

US EPA ARCHIVE DOCUMENT

Electronic Labeling and Structured Label Content

Robert Schultz

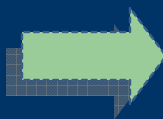
US EPA, Office of Pesticide Programs

PPDC WDL Workgroup

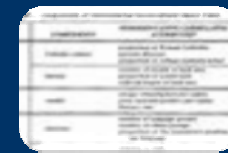
April 21, 2009

Current Challenges and Goals for Change

Challenges



Goals of e-Label



- Multiple definitions of e-Label exist.
- Paper copies of labels and amendments must be submitted.
- Manual processes dominate the review cycle:
 - Propagating consistent label changes
 - Enforcement of standardized text
 - Hand-keying data into EPA databases
 - Searching for “me too” and past versions
 - Comparing labels
- Distribution of labels is container-based and processing requirements delay changes to printed products.
- Structured label fields set the standard for incoming electronic data.
- Provide an e-Label Builder to support the creation of electronic labels.
- Label approval will move from a manual, paper-based process to an electronic stream of data and decisions.
- Provide the public and registrants with the latest approved and historical versions of labels online.

Benefits

- Process labels more efficiently by allowing EPA resources to focus on critical tasks.
- Compare e-Label content against current rules, requirements, guidance and laws.
- Improve data quality, including the accuracy and completeness of data received from registrants
- Provide a level playing field for registrants.
- Automate entry into backend systems.



What is Structured Content?

- **Structured content** refers to information or content that has been broken down and classified using metadata.
- **Metadata** is “data about data”
 - “Information that describes the *content*, quality, condition, *origin*, and other characteristics of data or other pieces of information. ...”

Source: www.sdbay.sdsu.edu/glossary/index.php

Simple Pesticide Label Structure

PRODUCT NAME

DIRECTIONS FOR USE
 It is a violation of federal law to use
 this product in a manner inconsistent
 with its labeling.

PRECAUTIONARY STATEMENTS
HAZARD TO HUMANS
(AND DOMESTIC ANIMALS)
DANGER

ENVIRONMENTAL HAZARDS

PHYSICAL OR CHEMICAL HAZARDS

STORAGE AND DISPOSAL

STORAGE _____

DISPOSAL _____

KEEP OUT OF THE REACH OF CHILDREN
DANGER

FIRST AID
 (STATEMENT OF PRACTICAL TREATMENT)

IF SWALLOWED _____

IF INHALED _____

IF IN EYES _____

IF ON SKIN _____

ACTIVE INGREDIENTS: _____%

OTHER (INERT) INGREDIENTS: _____%

TOTAL: _____
 100.00%

THIS PRODUCT _____ **WARRANTY STATEMENT**
 CONTAINS XX LBS. _____
 OF XXXX PER GALLON _____

MANUFACTURER'S ADDRESS _____

NET WT. / NET CONTENTS STATEMENT: _____

EPA Registration No. / EPA Reg. No: _____

EPA Establishment No. / EPA Est. No: _____

OPP's Basis for Structure

- Label Review Manual
- Data fields from
 - OPPIN
 - Label Use Information System (LUIS)
- OPP Workgroup
- XML schema for submission to OPP only
- Envision additional schema for output



Content Organizational Categories

- General Information
 - overall product and company information.
- Ingredient Statement
 - details about the active ingredients and diluents.
- Precautionary Statements
 - restrictions regarding environmental, human and user safety.
- Directions for Use
 - instructions on how to mix and apply the product.
- Additional Information
 - product warranty and marketing information.
- Regulatory Information
 - EPA tracking and processing information.



Degree of structure

- Large free-text blocks
- Discrete values
- Mixed
 - Re-entry interval contained within a text block
- Non-label information
 - Required for validation
 - LD50



Label content from discrete data

Active Ingredients:

2,4-dichlorophenoxyacetic acid, triisopropanolamine salt	34.05%
2,4-dichlorophenoxyacetic acid, dimethylamine salt	21.97%
Other Ingredients	43.98%
Total	100.00%

