

Structured Product Labeling (SPL) Implementation Guide with Validation Procedures

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry – Electronic Submission of Lot Distribution Reports
Guidance to industry - Providing Regulatory Submissions in Electronic Format – Content of Labeling
Guidance for Industry - Providing Regulatory Submissions in Electronic Format – Drug Establishment
Registration and Drug Listing
Guidance for Industry - SPL Standard for Content of Labeling Technical Questions and Answers
Guidance for Industry - Indexing Structured Product Labeling (Final)
Guidance for Industry: Self-Identification of Generic Drug Facilities, Sites, and Organizations
Guidance for Industry - Electronic Drug Product Reporting for Human Drug Compounding Outsourcing
Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act
Guidance for Industry - Registration of Human Drug Compounding Outsourcing Facilities Under Section
503B of the FD&C Act
Guidance for Industry - DSCSA Implementation: Annual Reporting by Prescription Drug Wholesale
Distributors and Third-Party Logistics
Guidance for Industry - Compounding Animal Drugs from Bulk Drug Substances
Guidance for Industry - Providing Regulatory Submissions in Electronic Format — Content of the Risk
Evaluation and Mitigation Strategies Document Using Structured Product Labeling
Guidance for Industry - Format and Content of a REMS Document
Registration and Listing of Cosmetic Product Facilities and Products: Guidance for Industry

For questions regarding these technical specifications document, contact spl@fda.hhs.gov.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
Center for Drug Evaluation and Research (CDER)
Center for Veterinary Medicine (CVM)
Office of Chief Scientist (OCS)**

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Structured Product Labeling (SPL) Implementation Guide with Validation Procedures

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1 Introduction

Structured Product Labeling (SPL) is a Health Level Seven (HL7) standard based on Clinical Document Architecture and HL7 Reference Information Model (RIM) accredited by the American National Standards Institute (ANSI) for the exchange of product information. Structured Product Labeling documents include a header and body. The header includes information about the document such as the type of product, author and versioning. The body of the document includes product information in both structured text and data element formats. The United States Food and Drug Administration (FDA) uses SPL documents to exchange information covering a growing number of product related topics.

This document provides technical conformance criteria for SPL documents used by FDA. This combines the information previously covered in separate implementation guide and validation procedures documents.* A link to the latest SPL schema and controlled terminology used in SPL and other technical documents may be found on the FDA Data Standards Council web site at: <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>.

1.1 Organization

This document is divided into three parts. The first part of this document describes the technical conformance criteria that are applicable to header and body of the SPL document Independent of the information being exchanged. The second part of the document describes product related technical conformance criteria. The third part describes the technical conformance criteria applicable to the type of information being exchanged.

1.2 Validation Procedures

Detailed validation procedures are presented at the end of most sub-sections and are clearly marked with the heading “Validation Procedures.” These procedures can be used by humans as check-lists to verify if their submission is correct. The validation procedures are written specific and operational so that they may be checked by systems processing SPL documents. Each validation procedure has a unique paragraph number. These paragraph numbers are generally stable over time, but they may change between versions of the document when – rarely – a validation procedure is inserted between existing ones; normally, however, new validation procedures are appended to the end of their respective sub-sections.

* Instead of 2 documents that both contain details on the structure of SPL files for various purposes with examples, explanations and conformance criteria at varying degree of detailing, the combined document is a systematic compilation of all such technical information in a new topical organization. As SPL is used for an increasing number of different types of products or aspects about products, the old organization became difficult to read and to maintain consistently. The new unified implementation guide with topical organization combines the discussion of consideration and detailed technical conformance rules for each aspect or use of SPL in one place.

2 SPL Documents in General

2.1 SPL Header

2.1.1 General

Validation Procedures

2.1.1.1 XML is well formed and valid against the schema

2.1.1.2 There are no data elements and attributes in addition to those described in this document

Certain exceptions apply to this rule, notably any default attribute that validating schemas would create are by default part of the document. These need not be stated, but cannot reasonably be forbidden.

```

<document classCode="DOC" moodCode="EVN"/>
<section ID="1" classCode="DOCSECT" moodCode="EVN"/>
<characteristic classCode="OBS" moodCode="EVN">
  <value xsi:type="ED" representation="TXT" integrityCheckAlgorithm="SHA-1"/>
</characteristic>
<policy moodCode="EVN"/>
<approval classCode="CNTRCT" moodCode="EVN"/>
<marketingAct classCode="ACT" moodCode="EVN"/>
<observationMedia classCode="OBS" moodCode="EVN">
  <value xsi:type="ED" representation="TXT" integrityCheckAlgorithm="SHA-1"/>
</observationMedia>
<effectiveTime xsi:type="IVL_TS" operator="I">
  <low value="20030203" inclusive="true"/>
  <high value="20040102" inclusive="true"/>
</effectiveTime>
<asContent>
  <quantity>
    <denominator value="1" unit="1"/>
  </quantity>
</asContent>
<actDefinition>
  <code nullFlavor="OTH"/>
</actDefinition>
<positionNumber nullFlavor="NA"/>
<relatedDocument typeCode="REFR">
  <relatedDocument>
    <setId extension="NCT01352845" root="2.16.840.1.113883.3.1077"/>
  </relatedDocument>
</relatedDocument>

```

- 2.1.1.3 There are no spaces in codes
- 2.1.1.4 Codes do not have a codeSystemName attribute
- 2.1.1.5 Display names are case insensitive
- 2.1.1.6 There are no spaces in id extensions
- 2.1.1.7 Letters in Globally Unique Identifiers (GUID) are lower case
- 2.1.1.8 There are no empty or incomplete elements except, in certain circumstances, code, title, text, and time (an id has a root, a code has a code system).
- 2.1.1.9 Characteristics have a class code of “OBS” or no class code at all.
- 2.1.1.10 There is no confidentiality code on anything but inactive ingredients, identified substance, registrant, and assigned establishments outside establishment registrations.
- 2.1.1.11 If there is a confidentiality code, then the code is “B” and the codeSystem is “2.16.840.1.113883.5.25”

2.1.2 XML references

This information includes the location of the current stylesheet for the FDA view of the SPL and the location of the current schema. The start of the SPL file is the same for every SPL document and is as follows:

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet
  href="https://www.accessdata.fda.gov/spl/stylesheet/spl.xsl"
  type="text/xsl"?>
<document xmlns="urn:hl7-org:v3"
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
  xsi:schemaLocation="urn:hl7-org:v3
  https://www.accessdata.fda.gov/spl/schema/spl.xsd">
```

Validation Procedures

- 2.1.2.1 XML reference is for version 1.0 and encoding “UTF-8”.
- 2.1.2.2 There is an xml-stylesheet reference to “https://www.accessdata.fda.gov/spl/stylesheet/spl.xsl”.
- 2.1.2.3 The schemaLocation of the urn:hl7-org:v3 namespace is provided as “https://www.accessdata.fda.gov/spl/schema/spl.xsd”.

- 2.1.2.4 There are no processing instructions other than the xml and xml-stylesheet declarations.
- 2.1.2.5 There are no comments.
- 2.1.2.6 SPL file name is the document id followed by “.xml”
- 2.1.2.7 A submission contains only the SPL file whose name ends in ‘.xml’ and, if appropriate, associated image files whose names end in '.jpg' except if the document types are *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)* or *Risk Evaluation & Mitigation Strategies* document (82351-8) having associated pdf files whose names end in '.pdf'.
- 2.1.2.8 All image files associated with the SPL document are actually referenced from that SPL document.

2.1.3 Document information

This provides basic information for the identity of the particular document, its type, title, date and versioning as a member of a document set.

Terminology: The SPL document types are from LOINC. This code provides information about the subject matter of the document e.g., prescription animal drug.

```
<document>
  <id root="50606941-3e5d-465c-b4e0-0f5a19eb41d4"/>
  <code code="51725-0" codeSystem="2.16.840.1.113883.6.1"
    displayName="Establishment registration"/>
  <title>Establishment Registration</title>
  <effectiveTime value="20070424"/>
  <setId root="a30accef-f437-4136-808c-9ed4ada5fcf8"/>
  <versionNumber value="1"/>
```

- The <id root> is a Globally Unique Identifier (GUID) and is unique for each version of the document. Letters used in a GUID are lower case.
- The <code> is the LOINC code which provides information on the document type.
- The <title> data element is used for the title for the document, if necessary. Images are not included in the title. Multiple lines may be used in the title with each line separated by the line break
 tag. (note: all titles can also be as follows: <title mediaType="text/x-hl7-title+xml">).
- The <effectiveTime> provides a date reference to the SPL version including the year, month and day as yyyyymmdd.
- The <setId> is a GUID and is a unique identifier for the document that remains constant through all versions/revisions of the document.

- The <versionNumber> is an integer greater than zero that provides a sequence to the versions of the document.

Validation Procedures

- 2.1.3.1 There is a document id
- 2.1.3.2 id root is a Globally Unique Identifier (GUID).
- 2.1.3.3 id does not have an extension.
- 2.1.3.4 id does not match any other id in the document.
- 2.1.3.5 id (document id) is unique across all documents, sections and any other ids
- 2.1.3.6 There is a code
- 2.1.3.7 Code system is 2.16.840.1.113883.6.1
- 2.1.3.8 Code comes from the *Document type* list
- 2.1.3.9 Display name matches the code
- 2.1.3.10 There are no figures in the title.
- 2.1.3.11 There is an effective time with at least the precision of day in the format YYYYMMDD
- 2.1.3.12 There is a set id
- 2.1.3.13 The set id is a GUID
- 2.1.3.14 There is a version number
- 2.1.3.15 Value of version number is a whole number > 0
- 2.1.3.16 Value of version number is greater than the value of any previously submitted version for the same set id
- 2.1.3.17 The preceding version of this set id has not been replaced by a document with a different set id, i.e., this set id has not been referenced as a related document of type "replace" (RPLC) from a document with a different set id.

2.1.3.18 If the document type is *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7) then the updated document type is *Intentional Animal Genomic Alteration Label* (101437-2).

2.1.3.19 If the previous document type is *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), (for the set id) then it has been replaced with *Intentional Animal Genomic Alteration Label* (101437-2).

2.1.4 Author Information

The author information is represented as follows:

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
```

Many times the author information is used to represent details on the businesses responsible for the products. This includes the labeler and registrant and establishments involved in manufacturing:

```
<author>
  <assignedEntity>
    <representedOrganization><!-- labeler -->
      <assignedEntity>
        <assignedOrganization> <!-- registrant -->
          <assignedEntity>
            <assignedOrganization> <!-- establishment -->
              <assignedEntity>
                <assignedOrganization><!-- US agent and importers -->
```

The following is a representative coding of the common structures in the header:

```
<document>
  <author>
    <time/>
    <assignedEntity>
      <representedOrganization><!-- labeler -->
        <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
        <id extension="NDC Labeler Code" root="2.16.840.1.113883.6.69"/>
        <name>business name</name>
        <contactParty>
          <addr>
            <streetAddressLine>address</streetAddressLine>
            <city>city</city>
            <state>state</state>
            <postalCode>postal code</postalCode>
            <country code="country code"
              codeSystem="1.0.3166.1.2.3">country name</country>
          </addr>
          <telecom value="tel:telephone number"/>
          <telecom value="mailto:email address"/>
          <contactPerson>
            <name>contact person name for labeler</name>
          </contactPerson>
        </contactParty>
```

```

<assignedEntity>
  <assignedOrganization><!-- registrant -->
    <id extension="DUNS number" root="1.3.6.1.4.1.519.1"/>
    <name>business name</name>
    <contactParty><!-- same structure as above --></contactParty>
  <assignedEntity>
    <assignedOrganization><!-- establishment -->
      <id extension="DUNS number" root="1.3.6.1.4.1.519.1"/>
      <id extension="FDA establishment identifier"
        root="2.16.840.1.113883.4.82"/>
      <name>Establishment name</name>
      <addr><!-- as above --></addr>
      <contactParty><!-- as above --></contactParty>
    <assignedEntity>
      <assignedOrganization><!-- U.S. agent -->
        <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
        <name>business name</name>
        <telecom value="tel: telephone number"/>
        <telecom value="mailto: email address"/>
      </assignedOrganization>
      <performance>
        <actDefinition>
          <code code="C73330"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="display name"/>
        </actDefinition>
      </performance>
    </assignedEntity>
  </assignedOrganization>
</performance>
  <actDefinition>
    <code code="establishment business operation code"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name"/>
  </actDefinition>
</performance>
</assignedEntity>
</assignedOrganization>
</assignedEntity>
</representedOrganization>
</assignedEntity>
</author>
</document>

```

2.1.5 Identified Organizations

Most organizations are identified using Dun and Bradstreet identifiers (DUNS numbers). These are identifiers with the root 1.3.6.1.4.1.519.1 and an extension.

```

<representedOrganization>
  <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>

```

The only reason for an organization not being identified is if the organization remains anonymous but has sub-organizations (e.g., a listing file may not contain any registrant information)

```

<representedOrganization>
  <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
  <name>business name</name>
  <assignedEntity>
    <assignedOrganization>
      <!-- pass-through organization without ids or name -->
    <assignedEntity>
      <assignedOrganization>
        <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
        <name>business name</name>

```

Validation Procedures

- 2.1.5.1 One id is a DUNS number with the root 1.3.6.1.4.1.519.1, except if the document type is *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), or *Cosmetic – Update* (X8888-5).
- 2.1.5.2 The id (DUNS number) with the root 1.3.6.1.4.1.519.1 has a 9-digit extension
- 2.1.5.3 There is a name, except if the document is an *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6), *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), or *Cosmetic – Update* (X8888-5).

2.1.6 Address

For addresses (addr) the following rules apply

```

<addr>
  <streetAddressLine>1625 29th street</streetAddressLine>
  <city>Camden</city>
  <state>NJ</state> <postalCode>08101</postalCode>
  <country code="USA" codeSystem="1.0.3166.1.2.3">USA</country>
</addr>

```

Validation Procedures

- 2.1.6.1 An address has one or two street address line, city, and country.
- 2.1.6.2 If there is a country code, then it is an ISO 3-letter country code (code system “1.0.3166.1.2.3”).
- 2.1.6.3 If there is no code attribute, then the country name may be the code, otherwise country is a full country name matching the code.

- 2.1.6.4 If the country is “USA”, then the contact party’s address has a state (2-letter abbreviation) and postal code
- 2.1.6.5 If the country is “USA”, then the postal code is 5 digits with optionally a dash followed by 4 numbers
- 2.1.6.6 If the country is **not** in the *postal code validation* list, then there is a postal code

2.1.7 Telecommunication Addresses

Some elements may have telecommunication addresses. If an element has telecommunication addresses it usually allows for a telephone number and an email address.

```
<contactParty>
...
<telecom value="tel:+1-800-555-1213;ext=112"/>
<telecom value="mailto:Bob.Jones@acme.com"/>
...
</contactParty>
```

However, there are exceptions noted in the validation procedures.

Telecommunication addresses are usually provided for an organization’s contact party, in which case telephone and email are the common standard. In no case is telephone or email missing for contact party. But in some cases a 3rd telecommunication address can be provided with the FAX number:

```
<contactParty>
...
<telecom value="tel:+1-800-555-1213;ext=112"/>
<telecom value="mailto:Bob.Jones@acme.com"/>
<telecom value="fax:+1-302-123-5433"/>
...
</contactParty>
```

Normally telecommunication addresses are associated with specific contact parties of organizations as shown above, such as, for registrant contact party or establishment contact party or labeler contact party. However, in some cases, telephone numbers of physical facilities can be specified directly without contact party:

```
<assignedOrganization>
...
<telecom value="tel:+1-800-555-1213;ext=112"/>
</assignedOrganization>
```

In several Establishment/Facility Registrations/Reporting use cases, traditionally the US Agents and Importers have been provided as abbreviated organizations without the added complexity of a contact party:

```

<assignedOrganization>
  ...
  <telecom value="tel:+1-800-555-1213;ext=112"/>
  <telecom value="mailto:Bob.Jones@acme.com"/>
</assignedOrganization>

```

Validation Procedures

- 2.1.7.1 There are two <telecom> elements, except if the document type is *Lot Distribution Data* (66105-8) or *Indexing - Substance* (64124-1) there is one telecom element, or for *Identification of CBER-Regulated Generic Drug Facility* (72090-4) or *Generic Drug Facility Identification Submission* (71743-9) there may be a third telecom element, or for any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types where all telecom elements are optional except in facility contact and U.S. Agent.
- 2.1.7.2 One telecom value begins with “tel:” and is a telephone number, except if the document code is *Lot Distribution Data* (66105-8) or *Indexing - Substance* (64124-1) or any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types, other than in facility contact party and U.S. Agent.
- 2.1.7.3 For telephone numbers, the following general rules apply:
- 2.1.7.4 Telephone numbers are global telephone numbers;
- 2.1.7.5 Telephone numbers contain no letters or spaces;
- 2.1.7.6 Telephone numbers begin with “+”;
- 2.1.7.7 Telephone numbers include hyphens to separate the country code, area codes and subscriber number;
- 2.1.7.8 US telephone numbers have the format +1-aaa-bbb-cccc where “aaa” is the area code, and “bbb-cccc” the usual digit grouping of a local phone number.
- 2.1.7.9 Telephone numbers have any extensions separated by “;ext=” (see Uniform Resource Identifier (URI) for Telephone Numbers RFC 3966).
- 2.1.7.10 If there is a semicolon in the telephone number, then it is followed by ext.
- 2.1.7.11 One telecom value begins with “mailto:” and encodes an email address, except for any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types, other than in facility contact party and U.S. Agent.
- 2.1.7.12 an email address is of the simple form <username>@<dns-name>

2.1.7.13 If there is a third telecom element (fax number), then its value begins with “fax:” and its format is the same as for a telephone number.

2.1.8 Contact Party

For most organizations, a contact party may be specified with a contact person as in the following example:

```
<contactParty>
  <addr>
    <streetAddressLine>1625 29th street</streetAddressLine>
    <city>Camden</city>
    <state>NJ</state> <postalCode>08101</postalCode>
    <country code="USA" codeSystem="1.0.3166.1.2.3">USA</country>
  </addr>
  <telecom value="tel:+1-800-555-1213;ext=112"/>
  <telecom value="mailto:Bob.Jones@acme.com"/>
  <contactPerson>
    <name>Bob Jones</name>
  </contactPerson>
</contactParty>
```

Validation Procedures

- 2.1.8.1 The contactParty has an address element (addr), except if the document is *Lot Distribution Data (66105-8)*, *Wholesale Drug Distributor and Third-Party Logistics Facility Report (75030-7)*, *Withdrawal of Wholesale Drug Distributors and Third-Party Logistics Facility Report (77573-4)*, *Blanket No Changes Certification Of Product Listing (86445-4)*, *Indexing - Substance (64124-1)*, or any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types.
- 2.1.8.2 The contactParty has telephone number and email addresses except for any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types.
- 2.1.8.3 There is one contact person name, except for any of the *Cosmetic Facility Registration* and *Cosmetic Product Listing* document types, where the name is optional.
- 2.1.8.4 If none of the contact party data are provided, then there is no contact party element at all.

2.1.9 “Doing Business As” (DBA) Name

```
<assignedOrganization> <!-- facility -->
...
```

```

<asNamedEntity> <!-- other "doing business as" name -->
  <code code="C117113" displayName="doing business as"
    codeSystem="2.16.840.1.113883.3.26.1.1"/>
  <name>A.C.M.E. Logistic</name>
</asNamedEntity>

<contactParty .../>

```

Validation Procedures

2.1.9.1 There is no “doing business as” (DBA) name element, except if the document type is *Wholesale Drug Distributors and Third-Party Logistics Facility Report* (75030-7).

2.1.9.2 DBA name has a name element

2.1.10 Core Document Reference

For some SPL documents it is permitted to specify a “core document” reference. A document with a core document reference “inherits” all the sections from the referenced core document and may override certain top-level sections with its own sections. A core document reference is specified as follows:

```

<document>
  ...
  <author .../>

  <relatedDocument typeCode="APND">
    <relatedDocument>
      <setId root="20d9b74e-e3d8-4511-9df9-cec2087372fc"/>
      <versionNumber value="1"/>
    </relatedDocument>
  </relatedDocument>

  <component .../>
</document>

```

The reference contains the setId of the referenced core-document. The document and the core-document can develop Independently. The core-document may be updated, but the reference remains to the latest core-document with the same setId. The version number in the reference may be provided to indicate which version of the core-document was used when at the time the referencing document was created or modified.

Validation Procedures

2.1.10.1 There is no document id

2.1.10.2 There is a set id

2.1.10.3 Set id is a GUID

2.1.10.4 Document set id is the set id of a core-document.

2.1.10.5 If there is a version number, then it is a whole number > 0.

2.1.10.6 If there is a version number, then it is less or equal than the version of the current core document with that set id.

2.1.11 Predecessor Document

Other documents may be merged into this document by providing a reference to the other predecessor documents that are replaced by this document. Do not provide a reference to the predecessor document under the same set id as the document being submitted, as this is implicitly given by the set id and incremented version number of this document. Only provide references to documents of different set ids. The reference contains only the id of the other predecessor document, code, the setId and the version number. All these ids must match the ids of the other documents that had previously been submitted.

```
<document>
...
<author .../>

<relatedDocument typeCode="RPLC">
  <relatedDocument>
    <id root="464239de-45c7-4d2f-a89a-45d303f428bd"/>
    <code code="Other Registration Document Type Code"
          codeSystem="2.16.840.1.113883.6.1"
          displayName="Other Registration Document Type Name"/>
    <setId root="9ea75e1e-84ef-4605-89ff-dd08a4c94f40"/>
    <versionNumber value="3"/>
  </relatedDocument>
</relatedDocument>

<component .../>
</document>
```

Validation Procedures

2.1.11.1 There is an id (document id)

2.1.11.2 The id (document id) is a GUID

2.1.11.3 There is a set id

2.1.11.4 The set id is a GUID

2.1.11.5 The set id is different from the present document's set id.

2.1.11.6 There is a version number, which is a whole number > 0.

2.1.11.7 The set id has been previously submitted.

- 2.1.11.8 Document id and version number match the latest document previously submitted under that set id excluding any No Change Notifications.
- 2.1.11.9 Document type matches the latest document type previously submitted under that set id excluding any No Change Notifications.
- 2.1.11.10 The referenced document has not already been replaced by another document.

2.2 *SPL Body*

The body of the SPL document includes structured text such as product labeling and specific data elements such as ingredients.

```
<document> <!-- SPL header material -->
  <component>
    <structuredBody> <!-- SPL body material -->
      <component>
        <section>
```

2.2.1 Sections and subsections

```
<component>
  <section>
    <id root="62abedf9-6bde-4787-beb0-abd214307427"/>
    <code code="34067-9"
      codeSystem="2.16.840.1.113883.6.1"
      displayName="Indications and Usage"/>
    <title>Indications and Usage</title>
    <text>labeling text</text>
    <effectiveTime value="20070822"/>
  </component/>
```

Sections and subsections have id, title, and code. LOINC codes are used for sections and subsections codes.

The <title>, if necessary, of the sections and subsections and order of the sections and subsections in the SPL are used to render the labeling contents. The numbering for the sections and subsections are included in the <title> text.

In the SPL schema, the <structuredBody> element contains multiple <component>s, and each <component> contains a <section>.

Sections are used to aggregate paragraphs into logical groupings. The order in which sections appear in an SPL document is the order the sections will appear when displayed (rendered) using the standard stylesheet. Major sections defined by the appropriate labeling regulations (e.g., 21 CFR 201.56 and 57 for human prescription drugs and 201.66 for human over the counter drugs) such as Indications and Usage are assigned LOINC codes. Sections that have not been assigned a LOINC code are

assigned the LOINC code for “SPL Unclassified Section”. Major sections may also be defined by parts of a container or carton label (e.g., Principal Display panel).

```
<section>
  <!-- this section's id, codes -->
  <text>
    <!-- actual text content in "narrative block" markup -->
  </text>
```

Each section has a unique identifier (<id>), an <effectiveTime>, and a LOINC code (i.e., the <code> element). A section may or may not contain a <title>.

