SPL 101 “THE BASICS”

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Transition from Paper to Electronic Drug Establishment Registration & Drug Listing

- Changes in FD&C Act require electronic registration of drug establishments and listing of human prescription drugs, OTC, animal drug, biologic products – September 2007
- Final guidance document for electronic drug establishment registration and listing – May 2009
- FDA is adopting the use of extensible markup language (XML) files in SPL format as the standard format for the exchange of drug establishment registration and drug listing information.

Transitioning from Paper to Electronic: Drug Registration and Listing

- No more **PAPER** drug registration and drug listing as of June 1, 2009 (unless waiver)
  - Form 2656 – NDC Labeler Code & Establishment Registration – replaced with
    - NDC Labeler Code SPL
    - Establishment Registration SPL
  - Form 2657 – Drug Product Listing & Form 2658 – Private Labeler Distributor – replaced with
    - Content of Labeling/Listing SPL

Introduction to SPL

The Standard:

Structured Product Labeling (SPL)

SPL Standard

- The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product information.
- American National Standards Institute (ANSI) accredited (SPL Release 4) – March 2009
- SPL is created using E**X**tensible **M**arkup **L**anguage

XML & XSL Stylesheet

- XML – E**X**tensible **M**arkup **L**anguage
  - Relatively human-legible
  - Machine readable
  - Tags (elements) permit search of key information
- XML Documents – created via Notepad, Word Pad, XML validation tools, Xforms, etc…
- XSL Stylesheet – transforms the XML data to be viewed via web browser or printed documents

Blocks of Text

PDF

Description:

This is the description of the product

Indications and Usage:

This is the indication for use of this product

Contraindications:

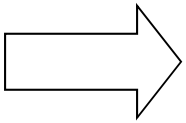
These are the contraindications

Warnings:

These are the warnings.

How supplied:

This is how the product is supplied.



SPL

<Description>

This is the description of this product

<Indication and Usage>

This is the indication of the product

<Contraindications>

These are the contraindications

<Warnings>

These are the warnings

<How supplied>

This is how the product is supplied

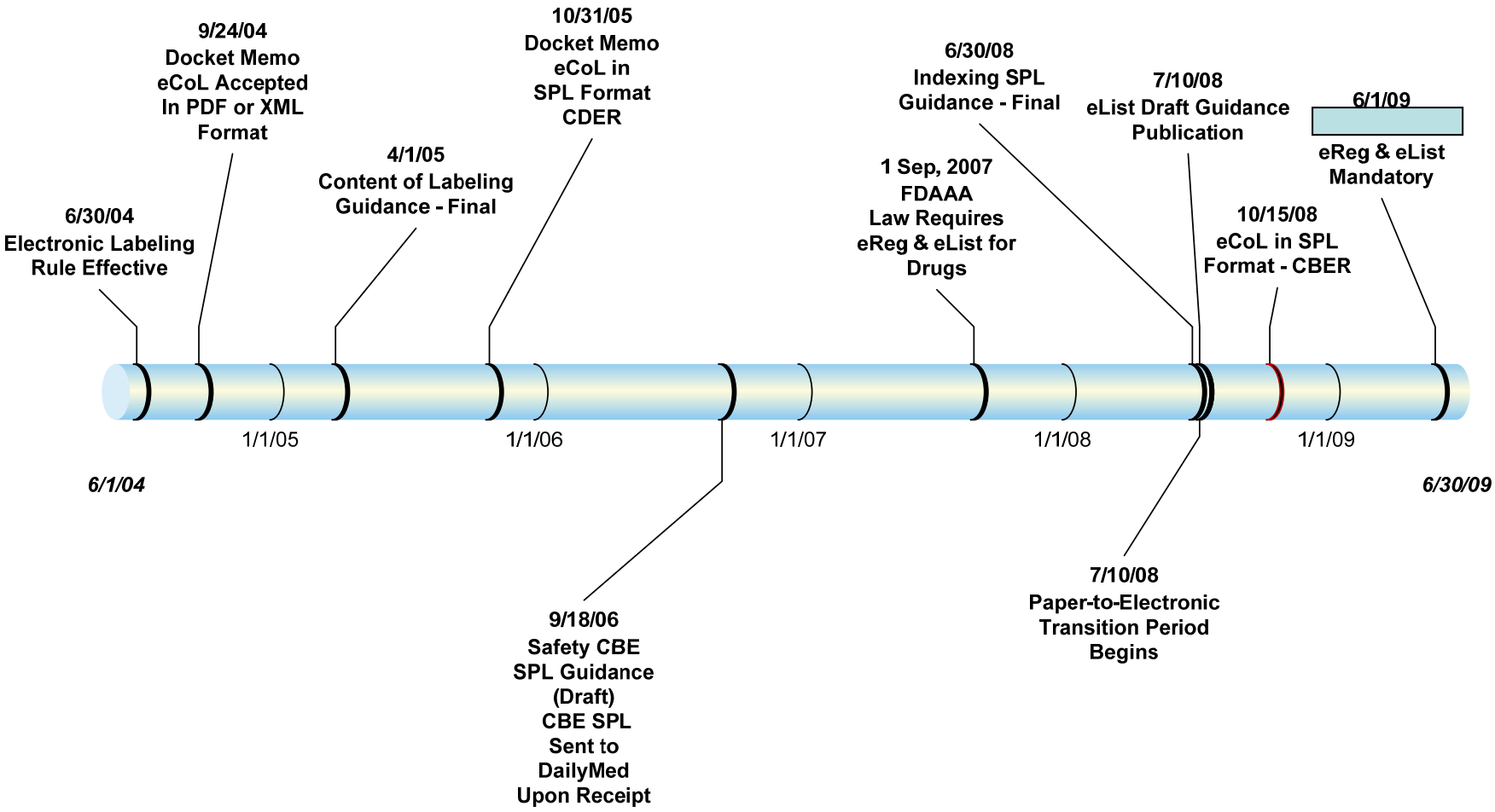
SPL Stylesheet View/Source Code

CONTRAINDICATIONS

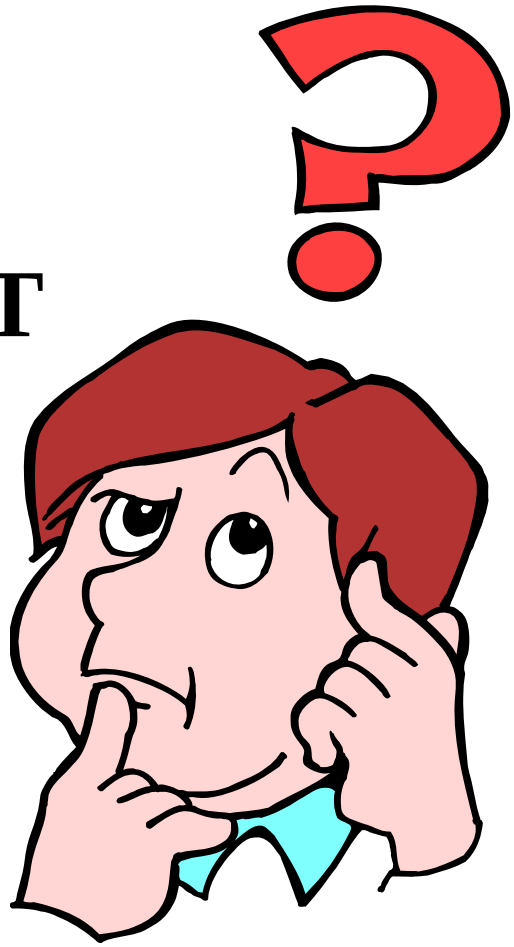
Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

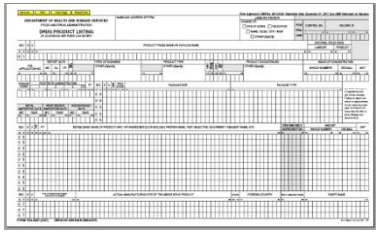
```
<component>
<section ID="_7CF4D228-65A6-6223-5A96-ECB4DBD620FC">
<id root="3A7D815A-A2B9-0389-5D92-4836E709B0FE" />
<code code="34070-3" codeSystem="2.16.840.1.113883.6.1" displayName="CONTRAINDICATIONS SECTION" />
<title mediaType="text/x-hl7-title+xml">CONTRAINDICATIONS</title>
<text><paragraph>Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson&amp;#8217;s disease.</paragraph></text>
<effectiveTime value="20070813" />
</section>
```

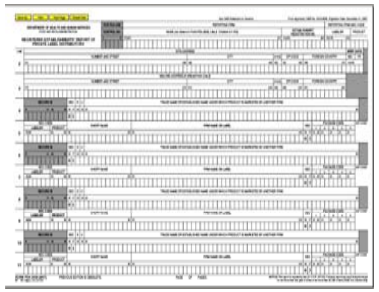
IMPLEMENTATION OF STRUCTURED PRODUCT LABELING AT FDA



WHY CHANGE
THE **DRUG LISTING AND ESTABLISHMENT REGISTRATION PROCESS** THAT HAS WORKED FOR DECADES ????







