduce errors into the content. This, in turn, increases the opportunities for costly product recalls.

Conversely, creating product information using XML enables you to streamline content creation and automate document publication so that you can reduce the opportunities for errors. Once you convert your labeling content to XML, you can begin to streamline additional processes beyond the creation of labeling content for regulatory approval. By creating reusable components of product information, you can automatically assemble and publish this content for a variety of purposes such as package inserts, product web sites, promotional materials, and package and label components. Automating the production of these various documents can greatly increase the productivity of your current staff, reduce the risk of label and packaging errors, accelerate the process of packaging changes, and improve regulatory compliance.

The following graphics, demonstrate how a single source of XML labeling content authored using Arbortext Epic Editor can be used to produce various outputs. Managing labeling content in a structured manner provides greater control over your product information, allowing for more accurate and consistent information and streamlined content creation and publishing processes.

Figure 6: Creation of XML Labeling Content

Labeling content created using Epic Editor, Arbortext's XML authoring tool, demonstrates a simple, intuitive way to create labeling information using all the features of traditional word processing tools. The advantage of this approach is that the content can be transformed automatically into multiple output formats including SPL.

Figure 7: FDA Browser Output of an SPL Document

The labeling content created in Epic Editor can be rendered to a Web browser using the FDA SPL common stylesheet. The process is entirely automatic; no additional changes to the content are required, thereby ensuring accuracy of the content. If a change is made to the XML labeling content, it is automatically reflected everywhere it is used.
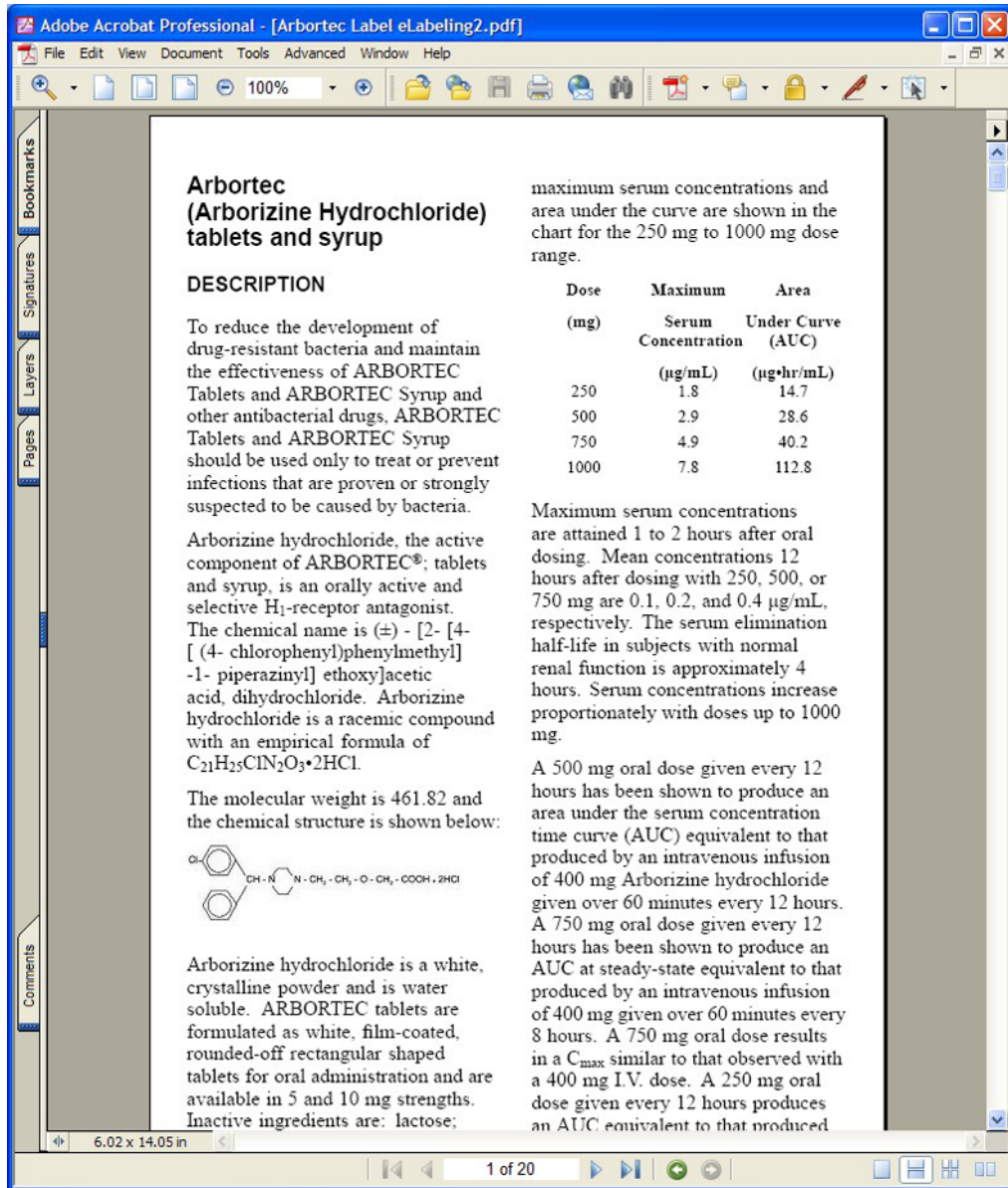
Figure 8: PDF Output for USPI