The human readable content of labeling is contained within the <text> element in the <section>. The <section> can be nested to form sub-sections. The schema for subsections in SPL requires that the nested <section> tag first be nested inside a <component> tag. Use nested sections to relate paragraphs. The section tag applies to all of the nested sections. By nesting sections, computer systems can use the section tags in SPL to display information useful for the care of patients. If information is not associated with the tag, it will not be displayed.

```
<section>
  <!-- this section's id, codes -->
  <text>
    <!-- actual text content in "narrative block" markup -->
  </text>

  <component>
    <section>
      <!-- subsection content -->
    </section>
  </component>

  <component>
    <section>
      <!-- subsection content -->
    </section>
  </component>
</section>
```

Using the following principles for markup of text information improves access to information in labeling:

- Capture the section heading using the <title> element rather than placing the text of the title within the <text> element. This allows computer systems to use and display this information properly.
- Capture the section heading even when the printed label does not include a heading. For example, tagging a pregnancy statement as a section in a label that does not have a heading for pregnancy is useful. Computer systems will be able to use the tag to capture the pregnancy use statement. Omitting the <title> would prevent the heading from appearing when the SPL is rendered.

- Link different parts of the labeling using the ID attribute to the <section> element. For example, <section ID="Clin_Pharm_Section"> serves as the target of a <linkHtml> element. Linking to the ID attribute of a section allows the link to 'reference' the section entirely, e.g., for retrieval of a whole section in a non-browser interface.
- For container or carton labels, when capturing text and figures outside the Drug Facts or equivalent sections, separate the text and figures for each concept using <paragraph> tags.
- The order of the placement of information is the content of the package insert, the content of the patient information and the carton and container labels with images.

Validation Procedures

- 2.2.1.1 Each section has zero to many subsections
- 2.2.1.2 Each section and subsection has an id root and no extension
- 2.2.1.3 id root (section id) is a GUID
- 2.2.1.4 id does not match any other id in the document
- 2.2.1.5 id (section id) does not match any other id across all sections, documents, or any id other than the id of the same section previously submitted
- 2.2.1.6 Each section and subsection has a code
- 2.2.1.7 Code system is 2.16.840.1.113883.6.1
- 2.2.1.8 Display name matches the code
- 2.2.1.9 Each section has an effective time with at least the precision of day in the format YYYYMMDD, except the *SPL Listing Data Elements Section* (48780-1) of *Lot Distribution Data* (66105-8), *Human Compounded Drug Label* (75031-5), *Animal Compounded Drug Label* (77647-6) and *Indexing - Warning Letter Alert* (77288-9) documents, and the *SPL Indexing Data Elements Section* (48779-3) of *Indexing - Biologic or Drug Substance* (77648-4) and *Indexing - Warning Letter Alert* (77288-9).
- 2.2.1.10 There are no figures in the title for a section or subsection.
- 2.2.1.11 The section for *SPL Medguide Section* (42231-1) and *SPL Patient Package Insert Section* (42230-3) is not a subsection.

2.2.2 Text

```
<section>
  <text>
    <paragraph>Lorem ipsum dolor sit amet, consectetur adipisicing elit,
    sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim
    ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip
    ex ea commodo consequat. Duis aute irure dolor in reprehenderit in
    voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint
    occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit
    anim id est laborum.</paragraph>
    <paragraph>At vero eos et accusamus et iusto odio dignissimos ducimus
    qui blanditiis praesentium voluptatum deleniti atque corrupti quos dolores
    et quas molestias excepturi sint occaecati cupiditate non provident,
    similique sunt in culpa qui officia deserunt mollitia animi, id est laborum
    et dolorum fuga.</paragraph>
  </text>
</section>
```

The human readable text content of SPL documents is contained within the `<text>` element. The actual content is contained within a `<paragraph>`, `<table>`, and/or `<list>`. If a section consists only of nested sections, the `<text>` tag is not included. Elements that can be used within the `<text>` element to capture the human readable content of SPL include paragraphs (`<paragraph>`), lists (`<list>`), tables (`<table>`) and images (`<renderMultimedia>`). Elements permitted as children of the `<text>` element, used as children of the `<paragraph>` element or within `<table>` and `<list>` include superscripts (`<sup>`), subscripts (`<sub>`), links (`<linkHtml>`), line breaks (`
`), footnotes (`<footnote>`), footnote references (`<footnoteRef>`). Images may be included in the content of labeling using the `<renderMultiMedia>` tag. This tag may be used as a direct child of `<text>` for ‘block’ images or as a child of `<paragraph>` for inline images.

2.2.2.1 Font effects

There are certain aspects of the rendering of SPL that must be specified in the SPL source to insure that the content of labeling is formatted correctly when rendered. For example:

```
<text>
  <paragraph>The next snippet <content styleCode="bold italics">will appear
  as bold italics</content> in the rendering.</paragraph>
```

Will be rendered as:

The next snippet *will appear as bold italics* in the rendering.

The `<content styleCode="">` can also be nested, for example:

```
<text>
  <paragraph>
    <content styleCode="bold italics"> will appear as bold
    italics</content>
```

Can also be represented as:

```
<text>
  <paragraph>
    <content styleCode="bold"><content styleCode="italics"> will appear as
    bold italics.</content></content>
```

The values for `<styleCode>` for font effect are bold, italics and underline. To assist people who are visually impaired, the `<styleCode="emphasis">` is used to prompt computer screen reader programs to emphasize text such as text in a box warning. The bold, italics and underline font effects may be used together with each other and the emphasis styleCode. For example, `<content styleCode="bold"><content styleCode="emphasis">` `</content></content>` will appear as bold and will be emphasized by the screen reader programs.

A special styleCode is used for recent major changes (see below).

2.2.2.2 Symbols and special characters

Special characters can be included in the text. Superscripts and subscripts are accomplished using the `<sup>` and `<sub>` tags. Because the SPL encoding is UTF-8, any Unicode character can be included as is. Unicode references may also be inserted as either `&#dddd;` where `dddd` is the Unicode value in decimal notation or `�` where `dddd` is the Unicode value in hexadecimal notation. The font used in the standard stylesheet is a Unicode font assuring that most Unicode characters will be rendered correctly if viewed by a browser supporting this font. The only prohibited characters in XML that can not be directly used are less-than “<” (because SPL XML tags begin with it) and ampersand “&” (because XML entity references begin with it). Use of these two symbols must be replaced by the XML entity references `<`, and `&`; respectively. For example, `<paragraph>The mean for group 1 was < 13.</paragraph>` will render as “The mean for group 1 was <13.” and “D&C Yellow #10” will render as “D&C Yellow #10”.

2.2.2.3 Footnotes

The SPL schema includes a specific footnote element `<footnote>`. Footnotes are rendered automatically by the standard SPL stylesheet. `<footnoteRef>` is used to refer to another (usually earlier) footnote. For example, `<footnote ID="testNote">This is the footnote content</footnote>` will generate the following footnote at the appropriate end of a section. “This is footnote content”

The `<footnoteRef>` element with the appropriate IDREF attribute, e.g., `<footnoteRef IDREF="testNote"/>` will display the footnote reference in the text corresponding to the footnote with the same ID, e.g., in this example footnote 6.

Footnotes are rendered by the default stylesheet using Arabic numbers (e.g., 1,2 3,). Within tables, footnotes are rendered using footnote marks in the series: * † ‡ § ¶ # ♣

♥ ♦ ♣, effectively separating numbered footnotes within general text and footnotes within tables. Footnotes within tables are rendered at the bottom of the table.

2.2.2.4 Lists

All lists are marked up using the <list> tag, and each item in a list is marked with an <item> tag. The 'listType' attribute identifies the list as ordered (numbered) or unordered (bulleted). The default numbering and bulleting are controlled by the stylesheet.

```
<text>
  <paragraph>Lorem ipsum dolor sit amet, consectetur adipisicing elit, sed
  do eiusmod tempor incididunt ut labore et ...</paragraph>

  <list listType="ordered" styleCode="BigRoman">
    <item>Lorem ipsum dolor sit amet,</item>
    <item>consectetur adipisicing slit</item>
  </list>

  <paragraph>At vero eos et accusamus et iusto ...</paragraph>
</text>
```

Lists featuring a standard set of specialized markers (standard specialized lists) can be created using the styleCode attribute with the <list> element. Options available for ordered lists are:

- Arabic (List is ordered using Arabic numerals: 1, 2, 3)
- LittleRoman (List is ordered using little Roman numerals: i, ii, iii)
- BigRoman (List is ordered using big Roman numerals: I, II, III)
- LittleAlpha (List is order using little alpha characters: a, b, c)
- BigAlpha (List is ordered using big alpha characters: A, B, C)

For example: <list listType="ordered" styleCode="LittleRoman">

For unordered lists the following options exist:

- Disc (List bullets are simple solid discs: ●)
- Circle (List bullets are hollow discs: ○)
- Square (List bullets are solid squares: ■)

For example: <list listType="unordered" styleCode="Disc">

In addition to the standard specialized lists, user-defined characters are also permitted as markers by nesting <caption> within the <item> tag. Note that any character, XML

entity, or Unicode symbol, may be used in the <caption>, and that the <caption> for each <item> are not restricted to the same character.

For example: <item><caption>*</caption> the asterisk is used as item marker here.<item>

2.2.2.5 Tables

Tables can be created with the full structure (header (e.g., for column names), body (e.g. for the rows of the table) and footer e.g. for table footnotes)). The element <tbody> is required for an SPL table while the elements <thead> and <tfoot> are optional in the SPL schema. The structure will display a standard typographical table with rules between the caption (table title) and head, the head and body, and the body and <tfoot>. If a <tfoot> element is included and footnotes are present in a table, then footnotes are rendered after the existing content of the <tfoot> element.

It is recommended to always start with a standard table (i.e., <thead> and <tbody> elements) and test to see whether the rendering is unambiguous and interpretable. It is important that the table communicate labeling content not that it duplicates the presentation in word processed or typeset versions of the package insert. In the unusual situation where additional formatting is needed, the rule styleCode specified or certain attributes may be used to modify the table.

The rule codes are as follows (note that the control names are case sensitive).

- Rule on left side of cell is Lrule
- Rule on right side of cell is Rrule
- Rule on top of cell is Toprule
- Rule on bottom of cell is Botrule

Note: More than one rule control may be used in a cell, e.g., <td styleCode code="Botrule Lrule">Cell content </td>.

Rule control codes should be used only when necessary for the interpretability of the table. Use of these codes may result in overriding the default rules for tables. Rather than setting the rule for each cell, table rules may also be controlled according to entire rows or columns by use of the styleCode attributes with <col>, <colgroup>, <thead>, <tfoot>, <tbody> and <tr> elements.

To make rowgroups appear with horizontal rules, use the styleCode attribute "Botrule" with the appropriate <tr> element. The Botrule value is rarely needed on the <td> element.

The preferred method for using vertical rules is to define colgroup with styleCode="Lrule" or "Rrule" (or both). Only if this does not yield the desired vertical rule should the Lrule or Rrule code value with styleCode attributes on the <td> or <th> element itself be used. Note: In general, vertical rules should not be used. Good typography for tables means using few vertical rules.

To merge cells vertically and horizontally, the rowspan and colspan attributes should be used on the <td>element.

To determine the width of a table, the width attribute may be used on the <table> element and to determine the width of a table column, the width attribute may be used on the <col> and <colgroup> elements.

For horizontal alignment, the preferred method for aligning cell content within the margins is to use <col align=".." /> in the <colgroup> element, though this can be used in the <colgroup> element as well. Valid values for align are "left", "center", "right", "justify" (for full justification of contents within the cells), and "char" (for character alignment within the cells). Using the <col align=".." /> markup ensures that the contents for all cells in the column share the same alignment.

For vertical alignment, the valign attribute can be used within cells. For cases in which the cell alignment must be different from other cells in the column, align is also available as an attribute on the other table elements, including <td>.

Markup for table footnote is rendered in the <tfoot> tag. This element does not need to be included in SPL; the standard stylesheet will include a <tfoot> tag if a <footnote> element is present within either the <thead> or <tbody> sections. A <tfoot> section should be included in SPL only if there is additional information other than footnotes that needs to be rendered in this section.

For table text spacing, in some instances, the use of a "tab" or text indentation is desirable in a given table cell. In an SPL document, this effect is achieved by using the nonbreaking space () as if it were a "tab" space. As the following snippet of XML shows, two nonbreaking spaces were used to offset the word "Male" from the margin: <td> Male</td>. The nonbreaking space can also be used to keep text in a table from breaking inappropriately due to browser resizing.

2.2.2.6 Hypertext links

SPL offers hypertext linking capabilities generally similar to those found in the HTML specification.

Links are specified by the <linkHtml> construct, where the value for the href attribute of <linkHtml> (the target of the link) is the ID attribute value of a <section>, <paragraph>, <table>, <list>, <content>,<renderMultimedia> element. The stylesheet does not support the styleCode attribute of the <linkHtml> element; if a styleCode is

needed for a link, this should be coded via the <content> element within the link as with other text.

2.2.2.7 Recent major changes in labeling text

SPL offers a notation to identify recent major changes in the labeling text including table elements <table> and table data <td>. The recent major text is tagged using the <content styleCode="xmChange">. For example,

```
<text>This is an example of text that is not changed.<content styleCode="xmChange">This is an example of text that is a recent major change</content>This is an example of changed text that is not considered a recent major change</text>
```

Validation Procedures

2.2.2.8 Text is enclosed under <paragraph>, <list>, or <table> elements.

2.2.2.9 The number of table data (<td>) elements is identical to the number of column (<col>) elements in each table (<table>).

2.2.3 Images

The SPL schema uses <observationMedia> elements to identify graphic files to be rendered at the locations where they are referenced by <renderMultiMedia> elements in the <section>. In other words, an image in an SPL will be rendered wherever it is referenced by the renderMultimedia markup, no matter where the observationMedia markup appears. The referencedObject attribute of the renderMultiMedia element identifies the corresponding observationMedia instance by means of its ID identifier such as <renderMultiMedia referencedObject="MM1"/>

```
<section>
  <text>
    <paragraph>...</paragraph>
    <renderMultiMedia referencedObject="MM1"/>
    <paragraph>...</paragraph>
  </text>
  <component>
    <observationMedia ID="MM1">
      <text>descriptive text</text>
      <value xsi:type="ED" mediaType="image/jpeg">
        <reference value="drug-01.jpg"/>
      </value>
    </observationMedia>
  </component>
</section>
```

The <observationMedia> element does not contain the graphics file, but instead points at the file. The <reference> value is the file name. The file name should not include spaces. The observationMedia identifies the graphic media type (i.e., JPEG). In addition, the observationMedia element includes the text description of the image

used by screen reader software for visually impaired users. This is included in the <text> child of <observationMedia>. Note also that observationMedia is always contained within a <component> element as illustrated.

For image placement, if an image is a block image (i.e., should appear in its own space), insert the renderMultimedia tag between <paragraph> elements. If an image is inline (i.e., should appear alongside text), insert the renderMultimedia tag in the text of a <paragraph> as appropriate. Inline images are expected to be uncommon and basically represent symbols that cannot be represented by Unicode characters. In addition, <caption> are not applicable for inline images since these are not offset from the surrounding text.

The SPL stylesheet does not perform any resizing graphics or changing the resolution of graphics files. Thus, all images are rendered in the browser as-is, with all characteristics of the actual graphic file itself. To ensure that a graphic will appear as desired, it is very important that the graphic file is edited to a dimension appropriate for its presentation within the browser. If this is not done, the appearance of the graphic may not be consistent with the narrative content reducing the readability of the file. JPEG image file type using appropriate pixels per inch for images for viewing in a browser using the standard stylesheet.

Validation Procedures

2.2.3.1 There is text

2.2.3.2 Value xsi:type is as above

2.2.3.3 Media type is image/jpeg

2.2.3.4 Reference value is the file name for a valid image

2.2.3.5 Size of image file is less than 1 MB

2.2.3.6 File is a JPEG image and the name has the extension “.jpg”

2.2.3.7 Image components are referenced at least once in the text of any section.

2.2.3.8 Image reference in text has an image “observationMedia” element with a matching ID in the same document.

2.2.4 Highlights

The actual Highlights of a rendered SPL are constructed from four sources: “boilerplate” text rendered directly from the stylesheet, information from data elements inserted into the boilerplate text, <title> in the header which includes the drug names, dosage form, route of administration, controlled substance symbol and

year of initial US approval, and text blocks corresponding to each major highlights part (Highlights text). Highlights section titles are derived from the FPI section LOINC codes. The Highlights text is captured for the following sections: Microbiology, Boxed Warning, Recent Major Changes, Indications and Usage, Dosage and Administration, Dosage Forms and Strengths, Contraindications, Warnings and Precautions, Adverse Reactions, Drug Interactions and Use in Specific Populations.

The text blocks for Highlights are coded with the <excerpt> <highlight> elements of the major section of labeling in which they are contained.

```
<section>
  <excerpt>
    <highlight>
      <text>...</text>
```

For example, the Highlights for Indications and Usage are located with the Indications and Usage section of the labeling. The Highlights text is placed under the main section and not under subsections. The following is an example:

```
<component>
  <section>
    <id root="47ef84cd-8314-48c3-8ee2-bdff3087f83f"/>
    <code code="43685-7" codeSystem="2.16.840.1.113883.6.1"
      displayName="warnings and precautions section"/>
    <title>5 WARNINGS AND PRECAUTIONS</title>
    <excerpt>
      <highlight>
        <text>
          <list listType="unordered">
            <item>Aplastic anemia has been observed in 8% of recipients and
is irreversible in the majority of patients who experience this. (<linkHtml
href="#Section_5.1">5.1</linkHtml>)</item>
            <item>Monitor for hematological adverse reactions every 2 weeks
through the second month of treatment (<linkHtml
href="#Section_5.2">5.2</linkHtml>)</item>
          </list>
        </text>
      </highlight>
    </excerpt>
    <component>
      <section ID="Section_5.1">
        <id root="a857689e-9563-43c0-a244-8a6d5a25966a"/>
        <title>5.1 Aplastic anemia</title>
        <text>
          <paragraph>Aplastic anemia has been observed in...</paragraph>
        </text>
      </section>
    </component>
  </section>
</component>
```

This example illustrates the following principles:

- a. The <text> block for the Highlights is included as the <excerpt> <highlight> <text> children of the respective section. In the example above, the text block rendered in the highlights section is the child of the “Warnings and Precautions” section.
- b. The coding of the highlights text block is not in a subsection.
- c. The text block is rendered similar to any other text block, although in a location separate from its actual position in the rendered SPL document.
- d. Links to the section or subsection where the primary content exists are explicitly entered in the Highlights text block.
- e. Section numbering is included in the title of sections and subsections (e.g., ‘5’ and ‘5.1’, above).

Highlights and labeling boilerplate items include:

- Statement -“Highlights of Prescribing Information”
- Highlights section titles
- Patient counseling statement with information taken from FPI section LOINC codes for patient information sections, specifically information for patient section (34076-0), SPL Medguide section (42231-1), SPL patient package insert section (42230-3) and SPL supplemental patient material (38056-8)
- Revision date is taken from the effective time
- Full Prescribing Information: Contents
- Statement – “Full Prescribing Information”

Validation Procedures

2.2.4.1 There may be excerpts (sections with highlights text).

2.2.4.2 Excerpts occur only in the following sections: *Boxed Warning Section* (34066-1), *Recent Major Changes Section* (43683-2), *Indications & Usage Section* (34067-9), *Dosage & Administration Section* (34068-7), *Dosage Forms & Strengths Section* (43678-2), *Contraindications Section* (34070-3), *Warnings and Precautions Section* (43685-7), *Adverse Reactions Section* (34084-4), *Drug Interactions Section* (34073-7), *Use in Specific Populations Section* (43684-0), and *Microbiology Section* (49489-8)

2.2.4.3 If there is an excerpt, then it only has highlight text.

- 2.2.4.4 An excerpt in the *Adverse Reactions Section* (34084-4) includes the statement: "to report suspected adverse reactions" and "1-800-332-1088" (different telephone number for documents of type *Vaccine Label* (53404-0)).
- 2.2.4.5 If there are highlights excerpts, then the title for the SPL file includes the text string (without the quotation marks): "These highlights do not include all the information needed to use" "see full prescribing information for" and "Initial U.S. Approval"

2.2.5 Product Data Elements Section

Currently most of the time the product data elements are in a separate section of their own followed by the content of labeling sections that contain only text and no data elements. Product data element section and other special data elements sections are described in Section 3 below; this section describes the features used from the free text (so called "narrative") part of the SPL documents.

```
<document>          <!-- SPL header material here -->
<component>
  <structuredBody><!-- SPL body material here -->
    <component>
      <section>  <!-- Product data element section -->
        <code code="48780-1" codeSystem="2.16.840.1.113883.6.1"
          displayName="SPL product data elements section"/>
        <subject>
          <manufacturedProduct>
            <!-- product data elements -->
          </manufacturedProduct>
        </subject>
      </section>
    </component>
    <!-- Other content of labeling material -->
  <component>
    <!-- ... -->
```

The beginning of the product data elements is as follows

```
<component>
  <section>
    <id root="e13a985b-f706-a5c8-e8ef-73891eb1c697"/>
    <code code="48780-1"
      codeSystem="2.16.840.1.113883.6.1"
      displayName="SPL product data elements section"/>
    <effectiveTime value="20070424"/>
    <subject>
      <manufacturedProduct>
```

Validation Procedures

- 2.2.5.1 Code, code system and display name are as above

- 2.2.5.2 There is one or more product, except in *Human Compounded Drug Label* (75031-5) and *Animal Compounded Drug Label* (77647-6) documents.
- 2.2.5.3 There is an effective time with at least the precision of day in the format YYYYMMDD.
- 2.2.5.4 There is only one product data element section.

3 Product Data Elements

This section describes with examples in general the capabilities of the product data elements that are currently implemented in the scope of this Implementation Guide. More specific sections follow with more detail and more specific guidelines and validation procedures. These subsequent sections may constrain and detail what is described here, but may also introduce details not described here in general. In case of discrepancies, the later specific ruling preempts the general description given here.

Terminology:

- FDA terminology is used for the proprietary, non proprietary and ingredient name.
- National Drug Codes (NDC) System is used for
 - NDC Labeler Code (4 or 5 digit code (e.g., 0001 or 11111)), to register the labeler prefix,
 - NDC Product Code (8 or 9 characters beginning with the NDC Labeler Code separated by a hyphen from the product segment of the code (e.g., 0001-0001 or 11111-001 or 11111-0001)) for products Independent of packaging, and
 - NDC Package Code (10 characters beginning with the NDC Product Code separated by a hyphen from the package segment of the code (e.g., 0001-0001-01, 11111-001-01 or 11111-0001-1)) for packaged products.
- NDC System is also used for identifiers for the National Health Related Item Code (NHRIC)
 - NHRIC Labeler Code (4 or 5 digit code),
 - NHRIC Product Code (8, 9 or 10 digits beginning with the NHRIC Labeler Code separated by a hyphen from the product segment of the code and
 - NHRIC Package Code (10 digits beginning with the NDC Product Code separated by a hyphen from the package segment of the code).
- ISBT-128 site and product codes are for licensed minimally manipulated cell products.
- GS1 GTIN and HIBCC codes are used for device item codes.
- FDA Substance Registration System (SRS) is used for the ingredient and active moiety Unique Ingredient Identifier (UNII).
- The FDA submission tracking system is used for application numbers.
- The National Cancer Institute Thesaurus (NCIt) is used for dosage form, product characteristics, DEA schedule, unit of presentation, route of administration and equivalent codes.
- The Unified Codes for Units of Measure (UCUM) is used for the unit of measure.
- HL7 confidentiality code “B” is for business confidential information.
- FDA Product Classification codes are for device and cosmetic products.