- Eliminate duplicative and redundant data entry
- Eliminate paper submissions
- Automate processing of data in a submission type in electronic format in a manner that FDA can adequately process, review, and archive.

Benefits of Electronic Registration and Listing

- Electronic registration and listing process is more efficient and effective for industry and the Agency
- Accurate, up-to-date inventory of marketed drugs
- Eliminates data entry errors
- Well formed and properly created SPL files can be processed in minutes
- Use existing technology and data standard – **SPL (Used by FDA (CDER) since 2004)(Required by CDER in 2005)**
- Standard was updated to SPL R4 to include data elements needed to register drug establishments and list drug products

More Benefits of Electronic Registration and Listing

- Data maintenance
  - Content of Labeling and listing information in one file.
  - Registrant can list all it's establishments in one file.
  - Update information – Use one file instead of creating several paper forms and resubmit.
- Eliminates the use of paper forms for listing and registration
- 24-hour submission window – FDA Gateway
- Manage data using same source (files) as FDA
- Reduces the amount of time for FDA to receive and process your information.

You Control the Published Electronic Drug Listing and Establishment Registration Data

Drug Company

Drug Listing Content of Labeling SPL file

Establishment Registration SPL file

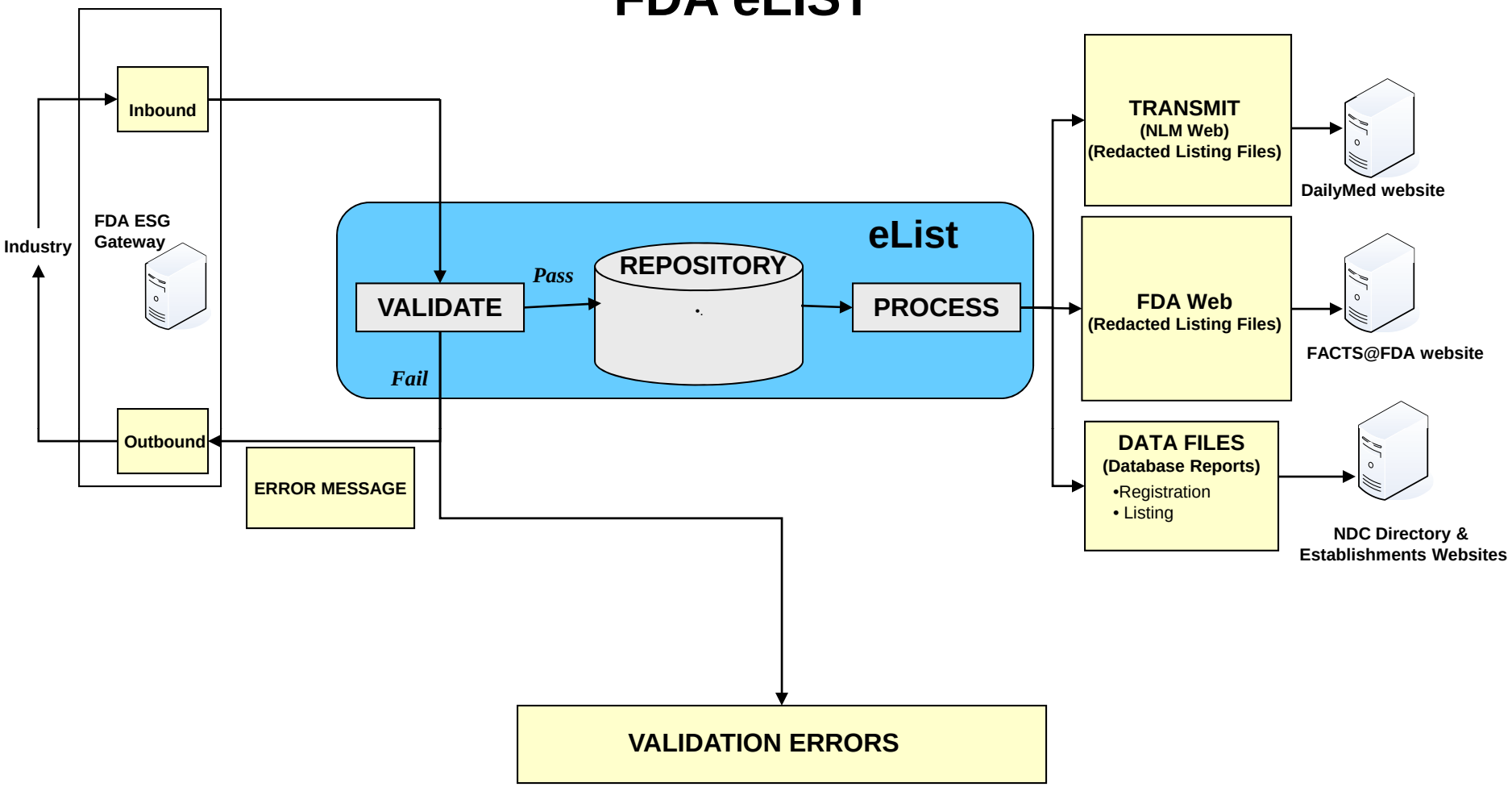
FDA Gateway and FDA eList System

DailyMed Website

FACTS @ FDA Website

Drug Firms & NDC Directory Websites

FDA eLIST


Inbound
FDA ESG Gateway
Industry
Outbound
eList
VALIDATE
Pass
REPOSITORY
PROCESS
Fail
ERROR MESSAGE
VALIDATION ERRORS
TRANSMIT
(NLM Web)
(Redacted Listing Files)
DailyMed website
FDA Web
(Redacted Listing Files)
FACTS@FDA website
DATA FILES
(Database Reports)
•Registration
• Listing
NDC Directory &
Establishments Websites

…three e-Files for Registration & Listing – SPL Format

- NDC Labeler Code Request
- Establishment Registration
- Content of labeling (CoL)/Listing

Order of Submissions

1. NDC Labeler Request (LCR) and Establishment Registration (ER) SPL
2. CoL/Listing SPL

- CoL/Listing validates against data submitted in NDC LCR and ER SPL

NDC Labeler Code

Administrative (Document Tracking Information)