Acid Equivalent: 2,4-dichlorophenoxyacetic acid - 36.5% - 3.8 lb/gal

Label content as free text

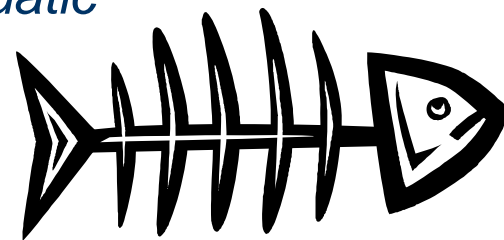
Mixing with Liquid Nitrogen Fertilizer

This product may be combined with liquid nitrogen fertilizer suitable for foliar application to accomplish broadleaf weed control and fertilization of corn, small grains, sorghum, or pastures in a single operation. Use Formula 40 in accordance with recommendations for these crops provided in this label. Use liquid fertilizer at rates recommended by the supplier or extension service specialist. Test for mixing compatibility by mixing spray ingredients in correct proportions in a clear glass jar before mixing in spray tank. A compatibility aids such as Unite or Compex may be needed in some situations. Compatibility is best with liquid fertilizer solutions containing only nitrogen. Mixing with N-P-K solutions may not be satisfactory, even with the addition of a compatibility aid. Pre-mixing Formula 40 with 1 to 4 parts water may help in situations when mixing difficulty occurs.

Fill the tank about half full with the liquid fertilizer, then add the required amount of Formula 40 with agitation.. Maintain agitation and complete filling the tank with liquid fertilizer. Apply immediately and continue spray tank agitation during application. **Do not store the spray mixture.** To avoid spray mixture compatibility problems, application during cold weather (less 40°F) is not recommended.

Non-target Organism Statement

- Label Review Manual Ch. 8, II, E
- 2. “The following statement has historically been required when a pesticide intended for outdoor use contains an active ingredient with a fish acute LC50 or aquatic invertebrate (including estuarine species such as oyster and mysid shrimp) EC50 = 1 ppm:”
 - *"This pesticide is toxic to [fish] [fish and aquatic invertebrates] [oysters/shrimp] or [fish, aquatic invertebrates, oysters and shrimp]."*



Label content built from standard text

Environmental Hazards

This product is toxic to aquatic invertebrates and may be toxic to fish. Do not apply directly to water, to areas where surface water is present, or to intertidal areas below the mean high water mark except as noted on appropriate labels. Drift or runoff may adversely affect aquatic invertebrates and nontarget plants. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. Do not contaminate water when disposing of equipment washwaters or rinsate.

This chemical has properties and characteristics associated with chemicals detected in groundwater. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination. Application around a cistern or well may result in contamination of drinking water or groundwater.

Advantages

- Standard statements allow for more efficient review
- Level playing field across products and companies
- Facilitates mitigation
- Supports web-distributed labeling

Label content – Combined text & structured content

Agricultural Use Requirements

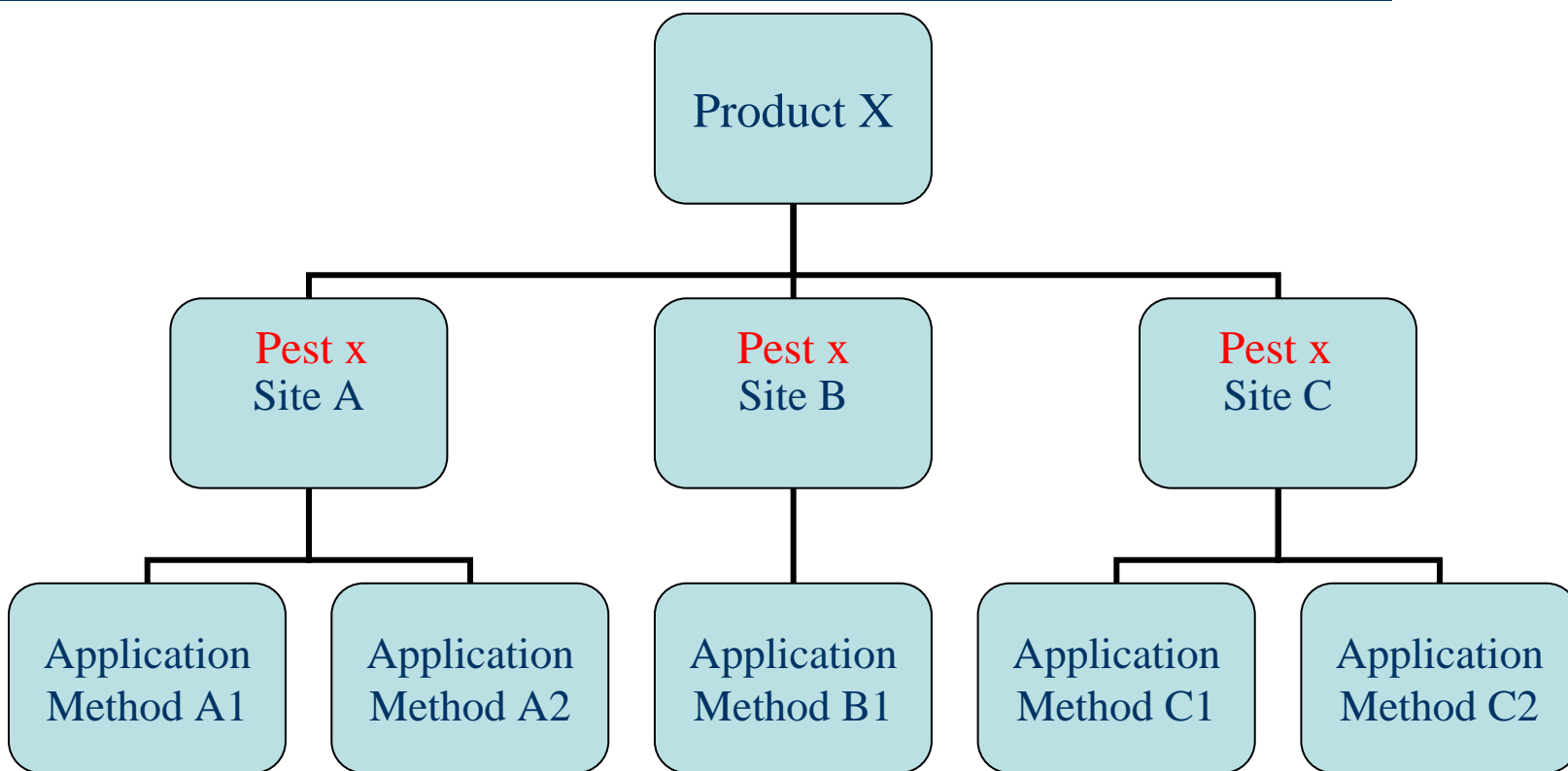
Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted entry interval. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 48 hours.

PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is:

- Coveralls
- Chemical-resistant gloves made of any waterproof material
- Shoes plus socks
- Protective eyewear

Data Hierarchy



Business Rules

- Precautionary Statement fields' content
 - Usually based on toxic category
 - Most fields will be standardized
 - Allow the users to edit the statements.
 - Edited fields will be flagged for further review.
- Each of the major label field categories should include an extra free text field to allow registrants to enter any additional information that did not fit into the pre-defined structure.
- EPA-defined pick lists will include an “other” option
 - allows the registrant to enter a value that is not on the lists..
- EPA-defined pick lists should include both the scientific and common names where applicable.

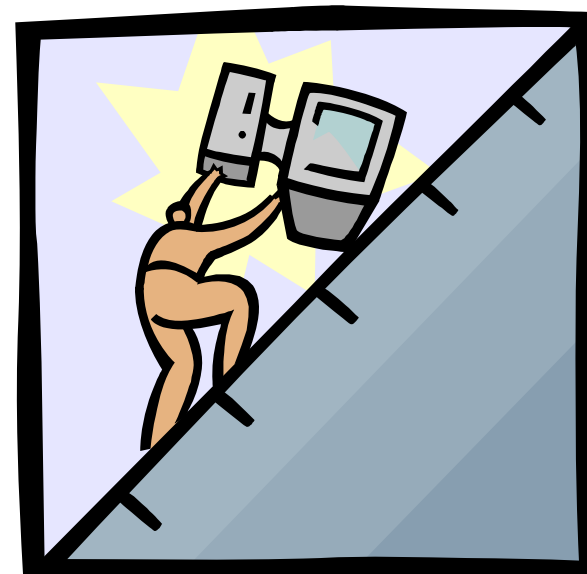
Key Elements of e-Label Submission

- XML Schema
 - Identifies label content
 - All content would be included
 - Includes some non-label information
- PDF
 - For visual/graphic requirements



Progress

- Defined structure requirements
 - Internal OPP Workgroup
- Developed XML Schema
 - Version 1
- Defined e-Label Builder requirements
 - Based on structure

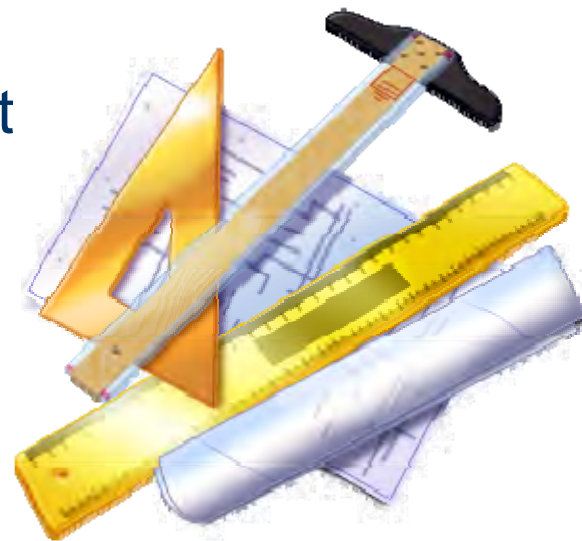


What is an XML Schema?