- Codes from the OTC Monograph are used for monograph IDs.
- Cosmetic Listing Number (CLN) assigned to each Cosmetic Product Name identified in each initial and updated technically valid cosmetic product SPL file for which a Listing Number has not been previously assigned. The Cosmetic Listing Number Format:
 - Cosmetic Listing Number (CLN) Prefix: 53 -
 - Product Segment of CLN: XXXXXX-XXXXXX
 - OID for Cosmetic Product Listing is 2.16.840.1.113883.3.9848.

3.1 *Product in General*

Among the product data elements that are always used are item code and name. These are children of <manufacturedProduct>.

Item Code is a unique identification of this product description whether or not the item code is printed on the product itself. Item codes must conform to the ISO 15459 system of codes. National Drug Code (NDC), National Health Related Item Code (NHRIC), GS1 GTIN, HIBCC all conform to ISO 15459. All these have in common that they are composed of a company prefix (e.g. NDC labeler segment) followed by the item reference that is assigned by the owner of the company prefix to create a unique item code. As long as the item code is unique, the digits (and letters) in it need not convey any other information.

Names: When specific manufactured or marketed products are described, the name is the proprietary name as it appears on the label divided between <name> and <suffix>. The <name> is the initial portion of the proprietary name describing the ingredients without any other descriptors including trademarks and dosage forms. If necessary, <suffix> is used for descriptors such as “extended release”. When using the <suffix>, a space after the proprietary name is added as necessary. Non-proprietary or generic names of drugs are found in the <genericMedicine><name> element. Device type codes and descriptions use <asSpecializedKind>.

A brief description is added in the <desc> element that states succinctly the kind of device. This text should be brief to be able to list it in short summary listings. While the text can be up to 512 characters in length, it should normally be much shorter so that it will be useful for listing in tables. A device also has a device-nomenclature code in the <asSpecializedKind> element. This code comes from the FDA Product Classification terminology.

Cosmetic Listing Number (CLN): Associated with each product name. For Code system name ‘Cosmetic Product Listing’ assigned Code system OID is ‘2.16.840.1.113883.3.9848’.

Marketing category and product type: The type of product is indicated by the “Marketing Category”.

Table 1: Marketing Category and Product Type

| Code | Type | Display Name |
|-------------|--------------------|--|
| C73583 | Drug | ANADA |
| C73584 | Drug | ANDA |
| C132333 | Drug | Approved drug product manufactured Under Contract |
| C95600 | Drug | Approved drug product manufactured Under Contract |
| C73585 | Biologic | BLA |
| C73626 | Drug | Bulk ingredient |
| C98252 | Drug | Bulk Ingredient for Animal Drug Compounding |
| C96793 | Drug | Bulk Ingredient for Human Prescription Compounding |
| C73588 | Drug | Conditional NADA |
| C86952 | Dietary Supplement | Dietary Supplement |
| C94795 | Drug | Drug for Further Processing |
| C80438 | Device | Exempt device |
| C73590 | Drug | Export only |
| C80440 | Device | Humanitarian Device Exemption |
| C75302 | Drug | IND |
| C92556 | Drug | Legally Marketed Unapproved New Animal Drugs for Minor Species |
| C86964 | Medical Food | Medical Food |
| C175238 | Drug or Biologic | Multi-Market Approved Product |
| C73593 | Drug | NADA |
| C73594 | Drug | NDA |
| C73605 | Drug | NDA authorized generic |
| C132334 | Drug | OTC monograph drug product manufactured Under Contract |
| C95601 | Drug | OTC monograph drug product manufactured Under Contract |
| C200263 | Drug | OTC Monograph Drug |
| C80441 | Device | Premarket Application |
| C80442 | Device | Premarket Notification |
| C175462 | Drug or Biologic | SIP Approved Drug |
| C101533 | Drug | unapproved drug for use in drug shortage |
| C73627 | Drug | unapproved drug other |
| C132335 | Drug | Unapproved drug product manufactured Under Contract |
| C95602 | Drug | Unapproved drug product manufactured Under Contract |
| C73614 | Drug | unapproved homeopathic |
| C73613 | Drug | unapproved medical gas |
| C181659 | Drug | Outsourcing Facility Compounded Human Drug Product (Exempt From Approval Requirements) |
| C96966 | Drug | Emergency Use Authorization |

The following is an example for a drug product:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="NDC Product Code" codeSystem="2.16.840.1.113883.6.69"/>
      <name>proprietary name <suffix>suffix to name</suffix></name>
      <formCode code="dose form code"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="display name"/>

      <asEntityWithGeneric>
        <genericMedicine>
          <name>non proprietary name</name>
        </genericMedicine>
      </asEntityWithGeneric>
    </manufacturedProduct>

    <subjectOf>
      <approval>
        <!-- possibly approval number -->
        <code code="C73594" displayName="NDA"
          codeSystem="2.16.840.1.113883.3.26.1.1" />
        <!-- possibly other attributes in the marketing category -->
      </approval>
    </subjectOf>
  </manufacturedProduct>
</subject>

```

The following is an example for a device:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="Device Item Code" codeSystem="Item Code System"/>
      <name>proprietary name <suffix>suffix to name</suffix></name>
      <desc>Brief description of product (up to 512 characters)</desc>

      <asSpecializedKind>
        <generalizedMaterialKind>
          <code code="product classification code"
            codeSystem="2.16.840.1.113883.6.303"
            displayName="display name"/>
        </generalizedMaterialKind>
      </asSpecializedKind>
    </manufacturedProduct>

    <subjectOf>
      <approval>
        <!-- possibly approval number -->
        <code code="C80441" displayName="Premarket Application"
          codeSystem="2.16.840.1.113883.3.26.1.1" />
        <!-- possibly other attributes in the marketing category -->
      </approval>
    </subjectOf>
  </manufacturedProduct>
</subject>

```

Validation Procedures

- 3.1.1.1 There is an Item Code, except for part products not requiring an Item Code or if the document type is *Human Compounded Drug Label (75031-5)*, *Animal Compounded Drug Label (77647-6)*, *Indexing - Biologic or Drug Substance*

(77648-4) or *Risk Evaluation & Mitigation Strategies* (82351-8), *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6), *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), or *Cosmetic – Update* (X8888-5).

3.1.1.2 General rules about the Item Code are:

3.1.1.3 Code system is 2.16.840.1.113883.6.69 (NDC, NHRIC), 1.3.160 (GS1), 2.16.840.1.113883.6.40 (HIBCC), 2.16.840.1.113883.6.18 (ISBT 128), or 2.16.840.1.113883.3.9848 (Cosmetic Product Listing Number) except if the document type is *Indexing – Product Concept* (73815-3).

3.1.1.4 Code is compliant with the code system’s allocation rules.

3.1.1.5 There is a name, i.e., proprietary name of the product as used in product labeling or in the catalog, except if the document type is *Indexing - Product Concept* (73815-3) or *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), or *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6), or if the marketing statusCode is *new* or *cancelled*.

3.1.1.6 If the document type is *Human Compounded Drug Label* (75031-5) then there may be an item code.

3.1.1.7 The product item code has not been previously submitted in an NDC reservation of a different document set id with marketing status *new*.

3.1.2 Equivalence to other Products, Product Source

The following is for referencing information already submitted for a source drug:

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="NDC Product Code" codeSystem="2.16.840.1.113883.6.69"/>
      <name>proprietary name <suffix>suffix to name</suffix></name>

      <asEquivalentEntity classCode="EQUIV">
        <code code="C64637" codeSystem="2.16.840.1.113883.3.26.1.1"/>
        <definingMaterialKind>
          <code code="source NDC Product Code"
            codeSystem="2.16.840.1.113883.6.69"/>
        </definingMaterialKind>
      </asEquivalentEntity>
    </manufacturedProduct>
  </manufacturedProduct>
</subject>
```

This is a special case of referencing other products for various purposes. Another purpose is for products that are updated with improvement, where it may be useful to indicate a succession to a previous version of the product identified by the item code of the predecessor product. This can be done using the equivalence relationship with `<asEquivalentEntity>` with a different Role code as in Table 2:

```
<manufacturedProduct>
  <manufacturedProduct>
    ...
  <asEquivalentEntity classCode="EQUIV">
    <code code="C?????" codeSystem="2.16.840.1.113883.3.26.1.1"/>
  <definingMaterialKind>
    <code code="81234567890008" codeSystem="1.3.160"/>
```

The following equivalence codes are defined:

| Equivalence | Code |
|---------------------|----------------|
| Same | C64637 |
| Predecessor Product | <i>pending</i> |

Product source may be specified under a product

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <asEquivalentEntity>
```

or under parts

```
<part>
  <partProduct>
    <asEquivalentEntity>
```

Validation Procedures

- 3.1.2.1 As equivalent entity class code is as above
- 3.1.2.2 If there is a classCode, it is “EQUIV”.
- 3.1.2.3 Code and code system are as above, except if the document type is *Indexing - Product Concept (73815-3)* or *Indexing - Warning Letter Alert (77288-9)*.
- 3.1.2.4 Source NDC product code (Defining material kind code) matches an NDC product code (Item Code) in an SPL file with a different set id.
- 3.1.2.5 Equivalent Item Code is not the same as the Item Code for the product

- 3.1.2.6 Equivalent Item Code is not the same as the Item Code for another equivalence stated for this product, except if the document type is *Indexing - Product Concept* (73815-3).
- 3.1.2.7 The Source NDC product code is not currently inactivated by an FDA Agency Initiated Compliance Action.
- 3.1.2.8 There is only one product source per product.
- 3.1.2.9 If the document type is *Human Compounded Drug Label* (75031-5) or *Animal Compounded Drug Label* (77647-6) then there is no product source.
- 3.1.2.10 If the source NDC product code (Defining Material Kind Code) matches an NDC product code (Item Code) with a marketing end date in an SPL file with a different set id, then the repackager's/relabeler's NDC product code is associated with a marketing end date which is identical or prior to the marketing end date for the source NDC product code (Defining Material Kind Code).

3.1.3 Additional Identifiers for this Product

A multitude of other identifiers may be assigned to some products by various parties, manufacturers, distributors, wholesalers, regulators. These identifiers are of a varying quality in terms of control for uniqueness and meaning. They may be unique item codes from other ISO 15459 item code systems, or they may be less well defined codes such as “model number” or “catalog number” etc. While those “model numbers” or “catalog numbers” are often not safe for referencing, such identifiers are customer facing and may encode minor product variants, which would be recognized by customers and hence listing such identifier cross references can aid in finding the correct item code.

```

<manufacturedProduct>
  <manufacturedProduct>
    ...
  <asIdentifiedEntity classCode="IDENT">
    <id extension="other identifier" root="other identifier root"/>
    <code code="other identifier type code"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="model number"/>

```

HL7 requires any identifier to be made globally unique, therefore submitters must acquire an OID of their own through any of several sources. Submitters must not allow conflicting assignments of model numbers among their own products. Submitters can still create unique identifiers from these model numbers by giving different root OIDs for each kind of identifiers that may be in conflict. Once a company has acquired a root OID this root OID can be freely sub-divided. For example, ACME Fine Devices Inc. may have acquired the OID 2.16.840.1.113883.3.98765 from the HL7 registry. ACME then decided to use a sub-branch .2 under their OID to manage model numbers for the models from models

release before 2007 and sub-branch .5 for models released after 2007. There is no specific rule that must be obeyed when sub-dividing OIDs as long as it results in the concatenation of model number code and codeSystem OID to be a unique identifier.

Different types of such identifications may be assigned different codes from the NCI Thesaurus for Model Number, Catalog Number and possibly other “types” of numbers:

Table 3: Miscellaneous Identifier Types

| Identifier Type | Code | Description |
|------------------|--------|--|
| Model Number | C99286 | the exact model number found on the device label or accompanying packaging. |
| Catalog Number | C99285 | the exact number as it appears in the manufacturer's catalog, device labeling, or accompanying packaging |
| Reference Number | C99287 | any secondary product identifier |

3.1.4 Ingredient

Ingredients may be specified for products

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <ingredient/>
```

and parts.

```
<part>
  <partProduct>
    <ingredient/>
```

Ingredient information includes the class code specifying the type of ingredient (e.g., active, inactive), code, name, and strength, and possibly active moiety name(s) and identifier and a reference ingredient name and identifier.

```
<ingredient classCode="class code including basis of strength">
  <quantity>
    <numerator value="value" unit="UCUM code"/>
    <denominator value="value" unit=" UCUM code"/>
  </quantity>
  <ingredientSubstance>
    <code code="UNII" codeSystem="2.16.840.1.113883.4.9"/>
    <name>active ingredient name</name>
    <activeMoiety>
      <activeMoiety>
        <code code="UNII" codeSystem="2.16.840.1.113883.4.9"/>
        <name>active moiety name</name>
      </activeMoiety>
    </activeMoiety>
```

```

<asEquivalentSubstance>
  <definingSubstance>
    <code code="UNI" codeSystem="2.16.840.1.113883.4.9"/>
    <name>reference substance name</name>
  </definingSubstance>
</asEquivalentSubstance>
</ingredientSubstance>
</ingredient>

```

Devices too may have active ingredients as discussed above (device with embedded ingredient.)

The ingredient element is also used to specify that a product “may contain” a certain substance (e.g., latex, milk, nuts) or that it “does not contain” such substances (e.g., wheat gluten).

“May contain” is expressed by specifying the ingredient using the class code “CNTM” without any quantity; e.g., product may contains latex:

```

<ingredient classCode="CNTM">
  <ingredientSubstance>
    <code code="2LQ0UUW8IN" codeSystem="2.16.840.1.113883.4.9"/>
    <name>NATURAL LATEX RUBBER</name>
  </ingredientSubstance>
</ingredient>

```

“Does not contain” is expressed by specifying the ingredient using the class code “CNTM” without a quantity with numerator 0 (zero); e.g. product is gluten free:

```

<ingredient classCode="CNTM">
  <quantity>
    <numerator value="0" unit="1"/>
    <denominator value="1" unit="1"/>
  </quantity>
  <ingredientSubstance>
    <code code="1534K8653J" codeSystem="2.16.840.1.113883.4.9"/>
    <name>WHEAT GLUTEN</name>
  </ingredientSubstance>
</ingredient>

```

If the ingredient comes from a product (such as in Human Compounded Drug Labels, 75031-5) one can specify the product item code for the ingredient as a source product, or, when the product item code is an NDC, called simply the ingredient’s source NDC.

```

<ingredient classCode="ingredient class code e.g., ACTI(M/B/R)">
  ...
  <ingredientSubstance .../>

  <subjectOf>
    <substanceSpecification>
      <code code="Source NDC" codeSystem="2.16.840.1.113883.6.69"/>
    </substanceSpecification>
  </subjectOf>
</ingredient>

```

Active ingredient class codes are “ACTIB”, “ACTIM”, and “ACTIR”. See Section 3.2.3 for details on active ingredients. Other ingredient classes exist aside from active ingredients. Drugs have inactive ingredients (also called “excipients”) described in Section 3.2.6. Devices, dietary supplements, cosmetics and certain compounded drugs may also have ingredients whose class is not further specified other than that it is an “ingredient” (INGR):

```
<ingredient classCode="INGR">  
  <ingredientSubstance>  
    <code code="PQ6CK8PD0R" codeSystem="2.16.840.1.113883.4.9"/>  
    <name>ASCORBIC ACID</name>
```

Validation Procedures

- 3.1.4.1 There is a class code.
- 3.1.4.2 There may be a strength with a numerator and denominator
- 3.1.4.3 Numerator and denominator have a value greater than zero and a unit, except the numerator when the ingredient class code is “CNTM”.
- 3.1.4.4 Unit comes from the *UCUM units of measures* list
- 3.1.4.5 For percentages numerator unit is not 1, instead use a volume unit for volume fractions and a mass unit for mass fractions.
- 3.1.4.6 The denominators values and units for all ingredients in this product are the same.
- 3.1.4.7 There is an ingredient code with code and code system, except for cosmetics product listings, where the code is optional.
- 3.1.4.8 Code system is 2.16.840.1.113883.4.9 except if the document type is *Human Compounded Drug Label (75031-5)*
- 3.1.4.9 The same ingredient substance code (UNII) is not used more than once per product.
- 3.1.4.10 There is an ingredient name.
- 3.1.4.11 Name matches the code (UNII)
- 3.1.4.12 If the document type is *Human Compounded Drug Label (75031-5)* or *Animal Compounded Drug Label (77647-6)* then there are source(s) of the active ingredient(s) which are identified using an item code (ingredient source NDC), or as ingredients (with the classCode “INGR”) such as a dietary supplement ingredients.

- 3.1.4.13 If the document type is not *Human Compounded Drug Label (75031-5)* or *Animal Compounded Drug Label (77647-6)* then there is no ingredient source product item code (ingredient source NDC).
- 3.1.4.14 Ingredient source product item code (source NDC) has been previously submitted (i.e. is a known listed product).
- 3.1.4.15 If the document type is *Animal Compounded Drug Label (77647-6)*, then the source of the active ingredient (bulk or finished drug(s)) identified by the item code (source NDC product code) has that same active ingredient as the compounded drug product.
- 3.1.4.16 If the document type is, *Animal Compounded Drug Label (77647-6)*, then the source of the active ingredient (bulk or finished drug(s)) identified by the item code (source NDC product code) can consist of more than one active ingredient, and in that case all the source's active ingredients must be mentioned in the compounded drug product.

3.1.5 Packaging

The packaging includes the quantity of product in the package and the package type and Package Item Code (such as NDC Package Code or other Item Code for the package).

Packaging may be specified for the product,

```
<manufacturedProduct>
  <manufacturedProduct>
    <asContent/>
```

for parts,

```
<part>
  <partProduct>
    <asContent/>
```

and for packages.

```
<asContent>
  <containerPackagedProduct>
    <asContent/>
```

The format for packaging specification is:

For example,

```

<asContent>
  <quantity>
    <numerator value="value" unit="UCUM code"/>
    <denominator value="1"/>
  </quantity>

  <containerPackagedProduct>
    <code code="Package Item Code" codeSystem="2.16.840.1.113883.6.69"/>
    <formCode code="value" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name"/>
  </containerPackagedProduct>
</asContent>

```

Validation Procedures

- 3.1.5.1 A product may have an “as content” (package information) element (optional for parts)
- 3.1.5.2 There is a quantity, except if the document type is *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), or *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6); see Section 30.
- 3.1.5.3 Quantity (for package information) includes a numerator and denominator.
- 3.1.5.4 Numerator (for package amount) has a value greater than zero and a unit
- 3.1.5.5 If the product has parts, then the initial numerator value and unit is “1”
- 3.1.5.6 Unit of the numerator (for package amount) of the initial package is the same as the units for the denominators of all the ingredient quantities (strengths)
- 3.1.5.7 Unit of the numerator (for package amount) of an outer package is the same as the unit for the denominator of the quantity of the inner package
- 3.1.5.8 Denominator has value 1 and either no unit or unit “1”.
- 3.1.5.9 There is a form code, except if the document type is *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), or *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6); see Section 30.
- 3.1.5.10 Code system for form code is 2.16.840.1.113883.3.26.1.1.
- 3.1.5.11 Display name matches form code
- 3.1.5.12 There is a package item code with code and code system for outermost package, except for parts or if the document type is *Human Compounded Drug Label* (75031-5) or *Animal Compounded Drug Label* (77647-6).

- 3.1.5.13 If document type is *Cellular Therapy* (60684-8), *Plasma Derivative* (60683-0), *Vaccine Label* (53404-0), then there is a package item code with code and code system for the inner, unit of use package, except if the inner package is wrapped into a pouch (C43200) the item code may be on the pouch level.
- 3.1.5.14 If the document type is *Human Compounded Drug Label* (75031-5) or *Animal Compounded Drug Label* (77647-6) and if there is a product NDC, then there should be an outermost package NDC.
- 3.1.5.15 If the package item code has been previously submitted, then the package form code and quantity value and unit are the same as in the most recent submission for this item code.
- 3.1.5.16 If the package item code is mentioned elsewhere in the document, then the package form code and quantity value and unit are the same and the content of both packages have an Item Code that is the same.
- 3.1.5.17 Package item code does not match any other package item code in the same package hierarchy.
- 3.1.5.18 If the package item code is an NDC/NHRIC (i.e., if the root is “2.16.840.1.113883.6.69”), then the following procedures apply:
- 3.1.5.19 NDC/NHRIC package item code is 10 digits (excluding any hyphens).
- 3.1.5.20 NDC/NHRIC package item code contains three segments divided by hyphens.
- 3.1.5.21 The first two segments of the NDC/NHRIC package item code matches the NDC/NHRIC product/item code.
- 3.1.5.22 The third segment of the NDC/NHRIC package item code is numeric.
- 3.1.5.23 If the package item code is an ISBT 128 code (i.e., if the root is “2.16.840.1.113883.6.18”), then the following procedures apply:
- 3.1.5.24 ISBT 128 package item code has three segments divided by hyphens.
- 3.1.5.25 The first two segments of the ISBT 128 package item code matches the ISBT 128 Product Item Code.
- 3.1.5.26 The third segment contains two digits.
- 3.1.5.27 Package Item Code code system is 2.16.840.1.113883.6.69 (NDC, NHRIC), 1.3.160 (GS1), 2.16.840.1.113883.6.40 (HIBCC), 2.16.840.1.113883.6.18 (ISBT 128), or 2.16.840.1.113883.3.9848 (Cosmetic Product Listing Number).

3.1.5.28 Package Item Code is compliant with the code system's allocation rules.

3.1.5.29 If the document type is not for *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Drug for Further Processing* (78744-0), *OTC Animal Drug Label* (50577-6), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type B Medicated Feed Animal Drug Label* (50574-3), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Prescription Animal Drug Label* (50578-4), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), *Cosmetic* (58474-8), *Dietary Supplement* (58476-3), *Medical Food* (58475-5), *Human Compounded Drug Label* (75031-5), *Animal Compounded Drug Label* (77647-6), *Lot Distribution Data* (66105-8), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6), or *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), then a combination product type characteristic is on the inner-most packaging.

3.1.6 Kits, Parts, Components and Accessories

Products may be combined in various ways such as:

- Drug kit with a device part
- Device kit with a drug part
- Device with an embedded drug
- Drug in a delivery device
- Products sold separately but meant to be used together

Kits and Parts: When products have more than one part, each part is described under <partProduct>. The total amount of the part in the product is included as follows:

```
<part>
  <quantity>
    <numerator value="total amount of part in product" unit="UCUM code"/>
    <denominator value="1"/>
  </quantity>
  <partProduct>
    <!-- same as above for drug or device. -->
```

Currently, when a drug product has parts, it is considered a Kit indicated by the formCode for KIT:

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="11234560012349" codeSystem="1.3.160"/>
    <name>Easy-Go PreciFuse PorterPump Kit</name>
    <formCode code=" C47916" displayName="KIT"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
  </part><!-- ... -->

```

Device products may also be kits (in this case a device with FDA product classification code but also with formCode specifying KIT. However, devices themselves may also be specified with parts, such as distinguishing component options or field replaceable parts, in this case the top-level device need not have a formCode for KIT:

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="item code of device" codeSystem="code system OID"/>
    <name>name of device</name>
    <desc>brief description of device</desc>