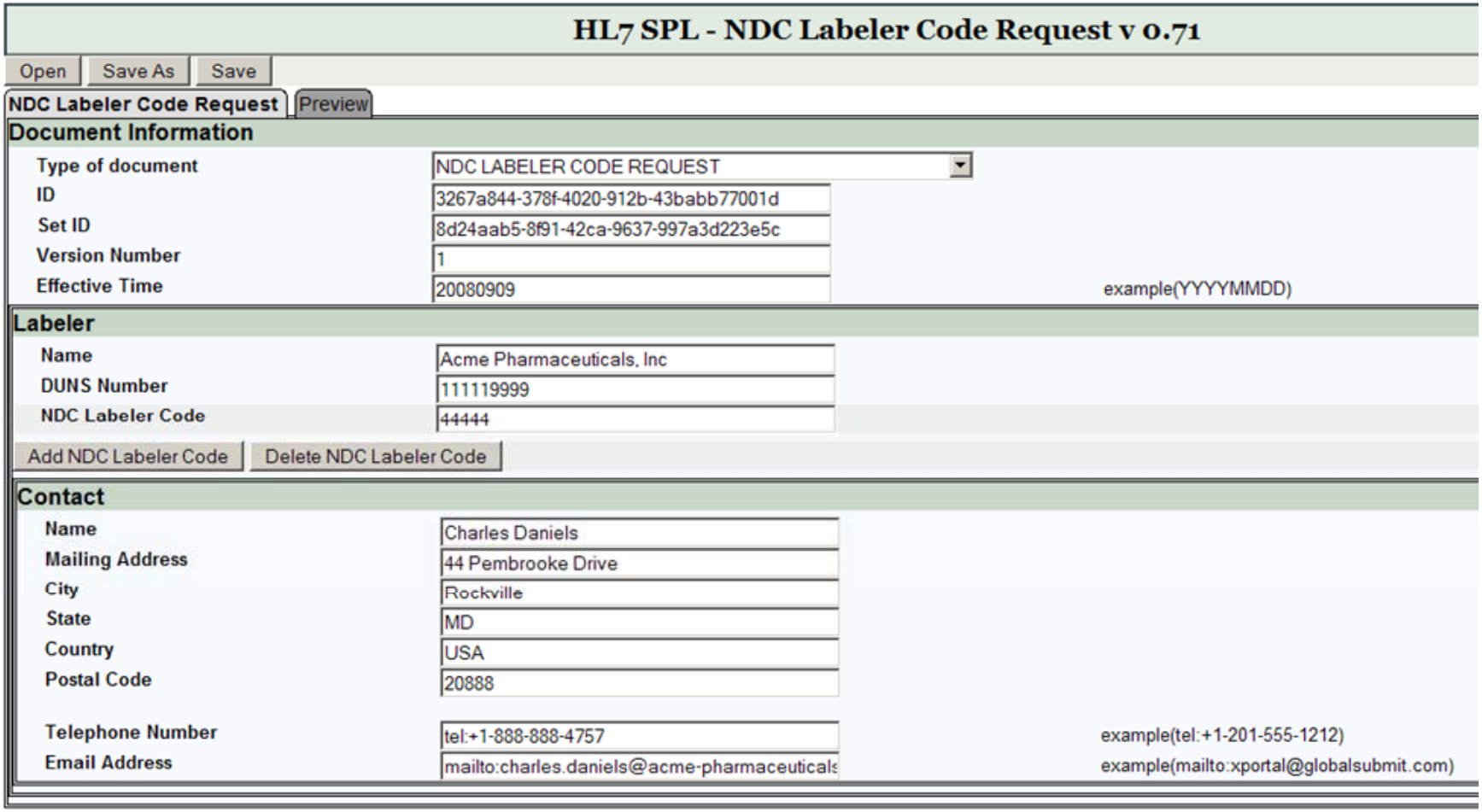
Basic information to identify the SPL document:

- **Document ID:** is a Globally Unique Identifier (GUID) and is unique for each version of the document. Letters used in a GUID are lower case.
- **Document Type:** The <code> is the LOINC code which provides information on the document type.
- **Effective Time:** provides a date reference to the SPL version including the year, month and day as yyyymmdd.
- **SetID:** is a GUID and is a unique identifier for the document that remains constant through all versions/revisions of the document.
- **Version number:** is an integer greater than zero that provides a sequence to the versions of the document.

NDC Labeler Code Request Data

- **Document Information**
  - Type of document
  - ID
  - Set ID
  - Version Number
  - Effective Time
- **Labeler**
  - Name
  - DUNS Number
  - NDC Labeler Code
- **Contact**
  - Name
  - Mailing Address
  - City
  - State
  - Country
  - Postal Code
  - Telephone Number
  - Email Address

NDC Labeler Code Request Xforms View



NDC Labeler Code Request SPL Document

Acme Pharmaceuticals, Inc

Product Information	
Product Type	NDC LABELER CODE REQUEST

Labeler – Acme Pharmaceuticals, Inc (111119999) **NDC Labeler Code:** 44444

Contact	Address	Telephone Number	Email Address
Charles Daniels	Address: 44 Pembrooke Drive City, State, Zip: Rockville , MD, 20888 Country: USA	+1-888-888-4757	charles.daniels@acme-pharmaceuticals.com

Revised: 09/2008

Acme Pharmaceuticals, Inc

NDC LCR SPL Scenarios

- **Requesting a new NDC Labeler Code**
  - Fill out the *NDC Labeler Code request* as described in sections 2.1 through 2.4 leaving the NDC Labeler Code field empty.
  - Requests for NDC Labeler Codes are individually evaluated prior to entry into the NDC System. The initial request will be automatically stopped because there is no NDC Labeler Code provided and is diverted to a FDA reviewer. Once the evaluation is completed, the response to the request is directed to the designated contact person.
  - Once the NDC Labeler Code is assigned, open the original SPL file and add the newly assigned NDC Labeler Code and resubmit the corrected file.
- **Initial electronic submission when NDC Labeler Code already assigned**
  - Fill out the *NDC Labeler Code request.* Only one NDC Labeler Code is included in an SPL file. In other words, use a different setId root for each NDC Labeler Code request.

NDC LCR SPL
Scenarios cont…

- **Correct SPL file validation error**
  - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.
- **Correct a mistake in an SPL file just submitted**
  - Open the SPL file, correct the mistake, and fill in a **new id root** and **new version number** with the **original setId root** and the appropriate effective time.

NDC LCR SPL
Scenarios cont…

- **Update the NDC Labeler Code information**
  - Open the previous SPL file and fill in the new information without changing the other existing information. Fill in a **new id root** and **new version number** with the **original setId root** and the appropriate effective time.
- **Requesting a second NDC Labeler Code**
  - Only one NDC Labeler Code is associated with each *NDC Labeler Code request*. If a second NDC Labeler Code is requested, fill out a separate SPL file with a **different setId root**. The labeler information and contact information is the same as the SPL file for the first NDC Labeler Code request

Notes

- Use NDC Labeler Code used in NDC Package Code (3-segment NDC)
- Submit NDC labeler codes that are used in NDCs associated with distributed products. (NDC on packaging)
- Only one NDC labeler code per NDC Labeler Code Request.
- NDC Labeler Code – Code should be identical to first segment of NDC (no leading zeros)

Establishment Registration

eRegistration of Drug Establishments

- Each Registrant (owner/operator firm) must submit one SPL file with registration information for all of its facilities (unlimited amount of domestic or foreign establishments per file)
- Updates of information require re-submission of the same updated SPL file (i.e., same setID; at least annually)
- Simplified SPL files are submitted for ‘No Change’ or ‘Out of Business’ notification

Registration Number

“FDA intends to use the Data Universal Numbering System (D-U-N-S®) as the registration number for the electronic system. Therefore, to facilitate and expedite processing of the SPL file, the registrant should submit their D-U-N-S® Number with the registration information. If the business entity does not submit a D-U-N-S® Number with its submission, FDA intends to make arrangements for obtaining a D-U-N-S® Number for that entity. An explanation of the D-U-N-S® Number and how to obtain one is described in section IV.B of this document.”

- ***from final “eList” guidance document.

Administrative (Document Tracking Information)

Basic information to identify the SPL document:

- **Document ID:** is a Globally Unique Identifier (GUID) and is unique for each version of the document. Letters used in a GUID are lower case.
- **Document Type:** The <code> is the LOINC code which provides information on the document type.
- **Effective Time:** provides a date reference to the SPL version including the year, month and day as yyyymmdd.
- **SetID:** is a GUID and is a unique identifier for the document that remains constant through all versions/revisions of the document.
- **Version number:** is an integer greater than zero that provides a sequence to the versions of the document.