Labeling content is used throughout the enterprise for many purposes beyond submission to the FDA. The XML labeling content from Figure 6 is formatted for a USPI in PDF format as shown here. Multiple PDF outputs from the same labeling content can be designed, such as promotional materials and USPI's in various paper sizes.
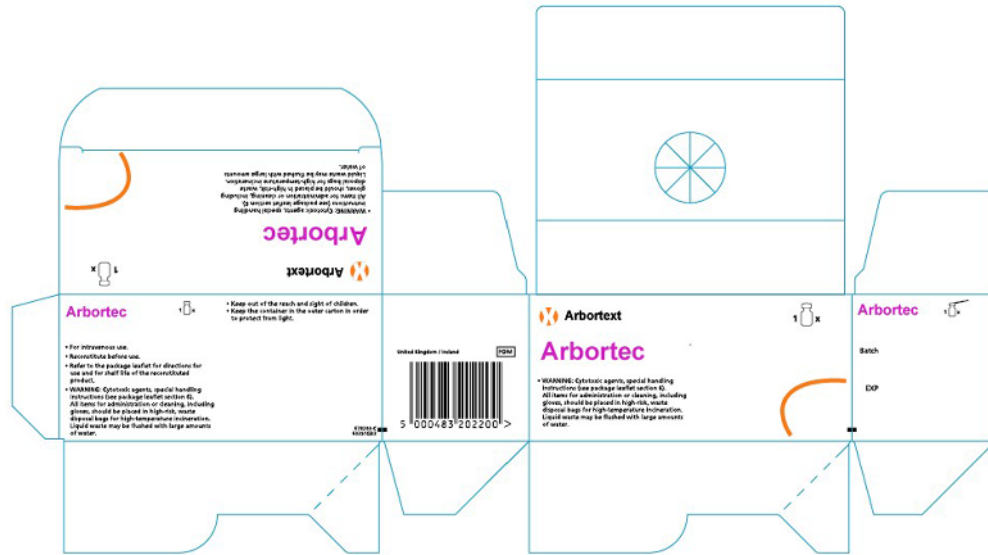
Arbortext

Figure 9: Artwork Output for Package Components

Using artwork templates, XML labeling content can be automatically integrated into package and labeling designs for box cartons, blister packs and other package components. This provides a streamlined process for package component creation which improves time to market, reduces the risk of errors, and reduces review cycles since the same content that has been reviewed and approved for regulatory purposes is inserted directly into the artwork.

SPL Resources

There are currently a variety of sources available to obtain further knowledge about Structured Product Labeling, some of which are listed below:

- http://www.fda.gov/oc/datacouncil/spl.html – The FDA created this web site specifically to address SPL. It contains links to valuable information regarding SPL, such as sample SPL documents, the common stylesheet files for viewing SPL documents in a browser, as well as many of the resources listed in this section of the document.

- http://www.fda.gov/cder/guidance/6028dft.doc – The FDA Draft Guidance, entitled "Providing Regulatory Submissions in Electronic Format – Content of Labeling."

- http://www.fda.gov/oc/datacouncil/SPL_schema.html – The Health Level 7 (HL7) Structured Product Labeling Specification is accessible from the FDA SPL web site, but is also located on the HL7 web site, http://www.hl7.org.

- http://www.fda.gov/oc/datacouncil/SPL_schema.html – The schemas used for SPL are accessible from the FDA SPL web site.

- http://www.fda.gov/oc/datacouncil/SPL_Stylesheets.html – The stylesheets used for presentation of the SPL content in a web browser.

- http://www.fda.gov/oc/datacouncil/spl.html – The SPL Implementation Guide for FDA Content of Labeling Submissions

- http://www.arbortext.com/spl – Arbortext maintains a site for SPL which contains information on SPL as well as solutions available to address SPL and other labeling content outputs across your enterprise.

These resources will continually be updated as SPL evolves.

Arbortext

Conclusion

While XML may be fairly new to many involved in managing labeling content, the use of XML for regulatory standards is not. However, SPL has gained a lot of attention since it is one of the first to mandate XML for electronic submissions. Great efforts have been put forth by HL7, FDA, the SPL Working Group and others to develop the SPL standard and increase the awareness and knowledge of it. As the industry and health authorities become more knowledgeable and comfortable with XML and understand the capabilities and possibilities of structured content, the evolution of XML-based standards in the life sciences industry will continue at a more rapid pace.

Creating and submitting SPL documents will require every company to make some type of additional investment, whether in the form of time, cost, new tools, or any combination of these. It is up to each one to determine how best to achieve SPL compliance, but the successful organizations will be those that look beyond SPL and recognize the opportunity to create measurable impacts throughout their enterprise.

About Arbortext

Arbortext is the leading global provider of automated publishing software that enables organizations to provide more personalized, dynamic and easily searchable content for Web, mobile and print usage. Arbortext's software is installed at over 1,400 organizations worldwide.

Current customers include American Express Financial Services, Audi, Aventis, Boeing, Bombardier, British Aerospace, Caterpillar, DaimlerChrysler, Ericsson Telecom, Ford, General Electric, GM, IBM, International Thomson Publishing, Lucent, Nokia, Nortel Networks, PeopleSoft, Pfizer, Ricoh, Sun Microsystems, Toyota, United Airlines, Volkswagen and Volvo. Arbortext is a founding member and active participant in the XML Activity of the World Wide Web Consortium (W3C). Headquartered in Ann Arbor, Michigan, USA, Arbortext has offices around the world. For more information, please visit www.arbortext.com.

Arbortext

Enterprise Publishing Software

Arbortext, Inc.
1000 Victors Way
Ann Arbor, MI 48108
USA

Tel: +1 734.997.0200
Fax: +1 734.997.0201

www.arbortext.com
info@arbortext.com