    <asSpecializedKind ... product classification for device ... />
  <part>
    <quantity>
      <numerator value="1"/>
      <denominator value="1"/>
    </quantity>
    <partProduct>
      <code code="item code of part" codeSystem="code system OID"/>
      <name>name of part</name>
      <desc>brief description of device part</desc>

```

Drug Kit with a Device Part: This sort of kit has been known from SPL R4 as well, examples being drugs sold as a kit with an applicator device.

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="NDC code of kit" codeSystem="2.16.840.1.113883.6.69"/>
    <name>name of kit</name>
    <formCode code="C47916" displayName="KIT"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <asEntityWithGeneric .../>
  <part>
    <quantity>
      <numerator value="amount of this part's content in one kit"
        unit="unit for amount"/>
      <denominator value="1"/>
    </quantity>
    <partProduct>
      <code code="NDC code of drug part"
        codeSystem="2.16.840.1.113883.6.69"/>
      <name>name of drug part</name>
      <formCode code="form code of drug part"
        displayName="form name of drug part"
        codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <ingredient ... />

```

```

    <asContent>
      <quantity>
        <numerator value="amount of this part in its package"
          unit="unit of amount"/>
        <denominator value="1"/>
      </quantity>
      <containerPackagedProduct>
        <code code="NDC code of part's package"
          codeSystem="2.16.840.1.113883.6.69"/>
        <formCode code="package type"
          displayName="package type name"
          codeSystem="2.16.840.1.113883.3.26.1.1"/>
      </containerPackagedProduct>
    </asContent>
  </partProduct>
</part>
<part>
  <quantity>
    <numerator value="amount of this device part in one kit"/>
    <denominator value="1"/>
  </quantity>
  <partProduct>
    <code code="item code of this device part"
      codeSystem="item code system OID"/>
    <name>name of device part</name>
    <desc>description of device part</desc>
    <asSpecializedKind>
      <generalizedMaterialKind>
        <code code="product classification code of device part"
          codeSystem="2.16.840.1.113883.6.303"
          displayName="display name of device part"/>
      </generalizedMaterialKind>
    </asSpecializedKind>
  </partProduct>
</part>

```

Device Kit with a Drug Part:

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="item code of device kit"
      codeSystem="item code system OID"/>
    <name>name of kit</name>
    <desc>brief description of kit</desc>
    <formCode code="C47916" displayName="KIT"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <asSpecializedKind>
      <generalizedMaterialKind>
        <code code="product classification code of kit"
          displayName="display name of kit"
          codeSystem="2.16.840.1.113883.6.303"/>
      </generalizedMaterialKind>
    </asSpecializedKind>
  <part>
    same as device part above
  </part>

```

```

<part>
  same as drug part above
</part>

```

Device with an embedded drug: For example, a drug eluting stent with an embedded active ingredient. Notice that such products do not involve kits and parts:

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="device item code"
      codeSystem="device item code system OID"/>
    <name>device name</name>
    <desc>brief description</desc>
    <asSpecializedKind>
      <generalizedMaterialKind>
        <code code="product classification code of device"
          displayName="display name of device"
          codeSystem="2.16.840.1.113883.6.303"/>
      </generalizedMaterialKind>
    </asSpecializedKind>
    <ingredient classCode="ACTIB">
      <quantity ../>
      <ingredientSubstance>
        <code code="UNII code of active ingredient"
          codeSystem="2.16.840.1.113883.4.9"/>
        <name>paclitaxel</name>

```

Drug in a delivery device: For example, drug in pre-filled syringe. Note that the syringe filled with the drug is a different product than the empty syringe. Hence it would not be correct to put the item code for the empty syringe on the one filled with the drug. In fact, since the pre-filled syringe already has (or should have) an NDC code, there is no need for another item code for it. However, one may want to refer to the item code for the empty syringe as a generalization of the filled syringe:

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="NDC code drug"
      codeSystem="2.16.840.1.113883.6.69"/>
    <name>name of drug</name>
    <formCode code="form code of drug"
      displayName="form display name of drug"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <ingredient classCode="ACTIB">
      <!-- active ingredient -->
    </ingredient>
    <asContent>
      <quantity>
        <numerator value="amount of drug in prefilled device"
          unit="unit of amount"/>
        <denominator value="1"/>
      </quantity>

```

```

<containerPackagedProduct>
  <code code="NDC code for prefilled device"
    codeSystem="2.16.840.1.113883.6.69"/>
  <formCode code="form code of prefilled device"
    displayName="form display name of prefilled device"
    codeSystem="2.16.840.1.113883.3.26.1.1"/>

  <asSpecializedKind>
    <generalizedMaterialKind>
      <code code="item code of empty device"
        codeSystem="item code system of empty device"/>
      <desc>brief description of empty device</desc>

    <asSpecializedKind>
      <generalizedMaterialKind>
        <code code="product classification code of device"
          displayName="display name of device"
          codeSystem="2.16.840.1.113883.6.303"/>
      </generalizedMaterialKind>
    </asSpecializedKind>
  </asSpecializedKind>

```

Products sold separately but meant to be used together: when products are used together but packaged separately, the data element `<asPartOfAssembly>` is used to identify the other product. The products could be drugs or devices.

```

<manufacturedProduct>
  <manufacturedProduct>
    <code code="item code of device" codeSystem="code system OID"/>
    <name>name of device</name>
    <desc>brief description of device</desc>

    <asSpecializedKind ... product classification for device .../>

    <asPartOfAssembly>
      <quantity>
        <numerator value="1"/>
        <denominator value="1"/>
      </quantity>

      <wholeProduct><!-- this is the assembly, but has no identifier -->
        <part>
          <quantity>
            <numerator value="1"/>
            <denominator value="1"/>
          </quantity>
          <partProduct>
            <code code="item code of accessory component"
              codeSystem="code system OID"/>
            <name>name of accessory component</name>
            <desc>brief description of accessory component</desc>

            <asSpecializedKind ... product classification for device .../>
          </partProduct>
        </part>
      </wholeProduct>
    </asPartOfAssembly>
  </manufacturedProduct>

```

Parts may be specified for the product,

```

<manufacturedProduct>
  <manufacturedProduct>
    <part/>

```

and for part products.

```

<part>
  <partProduct>
    <part/>

```

Validation Procedures

- 3.1.6.1 If the product form code is for a *Kit* (C47916), then there is one or more parts.
- 3.1.6.2 Each part has an overall quantity
- 3.1.6.3 If there is an “as content” (package information) data element in the part, then the numerator unit is the same as the numerator unit for the “as content” data element
- 3.1.6.4 If there is no “as content” (package information) data element in the part, then the numerator unit is 1, except if the document type is *Indexing - Product Concept* (73815-3) or marketing status is *new* or *cancelled*.
- 3.1.6.5 If there is a code, then the general rules for product code apply (see 3.1.1.1ff).
- 3.1.6.6 There is a name, except if the document type is *Indexing - Product Concept* (73815-3).
- 3.1.6.7 Procedures for source, ingredients, characteristics and packaging are the same as for products without parts
- 3.1.6.8 If the product is a kit/co-packaged product with the form code, C47916 (for *Kit*), the document type/product type is *Bulk Ingredient* (53409-9), *Human OTC Drug Label* (34390-5) or *Human Prescription Drug Label* (34391-3), the marketing start date for the co-packaged product is on or after November 1st, 2020 and the marketing category is not *Cosmetic* (C86965), *Dietary Supplement* (C86952), *Exempt Device* (C80438), *Humanitarian Device Exemption* (C80440), *Medical Food* (C86964), *Premarket Application* (C80441) or *Premarket Notification* (C80442), then each inner component product (<partProduct>) with a drug marketing category (see Table 1) has a unique NDC product code.

3.1.7 Marketing Category and Application Number

The approval structure specifies in the <code> the marketing category under which the product is approved for marketing. Products marketed under an approved application have an application number in the <id extension> and application tracking system under <id root>. Products marketed under a monograph provide the monograph ID for the monograph <id extension> and the OTC Monograph ID under <id root>. If there is no application number or monograph ID, the id element is omitted.

```

<subjectOf>
  <approval>
    <id extension="application, monograph ID, or monograph number"
      root="FDA document tracking system OID, OTC Monograph ID OID, or
CFR OID"/>
    <code code="code for marketing category"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name"/>
    <effectiveTime>
      <low value="approval date"/>
    </effectiveTime>
    <author>
      <territorialAuthority>
        <territory>
          <code code="USA" codeSystem="1.0.3166.1.2.3"/>
        </territory>
      </territorialAuthority>
    </author>
  </approval>
</subjectOf>

```

Marketing category is connected through the <subjectOf> element which may appear on the main product:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct/>
  <subjectOf/>

```

or on parts:

```

<part>
  <partProduct/>
  <subjectOf/>

```

Example:

```

<subjectOf>
  <approval>
    <id extension="NDA123456" root="2.16.840.1.113883.3.150"/>
    <code code="C73594"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="NDA"/>
    <author>
      <territorialAuthority>
        <territory>
          <code code="USA" codeSystem="1.0.3166.1.2.3"/>
        </territory>
      </territorialAuthority>
    </author>
  </approval>
</subjectOf>

```

Validation Procedures

- 3.1.7.1 There is one marketing category for every product and product part, except if the document type is *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), *Cosmetic – Update* (X8888-5), *Indexing – Product Concept* (73815-3), *Indexing - Warning*

Letter Alert (77288-9), or Out of Business Notification (53411-5), FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation (89600-1), or FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug (99282-6), or there is no marketing status other than new or cancelled.

- 3.1.7.2 There is a marketing category code.
- 3.1.7.3 Code comes from the *Marketing category* list.
- 3.1.7.4 Display name matches the code
- 3.1.7.5 Code system is 2.16.840.1.113883.3.26.1.1
- 3.1.7.6 Territorial authority is as above

Marketing Category vs. Application Number

The following are validation procedures relating marketing category to application numbers:

- 3.1.7.7 If the code is C73583 (ANADA), C73584 (ANDA), C73585 (BLA), C73588 (conditional NADA), C73593 (NADA), C73594 (NDA), C73605 (NDA authorized generic), C75302 (IND), C80438 (Exempt device), C80440 (Humanitarian Device Exemption), C80441 (Premarket Application), C80442 (Premarket Notification), C92556 (Legally Marketed Unapproved New Animal Drugs for Minor Species), C175238 (Multi-Market Approved Product) or C175462 (SIP Approved Drug), then the id root is 2.16.840.1.113883.3.150 (FDA application tracking system).
- 3.1.7.8 [RESERVED]
- 3.1.7.9 If the code is C73583 (ANADA), then the id extension has the prefix “ANADA” followed by 6 digits
- 3.1.7.10 If the code is C73584 (ANDA), then the id extension has the prefix “ANDA” or “BA” followed by 6 digits
- 3.1.7.11 If the code is C73585 (BLA), then the id extension has the prefix “BLA” followed by 6 digits
- 3.1.7.12 If the code is C73593 (NADA) or C73588 (Conditional NADA), then the id extension has the prefix “NADA” followed by 6 digits
- 3.1.7.13 If the code is C73594 (NDA), or C73605 (NDA authorized generic), then the id extension has the prefix “NDA” or “BN” followed by 6 digits

- 3.1.7.14 If the code is C75302 (IND), then the id extension has the prefix “IND” followed by 6 digits
- 3.1.7.15 [RESERVED].
- 3.1.7.16 [RESERVED].
- 3.1.7.17 [RESERVED].
- 3.1.7.18 If the code is C92556 (Legally Marketed Unapproved New Animal Drugs for Minor Species), then the id extension has the prefix “MIF” followed by 6 digits.
- 3.1.7.19 If the code is C80438 (Exempt device), then the id extension consists of 3 letters
- 3.1.7.20 If the code is C80440 (Humanitarian Device Exemption), then the id extension has a prefix “H” followed by 6 digits
- 3.1.7.21 If the code is C80441 (Premarket Application), then the id extension has a prefix “P” or “BP” followed by 6 digits
- 3.1.7.22 If the code is C80442 (Premarket Notification), then the id extension has a prefix “K” or “BK” followed by 6 digits.
- 3.1.7.23 If the code is not C73583 (ANADA), C73584 (ANDA), C73585 (BLA), C73588 (Conditional NADA), C73593 (NADA), C73594 (NDA), C200263 (OTC Monograph Drug), C73605 (NDA authorized generic), C75302 (IND), C80438 (Exempt device), C80440 (Humanitarian Device Exemption), C80441 (Premarket Application), C80442 (Premarket Notification), C132333 (Approved drug product manufactured Under Contract), C73626 (bulk ingredient), C96793 (bulk ingredient for human prescription compounding), or C98252 (bulk ingredient for animal drug compounding), C94795 (Drug for further processing), C92556 (Legally Marketed Unapproved New Animal Drugs for Minor Species), C175238 (Multi-Market Approved Product) or C175462 (SIP Approved Drug), then there is no id (application number or regulatory citation or monograph ID).
- 3.1.7.24 If the marketing category is *Approved drug product manufactured Under Contract* (C132333), then there is an id (application number or regulatory citation).
- 3.1.7.25 If the marketing category is *Approved drug product manufactured Under Contract* (C132333), then the id extension has the prefix “NDA”, “ANDA”, or “BLA” followed by 6 digits
- 3.1.7.26 If the marketing category is *Bulk Ingredient* (C73626), *Bulk Ingredient for Human Prescription Compounding* (C96793), or *Bulk Ingredient for Animal*

Drug Compounding (C98252), or Drug for Further Processing (C94795) and there is an id, then the id extension has the prefix “DMF” or “VMF” followed by 6 digits.

- 3.1.7.27 If the marketing category is C175238 (Multi-Market Approved Product) or C175462 (SIP Approved Drug), then the id extension has the prefix NDA, BN, or BLA followed by 6 digits.
- 3.1.7.28 If the marketing category is C200263 (OTC Monograph Drug), then the id root is 2.16.840.1.113883.3.9421 (OTC Monograph ID)

Application Number Consistency

- 3.1.7.29 If the marketing category is *ANDA (C73584), BLA (C73585), or NDA (C73594)* and the SPL document type is not *Lot Distribution Data (66105-8)* or *Vaccine Label (53404-0)* and the application number was already submitted, then the active ingredient UNIIs are the same as in any previous submission of a product with the same application number.
- 3.1.7.30 If the application number is referenced in any Product Concept Indexing file, then the active ingredient, strength and active moiety match a Product Concept Indexing file, except if the document type is *Lot Distribution Data (66105-8)* or the *Indexing – Product Concept (73815-3)* file itself.
- 3.1.7.31 If the application number or citation is referenced in the OTC drug product application list, then the active ingredient (UNII) and route of administration associated with the application number matches the entry in the list.
- 3.1.7.32 If on or after March 23th 2020, the application number is present in the *NDA to BLA Conversion List*, then the marketing category and application number prefix must be changed to BLA.

Application Approval Date

- 3.1.7.33 There may be an approval date (effective time).
- 3.1.7.34 Approval date (effectiveTime) has a low boundary.
- 3.1.7.35 Approval date has no high boundary.
- 3.1.7.36 Approval date has at least the precision of day (YYYYMMDD).
- 3.1.7.37 If the marketing category code is not C73584 (ANDA), C73585 (BLA), C73594 (NDA), or C175462 (SIP approved drug), then there is no approval date.
- 3.1.7.38 [RESERVED].

3.1.8 Marketing status

The marketing status provides information on when the product is on or off the market.

```
<subject>
  <manufacturedProduct>...</manufacturedProduct>

  <subjectOf>
    <marketingAct>
      <code code="C53292" codeSystem="2.16.840.1.113883.3.26.1.1"/>
      <statusCode code="active"/>
      <effectiveTime>
        <low value="20040120"/>

```

The `<code>` indicates the activity of “marketing” (or in cases of some packages as “marketing of sample packages not for sale”). The status of the product is described in the `<statusCode>` as either “active” for being on the market or “completed” when a product is discontinued, or “new” to indicate that the product item code is being reserved for future use. If the status of the product is cancelled, the NDC reservation is being cancelled. The date when the product is on or marketed or discontinued is included in the `<effectiveTime>`. The date when the product is on the market is characterized by the `<low value>`.

Example of a currently marketed product:

```
<subjectOf>
  <marketingAct>
    <code code="C53292" codeSystem="2.16.840.1.112883.3.26.1.1"/>
    <statusCode code="active"/>
    <effectiveTime>
      <low value="date when on the market"/>
    </effectiveTime>
  </marketingAct>
</subjectOf>
```

The marketing discontinuation date such as the expiration date of the last lot released to the market is characterized by the `<high value>`.

Example of a product that is discontinued:

```
<subjectOf>
  <marketingAct>
    <code code="C53292" codeSystem="2.16.840.1.112883.3.26.1.1"/>
    <statusCode code="completed"/>
    <effectiveTime>
      <low value="date when the product is on the market"/>
      <high value="date when the product is going to be off the market"/>
    </effectiveTime>
  </marketingAct>
</subjectOf>
```

For some types of products, a marketing status may be provided on the package level:

```

<asContent>
  <containerPackagedProduct>...</containerPackagedProduct>

  <subjectOf>
    <marketingAct>
      <code code="C53292" codeSystem="2.16.840.1.113883.3.26.1.1"/>
      <statusCode code="active"/>
      <effectiveTime>
        <low value="20040120"/>

```

Packages may also be marked as being a drug sample rather than regularly marketed for sale, Packages that are samples are marked with a marketingAct with the code C96974 instead of the default marketing act code C53292:

```

<asContent>
  <containerPackagedProduct>...</containerPackagedProduct>

  <subjectOf>
    <marketingAct>
      <code code="C96974" codeSystem="2.16.840.1.113883.3.26.1.1"/>
      <statusCode code="active"/>
      <effectiveTime>
        <low value="20040120"/>

```

The package marketing status and start and end date (if applicable) are in the same marketing act.

NDC Code Reservations

For human and animal drug products, NDC code reservations may be sent. This is done in a listing file, except that content of labeling is not included. The products that appear in the listing file, do not need a marketing category. Therefore it is not determined if they are drugs, dietary supplements, cosmetics, devices or biologic products.

All products require

- a non-proprietary name and
- a dose form.

Note that a proprietary name is not required. Packaging is also not required.

There are 3 types of products with further data requirements.

- drugs need at least one full active ingredient specification, with ingredient name, UNII, strength, active moiety, and basis of strength.
- dietary supplements need an ingredient (classCode INGR) with ingredient name and UNII.

A marketing status is required for every product, and the status 'new' indicates that this product is provided to reserve an NDC product code.

If the marketing status is 'new' a marketing start date should be provided up to 2 years in the future.

An NDC reservation should be sent as one document those products which will likely be contained in the same listing file once these products begin to be marketed. The document set id will then be used by the listing file, i.e., the next version of an NDC reservation will be a listing file. In a listing file which follows an NDC reservation, every NDC code that has been reserved needs to be disposed of as either active or cancelled. The active products become the actively listed products (their marketing start dates may still be in the future), and the NDC codes that are released will be marked as cancelled. Once cancelled, these NDC codes do not need to be mentioned any more in subsequent listing files.

Note that currently it is not expected that NDC reservations will be updated before the submission of the first listing files.

Validation Procedures

- 3.1.8.1 There is one marketing status for each top-level product (part products do not need this), except if the document type is a *Animal Compounded Drug Label* (77647-6), *Human Compounded Drug Label* (75031-5), *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), *Cosmetic – Update* (X8888-5), *Cosmetic – Abbreviated Renewal* (X8888-6), *Indexing - Product Concept* (73815-3), *Lot Distribution Data* (66105-8), *Indexing - Warning Letter Alert* (77288-9), *Indexing - Biologic or Drug Substance* (77648-4), *Risk Evaluation & Mitigation Strategies* related (82353-4, 85273-1, 85274-9, 82351-8), *Out of Business Notification* (53411-5), *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), or *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation – Animal Drug* (99282-6), or if the SPL file is for *Salvaged Drugs* (having business operation as *salvage*, C70827).
- 3.1.8.2 There is not more than one marketing status on any one item.
- 3.1.8.3 Marketing act code is C53292 (or C96974 for packages marked as *Drug Sample*) and code system is 2.16.840.1.113883.3.26.1.1.
- 3.1.8.4 Marketing status code is *active*, or *completed*, or *new*, or *cancelled*.
- 3.1.8.5 If the status code is *active* or *new*, then there is a low value (marketing start date) and no high value (marketing end date)
- 3.1.8.6 If the marketing status code is *completed*, (discontinued) then there is a low and high value, except if the document type is *Cosmetic Product Listing* (103572-4) or *Cosmetic – Update* (X8888-5).

- 3.1.8.7 The effective time low (marketing start date) and high boundary (marketing end date) have at least the precision of day in the format YYYYMMDD
- 3.1.8.8 If there is a high value (marketing end date), then it is not less than the low value (marketing start date).
- 3.1.8.9 A marketing status can not be on an inner package, except if the status code is *new*.
- 3.1.8.10 A marketing status can not be on a package for a part of a kit, except if the status code is *new*.
- 3.1.8.11 If the marketing start or end date is on a package, then the start date is not before the marketing start date of the product and the end date not after the end date of the product.
- 3.1.8.12 If any of the products in the document has the application number prefix BA or BN, then there is no package marketing status.
- 3.1.8.13 A marketing status can only be on a package in documents of types *Human Prescription Drug Label* (34391-3), *Human OTC Drug Label* (34390-5), *Drug for Further Processing* (78744-0), or *Bulk Ingredient* (53409-9),.
- 3.1.8.14 If the document type is *Human Compounded Drug Label* (75031-5) or *Animal Compounded Drug Label* (77647-6) then there is no marketing status.
- 3.1.8.15 A marketing act with code *Drug Sample* (C96974) is on a package only.
- 3.1.8.16 If the package is marked as a drug sample, then there is a package item code.
- 3.1.8.17 If an item has a marketing status *active*, then at least one of its packages has either no explicit marketing status at all, or a marketing status of *active*, except if the document type is *Risk Evaluation & Mitigation Strategies* (82351-8), *Cosmetic Product Listing* (103572-4), *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration - Biennial Renewal* (X8888-4), or *Cosmetic – Update* (X8888-5).
- 3.1.8.18 If the marketing status code is *active* or *completed*, then previous marketing status code for the item code (NDC product code) is not *cancelled*.
- 3.1.8.19 If the marketing status code is *completed*, then previous marketing status code for the item code (NDC product code) is not *new*.
- 3.1.8.20 If the product is regulated by CDER, then the marketing start or end date are present at the outermost package level, except for *Human Compounded Drug Label* (75031-5) or if marketing status is *new* or *cancelled*.

Validation Procedures for NDC Reservations

- 3.1.8.21 Marketing Status code new or cancelled can not be used at package level.
- 3.1.8.22 If the marketing status code is *new* or *cancelled*, then there is a start marketing date.
- 3.1.8.23 If the marketing status code is *new*, then marketing start date is two years or less from the date of the submission of the NDC reservation request.
- 3.1.8.24 If the marketing status code is *new* or *cancelled*, then marketing start date is the same for all products.
- 3.1.8.25 If the marketing status is *cancelled*, then there is no marketing end date.
- 3.1.8.26 If the marketing status code is *cancelled*, then previous marketing status code for the item code (NDC product code) is *new*.
- 3.1.8.27 If the marketing status code is *new* or *cancelled*, then marketing start date cannot be changed from the previous version.
- 3.1.8.28 If the marketing status code is *new* or *cancelled*, then there is an item code (NDC product code.)
- 3.1.8.29 If the marketing status is *new*, then the product item code has not been previously submitted in a document of a different set id, except if in that other document its marketing status is *cancelled*.
- 3.1.8.30 If the marketing status code is *new* or *cancelled*, then there is a non-proprietary name (generic medicine name.)
- 3.1.8.31 If the marketing status code is new or cancelled, then there is an active ingredient.
- 3.1.8.32 If any of the products have the marketing status of *new*, then products having any active ingredients have the same set of active ingredient substances.
- 3.1.8.33 Additional validation procedures for NDC product codes apply, see: 3.2.1.2 – 5 and 3.2.1.10 – 15.
- 3.1.8.34 NDCs can be reserved for drugs in development for a period of up to two years from the date of receipt of the initial reservation. Once the product(s) included on an NDC Reservation SPL are ready to launch in the U.S. market, the NDC Reservation SPL for the product(s) should be revised (change Marketing Status for ALL products on the SPL to “active”) and converted into a full product listing SPL.