- Describes the structure of an XML document.
- Defines the legal building blocks of an XML document
 - defines **elements** that can appear in a document
 - defines **attributes** that can appear in a document
 - defines which elements are **child elements**
 - defines the **order** of child elements
 - defines the **number** of child elements
 - defines whether an element is **empty** or can include text
 - defines **data types** for elements and attributes
 - defines **default** and **fixed values** for elements and attributes
- Source: <http://www.w3schools.com/Schema>

Data Fields

- 280 Data elements
- 7 Categories
- 34 Label sections
 - Active ingredient
 - Personal protective equipment
- 25 Subsections
 - AI name, percent
 - Respirator type, Role



Current Thinking

- Less granularity of Use Directions
 - Application instructions too complicated
 - Maintain some discrete data
 - Site
 - Pest
 - Restrictions
 - PHI, PGI, etc.
- Alternatives to “Turbo Tax”-style for Builder
- Identify “problem” areas of labels



Real Life Web Label – NIH Daily Med & FDA SPL

DailyMed: About DailyMed - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Home Search Favorites Refresh Print

Address <http://dailymed.nlm.nih.gov/dailymed/about.cfm> Go

Links Weather & News Google SDDB Tracker & Version Mgr BusinessObjects InfoView IT reference and online magazines

Skip to content Skip to Drug Search

Daily Med
Current Medication Information

DailyMed provides high quality information about marketed drugs.
Drug labeling on this Web site is the most recent submitted to the Food and Drug Administration (FDA) and currently in use; it may include, for example, strengthened warnings undergoing FDA review or minor editorial changes. These labels have been reformatted to make them easier to read.

Options

- Home
- E-mail Label Information
- Downloads
- Archives
- Notify of Updates
- Contact Us

Additional Resources

- Report Adverse Event
- SPL Format Previewer for Label Authors

At the present time this Web site does not contain a complete listing of labels for approved prescription drugs. Currently this Web site contains 4356 approved prescription drugs.

Search By Drug Name: **GO**

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z All

About DailyMed

DailyMed provides high quality information about marketed drugs. This information includes FDA approved labels (package inserts). This Web site provides health information providers and the public with a standard, comprehensive, up-to-date, look-up and download resource of medication content and labeling as found in medication package inserts.

Other information about prescription drugs may also be available. NLM regularly processes data files uploaded from FDA's system and provides and maintains this Web site for the public to use in accessing the information. Additional information about medicines is available on NLM's MedlinePlus Web site <http://www.nlm.nih.gov/medlineplus/medicines.html>.

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Internet

Real Life Web Label – Atenolol Search

The screenshot shows a Microsoft Internet Explorer browser window displaying the DailyMed search results for 'atenolol'. The browser's address bar shows the URL: <http://dailymed.nlm.nih.gov/dailymed/search.cfm?startswith=atenolol>. The page features a navigation menu on the left with sections for 'Options' (Home, E-mail Label Information, Downloads, Archives, Notify of Updates, Contact Us) and 'Additional Resources' (Report Adverse Event, SPL Format Previewer for Label Authors). The main content area includes an 'Information' banner, a search bar with the text 'Search By Drug Name:' and a 'GO' button, and a list of search results for 'atenolol'. The results are displayed in a table with columns for drug name, strength, and manufacturer. The search results section also includes a 'Search results for' header and a 'Total Results Found: [Count: 15]' indicator.

Options

- Home
- E-mail Label Information
- Downloads
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- Notify of Updates
- Contact Us

Additional Resources

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Information

DailyMed provides high quality information about marketed drugs. Drug labeling on this Web site is the most recent submitted to the Food and Drug Administration (FDA) and currently in use; it may include, for example, strengthened warnings undergoing FDA review or minor editorial changes. These labels have been reformatted to make them easier to read.