Establishment Registration Data

- **Document Information**
  - Type of Document
  - ID
  - Set ID
  - Version Number
  - Effective Time
- **Registrant**
  - Name
  - DUNS Number
- **Registrant Contact**
  - Name
  - Mailing Address
  - City
  - State
  - Country
  - Postal Code
  - Telephone Number
  - Email Address

Establishment Registration Data (cont…)

- **Establishment**
  - Name
  - DUNS Number
  - FEI
  - Street Address
  - City
  - State
  - Country
  - Postal Code
  - Type of Operation(s)
- **Establishment Contact**
  - Name
  - Mailing Address
  - City
  - State
  - Country
  - Postal Code
  - Telephone Number
  - Email Address

Establishment Registration Data (cont…)

- **US Agent**
  - Name
  - DUNS number
  - Telephone Number
  - Email Address
- **Importer (if applicable)**
  - Name
  - DUNS number
  - Telephone Number
  - Email Address

Types of Operations

- Acceptable types of operations for establishments:
  - API Manufacturer
  - ANALYSIS
  - MANUFACTURE
  - RECOVERY
  - RELABEL
  - REPACK
- Unacceptable types of operations for establishments:
  - IMPORT
  - UNITED STATES AGENT

(as of February 2009)

Importer

– *…under section 510(i)(1)(A) of the Act, the name of each importer that is known to the establishment (this means each U.S. company or individual in the United States that is an owner, consignee, or recipient, of the foreign establishment's drug, that is imported into the United States. An importer does not include the consumer or patient who ultimately purchases, receives, or is administered the drug, unless the foreign establishment ships the drug directly to the consumer or patient.); and the name of each person who imports or offers for import (this means the name of each agent, broker, or other entity, other than a carrier, that the foreign drug establishment uses to facilitate the import of their drug into the United States).*

(from "*Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing")*

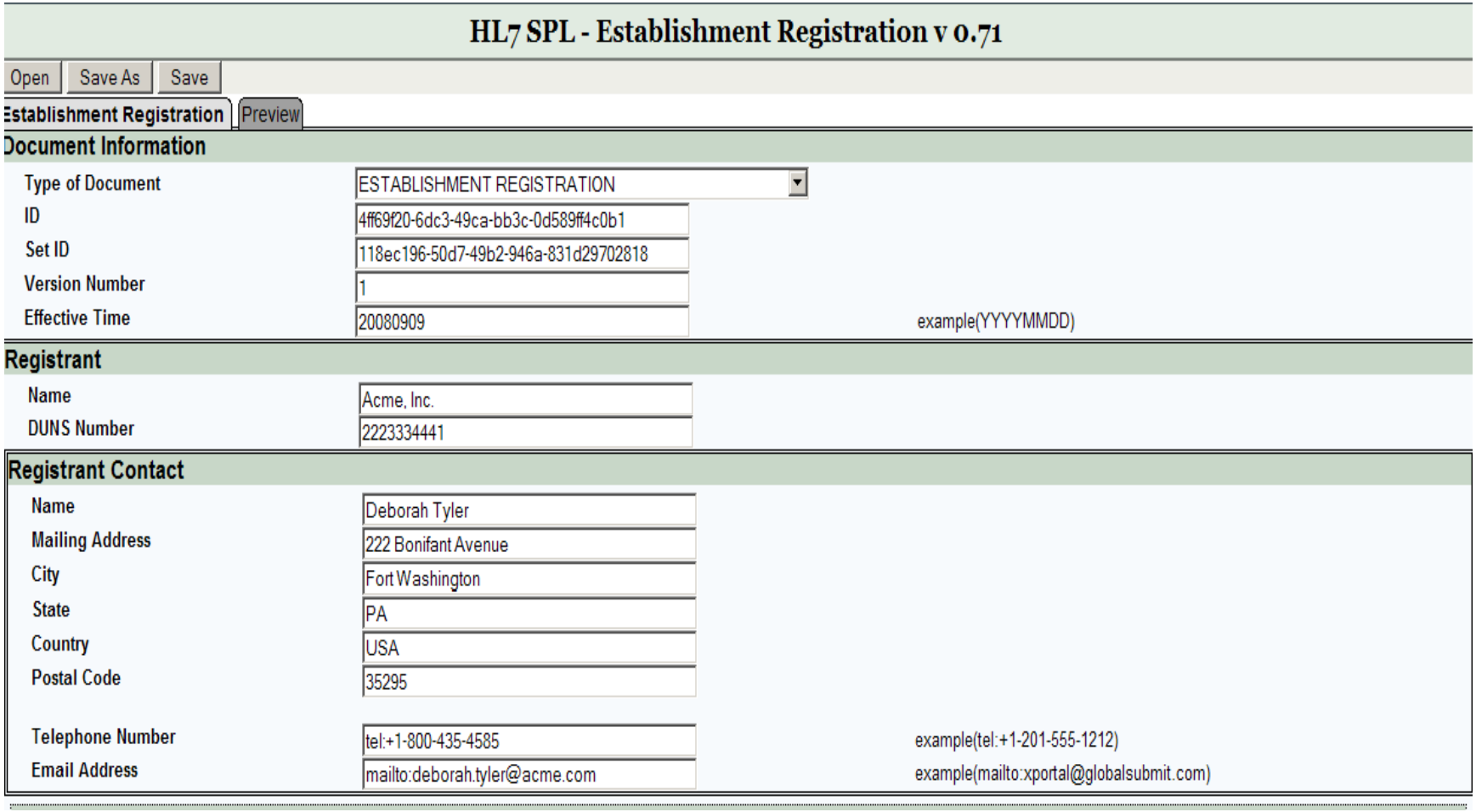
Importer cont…

- May or may not be an importer for each foreign establishment

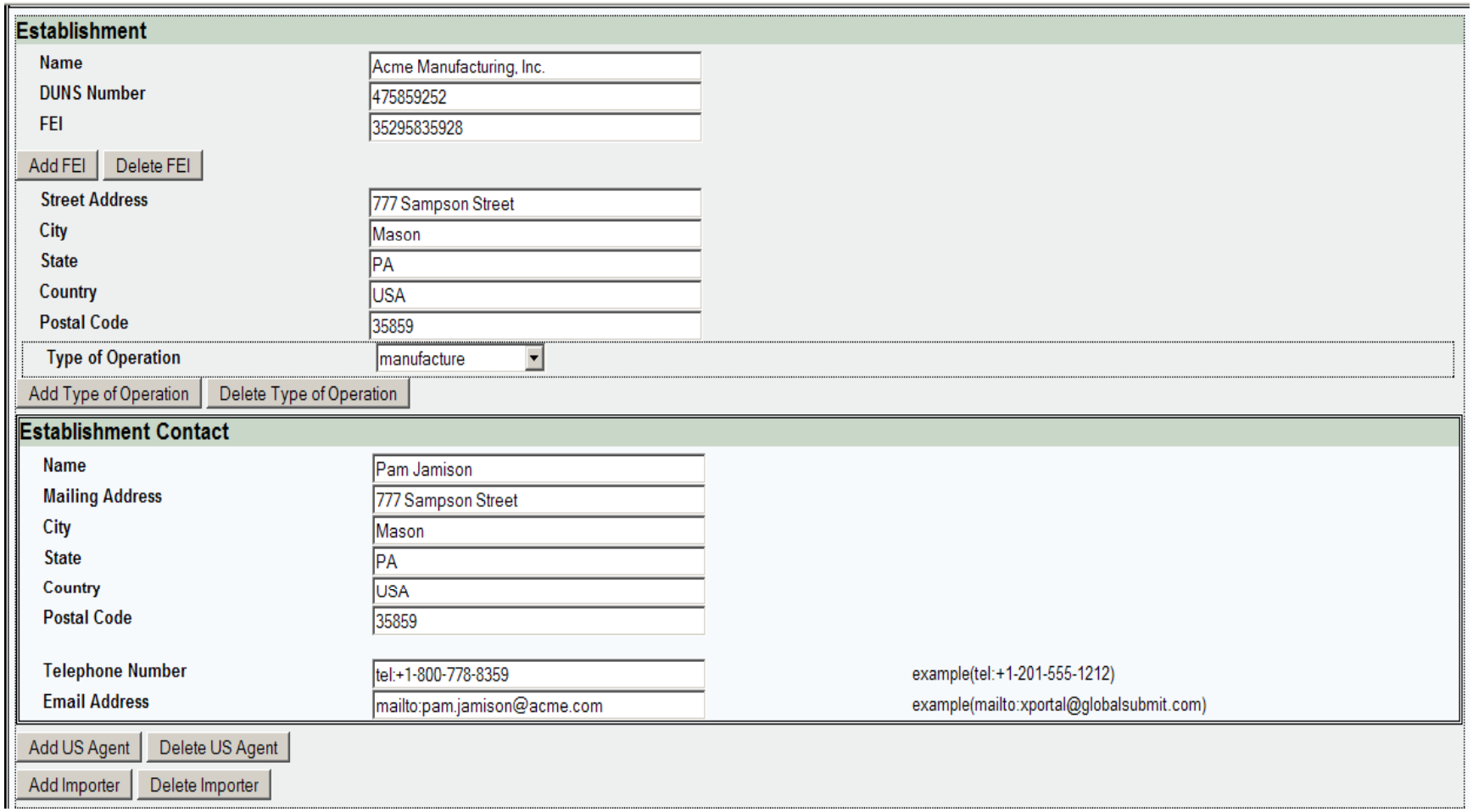
US Agent

- Submission of information about US Agent replaces the paper letter
- Each foreign establishment in an ER SPL should have a US agent