- 3.1.8.35 For NDC reservation questions for CDER products, contact eDRLS@fda.hhs.gov.
- 3.1.8.36 For NDC reservation questions for CVM products, contact Charise.Kasser@fda.hhs.gov.
- 3.1.8.37 If a document contains any item code reservation (marketing status codes is *new*), then the SPL document type is *Bulk Ingredient* (53409-9), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *Plasma Derivative* (60683-0), *Standardized Allergenic* (60682-2), or *Vaccine Label* (53404-0) or CVM products.
- 3.1.8.38 If a document contains any item code reservation (marketing status codes is *new* or *cancelled*), then there are no marketing status codes of *active* or *completed*, except a part of a kit may be active if the kit is new or cancelled.
- 3.1.8.39 [POSTPONED] If the product information has previously been submitted, and the marketing start date is not in the future, then the marketing start date is not later than the previously submitted marketing start date.
- 3.1.8.40 [POSTPONED] The product marketing start date is not after any of the start dates of any active or completed marketing status for any of its previously submitted packages.

3.1.9 Characteristics

Many characteristics may be specified for products as specified later for specific product types. In general, the characteristic structure allows specifying any properties of the product in a code-value pair, the code saying which property is being specified, the value saying what the property is for the given product. The characteristics structure connects to the product Role through the `subjectOf` element.

```
<manufacturedProduct>
  <manufacturedProduct>
    ...
  </manufacturedProduct>
  <subjectOf>
    <characteristic>
      <code code="characteristic code"
            codeSystem="characteristic code system"/>
      <value xsi:type="characteristic value type" ...>
```

Some characteristics may be specified for packaged products:

```

<manufacturedProduct>
  <manufacturedProduct>
    ...
    <asContent>
      <containerPackagedProduct>
        ...
      </containerPackagedProduct>
      <subjectOf>
        <characteristic>
          <code code="characteristic code"
                codeSystem="characteristic code system"/>
          <value xsi:type="characteristic value type" ...>

```

Characteristics listed in Table 6 use one of a number of different data types. Each data type uses slightly different XML elements and attributes as shown in the templates below:

Characteristic of type physical quantity (PQ):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
          codeSystem="characteristic code system"/>
    <value xsi:type="PQ" value="quantity value" unit="quantity unit">

```

Characteristic of type number (REAL):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
          codeSystem="characteristic code system"/>
    <value xsi:type="REAL" value="quantity value"/>

```

Characteristic of type integer number (INT):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
          codeSystem="characteristic code system"/>
    <value xsi:type="INT" value="quantity value"/>

```

Characteristic of coded type (CV):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
          codeSystem="characteristic code system"/>
    <value xsi:type="CV" code="value code"
          codeSystem="value code system OID"
          displayName="value code display name">

```

Characteristic of type character string (ST):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
      codeSystem="characteristic code system"/>
    <value xsi:type="ST">value string</value>

```

Characteristic of type interval of physical quantity (IVL<PQ>):

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
      codeSystem="characteristic code system"/>
    <value xsi:type="IVL_PQ">
      <low value="quantity value low boundary" unit="quantity unit"/>
      <high value="quantity value high boundary" unit="quantity unit"/>
    </value>

```

Characteristic of type Boolean (true/false value)

```

<subjectOf>
  <characteristic>
    <code code="characteristic code"
      codeSystem="characteristic code system"/>
    <value xsi:type="BL" value="true or false"/>

```

Table 4: Characteristic codes and code systems.

| Name | Code System OID / Code | Data Type | Description |
|------------------------|------------------------------|-----------|---|
| SPL Characteristics | 2.16.840.1.113883.1.11.19255 | | Used early on with Existing SPL for drugs characteristics codes that are possibly applicable for devices: |
| | SPLSIZE | PQ | Greatest dimension in millimeter |
| | SPLCOLOR | CV | color code from NCI Thesaurus |
| | SPLIMAGE | ED | Photographic image of the product for the purpose of identification, taken under standardized conditions. |
| LOINC | 2.16.840.1.113883.6.1 | | Used for metrologically well defined properties. |
| NCI Thesaurus | 2.16.840.1.113883.3.26.1.1 | | Used rarely (if at all) for characteristic codes. |

Validation Procedures

- 3.1.9.1 There is a characteristic property code with code and code system
- 3.1.9.2 Characteristic property code system is 2.16.840.1.113883.1.11.19255, 2.16.840.1.113883.6.1, or 2.16.840.1.113883.3.26.1.1.
- 3.1.9.3 There is a characteristic value with specified type appropriate for the characteristic property.

3.1.9.4 Value type is PQ, INT, IVL_PQ, CV, CE, ST, ED, or BL

3.1.10 Combination Product Type

Combination products are defined in 21 CFR 3.2(e).

To mark products as combination products, the nearest combining package should bear the combination product type characteristic:

```
<manufacturedProduct>
  <manufacturedProduct>
    ...
    <asContent>
      ...
      <subjectOf>
        <characteristic>
          <code code="SPLCMBPRDTP"
            codeSystem="2.16.840.1.113883.1.11.19255"/>
          <value code="C102835"
            codeSystem="2.16.840.1.113883.3.26.1.1" xsi:type="CV"
            displayName="Type 2: Prefilled Drug Delivery Device/System">
```

Validation Procedures

3.1.10.1 Code and code system are as above

3.1.10.2 Value code system is 2.16.840.1.113883.3.26.1.1

3.1.10.3 Value comes from the Combination Product Type list.

3.1.10.4 Display name matches the value code

3.1.10.5 If the document type is for *Bulk Ingredient (53409-9)*, *Bulk Ingredient – Animal Drug (81203-2)*, *OTC Animal Drug Label (50577-6)*, *OTC Type A Medicated Article Animal Drug Label (50576-8)*, *OTC Type B Medicated Feed Animal Drug Label (50574-3)*, *OTC Type C Medicated Feed Animal Drug Label (50573-5)*, *Prescription Animal Drug Label (50578-4)*, *VFD Type A Medicated Article Animal Drug Label (50575-0)*, *VFD Type B Medicated Feed Animal Drug Label (50572-7)*, *VFD Type C Medicated Feed Animal Drug Label (50571-9)*, *Cosmetic (58474-8)*, *Dietary Supplement (58476-3)*, *Medical Food (58475-5)*, *Human Compounded Drug Label (75031-5)*, *Licensed Vaccine Bulk Intermediate Label (53406-5)*, *Drug for Further Processing (78744-0)*, *Animal Compounded Drug Label (77647-6)*, or *Animal Cells, Tissues, and Cell and Tissue Based Product Label (98075-5)*, then there is no combination product type characteristic on any package.

3.1.10.6 If the dosage form (form code) is *Aerosol, Metered (C42960)*, *Gel, Metered (C60930)*, *Powder, Metered (C42961)*, *Spray, Metered (C42962)* or *Tablet with*

Sensor (C147579), then there is a combination product type other than *Type 0: Not a Combination Product* (C112160).

- 3.1.10.7 If the dosage form (form code) is *Aerosol, Metered* (C42960), *Gel, Metered* (C60930), *Powder, Metered* (C42961), or *Spray, Metered* (C42962), then the combination product type is *Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)* (C102835) or *Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)* (C102836).
- 3.1.10.8 If the dosage form (form code) is *Tablet with Sensor* (C147579), then the combination product type is *Type 4: Device Coated/Impregnated/Otherwise Combined with Drug* (C102837).
- 3.1.10.9 If the package type is *Inhaler* (C16738), *Syringe* (C43202), *Syringe, Glass* (C43203), or *Syringe, Plastic* (C43204), then there is a combination product type other than *Type 0: Not a Combination Product* (C112160).
- 3.1.10.10 If the package type is *Inhaler* (C16738), then the combination product type is *Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)* (C102835) or *Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)* (C102836).
- 3.1.10.11 If the package type is *Syringe* (C43202), *Syringe, Glass* (C43203), or *Syringe, Plastic* (C43204), then the combination product type is *Type 1: Convenience Kit of Co-Package* (C102834), *Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)* (C102835), *Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)* (C102836) or *Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)* (C102842).

3.1.11 Production Amount

The production amount for a package is specified as:

```
<manufacturedProduct>
  <manufacturedProduct>
    ...
    <asContent>
      ...
      <subjectOf>
        <characteristic>
          <code code="SPLPRODUCTIONAMOUNT"
            codeSystem="2.16.840.1.113883.1.11.19255"/>
          <value xsi:type="INT" value="10000"/>
        </characteristic>
      </subjectOf>
    </asContent>
  </manufacturedProduct>
</manufacturedProduct>
```

Unlimited production amounts are specified as:

```
<value xsi:type="INT" nullFlavor="PINF"/>
```

Validation Procedures

3.1.11.1 Code and code system are as above

3.1.11.2 The value is an integer number or null flavor “PINF” to indicate unlimited.

3.2 Drug, Biologics, Dietary Supplement and Medical Food Products

The drug, dietary supplement and medical food product data elements includes the product codes, proprietary and non proprietary name, dosage form, ingredient and active moiety name, ingredient identifier, ingredient strength, package quantity, type and code, marketing category, marketing status, dosage form appearance, DEA schedule, and route of administration.

Drug products are those products with the appropriate marketing categories listed in Table 1: Marketing Category and Product Type. Dietary supplement are those products that are associated with the dietary supplement (C86952) marketing category. Medical foods are associated with the medical food marketing category (C86964).

The drug product consists of a product item code (NDC for drugs and NHRIC for dietary supplements or medical foods), proprietary and non proprietary name, and dosage form. These are children of <manufacturedProduct>. The proprietary name is the name as it appears on the label divided between <name> and <suffix>. The <name> is the initial portion of the proprietary name describing the ingredients without any other descriptors including trademarks and dosage forms. If necessary, <suffix> is used for descriptors such as “extended release”. When using the <suffix>, a space after the proprietary name is added as necessary. If there is no proprietary name, the non proprietary name is used without any descriptors. The dosage form is described in <formCode>. The <genericMedicine><name> is the non proprietary name of the product.

3.2.1 Code and Name

```

<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="0001-0001" codeSystem="2.16.840.1.113883.6.69"/>
        <name>Tazmin <suffix>XR</suffix></name>
        <formCode code="C42998"
          codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="tablet"/>
        <asEntityWithGeneric>
          <genericMedicine>
            <name>tazminate hydrochloride</name>
          </genericMedicine>

```

Phonetic spellings of the product and generic names may also be specified:

```

<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        ...
        <name>Tazmin <suffix>XR</suffix></name>
        <name use="PHON">Tas-meen</name>
        ...
      <asEntityWithGeneric>
        <genericMedicine>
          <name>tazminate hydrochloride</name>
          <name use="PHON">tas-meen-at hy-droh-clor-aide</name>
        </genericMedicine>
      </asEntityWithGeneric>
    </manufacturedProduct>
  </subject>
</section>

```

Validation Procedures

- 3.2.1.1 If the product item code is an NDC/NHRIC (i.e., if the root is “2.16.840.1.113883.6.69”), then the following procedures apply:
- 3.2.1.2 Code (NDC/NHRIC product code) has two segments separated by a hyphen
- 3.2.1.3 The first segment (NDC/NHRIC labeler code) is numeric.
- 3.2.1.4 Segments (NDC/NHRIC product codes) follow the pattern of 4-4, 5-4 or 5-3
- 3.2.1.5 The second segment (middle segment of three-segment NDC) is numeric (no letters allowed).
- 3.2.1.6 If the product item code is an ISBT 128 code (i.e., if the root is “2.16.840.1.113883.6.18”), then the following procedures apply:
- 3.2.1.7 Code contains two segments separated by a hyphen.
- 3.2.1.8 The first segment contains the ISBT 128 Facility Identification Number (FIN) beginning with a capital letter A-N, P-Z (i.e., all 26 letters except O) followed by two alphanumerics A-N, P-Z, 0-9, and two digits.
- 3.2.1.9 The second segment contains the ISBT 128 product code beginning with a capital letter (A-Z) followed by 4 digits (0-9) and optionally followed by three alphanumeric characters.
- 3.2.1.10 First segment (NDC/NHRIC labeler code) matches a labeler code associated with the Labeler id (labeler’s DUNS Number) in a previously submitted NDC/NHRIC Labeler Code or NDC Labeler Code – Animal Drug SPL document, except for parts.
- 3.2.1.11 Code (NDC product code) has the same labeler segment as the NDC product/item code of all top-level products in this document, except under parts.

- 3.2.1.12 Code (NDC product code) has the same length as all other NDC product/item codes with the same labeler segment in this document (i.e., all NDC product/item codes from one labeler have the same consistent length and hence all package item codes have the same consistent configuration.)
- 3.2.1.13 Code (NDC product code) has the same length as any other NDC product/item codes of the same labeler (i.e., all NDC product/item codes by the same labeler have the same consistent length and hence all package item codes have the same consistent configuration.)
- 3.2.1.14 There is only one product data elements section for each NDC product/item code, i.e., the same product is not described more than once except under parts.
- 3.2.1.15 If the NDC product/item code is mentioned elsewhere in the document, then the product and generic name (along with their phonetic names, if any are specified), dosage form, UNII and strength of all ingredients are the same.
- 3.2.1.16 There is a product name, except if the document type is *Indexing - Product Concept* (73815-3) or there is no marketing status other than *new* or *cancelled*.
- 3.2.1.17 Product name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” or dosage forms.
- 3.2.1.18 There may be one phonetic name after the product name.
- 3.2.1.19 Phonetic name conforms to the phonetic name specification.
- 3.2.1.20 There is a form code (dosage form), except if the document type is *Indexing - Product Concept* (73815-3) or *Lot Distribution Data* (66105-8), *Indexing - Biologic or Drug Substance* (77648-4) or *Risk Evaluation & Mitigation Strategies* (82351-8) or *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4).
- 3.2.1.21 Form code (dosage form) has the code system 2.16.840.1.113883.3.26.1.1
- 3.2.1.22 If the product has parts, then the form code is C47916 (for KIT)
- 3.2.1.23 Display name matches the code
- 3.2.1.24 There is a non-proprietary (generic medicine) name, except if the document type is *Indexing - Product Concept* (73815-3) or *Lot Distribution Data* (66105-8) or *Indexing - Biologic or Drug Substance* (77648-4) or *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4).
- 3.2.1.25 Non-proprietary (generic medicine) name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” or dosage forms.

- 3.2.1.26 Non-proprietary (generic medicine) name contains no suffix.
- 3.2.1.27 Non-proprietary (generic medicine) name contains no more than 512 characters.
- 3.2.1.28 There may be one phonetic name after the non proprietary name.
- 3.2.1.29 Phonetic name conforms to the phonetic name specification.
- 3.2.1.30 If the NDC product/item code was previously submitted, then the product name is same as in the most recent submission for this NDC product/item code.
- 3.2.1.31 If the NDC product/item code was previously submitted, then the non-proprietary (generic) name is the same as in the most recent submission for this NDC product/item code, except if there is no marketing status other than new or cancelled.
- 3.2.1.32 If the NDC product/item code was previously submitted, then the active ingredient UNIs and active ingredient strengths are the same as in the most recent submission for this NDC product/item, except if there is no marketing status other than new or cancelled.
- 3.2.1.33 If the NDC product/item code was previously submitted, then the product dosage form is same as in the most recent submission for this NDC product/item code.
- 3.2.1.34 If the NDC product/item code was previously submitted, then the product characteristic of size is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.35 If the NDC product/item code was previously submitted, then the product characteristic of shape is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.36 If the NDC product/item code was previously submitted, then the product characteristic of color are same as in the most recent submission for this NDC product/item code.
- 3.2.1.37 If the NDC product/item code was previously submitted, then the product characteristic of imprint code is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.38 [RESERVED]
- 3.2.1.39 If the NDC product/item code was previously submitted, then the application number is the same as in the most recent submission for this NDC product/item

code except if after March 23rd, 2020 the application number is present in the NDA to BLA conversion list and changed to the BLA prefix.

- 3.2.1.40 The dosage form code cannot be “not applicable” (C48624), for document types other than *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), or *Intentional Animal Genomic Alteration Label* (101437-2).
- 3.2.1.41 If the NDC product/item code was previously submitted, then the product characteristic of flavor is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.42 If the NDC product/item code was previously submitted, then the product characteristic of scoring is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.43 If the NDC product/item code was previously submitted, then the product phonetic name (if specified) is the same as in the most recent submission for this NDC product/item code.
- 3.2.1.44 If the NDC product/item code was previously submitted, then the non-proprietary (generic) phonetic name (if specified) is the same as in the most recent submission for this NDC product/item code, except if there is no marketing status other than new or cancelled.
- 3.2.1.45 If the document type is *human OTC drug label* (34390-5), then there may be a cosmetic product category (asSpecializedKind element) with a code (see Section 3.4.3.2 and following).
- 3.2.1.46 If the document type is not *human OTC drug label* (34390-5), then there is no cosmetic product category (asSpecializedKind element).

3.2.2 Product source

```
<asEquivalentEntity classCode="EQUIV">  
  <code code="C64637" codeSystem="2.16.840.1.113883.3.26.1.1"/>  
  <definingMaterialKind>  
    <code code="source product item code"  
      codeSystem="2.16.840.1.113883.6.69"/>  
  </definingMaterialKind>  
</asEquivalentEntity>
```

Validation Procedures

- 3.2.2.1 As equivalent entity class code, code and code system are as above
- 3.2.2.2 If there is a classCode, it is “EQUIV”.
- 3.2.2.3 If the NDC product source (equivalent product) is present, then the active ingredients UNII and active ingredients strengths are the same as that of product source.

- 3.2.2.4 If the NDC product source (equivalent product) is present, then the product characteristic of size is the same as that of the product source.
- 3.2.2.5 If the NDC product source (equivalent product) is present, then the product characteristic of shape is the same as that of the product source.
- 3.2.2.6 If the NDC product source (equivalent product) is present, then the product characteristics of color are the same as that of the product source.
- 3.2.2.7 If the NDC product source (equivalent product) is present, then the product characteristic of imprint code is the same as that of the product source.
- 3.2.2.8 If the NDC product source (equivalent product) is present, then the product characteristic of flavor is the same as that of the product source.
- 3.2.2.9 If the NDC product source (equivalent product) is present, then the product characteristic of scoring is the same as that of the product source.
- 3.2.2.10 If the NDC product source (equivalent product) is present, then the product dosage form is the same as that of the product source.
- 3.2.2.11 If one of the listed establishment operations is Repack (C73606) or Relabel (C73607), then there is a product source reference.

3.2.3 Active ingredient

Active ingredients are specified as follows:

```
<ingredient classCode="ACTIM, ACTIB, or ACTIR">
  <quantity>
    <numerator value="10" unit="mg"/>
    <denominator value="1" unit="1"/>
  </quantity>
  <ingredientSubstance>
    <code code="1234567890" codeSystem="2.16.840.1.113883.4.9"/>
    <name>tazminate malate</name>
  </ingredientSubstance>
</ingredient>
```

The class code for active ingredient is dependent on the basis of the strength. If the basis of strength is the active ingredient, the class code is “ACTIB”. If the basis of strength is the active moiety, the class code is “ACTIM”. If the basis of strength is a reference drug, the class code is “ACTIR”. The strength is represented as a numerator and denominator. The UCUM code is used for the unit of measure. The UCUM code for a unit that is an “each” is “1” Examples of “each” is in the table below.

In most cases, the strength used is that for a single dose following the conventions in Table 5. In the table, an example of “mass” is milligrams, an example of “volume” is milliliter, an example of “time” is hour, and an example of “each” is tablet.

Table 5: Conventions for expressing strength

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

Validation Procedures

- 3.2.3.1 Class code for active ingredients are ACTIB, ACTIM or ACTIR
- 3.2.3.2 If the document type is *Bulk ingredient* (53409-9) or *Bulk ingredient – Animal drug* (81203-2) with a marketing category of *Bulk ingredient* (C73626), then there is one and only one active ingredient.
- 3.2.3.3 If the product has no parts and is not a part, then there are one or more active ingredients except if the document is a *Indexing - Product Concept* (73815-3) or *Lot Distribution Data* (66105-8), *Indexing - Warning Letter Alert* (77288-9), *Risk Evaluation & Mitigation Strategies* (82351-8), *Indexing - Risk Evaluation & Mitigation Strategies* (82353-4), or if the SPL file is for *Salvaged Drugs*, i.e., having business operation as *salvage* (C70827), or there is no marketing status other than *new* or *cancelled*.
- 3.2.3.4 If the product has parts, then the active ingredients are under parts
- 3.2.3.5 There is a strength with a numerator and denominator, except if the document is a *Indexing - Biologic* or *Drug Substance* (77648-4).
- 3.2.3.6 If the document type is *Bulk ingredient* (53409-9) or *Bulk ingredient – Animal drug* (81203-2) with a marketing category of *Bulk ingredient* (C73626), then numerator and denominator (representing strength amount) are the same.
- 3.2.3.7 The strength numerator is based on mass (e.g., mg or g) and not volume (e.g. mL or L), except for ingredients such as water, alcohol, and gases.

- 3.2.3.8 There is a unit of measure in the strength amount's numerator and denominator, except if the document type is *Licensed Minimally Manipulated Cells Label* (53408-1).
- 3.2.3.9 If the document type is *Bulk Ingredient* (53409-9), *Drug for Further Processing* (78744-0), *Human Compounded Drug Label* (75031-5), *Human OTC Drug Label* (34390-5) or *Human Prescription Drug Label* (34391-3), then the numerator unit cannot be “1”.
- 3.2.3.10 If the document type code is *Vaccine Label* (53404-0) and if there is any active ingredient under the main product or under its first part, then at least one active ingredient code is on the list of active ingredients approved for vaccines.

3.2.4 Active moiety

```
<ingredient classCode="ACTIR">
  <ingredientSubstance>
    <activeMoiety>
      <activeMoiety>
        <code code="0987654321" codeSystem="2.16.840.1.113883.4.9"/>
        <name>tazminic acid</name>
      </activeMoiety>
    </activeMoiety>
  </ingredientSubstance>
</ingredient>
```

Validation Procedures

- 3.2.4.1 There are one or two active moieties, except if the document type is *Indexing - Biologic or Drug Substance* (77648-4).
- 3.2.4.2 There is an active moiety code (UNII)
- 3.2.4.3 Code system is 2.16.840.1.113883.4.9
- 3.2.4.4 There is an active moiety name for each active moiety
- 3.2.4.5 If the active ingredient is in the active-ingredient-active-moiety-validation-list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then the active moiety and basis of strength is the corresponding active moiety and basis of strength respectively in this list, except if the document type is for *Bulk ingredient* (53409-9), *Bulk ingredient – Animal drug* (81203-2), or *Drug for Further Processing* (78744-0) or there is no marketing status other than new or cancelled.
- 3.2.4.6 If the active ingredient is not in the active-ingredient-active-moiety-validation-list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then the active moiety name does not include any of the names in the *active moiety validation* (counterion) list (see FDA SPL web page for list), except if the word appears by itself optionally followed by “(ester)”, “cation” or “anion” or “ion”.