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Search By Drug Name: **GO**

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z All

Search results for

atenolol

Total Results Found: [Count: 15]

Atenolol (atenolol) Tablet	[CARACO PHARMACEUTICAL LABORATORIES, LTD.]
Atenolol (atenolol) Tablet	[Genpharm Inc.]
Atenolol (atenolol) Tablet	[Mutual Pharmaceutical Company]
Atenolol (atenolol) Tablet	[Mylan Pharmaceuticals Inc]

Label – Atenolol Label Content

DailyMed: About DailyMed - Microsoft Internet Explorer


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Address http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=4622

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Skip to DrugLabel content Skip to DrugLabel sections



Options

- Home
- E-mail Label Information
- Downloads
- SPL History
- Print this Label
- Notify of Updates
- Contact Us

Additional Resources

- Report Adverse Event
- MedlinePlus Information
- Find Clinical Trials
- Biochemical Data Summary
- Search PubMed Articles
- Presence in Breast Milk

Merriam-Webster Turn Dictionary On

Download the FDA official PDF of this label

Search By Drug Name: GO

Atenolol (atenolol) Tablet
[Genpharm Inc.]

RxNorm Names
[Review RxNorm Normal Forms](#)

Drug Label Sections

- Description
- Clinical Pharmacology
- Indications & Usage
- Contraindications
- Warnings
- Precautions
- Adverse Reactions
- Overdosage
- Dosage & Administration
- How Supplied
- Patient Counseling Information
- Controlled Substance Material
- Boxed Warning
- Routes, Dosages, Uses
- Stability
- Full Text of Contents
- Other Information

Cessation of Therapy with Atenolol: Patients with coronary artery disease, who are being treated with atenolol, should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported in angina patients following the abrupt discontinuation of therapy with beta blockers. The last two complications may occur with or without preceding exacerbation of the angina pectoris. As with other beta blockers, when discontinuation of atenolol is planned, the patients should be carefully observed and advised to limit physical activity to a minimum. If the angina worsens or acute coronary insufficiency develops, it is recommended that atenolol be promptly reinstated, at least temporarily. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue atenolol therapy abruptly even in patients treated only for hypertension. (See **DOSAGE AND ADMINISTRATION**.)

DESCRIPTION

Atenolol, a synthetic, beta₁-selective (cardioselective) adrenoreceptor blocking agent, may be chemically described as benzeneacetamide, 2-[p-[2-hydroxy-3-(isopropylamino) propoxy]-phenyl]-acetamide.

javascript:nlmftoc("nlmftoc");

Internet

Real Life Web Label – Drug Interactions

DailyMed: About DailyMed - Microsoft Internet Explorer

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Back Search Favorites

Address <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=4622#nml34068-7> Go

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The drug should be used with caution in patients with impaired renal function. (See **DOSAGE AND ADMINISTRATION**.)

Drug Interactions

Catecholamine-depleting drugs (e.g. reserpine) may have an additive effect when given with beta blocking agents. Patients treated with atenolol plus a catecholamine depletor should therefore be closely observed for evidence of hypotension and/or marked bradycardia which may produce vertigo, syncope, or postural hypotension.

Calcium channel blockers may also have an additive effect when given with atenolol (see **WARNINGS**).

Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are coadministered, the beta blocker should be withdrawn several days before the gradual withdrawal of clonidine. If replacing clonidine by beta blocker therapy, the introduction of beta blockers should be delayed for several days after clonidine administration has stopped.

Concomitant use of prostaglandin synthase inhibiting drugs, e.g., indomethacin, may decrease the hypotensive effects of beta-blockers.