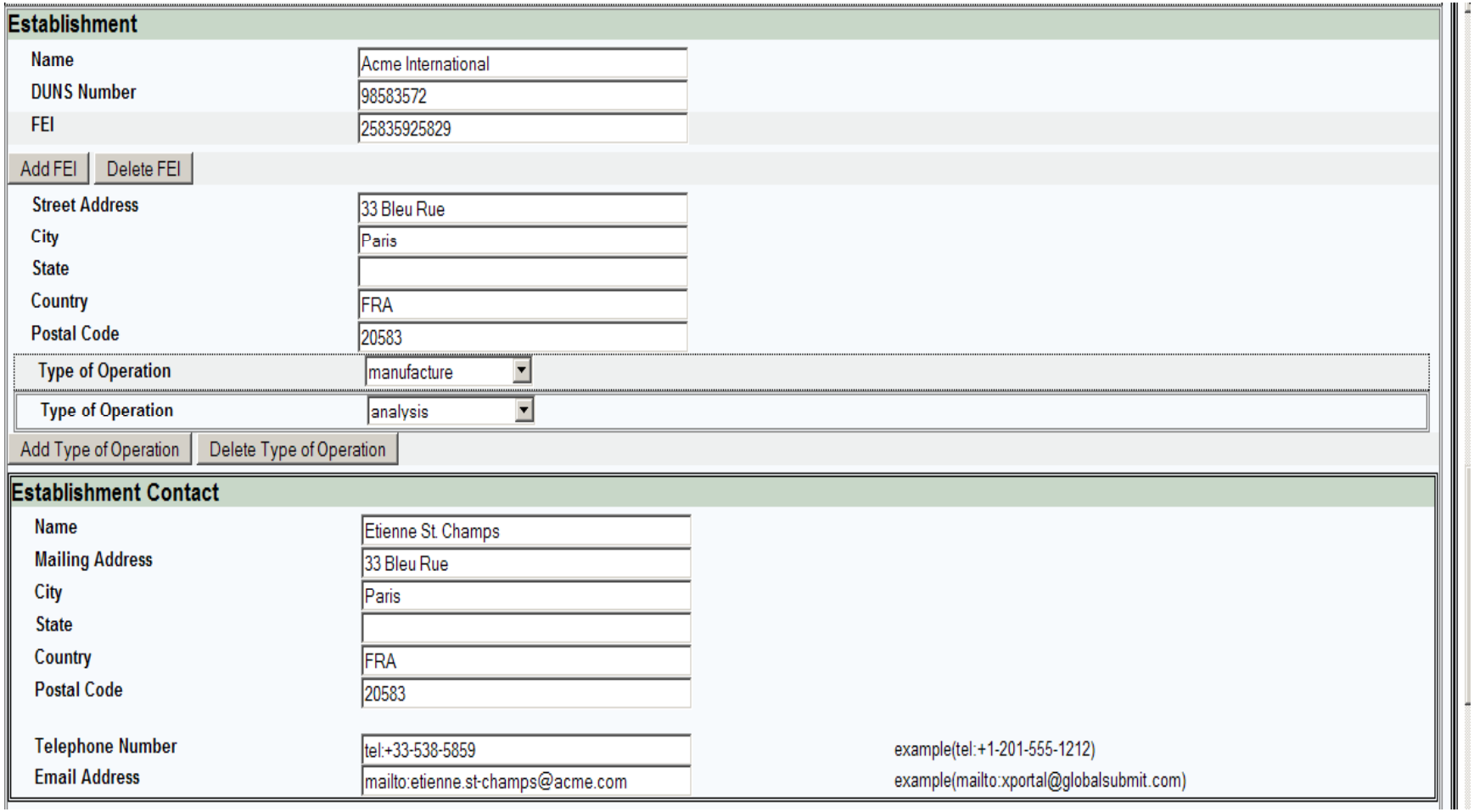
Establishment Registration SPL Xforms



Establishment Registration
SPL Xforms cont…



Establishment Registration
SPL Xforms cont…



Establishment Registration SPL Document

Product Information	
Product Type	ESTABLISHMENT REGISTRATION

Registrant – Acme, Inc. (2223334441)

Contact	Address	Telephone Number	Email Address
Deborah Tyler	Address: 222 Bonifant Avenue City, State, Zip: Fort Washington, PA, 35295 Country: USA	+1-800-435-4585	deborah.tyler@acme.com

Establishment

Name	Address	ID/FEI	Operations
Acme Manufacturing, Inc.	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	475859252	manufacture

Contact	Address	Telephone Number	Email Address
Pam Jamison	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	+1-800-778-8359	pam.jamison@acme.com

Establishment Registration SPL Document cont…

Establishment			
Name	**Address**	**ID/FEI**	**Operations**
Acme International	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	98583572	manufacture, analysis
Contact	**Address**	**Telephone Number**	**Email Address**
Etienne St. Champs	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	+33-538-5859	etienne.st-champs@acme.com
US Agent (ID)	**Address**	**Telephone Number**	**Email Address**
Acme USA (359582424)		+1-800-999-5542	jacob.goodman@acme.com
Importer (ID)	**Address**	**Telephone Number**	**Email Address**
Franklin Imports (252597793)		+1-888-444-5835	paula.johansen@franklin.com

Revised: 09/2008

Electronically Registered Drug Establishments

- Example of actual Drug Firms Annual Registration Status Website Display

Pfizer approved use of their name in presentation

Website address: **http://www.fda.gov/cder/dfars/docs/querydrls.htm**

Pfizer Ireland Pharmaceuticals	3003047405	300348730	Loughbeg Ringaskiddy, County Cork IRL	2008
Pfizer Ireland Pharmaceuticals	3003348730	986948909	Pottery Road, Dun Laoghaire Dublin IRL	2008
Pfizer Ireland Pharmaceuticals	3003382089	989811526	Little Island Cork IRL	2008
Pfizer Ireland Pharmaceuticals	3003882524	896090987	Ringaskiddy API Plant Cork IRL	2008
Pfizer Italia S.r.l.	3003637173	431227388	63046 Marino Del Tronto Ascoli Piceno (AP) ITA	2008
Pfizer Japan Inc	1000172081	705466860	Aza 5-Gochi, 2-banchi, Taketoyo-cho Chita-gun, Aichi-Ken Nagoya 470-2393 JPN	2008
Pfizer Laboratories Div Pfizer	1819508	006050075	100 Pfizer Drive Terre Haute IN	2008

Initial Establishment Registration Submission

- Initial electronic submission for establishments already registered
  - Registrants include information for **all** of their establishments in one *Establishment Registration* SPL file. Each establishment is in only one **ER** SPL file.
  - If establishment is included in another **ER** SPL w/different setID, SPL will FAIL validation

Electronically Requesting an FEI Number

- Request an FEI Number using SPL
  - Include all establishments in one file.
  - Add the FEI numbers for all of the previously registered establishments (registered in paper or electronic format)
  - Include information for new establishment (leave FEI number field empty)
  - Request for FEI will be routed to appropriate FDA team

Correcting an ER SPL with Validation Error

- Correct SPL file validation error

  – If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.

  SPL file **never** made it into the FDA eList system

Correcting Mistake in Valid SPL Just Submitted

- Correct a mistake in an SPL file just submitted

  – Open the SPL file, correct the mistake,
  – Use
    - **new id root**
    - **new version number**
    - **original setId root**
    - appropriate effective time.

***SPL file was **valid** and loaded into FDA eList system

Updating an ER SPL

- Update information for an **electronically** registered establishment
- Update anytime during year **or** for annual registration

  - Open the previous SPL file and fill in the new information **without changing the other existing information.**
  - Use
    - **new id root**
    - **new version number**
    - **original setId root**
    - appropriate effective time.