3.2.4.7 Active moiety name matches the code (UNII)

3.2.5 Reference Ingredient for Strength

```
<ingredient classCode="ACTIR">
  <ingredientSubstance>
    <asEquivalentSubstance>
      <definingSubstance>
        <code code="A123455678" codeSystem="2.16.840.1.113883.4.9"/>
        <name>tazemate formate</name>
      </definingSubstance>
    </asEquivalentSubstance>
  </ingredientSubstance>
</ingredient>
```

Validation Procedures

- 3.2.5.1 If the class code is ACTIR, then there is an asEquivalentSubstance element with a defining substance, except if there is no marketing status other than *new* or *cancelled*.
- 3.2.5.2 If the class code is not ACTIR, then there is no asEquivalentSubstance element
- 3.2.5.3 There is a reference ingredient code
- 3.2.5.4 Code system is 2.16.840.1.113883.4.9
- 3.2.5.5 There is a name (preferred substance name)
- 3.2.5.6 The name matches the code (UNII)

3.2.6 Inactive ingredient

The inactive ingredient includes the inactive ingredient class code, ingredient name, identifier, and strength. The element `<ingredient>` is a child of `<manufacturedProduct>`. The class code for inactive ingredient is "IACT". The strength, if needed, is represented as a numerator and denominator and is described using UCUM units of measure. If the inactive ingredient is confidential, the element `<ingredient>` includes `<confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>`.

```
<ingredient classCode="IACT">
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
  <quantity>
    <numerator value="value" unit="UCUM code"/>
    <denominator value="value" unit="UCUM code"/>
  </quantity>
  <ingredientSubstance>
    <code code="UNII" codeSystem="2.16.840.1.113883.4.9"/>
    <name>inactive ingredient name</name>
  </ingredientSubstance>
</ingredient>
```

Validation Procedures

- 3.2.6.1 There are zero to many inactive ingredients.
- 3.2.6.2 If the document type is *human OTC drug label* (34390-5), then there is at least one inactive ingredient, except if the active ingredient(s) comprise 100% of the product or there is no marketing status other than new or cancelled, or the inactive ingredient section (51727-6) has the text “none”.
- 3.2.6.3 Class code is IACT
- 3.2.6.4 If the product has parts, then the inactive ingredients are under parts
- 3.2.6.5 If the document type is *human OTC drug label* (34390-5), then there is no confidentiality code.
- 3.2.6.6 There is no ingredient other than active ingredient (having class code ACTIM, ACTIR, ACTIB), inactive ingredient (having class code IACT), adjuvant (having class code ADJV), and those having class code CNTM, except if the document is a *Human Compounded Drug Label* (75031-5) or *Animal Compounded Drug Label* (77647-6) or there is no marketing status other than *new* or *cancelled*.

3.2.7 Packaging

The format for packaging specification is:

```
<asContent>
  <quantity>
    <numerator value="100" unit="1"/>
    <denominator value="1"/>
  </quantity>
  <containerPackagedProduct>
    <code code="0001-0001-05" codeSystem="2.16.840.1.113883.6.69"/>
    <formCode code="C43169"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="bottle"/>
  </containerPackagedProduct>
</asContent>
```

Validation Procedures

- 3.2.7.1 Every top-level product has an “as content” (package information) element (optional for parts), except if the document is a *Indexing - Product Concept* (73815-3), *Lot Distribution Data* (66105-8), *Indexing - Warning Letter Alert* (77288-9), *Indexing - Biologic or Drug Substance* (77648-4), *Risk Evaluation & Mitigation Strategies* (82351-8) or *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4), or there is no marketing status other than *new* or *cancelled*, or if the SPL file is for *Salvaged Drugs*, i.e., having business operation as *salvage* (C70827).

- 3.2.7.2 If outer package description has a production quantity characteristic, then document type is *Human Compounded Drug Label (75031-5)* or *Animal Compounded Drug Label (77647-6)*.
- 3.2.7.3 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) then each outer package description has a production quantity characteristic.
- 3.2.7.4 The outer package item code is not associated with another set id except under parts; therefore the original set ID included in the previous version of the file with the outer package item code should be used.
- 3.2.7.5 If the package item code has been previously submitted, then the package form code (package type) and quantity value and unit are the same as in the most recent submission for this package item code.
- 3.2.7.6 There are no drug package characteristics other than the ones mentioned in this document.
- 3.2.7.7 The package type code cannot be *not applicable (C123723)*, for documents of types other than *Recombinant Deoxyribonucleic Acid Construct Label (78745-7)* or *Intentional Animal Genomic Alteration Label (101437-2)*.

3.2.8 Parts

Products with one or more parts

```
<part>
  <quantity>
    <numerator value="1" unit="1"/>
    <denominator value="1"/>
  </quantity>
  <partProduct>
    <code code="0001-0001" codeSystem="2.16.840.1.113883.6.69"/>
    <name>Tazmin <suffix>XR</suffix></name>
    <name use="PHON">Taz-min</name>
    <formCode code="C42916"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="capsule, extended release"/>
    <asEntityWithGeneric>
      <genericMedicine>
        <name>tazminate hydrochloride</name>
```

Validation Procedures

- 3.2.8.1 If the product form code is *Kit (C47916)*, then there is one or more parts
- 3.2.8.2 If the product has parts, then at least one part has one or more active ingredients.

- 3.2.8.3 Procedures for code, name, dosage form code, source, ingredients, characteristics and packaging are the same as for the main products (see Sections 3.2.1ff)

3.2.9 Marketing Category

Example:

```
<subjectOf>
  <approval>
    <id extension="NDA123456" root="2.16.840.1.113883.3.150"/>
    <code code="C73594"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="NDA"/>
    <author>
      <territorialAuthority>
        <territory>
          <code code="USA" codeSystem="1.0.3166.1.2.3"/>
        </territory>
      </territorialAuthority>
    </author>
  </approval>
</subjectOf>
```

Validation Procedures

- 3.2.9.1 If the marketing category is *Exempt device (C80438)*, *Humanitarian Device Exemption (C80440)*, *Premarket Application (C80441)*, or *Premarket Notification (C80442)*, then there is at least one part.
- 3.2.9.2 If the document type is: *OTC Animal Drug Label (50577-6)*, *OTC Type A Medicated Article Animal Drug Label (50576-8)*, *OTC Type B Medicated Feed Animal Drug Label (50574-3)*, *OTC Type C Medicated Feed Animal Drug Label (50573-5)*, *Prescription Animal Drug Label (50578-4)*, *VFD Type A Medicated Article Animal Drug Label (50575-0)*, *VFD Type B Medicated Feed Animal Drug Label (50572-7)*, *VFD Type C Medicated Feed Animal Drug Label (50571-9)*, or *Animal Cells, Tissues, and Cell and Tissue Based Product Label (98075-5)*, then the marketing category is: *ANADA (C73583)*, *Conditional NADA (C73588)*, *NADA (C73593)*, *Legally Marketed Unapproved New Animal Drugs for Minor Species (C92556)*, *Unapproved Homeopathic (C73614)*, *Unapproved Medical Gas (C73613)*, *Unapproved Drug Other (C73627)* or *Export Only (C73590)*.
- 3.2.9.3 If the marketing category is *ANADA (C73583)*, *Conditional NADA (C73588)*, *NADA (C73593)*, then the document type code is: *OTC Animal Drug Label (50577-6)*, *OTC Type A Medicated Article Animal Drug Label (50576-8)*, *OTC Type B Medicated Feed Animal Drug Label (50574-3)*, *OTC Type C Medicated Feed Animal Drug Label (50573-5)*, *Prescription Animal Drug Label (50578-4)*, *VFD Type A Medicated Article Animal Drug Label (50575-0)*, *VFD Type B Medicated Feed Animal Drug Label (50572-7)*, *VFD Type C Medicated Feed Animal Drug Label (50571-9)*, *Recombinant Deoxyribonucleic Acid Construct Label (78745-7)*, *Intentional Animal Genomic Alteration Label (101437-2)*, or *Animal Cells, Tissues, and Cell and Tissue Based Product Label (98075-5)*.

- 3.2.9.4 If the marketing category is *Bulk Ingredient* (C73626), *Bulk Ingredient for Human Prescription Compounding* (C96793), or *Bulk Ingredient for Animal Drug Compounding* (C98252), then the document type is *Bulk Ingredient* (53409-9) or *Bulk Ingredient – Animal drug* (81203-2).
- 3.2.9.5 If the document type is *Bulk Ingredient* (53409-9), then the marketing category is *Bulk Ingredient* (C73626), *Bulk Ingredient for Human Prescription Compounding* (C96793), or *Export Only* (C73590).
- 3.2.9.6 If the code is *ANDA* (C73584), *BLA* (C73585), *NDA* (C73594), *Approved Drug Product Manufactured under Contract* (C132333), *NDA authorized generic* (C73605), *Multi-Market Approved Product* (C175238), or *SIP Approved Drug* (C175462) and the marketing status is *active*, then there exists a record of an application for the application number, except if the document is an *Indexing - Product Concept* (73815-3), *Indexing - Warning Letter Alert* (77288-9) or *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4).
- 3.2.9.7 If the code is *ANDA* (C73584), *BLA* (C73585), *NDA* (C73594), *Approved Drug Product Manufactured under Contract* (C132333), *NDA authorized generic* (C73605), *Multi-Market Approved Product* (C175238), or *SIP Approved Drug* (C175462) and the marketing is *active* with a start date on or before the current date, then there exists a record of an approved application for the application number.
- 3.2.9.8 If the code is *ANDA* (C73584), *BLA* (C73585), *NDA* (C73594), *Approved Drug Product Manufactured under Contract* (C132333), *NDA authorized generic* (C73605), *Multi-Market Approved Product* (C175238), or *SIP Approved Drug* (C175462) and the marketing status is *completed*, then there exists a record of an approved or withdrawn application for the application number.
- 3.2.9.9 If the marketing category is *Approved Drug Product Manufactured under Contract* (C132333), *OTC Monograph Drug Product Manufactured Under Contract* (C132334), *Unapproved Drug Product Manufactured Under Contract* (C132335), then the document type is *Human Prescription Drug Label* (34391-3) or *Human OTC Drug Label* (34390-5).
- 3.2.9.10 If the marketing category is *Medical Food* (C86964), then the document type is *Medical Food* (58475-5), except under parts.
- 3.2.9.11 If the document type is *Medical Food* (58475-5), then the marketing category is *Medical Food* (C86964).
- 3.2.9.12 If the marketing category is *Dietary Supplement* (C86952), then the document type is *Dietary Supplement* (58476-3), except under parts.

- 3.2.9.13 If the document type is *Dietary Supplement* (58476-3), then the marketing category is *Dietary Supplement* (C86952).
- 3.2.9.14 If the document type is *Human prescription drug label* (34391-3), then the marketing category is not *OTC Monograph Drug Product Manufactured Under Contract* (C132334), or *OTC Monograph Drug* (C200263) except under parts.
- 3.2.9.15 If the document type is *Drug for Further Processing* (78744-0), then the marketing category is *Drug for further processing* (C94795) or *Export Only* (C73590).
- 3.2.9.16 If the document type is *Bulk ingredient - Animal drug* (81203-2), then the marketing category is *Bulk Ingredient* (C73626), (*Bulk ingredient for animal drug compounding* (C98252), *Drug for further processing* (C94795) or *Export only* (C73590).
- 3.2.9.17 If the document type is *Human Compounded Drug Label* (75031-5), then the marketing category is *Outsourcing Facility Compounded Human Drug Product (Exempt From Approval Requirements)* (C181659) or *Outsourcing Facility Compounded Human Drug Product (Not Marketed - Not Distributed)* (C190698).
- 3.2.9.18 If the document type is *Animal Compounded Drug Label* (77647-6), then the marketing category is *unapproved drug other* (C73627).
- 3.2.9.19 If the marketing category is *Emergency Use Authorization* (C96966), then the document type is *Human Prescription Drug Label* (34391-3) or *Vaccine Label* (53404-0).
- 3.2.9.20 If the marketing category is *Outsourcing Facility Compounded Human Drug Product (Exempt From Approval Requirements)* (C181659) or *Outsourcing Facility Compounded Human Drug Product (Not Marketed - Not Distributed)* (C190698), then the document type is *Human Compounded Drug Label* (75031-5).

3.2.10 Marketing Status and Date

The procedures for marketing status and date (if any) are the same for all products and described in Section 3.1.8.

Validation Procedures

- 3.2.10.1 There is one marketing status code for each top-level product (part products do not need this), except if the document is a *Indexing - Product Concept* (73815-3) or *Lot Distribution Data* (66105-8) or *Indexing - Biologic or Drug Substance* (77648-4) or *Human Compounded Drug Label* (75031-5) or *Animal*

Compounded Drug Label (77647-6) or Risk Evaluation & Mitigation Strategies (82351-8) or Indexing – Risk Evaluation & Mitigation Strategies (82353-4) or if the SPL file is for Salvaged Drugs (having business operation as salvage, C70827).

3.2.11 DEA schedule

The DEA schedule, when applicable, is described under <policy> which is a child of <subjectOf> which is a child of <manufacturedProduct> as illustrated in the following example of a drug that is schedule II.

```
<subjectOf>
  <policy classCode="DEADrugSchedule">
    <code code="C48675"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="CII"/>
```

Validation Procedures

3.2.11.1 If the product item code (NDC) is on the DEA Exempt Products List, then there is no DEA schedule.

3.2.11.2 There is only one DEA schedule element.

3.2.11.3 If there is a DEA schedule, then the code system is 2.16.840.1.113883.3.26.1.1

3.2.11.4 Display name matches the code

3.2.11.5 The policy element has a class code of 'DEADrugSchedule'.

3.2.11.6 If the product item code (NDC) is not on the DEA Exempt Products List, then the DEA Schedule matches the one in the Controlled Substance Table where all supplied constraints match, except for products regulated by CVM.

3.2.11.7 If the product item code (NDC) is not on the DEA Exempt Products List and the product's active ingredient(s) is in the Controlled Substance Table with DEA Schedule CI, CII, CIII, CIV, or CV, and all supplied constraints matching, then there is a DEA Schedule, except for products regulated by CVM.

3.2.12 Solid Oral Drug Product characteristics

Product characteristics include dosage form appearance. Dosage form characteristics are used to describe the appearance of the drug product and include the color, score, shape, size, imprint code and image. These are all under <subjectOf> which is a child of <manufacturedProduct>. Product characteristics also include product flavor and what the product contains.

```

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLCOLOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value code="code for color" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name for color" xsi:type="CE">
      <originalText>optional original color description text</originalText>
    </value>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLSCORE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value value="value for score" xsi:type="INT"/>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLSHAPE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value code="code for shape" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name for shape" xsi:type="CE">
      <originalText>optional original shape description text</originalText>
    </value>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLSIZE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value unit="mm" value="value for size in mm" xsi:type="PQ"/>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLIMPRINT" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ST">imprint separated by semicolon</value>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLFLAVOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value code="code for flavor" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="display name for flavor" xsi:type="CE">
      <originalText>optional flavor description text</originalText>
    </value>
  </characteristic>
</subjectOf>

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLIMAGE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ED" mediaType="image/jpeg">
      <reference value="file name.jpg"/>
    </value>
  </characteristic>
</subjectOf>

```

3.2.13 Color

```

<subjectOf>
  <characteristic>

```

```
<code code="SPLCOLOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
<value code="C48333"
  codeSystem="2.16.840.1.113883.3.26.1.1"
  displayName="blue" xsi:type="CE">
  <originalText>LIGHT BLUE</originalText>
```

Validation Procedures

3.2.13.1 If the dosage form is on the *solid oral dosage form* list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then there is a color, except if there is no marketing status other than *new* or *cancelled*.

3.2.13.2 Code and code system is as above (for SPLCOLOR)

3.2.13.3 Value code system is 2.16.840.1.113883.3.26.1.1

3.2.13.4 Display name matches the value code

3.2.14 Shape

```
<subjectOf>
  <characteristic>
    <code code="SPLSHAPE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value code="C48336"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="capsule" xsi:type="CE"/>
    <originalText>capsule like</originalText>
```

Validation Procedures

3.2.14.1 If the dosage form is on the *solid oral dosage form* list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then there is a shape, except if there is no marketing status other than *new* or *cancelled*.

3.2.14.2 Code and code system is as above (for SPLSHAPE)

3.2.14.3 Value code system is 2.16.840.1.113883.3.26.1.1

3.2.14.4 Display name matches the value code

3.2.14.5 There is only one shape element

3.2.15 Size

```
<subjectOf>
  <characteristic>
    <code code="SPLSIZE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value unit="mm" value="18" xsi:type="PQ"/>
```

Validation Procedures

3.2.15.1 If the dosage form is on the *solid oral dosage form* list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then there is a size, except if there is no marketing status other than *new* or *cancelled*.

3.2.15.2 Code and code system is as above (for SPLSIZE)

3.2.15.3 There is a unit and value for size element

3.2.15.4 Value units is mm for size element

3.2.15.5 Value is a whole number greater than zero for size element

3.2.15.6 There is only one size element

3.2.16 Scoring

```
<subjectOf>
  <characteristic>
    <code code="SPLSCORE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value value="1" xsi:type="INT"/>
```

Validation Procedures

3.2.16.1 If the dosage form is on the *solid oral dosage form* list (see FDA SPL web page for list <https://www.fda.gov/industry/fda-resources-data-standards/structured-product-labeling-resources>), then there is scoring, except if there is no marketing status other than *new* or *cancelled*.

3.2.16.2 Code and code system is as above (for SPLSCORE)

3.2.16.3 The value is 1, 2, 3, 4 or nullFlavor="OTH" (for SPLSCORE)

```
<characteristic>
  <code code="SPLSCORE" codeSystem="2.16.840.1.113883.1.11.19255"/>
  <value nullFlavor="OTH" xsi:type="INT"/>
```

3.2.16.4 There is only one score element

3.2.17 Imprint code

```
<subjectOf>
  <characteristic>
    <code code="SPLIMPRINT" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ST">05</value>
```

Validation Procedures

3.2.17.1 Code and code system is as above (for SPLIMPRINT)

3.2.17.2 Value has only letters and numbers separated by semicolon without spaces (for SPLIMPRINT)

3.2.17.3 There is only one imprint code element

3.2.18 Flavor

```
<subjectOf>
  <characteristic>
    <code code="SPLFLAVOR" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value code="C73391"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="grape" xsi:type="CE">
      <originalText>wild grape</originalText>
```

Validation Procedures

3.2.18.1 If there is a flavor, then code and code system is as above

3.2.18.2 Value code system is 2.16.840.1.113883.3.26.1.1

3.2.18.3 Display name matches the value code

3.2.19 Image for Solid Oral Dosage Forms

```
<subjectOf>
  <characteristic>
    <code code="SPLIMAGE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ED" mediaType="image/jpeg">
      <reference value="8837a946-1912-4c1f-8035-e313fdd11ef2.jpg"/>
```

Validation Procedures

3.2.19.1 If there is SPL image of the solid oral dosage form, then code and code system are as above

3.2.19.2 Value xsi:type is as above

3.2.19.3 mediaType is “image/jpeg”

3.2.19.4 Reference value is the file name for a valid image

3.2.19.5 The image file is submitted together with the SPL file.

3.2.19.6 There are no product characteristics other than the ones mentioned above.

3.2.20 Route of administration

Route of administration may be specified for products

```
<subject>
  <manufacturedProduct>
    <consumedIn/>
```

and their parts:

```
<part>
  <consumedIn/>
```

Route of administration is specified as follows:

```
<consumedIn>
  <substanceAdministration>
    <routeCode code="C38288"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="oral"/>
```

Validation Procedures

3.2.20.1 If the document type is not for *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Licensed Vaccine Bulk Intermediate Label* (53406-5) or *Drug for Further Processing* (78744-0) and product is not a top-level product whose form code is *Kit* (C47916) or there is no marketing status other than *new* or *cancelled*, then there is one or more route of administration (consumedIn/substanceAdministration element with routeCode), except if the document type is *Indexing - Product Concept* (73815-3) or *Lot Distribution Data* (66105-8) or *Indexing - Biologic or Drug Substance* (77648-4) or *Risk Evaluation & Mitigation Strategies* (82351-8) or *Indexing – Risk Evaluation & Mitigation Strategies* (82353-4) or if the SPL file is for *Salvaged Drugs*, i.e., having business operation as *salvage* (C70827).

3.2.20.2 Route code system is 2.16.840.1.113883.3.26.1.1

3.2.20.3 There is a display name that matches the code

3.2.20.4 If the document type is for *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Licensed Vaccine Bulk Intermediate Label* (53406-5) or *Drug for Further Processing* (78744-0) then route code is *not applicable* (nullFlavor NA) or not present at all.

```
<routeCode nullFlavor="NA"/>
```

3.2.20.5 The route (of administration) code cannot be “not applicable” (C48623) for document types other than *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Licensed Vaccine Bulk Intermediate Label* (53406-5) ,

Recombinant Deoxyribonucleic Acid Construct Label (78745-7), Intentional Animal Genomic Alteration Label (101437-2), or Drug for Further Processing (78744-0).

3.3 Device Product

```
<manufacturedProduct>
  <code code="91234561234569" codeSystem="1.3.160"/>
  <name>SuperTape 2000</name>
  <desc>Adhesive tape for orthopedic use.</desc>
  <asSpecializedKind classCode="GEN">
    <generalizedMaterialKind>
      <code code="MCA" displayName="Tape, Surgical, Internal"
        codeSystem="2.16.840.1.113883.6.303"/>
    </generalizedMaterialKind>
  </asSpecializedKind>
```

Device products are those products with the appropriate marketing categories listed in Table 1: Marketing Category and Product Type.

3.3.1 Item Code and Name

Validation Procedures

- 3.3.1.1 There may be an NDC product/item code
- 3.3.1.2 If there is a NDC product/item code, the following general procedures apply:
- 3.3.1.3 Code system is 2.16.840.1.113883.6.69 (NHRIC), 1.3.160(GS1), or 2.16.840.1.113883.6.40 (HIBCC).
- 3.3.1.4 Code is compliant with the code system's allocation rules.
- 3.3.1.5 There is a name, i.e., the trade or proprietary name of the medical device as used in product labeling or in the catalog
- 3.3.1.6 Markings such as ®, or ™ should not be included
- 3.3.1.7 There is a device type (asSpecializedKind element) with a code.
- 3.3.1.8 code system is 2.16.840.1.113883.6.303 for FDA Product Classification System
- 3.3.1.9 there is a valid medical device product classification code
- 3.3.1.10 there is a displayName which matches the code

3.3.2 Additional Device Identifiers

```

<document>
  <section>
    <subject>
      <manufacturedProduct>
        <manufacturedProduct>
          <asIdentifiedEntity classCode="IDENT">
            <id extension="ST2000/A" root="1.2.3.99.1"/>
            <code code="C99286" displayName="model number"
              codeSystem="2.16.840.1.113883.3.26.1.1"/>
          </asIdentifiedEntity>
        </manufacturedProduct>
      </subject>
    </section>
  </document>

```

These additional identifiers may also appear under device parts:

```

<part>
  <partProduct>
    <asIdentifiedEntity>

```

- 3.3.2.1 There may be one or more additional identifiers, including *model number* (C99286), *catalog number* (C99285), and *reference number* (C99287).
- 3.3.2.2 There is a code with code system 2.16.840.1.113883.3.26.1.1.
- 3.3.2.3 Code is from the Table 3: Miscellaneous Identifier Types.
- 3.3.2.4 There is one id
- 3.3.2.5 Id has a root OID
- 3.3.2.6 The actual identifier is in the extension.
- 3.3.2.7 There is at most one *Model Number* reference (C99286)
- 3.3.2.8 The id root can be any root OID over which the labeler has authority. If the labeler has no such root OID of its own, then the root is constructed by concatenating the DUNS number (without leading zeroes) to the fixed string "1.3.6.1.4.1.32366.3."
- 3.3.2.9 There is at most one *Catalog Number* (C99285)
- 3.3.2.10 The id root can be any root OID over which the labeler has authority. If the labeler has no such root OID of its own, then the root is constructed by concatenating the DUNS number (without leading zeroes) to the fixed string "1.3.6.1.4.1.32366.3."
- 3.3.2.11 The product may have multiple reference numbers (i.e., *secondary identifiers*, C99287).

3.3.2.12 The id root is 2.16.840.1.113883.6.69 (NHRIC), 1.3.160 (GS1), 2.16.840.1.113883.6.40 (HIBCC), or may be constructed by concatenating the DUNS number (without leading zeroes) to the fixed string “1.3.6.1.4.1.32366.3.”