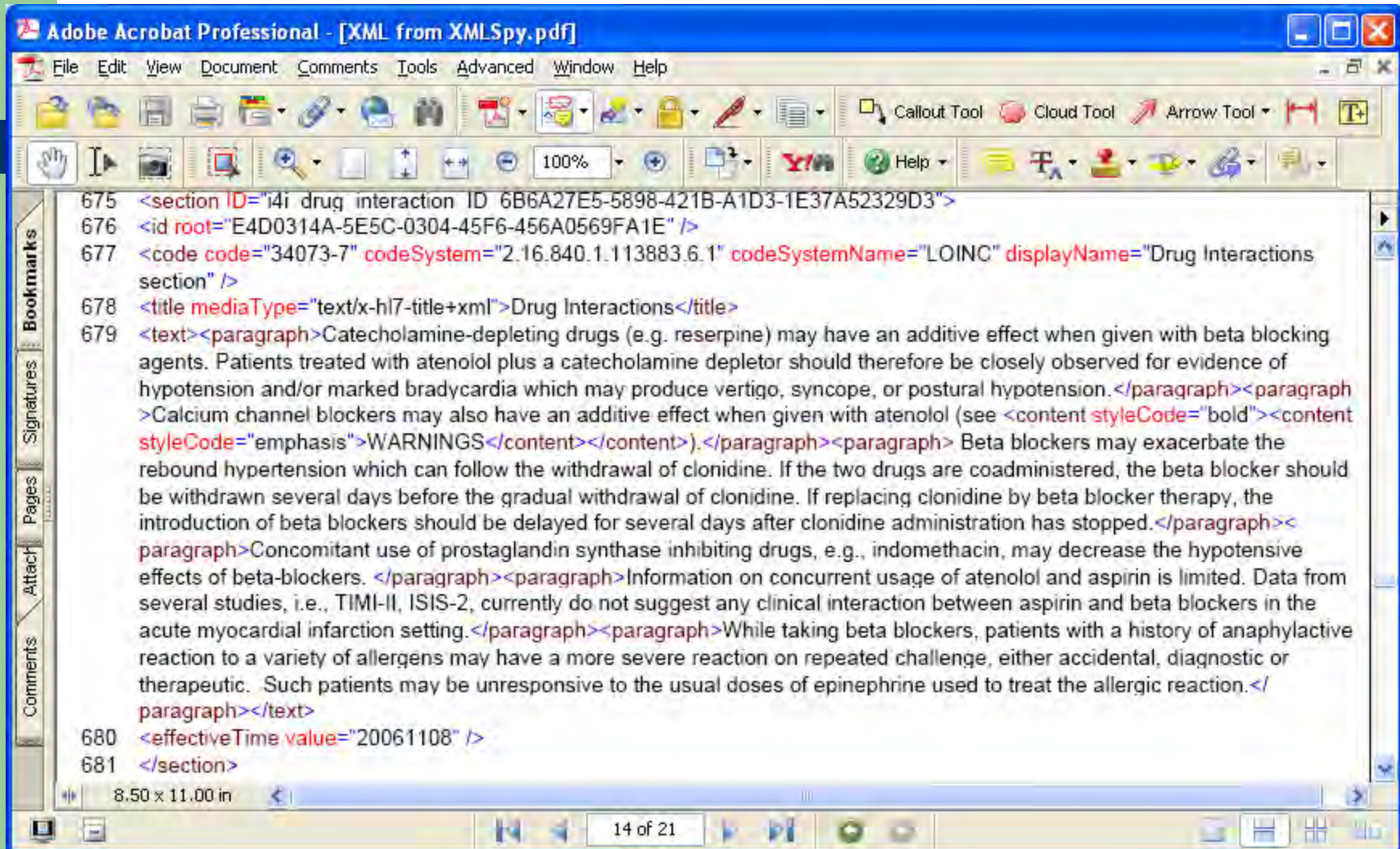
Done Internet

Real Life Web Label - Structuring

The screenshot displays a Microsoft Word window titled "77331CAD-4576-4AF6-88F4-6F0F70CB0D68.xml - Microsoft Word". The window shows the XML markup for a document section. The markup is as follows:

```
<code />  
<title>Drug Interactions</title>  
<text>  
  <paragraph>Catecholamine-depleting drugs (e.g. reserpine) may have an additive effect when given with beta blocking agents. Patients treated with atenolol plus a catecholamine depletor should therefore be closely observed for evidence of hypotension and/or marked bradycardia which may produce vertigo, syncope, or postural hypotension.</paragraph>  
  <paragraph>  
    Calcium channel blockers may also have an additive effect when given with atenolol (see  
    <content>  
      <content>WARNINGS</content>  
    </content>  
  </paragraph>  
<paragraph>Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are coadministered, the beta blocker should be withdrawn several days before the gradual withdrawal of clonidine. If replacing clonidine by beta blocker therapy, the introduction of beta blockers should be delayed for several days after clonidine administration has stopped.</paragraph>
```