Adding a New Establishment

- Add a new establishment to your ER SPL file:
  - Open the previous SPL file
  - Fill in the information on a new establishment **without changing the information on the other establishments.**
  - Use
    - **new** id root
    - **new** version number
    - **original** setId root
    - appropriate effective time.

Removing an Establishment

- Remove a previously **electronically** registered establishment

  - Open the previous ER SPL file, **without changing the existing information on the other establishments,** and remove the specific establishment information.
  - Use
    - **new** id root
    - **new** version number
    - **original** setId of your ER SPL
    - appropriate effective time.

Establishment Re-Registration No Changes

- Simple process for annually re-registering establishments which have no changes
- Must have already **electronically** registered the establishments once.
- Submit No Change Notification SPL

Establishment Re-Registration No Changes

- No changes to registration information
  - Each year when the information is updated, if there is no change:
    - Create an SPL file with the *document type* **No change notification** with a **new** id root and **new** version number with the **original** setId and the appropriate effective time.
    - Registrant and establishment information is **not** included with an SPL file with the *document type* **No change notification**.

Establishment
No Change Notification SPL

Product Information	
Product Type	NO CHANGE NOTIFICATION

Revised: 04/2008

Going Out of Business?

- Registrant goes out of business
  - If the registrant goes out of business, create an SPL file with the *document type* **Out of business notification** using a **new** id root and **new** version number with the **original** setId and the appropriate effective time. Registrant and establishment information is not included with an SPL file with the *document type* **Out of business notification**.
  - Applicable for registrants who electronically registered establishments

Establishment
Out of Business Notification

Product Information	
Product Type	OUT OF BUSINESS NOTIFICATION

Revised: 09/2008

Certified 2656 Paper Form?

- No certified paper forms for e-registered establishments
- Check DFARS website for electronically registered establishments

ER SPL Notes

- In eReg & eList system for current relationship (for paper) between labeler code & establishment is non-existent
- Entering provinces - The province, "BC", goes in the <state> tag.
- No limit to amount of importers
- No limit to number of establishments in one SPL
- Use “USA” as the country code for Puerto Rico

Common Errors in Establishment Registration SPL

- Incorrect telephone format
- Wrong e-mail format
- Including registrant and establishment information & coding in a “No Change Notification” SPL document.
- Incorrect ISO-3166 Country Code
- Mismatch for DUNS Number & Establishment name
- Files uploaded to Gateway without a folder

Content of Labeling

- Sections and Subsections
- Symbols and Characters
- Font Effects
- Footnotes
- Lists
- Tables
- Images

CoL & eList Data

- Content of labeling and product data elements are included in ONE document
- Keeps content of labeling and data elements for listing in one document

Approved Rx Drugs - Fulfill Two Regulatory Requirements

- Companies with application products regulated by CBER & CDER can fulfill two regulatory requirements using SPL
  - Electronic Labeling Rule – Prescription drug products
  - Drug listing (electronically)

CoL for API, Medical Gas, Homeopathic

- Add Section - PACKAGE LABEL.PRINCIPAL DISPLAY PANEL
- Include text from principal display panel
- Insert image of carton or container

Drug Listing/CoL
SPL Document

MIRACLE XR - good drug tablet
Acme Pharmaceuticals, Inc

Miracle XR

Description

Description text placeholder

Listing

Data Elements

- Data Element
  - A basic unit of identifiable and definable information. It occupies the space provided by a field in a record or a block on a form, and has an identifying name and value or values for expressing a specific fact. A data element is defined by its name, description, source, length, structure, and format.

- Product Data Elements
  - Formerly known as Drug Listing Data Elements
  - Drug listing data elements are **metadata** displayed via SPL stylesheet for purpose of review
  - Computer friendly information - product information which is tagged that permits search of key information.
  - Information system friendly – Medication information in computer readable form - Easily imported into information systems

Terminology

- **Standard terminology** is used for SPL product data elements. Information about the controlled vocabulary for SPL is available at http://www.fda.gov/oc/datacouncil/spl.html under “SPL Terminology.”

Terminology

- Product
  - Proprietary and nonproprietary name and code
- Description
  - Ingredients
    - Active and inactive ingredient and active moiety name and code (Unique Ingredient Identifier (UNII) from FDA Substance Registration System (SRS)
    - Active and inactive ingredient strength (National Cancer Institute (NCI) Thesaurus, Unified Codes for Units of Measure (UCUM)
    - Dosage form (NCI Thesaurus)
    - Appearance (imprint, color, shape, size, score, coating, symbol) (NCI Thesaurus and HL7)
    - Route of administration (NCI Thesaurus)
    - DEA schedule (NCI Thesaurus)
- Packaging
  - Package type (NCI Thesaurus), quantity and packaging code

Ingredients (Terminology)

- Ingredient name (substance name)
  - SRS preferred name of ingredient (active and inactive)
  - Source – FDA SRS
- Ingredient code (substance code)
  - Unique Ingredient Identifier
  - Source –FDA SRS
- Active moiety name (active moiety entity name)
  - active ingredient or portion of active ingredient without counter ion (if relevant)
  - Source –FDA SRS
- Active moiety code (active moiety code)
  - Unique Ingredient Identifier (UNII)
  - Source –FDA SRS

Unique Ingredient Identifier (UNII)

- Joint FDA/USP Substance Registration System (SRS) to support health information technology initiatives by generating unique ingredient identifiers (UNIIs) for substances in drugs, biologics, foods, and devices.

- Non-proprietary, free, unique, unambiguous, alphanumeric identifier based on a substance's molecular structure and/or descriptive information

UNII Assignment

- UNII, an ingredient must be a ‘substance’, which is defined as “Any physical material that has a discrete existence, irrespective of origin.” **Products will not be assigned a UNII.**
- More information about UNII codes and the SRS is available at: http://www.fda.gov/oc/datacouncil/SRS.htm
- Missing UNIIs or other terms? – Send request to spl@fda.hhs.gov

Listing Data

- **Drug Listing**
- **Labeler**
  - Name
  - DUNS Number
- **Registrant**
  - Name
  - DUNS number
  - Mark as Confidential
- **Establishment**
  - Name
  - DUNS number
  - Mark as Confidential
  - Type of operation

Listing Data cont…

- **Product Information**
  - Proprietary Name
  - Proprietary Name Suffix
  - Non-Proprietary Name
  - NDC Product Code
  - Dosage Form
  - Source NDC Product Code (if applicable)
  - DEA Schedule (if applicable)
  - Route(s) of Administration
- **Active Ingredient**
  - Name(s)
  - Unique Ingredient Identifier(s) (UNII)
  - Strength
- **Reference Drug**
  - Name
  - Unique Ingredient Identifier (UNII)

Listing Data cont…

- **Active Moiety**
  - Name(s)
  - Unique Ingredient Identifier(s) (UNII)
  - Basis of Strength
- **Inactive Ingredient**
  - Name(s)
  - Unique Ingredient Identifier(s) (UNII)
  - Mark as Confidential
  - Strength
- **Flavor**
  - Name(s)
    - Original Text

Listing Data cont…

- **Imprint Information**
  - Color(s)
    - Original Text
  - Score
  - Shape
    - Original Text
  - Imprint Code
  - Size
  - Size Unit

Listing Data cont…

- **Packaging**
  - **Immediate packaging**
    - NDC Package Code (10 digit)
    - Quantity
    - Package Type
  - **Outer package**
    - NDC Package Code (10 digit)
    - Quantity
    - Package Type

Listing Data cont…

- **Marketing Date**
  - Product Status
  - Start Marketing Date
  - End Marketing Date (if applicable)
- **Marketing Category**
  - Marketing Category
  - Application or citation number
  - Application or citation number code system

Registrant, Labeler & Establishment Info in Listing File

Labeler Information in Listing SPL

- Name
- DUNS number

Labeler Information in Listing SPL

- The labeler uses their assigned NDC Labeler Code to create the NDC for the drug product. The information includes the name and DUNS Number.