3.3.2.13 Id extension is compliant with the code system’s allocation rules.

3.3.3 [RESERVED]

3.3.4 Device Ingredient

Ingredients included in devices that are not identified as active ingredients include the ingredient class code, ingredient name, identifier, and strength. The element `<ingredient>` is a child of `<manufacturedProduct>`. The class code for ingredient is “INGR”. The strength, if needed, is represented as a numerator and denominator and is described using UCUM units of measure.

```
<ingredient classCode="INGR">
  <quantity>
    <numerator value="value" unit="UCUM code"/>
    <denominator value="value" unit="UCUM code"/>
  </quantity>
  <ingredientSubstance>
    <code code="UNII" codeSystem="2.16.840.1.113883.4.9"/>
    <name>ingredient name</name>
  </ingredientSubstance>
</ingredient>
```

This structure is also used to indicate that a product contains latex (UNII code for latex).

Note that devices may have active ingredients as well, such as in a medicated stent, i.e., where the device serves in part the function of releasing a built-in drug. This is to be distinguished from devices such as syringes which are delivery devices for a drug product that they contain.

3.3.5 [RESERVED]

3.3.6 [RESERVED]

3.3.7 Device Parts

Device parts may be specified for the product in the same way as for other product kits (see Section 3.1.6 Kits, Parts, Components and Accessories above),

```
<partProduct>
  <code code="91234561234569" codeSystem="1.3.160"/>
```

```

<name>SuperTape 200</name>
<asSpecializedKind classCode="GEN">
  <generalizedMaterialKind>
    <code code="MCA"
      codeSystem="2.16.840.1.113883.6.303"/>
  </generalizedMaterialKind>
</asSpecializedKind>

```

Validation Procedures

3.3.7.1 There is a name, i.e., the trade or proprietary name of the medical device as used in product labeling or in the catalog

3.3.7.2 Markings such as ®, or ™ should not be included

3.3.8 Part of Assembly

When products are used together but packaged separately, the data element <asPartOfAssembly> is used to identify the other product. The products could be drugs or devices.

```

<asPartOfAssembly>
  <wholeProduct><!-- this is the assembly, but has no identifier -->
  <part>
    <partProduct>
      <code code="item code of accessory component"
        codeSystem="code system OID"/>

```

3.3.9 Regulatory Identifiers

Regulatory identifiers, marketing status and characteristics are all connected through the <subjectOf> element which may appear on the main product:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct/>
  <subjectOf/>

```

The regulatory identifier:

```

<subjectOf>
  <approval>
    <id extension="K123456" root="2.16.840.1.113883.3.150"/>
    <code code="C80442"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="Premarket Notification"/>
    <author>
      <territorialAuthority>
        <territory>
          <code code="USA" codeSystem="1.0.3166.1.2.3"/>

```

Validation Procedures

- 3.3.9.1 There is one regulatory identifier for each product
- 3.3.9.2 Code comes from Table 1 for product type “device”.
- 3.3.9.3 Display name matches the code
- 3.3.9.4 Code system is 2.16.840.1.113883.3.26.1.1
- 3.3.9.5 If the marketing category (code) is *Premarket Application* (C80441), *510(k) Premarket Notification* (C80442), *Exempt Device* (C80438), or *Humanitarian Device Exemption* (C80440), then the id root is 2.16.840.1.113883.3.150.
- 3.3.9.6 If the marketing category (code) is *Premarket Application* (C80441), then the id extension has a prefix “P” or “BP” followed by 6 digits
- 3.3.9.7 If the marketing category (code) is *Premarket Notification* (C80442), then the id extension has a prefix “K” or “BK” followed by 6 digits.
- 3.3.9.8 If the marketing category (code) is *Exempt Device* (C80438), then the id extension consists of 3 letters
- 3.3.9.9 If the marketing category (code) is *Humanitarian Device Exemption* (C80440), then the id extension has a prefix “H” followed by 6 digits
- 3.3.9.10 Territorial authority is as above
- 3.3.9.11 If the form code is *kit* (C47916) and the top/kit-level marketing category is *Exempt device* (C80438), *Humanitarian Device Exemption* (C80440), *Premarket Application* (C80441) or *Premarket Notification* (C80442), then the document type is not *Bulk Ingredient* (53409-9), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Plasma Derivative* (60683-0), *Prescription Animal Drug Label* (50578-4), *Standardized Allergenic* (60682-2), *Vaccine Label* (53404-0), *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), *OTC Animal Drug Label* (50577-6), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), *Animal*

Compounded Drug Label (77647-6), Bulk Ingredient - Animal Drug (81203-2), or Human Compounded Drug Label (75031-5).

3.3.9.12 If the form code is not *kit* (C47916) and the document type is *Bulk Ingredient* (53409-9), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste? Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *OTC Type A Medicated Animal Drug Label* (50576-8), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Plasma Derivative* (60683-0), *Prescription Animal Drug Label* (50578-4), *Standardized Allergenic* (60682-2), or *Vaccine Label* (53404-0), *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), *OTC Animal Drug Label* (50577-6), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), *Animal Compounded Drug Label* (77647-6), *Bulk Ingredient - Animal Drug* (81203-2), or *Human Compounded Drug Label* (75031-5), then the marketing category is not *Exempt device* (C80438), *Humanitarian Device Exemption* (C80440), *Premarket Application* (C80441) or *Premarket Notification* (C80442).

3.3.10 Marketing status and date

The procedures for marketing status and date (if any) are the same for all products and described in Section 3.1.8.

Validation Procedures

3.3.10.1 There is one marketing status code for each top-level product (part products do not need this)

3.3.11 Device Characteristics

Many characteristics exist for devices and are listed here in tabular form. The characteristic structure allows specifying any properties of the product in a code-value pair, the code saying which property is being specified, the value saying what the property is for the given product. The characteristics structure connects to the product Role through the subjectOf element.

```
<manufacturedProduct>
  <manufacturedProduct>
    ...
</manufacturedProduct>
```

```
<subjectOf>
  <characteristic>
    <code code="characteristic code"
      codeSystem="characteristic code system"/>
    <value xsi:type="characteristic value type" ...>
```

Characteristics listed in Table 6 use one of a number of different data types. Each data type uses slightly different XML elements and attributes as shown in the templates in Section 3.1.8.34

Table 6: Characteristic codes and code systems.

| Name | Code / Code System OID | Data Type | Description |
|--------------------------|---|-----------|---|
| Number of times useable. | SPLUSE 2.16.840.1.113883.1.11.19255 | INT | Specifies how often a product may be re-used. While a number could be specified, the common distinction is between single disposable and multiple use products. A product that has unlimited reuses uses the <value nullFlavor="PINF" xsi:type="INT"/>. |
| Sterile Use | SPLSTERILEUSE 2.16.840.1.113883.1.11.19255 | BL | Specifies whether the device is intended or not intended to be used where sterile conditions are necessary (e.g., pens). |
| MRI Safety | SPLMRISAFE 2.16.840.1.113883.1.11.19255 | BL | Yes (MRI Safe), No (MRI unsafe) |

Validation Procedures

3.3.11.1 There are no device characteristics other than the ones mentioned in this document.

3.3.12 Reusability

```
<subjectOf>
  <characteristic>
    <code code="SPLUSE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value value="1" xsi:type="INT"/>
```

Unlimited reusability is represented as follows:

```
<subjectOf>
  <characteristic>
    <code code="SPLUSE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value nullFlavor="PINF" xsi:type="INT"/>.
```

Validation Procedures

3.3.12.1 Code and code system is as above

3.3.12.2 The value is an integer number greater or equal 1 (1 meaning single use, and number greater than 1 meaning reusable up to this many times) or there is nullFlavor “PINF” and no value.

3.3.12.3 There is only one reusability element

3.3.13 [RESERVED]

3.3.14 Sterile Use

```
<subjectOf>
  <characteristic>
    <code code="SPLSTERILEUSE"
          codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="BL" value="true"/>
```

Validation Procedures

3.3.14.1 Code and code system are as above

3.3.14.2 Value type is “BL” (Boolean)

3.3.14.3 Value is “true” or “false”

3.4 *Cosmetic Product*

Cosmetic products are those products with marketing category C86965 (cosmetic) or any product inside a document of type *Cosmetic Product Listing* (103572-4), or *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration – Amendment* (X8888-1), or *Cosmetic – Update* (X8888-5).

3.4.1 *Cosmetic Product Item Code*

```
<manufacturedProduct>
  <manufacturedProduct>
    <code .../>
    <name>Juvenia Soft</name>
```

Validation Procedures

3.4.1.1 If the document is a Cosmetic Product Listing, then the item code is a cosmetic product listing number (see Section 36.2.2.1 and following).

3.4.1.2 If the document is not a Cosmetic Product Listing or Cosmetic Facility Registration, then the item code should be a GS1 GTIN.

3.4.1.3 If the document is a Cosmetic Facility Registration, then there is no item code.

3.4.2 *Cosmetic Product Name*

The product name is the statement of identity, as such name appears on the label. If the product names in the listing are not unique, then also include distinguishing information for identification purposes, for example brand name or a code that the

responsible person uses to distinguish the product. Such information may also be included in addition to the product name even when product names in the listing are unique. If you believe certain distinguishing information is confidential, include that distinguishing information in parenthesis.

```
<manufacturedProduct>
  <manufacturedProduct>
    <code .../>
    <name>Juvenia Soft</name>
```

Validation Procedures

3.4.2.1 There is a name, i.e., the product name of the cosmetic as used in product labeling or in the catalog.

3.4.2.2 Markings such as ®, or ™ should not be included

3.4.3 Cosmetic Product Category

```
<manufacturedProduct>
  <manufacturedProduct>
    <code .../>
    <name .../>

    <asSpecializedKind classCode="GEN">
      <generalizedMaterialKind>
        <code code="01B" displayName="lotions, oils, powders, and creams"
          codeSystem="2.16.840.1.113883.6.303"/>
      </generalizedMaterialKind>
    </asSpecializedKind>
```

3.4.3.1 There are one or more cosmetic product category codes (asSpecializedKind element) with a code.

3.4.3.2 code system is 2.16.840.1.113883.6.303 for FDA Product Classification System

3.4.3.3 there is a valid cosmetic product category code

3.4.3.4 there is a displayName which matches the code

3.4.3.5 If one cosmetic product category code is “Other baby products, leave-on [Baby products]” (01D1), then another cannot be “Other baby products, rinse-off [Baby products]” (01D2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).

3.4.3.6 If one cosmetic product category code is “Other baby products, rinse-off [Baby products]” (01D2), then another cannot be “Other baby products, leave-on [Baby products]” (01D1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).

- 3.4.3.7 If one cosmetic product category code is “Shampoos (non-coloring), leave-on [Hair preparations (non-coloring)]” (06F1), then another cannot be “Shampoos (non-coloring), rinse-off [Hair preparations (non-coloring)]” (06F2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.8 If one cosmetic product category code is “Shampoos (non-coloring), rinse-off [Hair preparations (non-coloring)]” (06F2), then another cannot be “Shampoos (non-coloring), leave-on [Hair preparations (non-coloring)]” (06F1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.9 If one cosmetic product category code is “Other hair preparations, leave-on [Hair preparations (non-coloring)]” (06I1), then another cannot be “Other hair preparations, rinse-off [Hair preparations (non-coloring)]” (06I2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.10 If one cosmetic product category code is “Other hair preparations, rinse-off [Hair preparations (non-coloring)]” (06I2), then another cannot be “Other hair preparations, leave-on [Hair preparations (non-coloring)]” (06I1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.11 If one cosmetic product category code is “Hair rinses (coloring), leave-on [Hair coloring preparations]” (07C1), then another cannot be “Hair rinses (coloring), rinse-off [Hair coloring preparations]” (07C2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.12 If one cosmetic product category code is “Hair rinses (coloring), rinse-off [Hair coloring preparations]” (07C2), then another cannot be “Hair rinses (coloring), leave-on [Hair coloring preparations]” (07C1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.13 If one cosmetic product category code is “Hair shampoos (coloring), leave-on [Hair coloring preparations]” (07D1), then another cannot be “Hair shampoos (coloring), rinse-off [Hair coloring preparations]” (07D2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility*

Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).

- 3.4.3.14 If one cosmetic product category code is “Hair shampoos (coloring), rinse-off [Hair coloring preparations]” (07D2), then another cannot be “Hair shampoos (coloring), leave-on [Hair coloring preparations]” (07D1), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*
- 3.4.3.15 If one cosmetic product category code is “Other hair coloring preparations, leave-on [Hair coloring preparations]” (07I1), then another cannot be “Other hair coloring preparations, rinse-off [Hair coloring preparations]” (07I2), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*
- 3.4.3.16 If one cosmetic product category code is “Other hair coloring preparations, rinse-off [Hair coloring preparations]” (07I2), then another cannot be “Other hair coloring preparations, leave-on [Hair coloring preparations]” (07I1), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*
- 3.4.3.17 If one cosmetic product category code is “Feminine deodorants, leave-on [Personal cleanliness]” (12D1), then another cannot be “Feminine deodorants, rinse-off [Personal cleanliness]” (12D2), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*
- 3.4.3.18 If one cosmetic product category code is “Feminine deodorants, rinse-off [Personal cleanliness]” (12D2), then another cannot be “Feminine deodorants, leave-on [Personal cleanliness]” (12D1), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*
- 3.4.3.19 [RESERVED].
- 3.4.3.20 If one cosmetic product category code is “Other personal cleanliness products, leave-on [Personal cleanliness]” (12F1), then another cannot be “Other personal cleanliness products, rinse-off [Personal cleanliness]” (12F2), except if the document type is *Cosmetic Facility Registration (103573-2), Cosmetic Facility Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).*

- 3.4.3.21 [RESERVED].
- 3.4.3.22 If one cosmetic product category code is “Other personal cleanliness products, rinse-off [Personal cleanliness]” (12F2), then another cannot be “Other personal cleanliness products, leave-on [Personal cleanliness]” (12F1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.23 If one cosmetic product category code is “Face and neck (excluding shaving preparations), leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14C1), then another cannot be “Face and neck (excluding shaving preparations), rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14C2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.24 If one cosmetic product category code is “Face and neck (excluding shaving preparations), rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14C2), then another cannot be “Face and neck (excluding shaving preparations), leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14C1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.25 If one cosmetic product category code is “Body and hand (excluding shaving preparations), leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14D1), then another cannot be “Body and hand (excluding shaving preparations), rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14D2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.26 If one cosmetic product category code is “Body and hand (excluding shaving preparations), rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14D2), then another cannot be “Body and hand (excluding shaving preparations), leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14D1), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1) and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).
- 3.4.3.27 If one cosmetic product category code is “Other skin care preparations, leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14J1), then another cannot be “Other skin care preparations, rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14J2), except if the document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility*

Registration - Amendment (X8888-1) and Cosmetic Facility Registration - Biennial Renewal (X8888-4).

3.4.3.28 If one cosmetic product category code is “Other skin care preparations, rinse-off [Skin care preparations (creams, lotions, powder, and sprays)]” (14J2), then another cannot be “Other skin care preparations, leave-on [Skin care preparations (creams, lotions, powder, and sprays)]” (14J1), except if the document type is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration - Amendment (X8888-1)* and *Cosmetic Facility Registration - Biennial Renewal (X8888-4)*.

3.4.3.29 If one cosmetic product category code is “Hair Conditioners (non-coloring), leave-on [Hair preparations]” (06A1), then another cannot be “Hair Conditioners (non-coloring), rinse-off [Hair preparations]” (06A2), except if the document type is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration - Amendment (X8888-1)* and *Cosmetic Facility Registration - Biennial Renewal (X8888-4)*.

3.4.3.30 If one cosmetic product category code is “Hair Conditioners (non-coloring), rinse-off [Hair preparations]” (06A2), then another cannot be “Hair Conditioners (non-coloring), leave-on [Hair preparations]” (06A1), except if the document type is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration - Amendment (X8888-1)* and *Cosmetic Facility Registration - Biennial Renewal (X8888-4)*.

3.4.4 Cosmetic Ingredient

Cosmetic ingredients use the class code INGR, or COLR for color additives. The ingredients are included in the order as in the label, i.e., generally descending order of predominance, with an alternative grouping as per 21 CFR 701.3(f).

```
<ingredient classCode="INGR">
  <ingredientSubstance>
    <code code="UNII" codeSystem="2.16.840.1.113883.4.9"/>
    <name>ingredient name</name>
  </ingredientSubstance>
</ingredient>
```

Validation Procedures

3.4.4.1 Class code for cosmetic ingredients is INGR or COLR

3.4.4.2 [RESERVED]

3.4.4.3 [RESERVED]

3.4.4.4 If the document type is one of the Cosmetic Facility Registrations (see Section 35), then there are no ingredients.

3.4.4.5 For cosmetics the ingredient substance (UNII) code is optional.

3.4.4.6 There may be one ingredient specified as flavor(s) by ingredient name simply “flavor” or “flavors” without a UNII code.

```
<ingredient classCode="INGR">
  <ingredientSubstance>
    <name>flavors</name>
  </ingredientSubstance>
</ingredient>
```

3.4.4.7 There may be one ingredient specified as fragrance(s) by ingredient name simply “fragrance” or “fragrances” without a UNII code.

```
<ingredient classCode="INGR">
  <ingredientSubstance>
    <name>fragrances</name>
  </ingredientSubstance>
</ingredient>
```

3.4.4.8 Cosmetic Product Listing documents (see Section 36) have no ingredient quantity.

3.4.5 Cosmetic Parts

Cosmetic parts may be specified for the product in the same way as for other product kits (see Section 3.1.6 Kits, Parts, Components and Accessories above),

```
<partProduct>
  <code code="91234561234569" codeSystem="1.3.160"/>
  <name>Juvenia Soft</name>
  <asSpecializedKind classCode="GEN">
    <generalizedMaterialKind>
      <code code="MCA"
        codeSystem="2.16.840.1.113883.6.303"/>
    </generalizedMaterialKind>
  </asSpecializedKind>
```

Note that in cosmetic product listing (Section 36) kits with parts are currently not expected.

Validation Procedures

3.4.5.1 There is a name, i.e., the trade or proprietary name of the cosmetic as used in product labeling or in the catalog

3.4.5.2 Markings such as ®, or ™ should not be included

3.4.6 Marketing status and date

The procedures for marketing status and date (if any) are the same for all products and described in Section 3.1.8, except that products listed in cosmetic product listing documents do not require a marketing status unless discontinued.

Validation Procedures

- 3.4.6.1 There is one marketing status code for each top-level product (part products do not need this), except if the document is a cosmetic product listing or cosmetics facility registration.
- 3.4.6.2 If the document is a cosmetics facility registration, then there is no marketing status.
- 3.4.6.3 If the document is a cosmetic product listing and the product is to be discontinued, then there is a marketing status code of “completed”.

3.4.7 Product Web Page Link

Web page to the product may be provided with an absolute URL reference with the “http://” or https://” protocol as follows:

```
<subjectOf>
  <document>
    <text>
      <reference value="https://aux-supreme.com/eau-claire.html"/>
    </text>
  </document>
```

Validation Procedures

- 3.4.7.1 Web page reference has a text element with reference (text reference) but no mediaType.
- 3.4.7.2 Text reference value is an absolute URL, starting with a URL scheme “http://” or “https://”.
- 3.4.7.3 There are no elements other than text.

3.4.8 Professional Use

To indicate that the cosmetic product is intended for use by professionals only, include the following characteristic:

```
<subject>
  <manufacturedProduct>
    ...
```

```

<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLPROFESSIONALUSE"
      codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="BL" value="true"/>
  </characteristic>
</subjectOf>

```

3.4.8.1 Code and code system is as above (“SPLPROFESSIONALUSE”)

3.4.8.2 There is a Boolean value is “true”.

3.4.8.3 Value may be “true” (professional use); to indicate general use, omit this property.

3.4.9 Image of Label for Cosmetics

```

<subjectOf>
  <characteristic>
    <code code="SPLIMAGE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ED" mediaType="image/jpeg">
      <reference value="shampoo-bottle-sticker.jpg"/>
    </value>
  </characteristic>
</subjectOf>

```

Validation Procedures

3.4.9.1 There may be one or more images of labels with the characteristic code and code system are as above.

3.4.9.2 Value xsi:type is as above

3.4.9.3 mediaType is “image/jpeg”

3.4.9.4 Reference value is the file name for a valid image

3.4.9.5 The image file is submitted together with the SPL file.

3.4.9.6 There are no product characteristics other than the ones mentioned above.

3.5 ***Summary of Product Data Elements***

This concludes the specific data elements recognized about various types of products. The following sections describe specific business processes which may or may not contain the above product data element structures.

Validation Procedures

3.5.1.1 There are no products or parts that do not follow the validation procedures for the major types described in this section, except if there is no marketing status other than *new* or *cancelled*.

4 Drug and Biologics Labeling, Listing, and other Product Submissions

Drug labeling provides a description of the product and information for its use. Drug listing links registered establishments to specific products.

4.1 Header

4.1.1 Document Type

4.1.1.1 Document types for labeling and listing are in the following Table 7. Some validation procedures vary by which FDA Center has authority over the types of products submitted with the respective document.

Table 7: Document Types for Labeling , Listing, and other Product Submissions

| Code | Display Name | FDA Center |
|-------------|--|-------------------|
| 53409-9 | BULK INGREDIENT | CDER |
| 81203-2 | BULK INGREDIENT – ANIMAL DRUG | CVM |
| 60684-8 | CELLULAR THERAPY | CDER |
| 58474-8 | COSMETIC | CFSAN |
| 103572-4 | COSMETIC PRODUCT LISTING | CFSAN |
| 58476-3 | DIETARY SUPPLEMENT | CFSAN |
| 34390-5 | HUMAN OTC DRUG LABEL | CDER |
| 34391-3 | HUMAN PRESCRIPTION DRUG LABEL, except if the application number prefix is "BN" or "BA" | CDER |
| 34391-3 | HUMAN PRESCRIPTION DRUG LABEL if the application number prefix is "BN" or "BA" | CDER |
| 75031-5 | HUMAN COMPOUNDED DRUG LABEL | CDER |
| 101437-2 | INTENTIONAL ANIMAL GENOMIC ALTERATION LABEL | CVM |
| 53407-3 | LICENSE BLOOD INTERMEDIATES/PASTE LABEL | CDER |
| 53408-1 | LICENSED MINIMALLY MANIPULATED CELLS LABEL | CDER |
| 53406-5 | LICENSED VACCINE BULK INTERMEDIATE LABEL | CDER |
| 55439-4 | MEDICAL DEVICE | CDRH |
| 58475-5 | MEDICAL FOOD | CFSAN |
| 53405-7 | NON-STANDARDIZED ALLERGENIC LABEL | CDER |
| 50577-6 | OTC ANIMAL DRUG LABEL | CVM |
| 69403-4 | OTC MEDICAL DEVICE LABEL | CDRH |
| 50576-8 | OTC TYPE A MEDICATED ARTICLE ANIMAL DRUG LABEL | CVM |
| 50574-3 | OTC TYPE B MEDICATED FEED ANIMAL DRUG LABEL | CVM |
| 50573-5 | OTC TYPE C MEDICATED FEED ANIMAL DRUG LABEL | CVM |
| 60683-0 | PLASMA DERIVATIVE | CDER |
| 50578-4 | PRESCRIPTION ANIMAL DRUG LABEL | CVM |
| 69404-2 | PRESCRIPTION MEDICAL DEVICE LABEL | CDRH |
| 60682-2 | STANDARDIZED ALLERGENIC | CDER |
| 53404-0 | VACCINE LABEL | CDER |
| 50575-0 | VFD TYPE A MEDICATED ARTICLE ANIMAL DRUG LABEL | CVM |
| 50572-7 | VFD TYPE B MEDICATED FEED ANIMAL DRUG LABEL | CVM |
| 50571-9 | VFD TYPE C MEDICATED FEED ANIMAL DRUG LABEL | CVM |

| | | |
|---------|--|------|
| 78745-7 | RECOMBINANT DEOXYRIBONUCLEIC ACID | CVM |
| 77647-6 | ANIMAL COMPOUNDED DRUG | CVM |
| 78744-0 | DRUG FOR FURTHER PROCESSING | CDER |
| 98075-5 | ANIMAL CELLS, TISSUES, AND CELL AND TISSUE BASED PRODUCT LABEL | CVM |

- 4.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type, except if the previous document type was *Bulk Ingredient* (53409-9) or *Bulk ingredient – Animal drug* (81203-2) and the present document type is *Drug for Further Processing* (78744-0).
- 4.1.1.3 If any active ingredient code is on the list of active ingredients approved for vaccines, then the document type code is *Vaccine Label* (53404-0) or *Licensed Vaccine Bulk Intermediate Label* (53406-5), except if the strength unit is a homeopathic unit.
- 4.1.1.4 If the document type changes from *Human Prescription Drug Label* (34391-3) to *Human OTC Drug Label* (34390-5), then submit a new listing file with new NDC product codes for the OTC drug.

4.1.2 Labeler information

```
<document>
  <code code="..." codeSystem="2.16.840.1.113883.6.1"
    displayName="..."/>
  <author>
  <assignedEntity>
    <representedOrganization>
      <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>
```

Validation Procedures

- 4.1.2.1 There is one labeler.
- 4.1.2.2 There is one id, the labeler's DUNS number, and name is as in Section 2.1.5.
- 4.1.2.3 The set id is not associated with any top level product with a different NDC Labeler Prefix
- 4.1.2.4 There is no other element besides id (the labeler's DUNS Number), name and registrant.

4.1.3 Registrant information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
```

```

<assignedEntity>
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
  <assignedOrganization>
    <id extension="100000008" root="1.3.6.1.4.1.519.1"/>
    <name>Acme drug company</name>
  
```

Validation Procedures

- 4.1.3.1 There may be registrant information
- 4.1.3.2 If there is a registrant, then there is one id, (the registrants DUNS number) and a name as in Section 2.1.5.
- 4.1.3.3 There is no other element besides registrant’s id, registrant’s name and establishments.
- 4.1.3.4 There is not more than one registrant element.