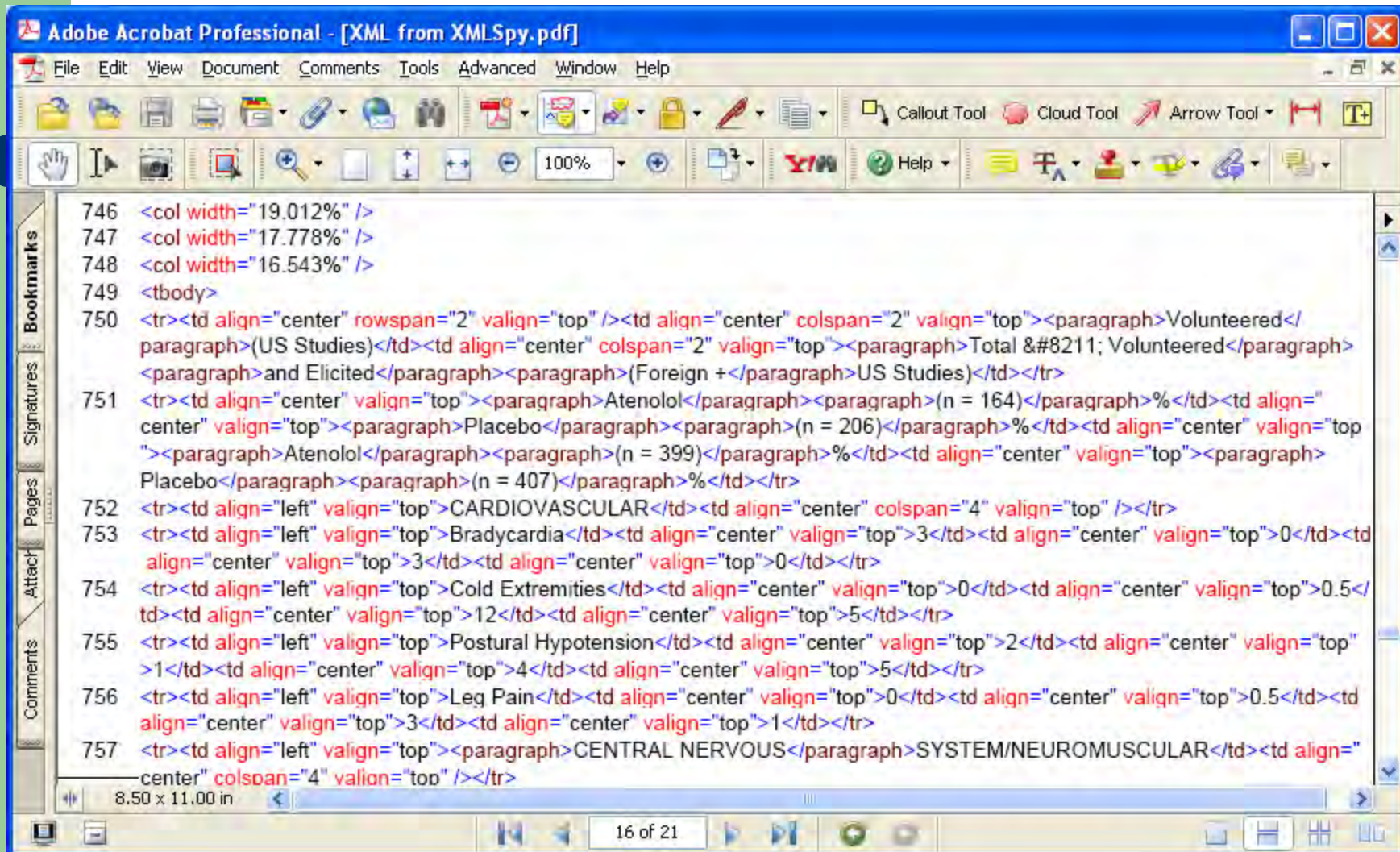
Real Life Web Label - XML



The screenshot shows the Adobe Acrobat Professional interface with the XML source code of a PDF document. The window title is "Adobe Acrobat Professional - [XML from XMLSpy.pdf]". The menu bar includes File, Edit, View, Document, Comments, Tools, Advanced, Window, and Help. The toolbar contains various icons for navigation and editing. The main content area displays XML code with line numbers 675 through 681. The code defines a section for drug interactions, including a title and a text block with several paragraphs of medical text. The text includes warnings about drug interactions with atenolol, calcium channel blockers, and beta blockers.

```
675 <section ID="i4i drug interaction ID 6B6A27E5-5898-421B-A1D3-1E37A52329D3">
676 <id root="E4D0314A-5E5C-0304-45F6-456A0569FA1E" />
677 <code code="34073-7" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC" displayName="Drug Interactions
section" />
678 <title mediaType="text/x-hl7-title+xml">Drug Interactions</title>
679 <text><paragraph>Catecholamine-depleting drugs (e.g. reserpine) may have an additive effect when given with beta blocking
agents. Patients treated with atenolol plus a catecholamine depletor should therefore be closely observed for evidence of
hypotension and/or marked bradycardia which may produce vertigo, syncope, or postural hypotension.</paragraph><paragraph
>Calcium channel blockers may also have an additive effect when given with atenolol (see <content styleCode="bold"><content
styleCode="emphasis">WARNINGS</content></content>).</paragraph><paragraph> Beta blockers may exacerbate the
rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are coadministered, the beta blocker should
be withdrawn several days before the gradual withdrawal of clonidine. If replacing clonidine by beta blocker therapy, the
introduction of beta blockers should be delayed for several days after clonidine administration has stopped.</paragraph><
paragraph>Concomitant use of prostaglandin synthase inhibiting drugs, e.g., indomethacin, may decrease the hypotensive
effects of beta-blockers. </paragraph><paragraph>Information on concurrent usage of atenolol and aspirin is limited. Data from
several studies, i.e., TIMI-II, ISIS-2, currently do not suggest any clinical interaction between aspirin and beta blockers in the
acute myocardial infarction setting.</paragraph><paragraph>While taking beta blockers, patients with a history of anaphylactic
reaction to a variety of allergens may have a more severe reaction on repeated challenge, either accidental, diagnostic or
therapeutic. Such patients may be unresponsive to the usual doses of epinephrine used to treat the allergic reaction.</
paragraph></text>
680 <effectiveTime value="20061108" />
681 </section>
```