Labeler – Labeler name here (labeler DUNS Number here)

Registrant Information in Listing SPL

- Name
- DUNS number
- Mark as Confidential, if applicable (check box)

Registrant Listing for PLD

- The registrant is included **if** they are listing a drug made for a private label distributor. The information includes the name and DUNS Number.
- Otherwise, do **not** complete this field

Establishment Information in Listing SPL

- Name
- DUNS number
- Mark as Confidential (check box)
- Type(s) of operations

Establishment			
Name	**Address**	**ID/FEI**	**Operations**
Establishment name here		Establishment DUNS Number here	manufacture

Establishment			
Name	**Address**	**ID/FEI**	**Operations**
Establishment name 2 here		establishment DUNS Number here	manufacture

Revised: 02/2009

Labeler name here

Establishments in Listing SPL

- The establishments are the entities involved in the manufacturing or processing the drug product.
- Enter one or more establishments.
- The information includes the name, DUNS Number and types of operations.
  - Types of operations for an establishment in the listing SPL should also be one of the types of operations for that establishment in Establishment Registration SPL.

Listing a API w/Finished Dosage Form Product

- Inclusion of the establishment for the API in the SPL file for the finished dosage form product. This electronically lists the API.
- Importation of API
  - The NDC for the finished product could be used for import purposes.

Drug Listing: Establishment Information for API Manufacturers

- Establishment information for manufacturers of your **active pharmaceutical ingredient (API)** used in your products
  - Recommendation that this information **should** be included in your **electronic drug listing document** (SPL file)

Drug Listing: Establishment Information for Inactive Ingredient Manufacturers

- Establishment information for manufacturers of **inactive ingredients** in your listed products – does **NOT** need to be included in your **electronic drug listing SPL.**

Product Data Elements

Product Data Elements

- Product
  - Product names
- Description
  - Ingredients
  - Strength
  - Dosage form
  - Route of administration
  - Controlled substance code
  - Appearance
- How supplied
  - Packaged product

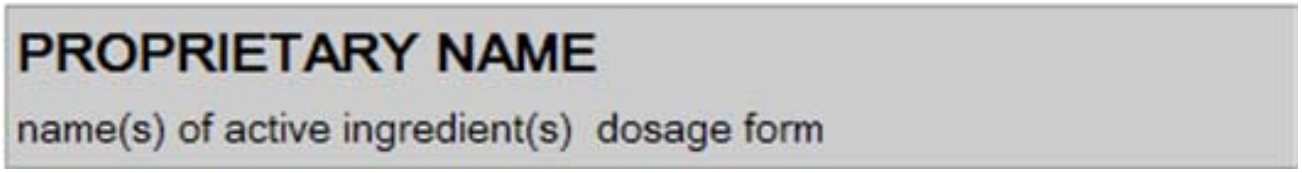
Only terms in the controlled terminology are allowed.

Product Name and NDC Product Code

- The proprietary/trade and ingredient name data elements only include the name and do not include any additional qualifiers such as trademark symbols, route of administration, or dosage forms. (SPL R4 only: Suffix element may contain “XL” “ER”)
- The NDC product code in SPL documents is comprised of the first two segments of the NDC

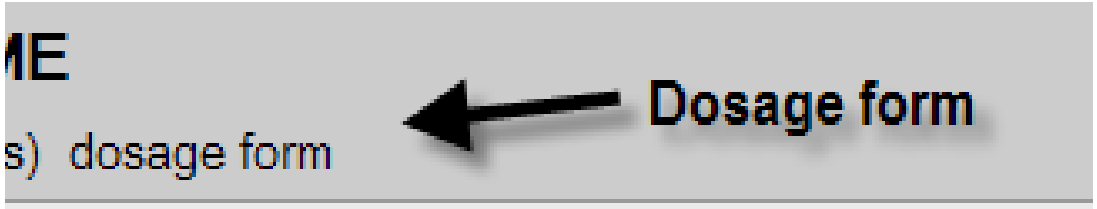
Proprietary name: “PROPRIETARY NAME”

Name of active ingredient: “name(s) of active ingredient(s)”



Dosage Form

- The dosage form is the name for the drug dosage form taken from the controlled terminology. Only terms in the controlled terminology are allowed.



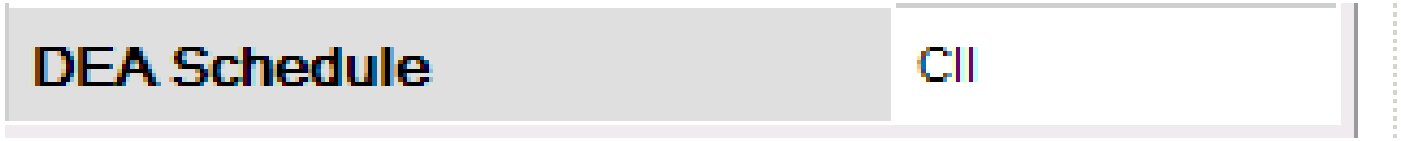
Route of Administration

- Labeled route of administration is the name of the route of administration taken from the controlled terminology. Only terms in the controlled terminology are allowed. A product may have one or more route of administration.

Route Of Administration	SUBCUTANEOUS, INTRAMUSCULAR

Controlled Substance Code

- The abuse potential category to which an active ingredient, or combination of active ingredients, is assigned, as regulated by both the United States Drug Enforcement Administration (DEA) and the United States Food and Drug Administration. The controlled schedule may be found near the title of the label or in the narrative portion of the label.



Active Ingredient

- The active ingredient includes the active ingredient name and identifier (Unique Ingredient Identifier (UNII) , strength, and the active moiety names and identifier (UNII). All active ingredients have at least one active moiety (in some cases two active moieties). Names of active ingredient **should not include designations such as USP or NF**. The name is taken from controlled terminology. Only terms in the controlled terminology are allowed. For ingredients, the controlled terminology is found in the FDA Substance Registration System/Ingredient Dictionary (SRS/ID). The **UNII is linked to the name** of the ingredient.

- Active moieties - more than one active moiety can be included for each active ingredient.

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
name(s) of active ingredient(s) (name of active moiety number 1 and name of active moiety number 2)	name(s) of active ingredient(s)	50 mg

Inactive Ingredient

- The inactive ingredient includes the ingredient name, identifier, and strength. The drug listing data elements may include the inactive ingredients listed in the labeling, however, products (proprietary mixtures of ingredients such as coatings and inks), ambiguous ingredients (such as flavors and fragrances) or other “ingredients” that don’t qualify for a UNII are not included. Only the ingredient name is included in the drug listing data elements. The inactive ingredient strength is included if it is in the label.
- Mark as confidential inactive ingredients. (trade secret ingredients or other confidential ingredients not in labeling)

Inactive Ingredients	
Ingredient Name	Strength
name of inactive ingredient	

Strength of Ingredient
SPL Release Four

- SPL R4 documents will allow companies to **designate strength based on the active ingredient, active moiety or a reference drug.**

  Example of non-solid dosage form

  Numerator: **10 mg**
  Denominator: **1 mL**

  Example of solid dosage form

  Numerator: **10 mg**
  Denominator: None

Strength cont…

Product	Numerator unit	Denominator unit
Oral solid	Weight	Each
Oral liquid	Weight	Volume
Oral powder for reconstitution with a known volume	Weight	Volume
Oral powder for reconstitution with a variable volume	Weight	Each
Suppository	Weight	Each
Injection liquid	Weight	Volume
Injection powder for reconstitution with a known volume	Weight	Volume
Injection powder for reconstitution with a variable volume	Weight	Each
Inhaler powder	Weight	Each
Inhaler liquid	Volume	Each
Inhaler blister	Weight	Each
Topical cream or ointment	Weight	Weight
Topical gel or lotion	Weight	Volume
Transdermal patch	Weight	Time
Bulk liquid	Weight	Volume
Bulk solid	Weight	Weight

Color

- The color of the solid or liquids dosage form is the **predominant color or approximate color**, not the specification for the name in the labeling. There can be **more than one color** such as the color of the sides of a tablet and halves of capsules. **Imprints and bands on capsules are not included in the color.**

- There are **twelve SPL colors** –black, gray, white, red, purple, pink, green, yellow, orange, brown, blue, turquoise. The name is taken from these terms and only terms in the controlled terminology are allowed. **An original text field may be used to more specifically describe colors.** However, applicant should not include “cap” or “body” in the description of color. (e.g. purple cap, yellow body)

Color	WHITE (white to off-white)

Shape

- 2-D representation of the outside perimeter of an oral solid dosage form
- **Includes rounding of corners; excludes embossing, scoring, debossing, internal cutouts**
- **19 SPL shapes**: bullet, capsule, clover, diamond, double circle, freeform, gear, heptagon, hexagon, octagon, oval, pentagon, rectangle, round, semi circle, square, tear, trapezoid, triangle.
- The name is taken from these terms and only terms in the controlled terminology are allowed. An **original text (free text) field is available to specifically describe a shape.**

Shape	OVAL (capsule-shaped)

Size

- The size is the longest single dimension for an oral solid dosage form; Length for rectangle, diameter for circle. **Millimeters rounded to the nearest millimeter**

Size	12mm

Score

- The score is the number of equal pieces that an oral, solid, dosage form can be divided using the score line(s).

