ElectronicLabeling and Structured Label Content

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PPDC WDL Workgroup
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Current Challenges and Goals for Change

Challenges

- 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.

Goals of e-Label

- 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](http://www.sdbay.sdsu.edu/glossary/index.php)
Simple Pesticide Label Structure

Source: http://www.epa.gov/pesticides/label/
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
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 aid 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].”
Environmental Hazards

Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas.

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
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

Product X

- Pest x Site A
  - Application Method A1
  - Application Method A2

- Pest x Site B
  - Application Method B1

- Pest x Site C
  - Application Method C1
  - Application Method C2
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 – Atenolol Search

Atenolol (atenolol) Tablet
[CARACO PHARMACEUTICAL LABORATORIES, LTD.]

Atenolol (atenolol) Tablet
[Genpharm Inc.]

Atenolol (atenolol) Tablet
[Mutual Pharmaceutical Company]

Atenolol (atenolol) Tablet
[Mylan Pharmaceuticals Inc]
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 re instituted, 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, beta-selective (cardioselective) adrenoreceptor blocking agent, may be chemically described as benzeneacetamide, 2-[p-[2-hydroxy-3-(isopropylamino)propoxy]phenyl]acetamide.
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 depleter 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.
Real Life Web Label - Structuring

```xml
<title>Drug Interactions</title>
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  <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 WARNING 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>
</text>
```
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 <content styleCode="bold">WARNINGS</content>).

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. 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.

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.
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The reported frequency 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.

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<th>Volunteered (US Studies)</th>
<th>Total – Volunteered and Elicited (Foreign + US Studies)</th>
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<td>Atenolol (n = 184) %</td>
<td>Placebo (n = 206) %</td>
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Questions and Discussion