Real Life Web Label – XML Table



```
746 <col width="19.012%" />
747 <col width="17.778%" />
748 <col width="16.543%" />
749 <tbody>
750 <tr><td align="center" rowspan="2" valign="top" /><td align="center" colspan="2" valign="top"><paragraph>Volunteered</
paragraph>(US Studies)</td><td align="center" colspan="2" valign="top"><paragraph>Total &#8211; Volunteered</paragraph>
<paragraph>and Elicited</paragraph><paragraph>(Foreign + </paragraph>US Studies)</td></tr>
751 <tr><td align="center" valign="top"><paragraph>Atenolol</paragraph><paragraph>(n = 164)</paragraph>%</td><td align="
center" valign="top"><paragraph>Placebo</paragraph><paragraph>(n = 206)</paragraph>%</td><td align="center" valign="top"
"><paragraph>Atenolol</paragraph><paragraph>(n = 399)</paragraph>%</td><td align="center" valign="top"><paragraph>
Placebo</paragraph><paragraph>(n = 407)</paragraph>%</td></tr>
752 <tr><td align="left" valign="top">CARDIOVASCULAR</td><td align="center" colspan="4" valign="top" /></tr>
753 <tr><td align="left" valign="top">Bradycardia</td><td align="center" valign="top">3</td><td align="center" valign="top">0</td><td
align="center" valign="top">3</td><td align="center" valign="top">0</td></tr>
754 <tr><td align="left" valign="top">Cold Extremities</td><td align="center" valign="top">0</td><td align="center" valign="top">0.5</
td><td align="center" valign="top">12</td><td align="center" valign="top">5</td></tr>
755 <tr><td align="left" valign="top">Postural Hypotension</td><td align="center" valign="top">2</td><td align="center" valign="top"
">1</td><td align="center" valign="top">4</td><td align="center" valign="top">5</td></tr>
756 <tr><td align="left" valign="top">Leg Pain</td><td align="center" valign="top">0</td><td align="center" valign="top">0.5</td><td
align="center" valign="top">3</td><td align="center" valign="top">1</td></tr>
757 <tr><td align="left" valign="top"><paragraph>CENTRAL NERVOUS</paragraph>SYSTEM/NEUROMUSCULAR</td><td align="
center" colspan="4" valign="top" /></tr>
```

Real Life Web Label – Display Table

DailyMed: About DailyMed - Microsoft Internet Explorer

Address: <http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=4622#nlm34068-7>

Links: Weather & News, Google, SDDB, Tracker & Version Mgr, BusinessObjects InfoView, IT reference and online magazines

(The severity of elicited adverse effects was higher for both atenolol and placebo-treated patients than when these reactions were volunteered. Where frequency of adverse effects of atenolol and placebo is similar, causal relationship to atenolol is uncertain.)

	Volunteered (US Studies)		Total – Volunteered and Elicited (Foreign + US Studies)	
	Atenolol (n = 164) %	Placebo (n = 206) %	Atenolol (n = 399) %	Placebo (n = 407) %
CARDIOVASCULAR				
Bradycardia	3	0	3	0
Cold Extremities	0	0.5	12	5
Postural Hypotension	2	1	4	5
Leg Pain	0	0.5	3	1
CENTRAL NERVOUS SYSTEM/NEUROMUSCULAR				

Done Internet

Questions and Discussion