Description	Value
No score	No score
Bisect (two equal pieces)	2 pieces
Trisect (three equal pieces)	3 pieces
Quadrisect (four equal pieces)	4 pieces
Unequal pieces	

Imprint Code

- The imprint code is the alphanumeric text on solid dosage forms. **Includes embossed, debossed, engraved, and printed; Excludes trademark letters, marks, symbols, internal and external cutouts**
- Start top left with **semi-colon** to show separation between words or line divides

Imprint Code	XXX;1234

Marketing Category

- Select the appropriate marketing category for the drug product.

Marketing Information	
Marketing Category	
NDA	

Application or Citation Number

- Application numbers include the character application abbreviation and the numbers without spaces or dashes (e.g., NDA123456). Monograph citations include the number of the regulatory part (e.g., part234).

Application Number or Monograph Citation
NDA000000

Marketing Status & Date

- The marketing status describes the activity of the product
- SPL file is removed from the public repository. The expiration date of the last lot released to the marketplace provides an estimate of the date when the SPL file is removed.

Marketing Status & Dates

- Status of product
  - **Active:** on the market
  - **Completed**: when marketing is done the drug is no longer going to be available on the market.
  - Active or completed timestamp: effectiveTime value.
- Low value
  - Time on the market
  - Determines release of CoL/Listing SPL to public
- High value
  - Time off the market (e.g. the expiration date of the last lot released to the market.)

Marketing Start Date	Marketing End Date
01/24/2005	

Packaging

Single level of packaging

PACKAGING			
#	NDC	Package Description	Multilevel Packaging
1	0009-3776-01	42.5 GRAM In 1 TUBE, WITH APPLICATOR	None

Multi-level of packaging

PACKAGING			
#	NDC	Package Description	Multilevel Packaging
1	63481-445-01	1 VIAL In 1 BOX	contains a VIAL, MULTI-DOSE
1		10 MILLILITER In 1 VIAL, MULTI-DOSE	This package is contained within the BOX (63481-445-01)

PROPRIETARY NAME - name(s) of active ingredient(s) dosage form
Labeler

SPL Release Four Drug Listing Data Elements (Example w/Nonsolid Oral Dosage Form) - Revised Stylesheet

PROPRIETARY NAME

name(s) of active ingredient(s) dosage form

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**NDC Product Code (Source)**	0001-0001
Route of Administration	ORAL	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
name(s) of active ingredient(s) (name of active moiety number 1 and name of active moiety number 2)	name(s) of active ingredient(s)	50 mg

Inactive Ingredients

Ingredient Name	Strength
name of inactive ingredient	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	NDC	Package Description	Multilevel Packaging
1	0001-0001-02	5 mL In 1 VIAL	None

Drug Listing/CoL
SPL Document

MIRACLE XR

good drug tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**NDC Product Code (Source)**	44444-333
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Good Drug (active moiety)	Good Drug	25 mg

Inactive Ingredients	
Ingredient Name	**Strength**
Inactive ingredient one	

Product Characteristics			
Color	yellow (yellow-orange)	**Score**	2 pieces
Shape	ROUND (ROUND)	**Size**	18mm
Flavor	CITRUS (citrus-flavored)	**Imprint Code**	AC;25;mg
Contains			

Packaging			
#	**NDC**	**Package Description**	**Multilevel Packaging**
1	44444-333-10	1 BOTTLE In 1 CARTON	contains a BOTTLE (44444-333-50)
1	44444-333-50	50 TABLET In 1 BOTTLE	This package is contained within the CARTON (44444-333-10)

Drug Listing/CoL
SPL Document

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**
NDA	NDA024380	04/13/2007	

Labeler - Acme Pharmaceuticals, Inc (111119999)

Establishment			
Name	**Address**	**ID/FEI**	**Operations**
Acme Manufacturing, Inc.		475859252	manufacture

Establishment			
Name	**Address**	**ID/FEI**	**Operations**
Acme International		98583572	manufacture, analysis

Revised: 09/2009

Acme Pharmaceuticals, Inc

Common Errors in eList Program Submissions

- XML file sent not enclosed within a folder
- XML file name is not the document ID root name
- Spaces before telephone number
- Hyphens in DUNS number
- SPL file created with outdated SPL xforms
- Two-character country code used in place of three-character country code (ISO-3166 - ftp://ftp1.nci.nih.gov/pub/cacore/EVS/FDA/SPL/)

Delisting Products in Paper

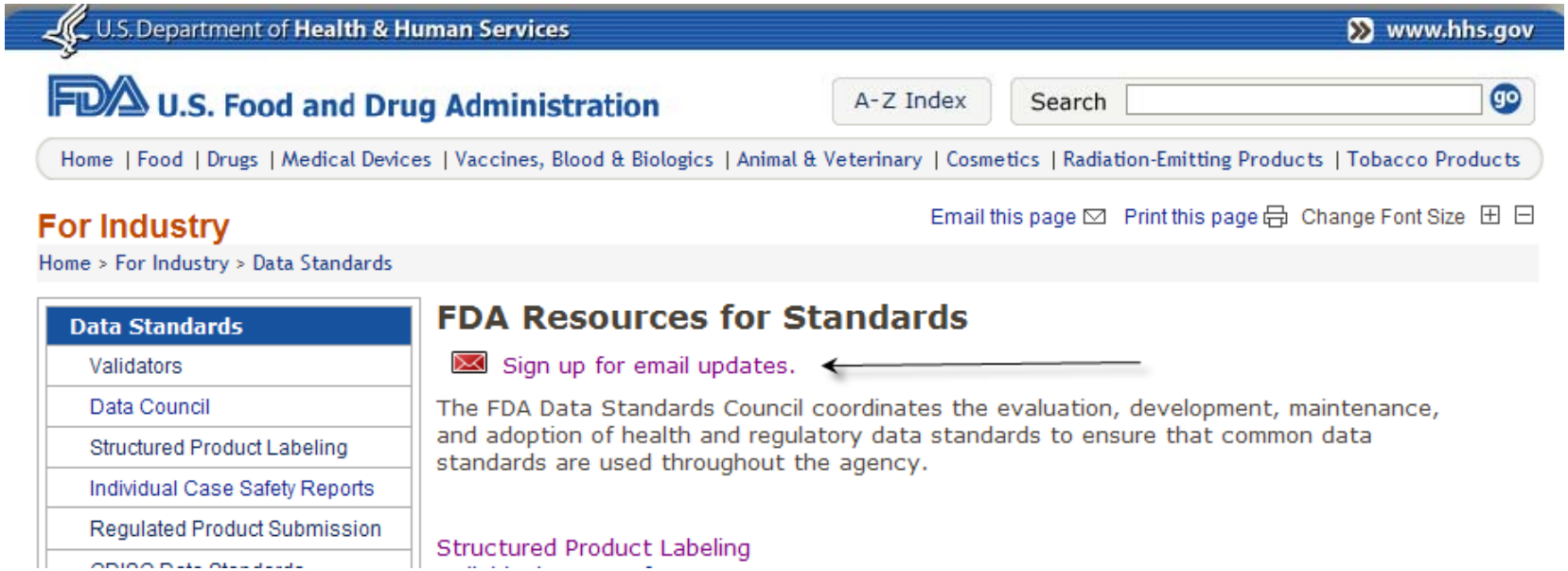
- Lots of discontinued products to delist?
- Contact FDA at spl@fda.hhs.gov.

SPL-related Technical Assistance/Questions

- SPL e-mail account (spl@fda.hhs.gov)

Stay Informed

- Join FDA Data Standards Council listserv
- http://www.fda.gov/ForIndustry/DataStandards/default.htm



Questions

Thank you!