4.1.4 Establishment information

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization> <!-- Labeler -->
        <assignedEntity>
          <assignedOrganization> <!-- Registrant -->
        
```

Validation Procedures

- 4.1.4.1 If the marketing status code for any of the products that is or includes a drug is active, then there are one or more establishments.
- 4.1.4.2 There is one id (the DUNS number) and name is as in Section 2.1.5.
- 4.1.4.3 Id (DUNS Number) is not used for other establishments in the file
- 4.1.4.4 Establishment (“assignedOrganization”) has no other element besides id (the DUNS Number) and name.

- 4.1.4.5 The establishment id (DUNS Number) has been submitted in a document of type *Establishment Registration* (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a document of type *No Change Notification* (53410-7) between October 1st and December 31st of the previous or the current year, and that has not been inactivated by an FDA Agency Initiated Compliance Action, except if all products have the marketing status *completed*.
- 4.1.4.6 There are one or more business operations.
- 4.1.4.7 Business operation name (act definition code display name) matches corresponding business operation code
- 4.1.4.8 The code comes from the business operations list except for *Import* (C73599), *United States Agent* (C73330), *Distributes Drug Products under own Private Label* (C73608), *API/FDF Analytical Testing* (C101509), *Clinical Bioequivalence or Bioavailability Study* (C101511), *FDF Manufacture* (C101510), *In Vitro Bioequivalence or Bioanalytical Testing* (C101512), *Wholesale Drug Distributor* (C118411), and *Third-Party Logistics Provider* (C118412).
- 4.1.4.9 Business operation code matches a business operation code for the establishment with same id in its most recent establishment registration.
- 4.1.4.10 If any of the products without a marketing completion date in a *Prescription Animal Drug Label* (50578-4), *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), *OTC Animal Drug Label* (50577-6) or *Animal Medicated Article or Medicated Feed Label* (50576-8, 50574-3, 50573-5, 50575-0, 50572-7, 50571-9) has establishments with operations of *manufacture* (C43360) and also *relabel* (C73607), or *repack* (C73606), then there is no product source.
- 4.1.4.11 If the document type is *Human Compounded Drug Label* (75031-5), then the establishment's business operation is *Human drug compounding outsourcing facility* (C112113).
- 4.1.4.12 If the document type is *Animal Compounded Drug Label* (77647-6), then the establishment's business operation is *Outsourcing Animal Drug Compounding* (C122061).
- 4.1.4.13 If the product has a product source reference (source NDC product code), then one of the operations is *Repack* (C73606) or *Relabel* (C73607) except if the SPL file is for *Salvaged Drugs*, i.e. having business operation as *salvage* (C70827).
- 4.1.4.14 If in a *Bulk Ingredient* (53409-9) or *Bulk ingredient – Animal Drug* (81203-2) listing there is a product with marketing category *Bulk Ingredient* (C73626) and

without a marketing completion date, then one or more establishments with operation of *API Manufacture* (C82401) are included.

4.1.4.15 If there is any product that is or includes a drug or biologic and has no marketing completion date and no product source, then at least one establishment with a manufacture operation is included such as *API Manufacture* (C82401), *Manufacture* (C43360), or *Positron Emission Tomography Drug Production* (C91403).

4.1.4.16 If in a *Prescription Animal Drug Label* (50578-4), *OTC Animal Drug Label* (50577-6) or *Animal Medicated Article* or *Medicated Feed Label* (50576-8, 50574-3, 50573-5, 50575-0, 50572-7, 50571-9) there is a product without a marketing completion date, with an active ingredient other than those in the designated medical gas validation list, and without product source, then one or more establishments with operation of *API Manufacture* (C82401) are included.

4.1.4.17 If the marketing status code for any of the products that is or includes a drug is completed and the document type and marketing categories are as follows, then there are one or more establishments. For document type *Bulk Ingredient* (53409-9) the marketing category *Bulk Ingredient for Human Prescription Compounding* (C96793); for document type *Human OTC Drug Label* (34390-5) the marketing categories *OTC Monograph Drug Product Manufactured Under Contract* (C132334), *Unapproved Drug Other* (C73627), *Unapproved Drug Homeopathic* (C73614), *Unapproved Drug Product Manufactured Under Contract* (C132335), and *OTC Monograph Drug* (C200263); for document type *Human Prescription Drug Label* (34391-3) the marketing categories *Approved Drug Product Manufactured Under Contract* (C132333), *NDA Authorized Generic* (C73605), *Export Only* (C73590), *ANDA* (C73584), *BLA* (C73585), *IND* (C75302), *NDA* (C73594), *Unapproved Drug for Use in Drug Shortage* (C101533), *Unapproved Homeopathic* (C73614), *Unapproved Medical Gas* (C73613), *Unapproved Drug Other* (C73627), and *Unapproved Drug Product Manufactured Under Contract* (C132335); and for the marketing category *BLA* (C73585) the document types *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Cellular Therapy* (60684-8), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *Plasma Derivative* (60683-0), *Standardized Allergenic* (60682-2), and *Vaccine Label* (53404-0).

Table 8: Document Types and Marketing Categories for which even completed product listings should have establishments.

| GRP | Document Type Name | DTCode Code | Marketing Category Name | MCCode Code |
|-----|--------------------|-------------|--|-------------|
| 1 | Bulk Ingredient | 53409-9 | Bulk Ingredient for Human Prescription Compounding | C96793 |
| 2 | Cellular Therapy | 60684-8 | BLA | C73585 |

4 Drug and Biologics Labeling, Listing, and other Product Submission

| | | | | |
|----|---|---------|---|---------|
| 3 | Human OTC Drug Label | 34390-5 | OTC Monograph Drug Product Manufactured Under Contract | C132334 |
| 3 | Human OTC Drug Label | 34390-5 | Unapproved Drug Other | C73627 |
| 3 | Human OTC Drug Label | 34390-5 | Unapproved Drug Homeopathic | C73614 |
| 3 | Human OTC Drug Label | 34390-5 | Unapproved Drug Product Manufactured Under Contract | C132335 |
| 3 | Human OTC Drug Label | 34390-5 | OTC Monograph Drug | C200263 |
| 4 | Human Prescription Drug Label | 34391-3 | Approved Drug Product Manufactured Under Contract | C132333 |
| 4 | Human Prescription Drug Label | 34391-3 | NDA Authorized Generic | C73605 |
| 4 | Human Prescription Drug Label | 34391-3 | Export Only | C73590 |
| 4 | Human Prescription Drug Label | 34391-3 | ANDA | C73584 |
| 4 | Human Prescription Drug Label | 34391-3 | BLA | C73585 |
| 4 | Human Prescription Drug Label | 34391-3 | IND | C75302 |
| 4 | Human Prescription Drug Label | 34391-3 | NDA | C73594 |
| 4 | Human Prescription Drug Label | 34391-3 | Unapproved Drug for Use in Drug Shortage | C101533 |
| 4 | Human Prescription Drug Label | 34391-3 | Unapproved Homeopathic | C73614 |
| 4 | Human Prescription Drug Label | 34391-3 | Unapproved Medical Gas | C73613 |
| 4 | Human Prescription Drug Label | 34391-3 | Unapproved Drug Other | C73627 |
| 4 | Human Prescription Drug Label | 34391-3 | Unapproved Drug Product Manufactured Under Contract | C132335 |
| 5 | License Blood Intermediates/Paste Label | 53407-3 | BLA | C73585 |
| 6 | Licensed Minimally Manipulated Cells Label | 53408-1 | BLA | C73585 |
| 7 | Licensed Vaccine Bulk Intermediate Label | 53406-5 | BLA | C73585 |
| 8 | Non-Standardized Allergenic Label | 53405-7 | BLA | C73585 |
| 9 | Plasma Derivative | 60683-0 | BLA | C73585 |
| 10 | Standardized Allergenic | 60682-2 | BLA | C73585 |
| 11 | Vaccine Label | 53404-0 | BLA | C73585 |

4.1.4.18 DUNS Number is not associated with any other set id for Compounded Drug report.

4.1.4.19 If the marketing category is *OTC Monograph Drug Product Manufactured Under Contract* (C132334), *OTC Monograph Drug* (C200263) and business operations is *label* (C84732), *manufacture* (C43360), *pack* (C84731), *relabel* (C73607), or *repack* (C73606), then one or more establishment ids (DUNS Numbers) matches an establishment with same id (DUNS Number) submitted in documents of type *Establishment Registration* (51725-0) in the same or previous calendar year which is associated with one or more of the business operation qualifiers *contract manufacturing for human over-the-counter drug products*

produced under a monograph (C170729) or manufactures human over-the-counter drug products produced under a monograph (C131708).

4.1.5 Business Operation Product

The following example shows how the business operations are specified for particular products. It is done by replicating the business operation (actDefinition) elements, and connecting each with one product as shown below:

```
<document>
  <author>
    <assignedEntity><representedOrganization>      <!-- Labeler -->
      <assignedEntity><assignedOrganization>      <!-- Registrant -->
        <assignedEntity><assignedOrganization/> <!-- Establishment -->

  <performance><actDefinition>
    <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="manufacture"/>

    <product><manufacturedProduct classCode="MANU"><manufacturedMaterialKind>
      <code code="0123-12345" codeSystem="2.16.840.1.113883.6.69"/>
    </manufacturedMaterialKind></manufacturedProduct></product>
  </actDefinition></performance>

  <performance><actDefinition>
    <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="manufacture"/>
    <product><manufacturedProduct classCode="MANU"><manufacturedMaterialKind>
      <code code="0123-12348" codeSystem="2.16.840.1.113883.6.69"/>
    </manufacturedMaterialKind></product>
  </actDefinition></performance>
```

Validation Procedures

- 4.1.5.1 If the product is regulated by CDER, then an establishment operation listed is linked to at least one listed product or part product, except for Human Compounded Drug Label (75031-5).
- 4.1.5.2 If the product is regulated by CDER, then each listed product having an active marketing status is linked from at least one establishment operation, except for Human Compounded Drug Label (75031-5).
- 4.1.5.3 If the product is regulated by CDRH, CFSAN, or CVM or if it is a *Human Compounded Drug Label (75031-5)* or *Animal Compounded Drug Label (77647-6)*, then there is no operation-product link (NDC product code-to-establishment-business operation data relationship).
- 4.1.5.4 If the product is regulated by CBER, then the operation-product link is optional. (NDC product code-to-establishment-business-operation data relationship)
- 4.1.5.5 An operation product link refers to the product item code of an existing product.

4.2 Body

4.2.1 Required Sections

Validation Procedures

- 4.2.1.1 The document body contains one or more sections
- 4.2.1.2 One section contains the product data elements
- 4.2.1.3 With the exception of inner components of kits or for products with item codes (NDC product codes) for which the marketing status code is *new* or *cancelled*, for each product there is a representative sample image of a carton/container label in a major SPL section with section heading *Package Label.Principal Display Panel* (51945-4), except for Positron Emission Tomography drug products (files with only one establishment and this establishment having business operation *Positron Emission Tomography Drug Production*, C91403) and *Non-Standardized Allergenic Label* (53405-7), *Animal Compounded Drug Label* (77647-6), and *Human Compounded Drug Label* (75031-5) or if the SPL file is for *Salvaged Drugs*, i.e., having business operation as salvage (C70827).
- 4.2.1.4 If the document type is *Non-Standardized Allergenic Label* (53405-7), then there is at least one carton/container label in a major SPL section with section heading *Package Label.Principal Display Panel* (51945-4) in the SPL, except if there is no marketing status other than *new* or *cancelled*.
- 4.2.1.5 If the document type is *Human Prescription Drug Label* (34391-3), *Prescription Animal Drug Label* (50578-4), *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), or CVM document types other than *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), or *Intentional Animal Genomic Alteration Label* (101437-2), then there is at least one other content of labeling section besides SPL Listing Data Elements Section (48780-1) and *Package Label.Principal Display Panel* (51945-4), except if there is no marketing category code other than *Bulk Ingredient* (C73626), *Drug for Further Processing* (C94795), *Unapproved Medical Gas* (C73613), *Approved Drug Product Manufactured under Contract* (C132333), *OTC Monograph Drug Product Manufactured under Contract* (C132334), *Unapproved Drug Product Manufactured under Contract* (C132335), *Bulk Ingredient for Human Prescription Compounding* (C96793), *Bulk Ingredient for Animal Drug Compounding* (C98252) or *Export Only* (C73590), or there is no active ingredient other than those in the designated medical gas validation list or there is no marketing status other than *new* or *cancelled*.
- 4.2.1.6 If the approval number is in the medication guide validation list and the marketing category is not *Approved Drug Product Manufactured Under*

Contract (C132333), then there is such an *SPL Medguide Section (42231-1)*, except if there is no marketing status other than *new* or *cancelled*.

- 4.2.1.7 If the document type is *Human OTC Drug Label (34390-5)* and the marketing category code is not *Approved Drug Product Manufactured under Contract (C132333)*, *OTC Monograph Drug Product Manufactured under Contract (C132334)*, *Unapproved drug Product Manufactured under Contract (C132335)* *Export Only (C73590)* or *OTC Monograph Drug (C200263)* and the citation is not *sunscreens (part352)*, then there is an *OTC - Active Ingredient Section (55106-9)*, except if there is no marketing status other than *new* or *cancelled*.
- 4.2.1.8 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved drug Product Manufactured Under Contract) or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is an OTC – Purpose section (55105-1), except if there is no marketing status other than new or cancelled.
- 4.2.1.9 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved Drug Product manufactured Under Contract) or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is an OTC – keep out of reach of children section (50565-1), except if there is no marketing status other than new or cancelled.
- 4.2.1.10 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved Drug Product Manufactured Under Contract) or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is an Indications & usage section (34067-9), except if there is no marketing status other than new or cancelled.
- 4.2.1.11 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved Drug Product Manufactured Under Contract) or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is a Warnings section (34071-1), except if there is no marketing status other than new or cancelled.
- 4.2.1.12 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved Drug Product Manufactured Under Contract)

or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is a Dosage & administration section (34068-7), except if there is no marketing status other than new or cancelled.

- 4.2.1.13 If the document type is 34390-5 (Human OTC Drug Label) and the marketing category code is not C132333 (Approved Drug Product Manufactured Under Contract), C132334 (OTC Monograph Drug Product Manufactured Under Contract), C132335 (Unapproved Drug Product Manufactured Under Contract) or C73590 (Export Only) and the citation is not part352 (sunscreens), then there is an Inactive ingredient section (51727-6), except if there is no marketing status other than new or cancelled.
- 4.2.1.14 If the marketing category is “unapproved drug for use in drug shortage” (C101533), then Health Care Provider Letter Section (71744-7) is present, except if there is no marketing status other than new or cancelled.
- 4.2.1.15 *Package Label.Principal Display Panel Section(s)* (51945-4) are the last section(s) in the document.
- 4.2.1.16 If any of the products has the marketing status code is new or cancelled, then there may not be a content of labeling section.

4.2.2 Reporting Period (for certain submissions)

For certain drug product submission files (currently Human Compounded Drug Label), a reporting period is provided as follows:

```
<component>
  <section>
    <id root="e13a985b-f706-a5c8-e8ef-73891eb1c697"/>
    <code code="48780-1"
      codeSystem="2.16.840.1.113883.6.1"
      displayName="SPL product data elements section"/>
    <effectiveTime>
      <low value="20150601"/>
      <high value="20151130" closed="false"/>
    </effectiveTime>
```

Validation Procedures

- 4.2.2.1 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then the product data element section’s effective time contains the reporting period.
- 4.2.2.2 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then reporting period (effective time) has low and high boundaries for reporting period start and end date respectively.

- 4.2.2.3 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then reporting start date has at least the precision of day in the format YYYYMMDD
- 4.2.2.4 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then reporting end date has at least the precision of day in the format YYYYMMDD
- 4.2.2.5 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then reporting start date is before reporting end date.
- 4.2.2.6 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), then reporting period start date (low value) is any day of any year between 2014 to current year.
- 4.2.2.7 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) and the reporting period start date (low value) is December 1, then the end date (high value) is May 31 of the following year.
- 4.2.2.8 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) and the reporting period start date (low value) is June 1, then the end date (high value) is November 30 of the same year.
- 4.2.2.9 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) and the reporting period start date (low value) is not Dec 1 or Jun 1, then the reporting period end date (high value) is 6 month from the start date.

```
<section>
  <id root="..." />
  <code code="48780-1" codeSystem="2.16.840.1.113883.6.1"
    displayName="SPL product data elements section" />
  <title />
  <text>
    <paragraph>No Products to Report.</paragraph>
  </text>
```

- 4.2.2.10 If no products are reported in the product data element section of a Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6), i.e., the product data elements section contains no subject element, then the product data elements section contains section text with the single paragraph “No Products to Report” and the only section is the product data elements section.
- 4.2.2.11 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) and the text section is included in the

product data elements section, then there is no subject element (for the product data elements).

4.2.2.12 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) and no products are reported, then the facility can not be associated with any compounded drug in this period.

4.2.2.13 If the document type is Human Compounded Drug Label (75031-5) or Animal Compounded Drug Label (77647-6) with products reported in this period, then the establishment can not be associated with another Human Compounded Drug Label that states “No Products to Report” for this period.

5 NDC/NHRIC Labeler Code Request

5.1 Header

5.1.1 Document type

```
<document>
  <code code="51726-8"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="NDC/NHRIC Labeler Code request"/>
```

Validation Procedures

- 5.1.1.1 Document code is NDC/NHRIC Labeler Code Request (51726-8), NDC Labeler Code Request - Animal Drug (72871-7), NDC Labeler Code Inactivation (69968-6), or NDC Labeler Code Inactivation – Animal Drug (81204-0).
- 5.1.1.2 There is no title
- 5.1.1.3 If a document with the same set id has been previously submitted, then it is an NDC/NHRIC Labeler Code Request (51726-8) or NDC Labeler Code Request - Animal Drug (72871-7), NDC Labeler Code Inactivation (69968-6), or NDC Labeler Code Inactivation – Animal Drug (81204-0).
- 5.1.1.4 If the document is an NDC Labeler Code Inactivation (69968-6) or NDC Labeler Code Inactivation – Animal Drug (81204-0), then an NDC/NHRIC Labeler Code Request (51726-8) or NDC Labeler Code Request - Animal Drug (72871-7) document with the same set id has been previously submitted
- 5.1.1.5 If the document is an NDC Labeler Code Inactivation (69968-6) or NDC Labeler Code Inactivation – Animal Drug (81204-0), then there is no labeler information.
- 5.1.1.6 If the document is an NDC Labeler Code Inactivation (69968-6), or NDC Labeler Code Inactivation – Animal Drug (81204-0), then all NDCs with the NDC Labeler Code linked to the NDC Labeler Code Inactivation file's set ID is associated with a product with a marketing end date, except if the NDC Labeler Code Inactivation file was initiated by the FDA.

5.1.2 Labeler information

```

<document>
  <author>
    <time/>
    <assignedEntity>
      <representedOrganization>
        <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
        <id extension="0001" root="2.16.840.1.113883.6.69"/>
        <name>Mann's drug Store</name>
        <contactParty>

```

Validation Procedures

- 5.1.2.1 If the document is an NDC/NHRIC Labeler Code Request (51726-8) or NDC Labeler Code Request - Animal Drug (72871-7), then there is a labeler organization.
- 5.1.2.2 There are two ids (NDC/NHRIC labeler code and DUNS Number) (except for an initial labeler code request, which should be submitted with only one id (DUNS Number.))
- 5.1.2.3 One id, the DUNS number, and name are as in Section 2.1.5.
- 5.1.2.4 One id has the root 2.16.840.1.113883.6.69 and an extension (except for an initial labeler code request, which should be submitted without this id (NDC/NHRIC labeler code.))
- 5.1.2.5 There is no id root besides 1.3.6.1.4.1.519.1 and 2.16.840.1.113883.6.69
- 5.1.2.6 If no document with the same set id has been previously submitted, then the NDC labeler code has not been associated previously with a different setId (regardless of version)
- 5.1.2.7 The set id is not associated with any other id(NDC/NHRIC labeler code) with root 2.16.840.1.113883.6.69
- 5.1.2.8 The id extension(NDC/NHRIC labeler code) with the root 2.16.840.1.113883.6.69 has 4 or 5 digits
- 5.1.2.9 The id extension(NDC/NHRIC labeler code) with the root 2.16.840.1.113883.6.69 with 5 digits does not have a leading zero
- 5.1.2.10 The labeler code (id extension with the root 2.16.840.1.113883.6.69) is not (0)0000, (0)0001, (0)1500, (0)1800 or (0)1900.
- 5.1.2.11 There is one contact party

- 5.1.2.12 If a document with the same set id has previously been submitted, then there is a labeler code (id with the root 2.16.840.1.113883.6.69) same as the one previously submitted under that set id (if any).

5.1.3 Labeler Detail Information

To describe details of a labeler such as physical address, US agent, and business operations the following structure is added

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
        <id extension="0001" root="2.16.840.1.113883.6.69"/>
        <name>Mann's drug Store</name>
        <contactParty>...</contactParty>
      </representedOrganization>
      <assignedEntity>
        <assignedOrganization>
          <assignedEntity><!-- Labeler Details -->
            <assignedOrganization>
              <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
              <name>Mann's drug Store</name>
              <addr>...</addr>
            </assignedOrganization>
          </assignedEntity>
        </assignedOrganization>
      </assignedEntity>
    </assignedEntity>
  </author>
</document>

```

The format is similar to the Establishment description. The only difference is that there is only one such “Establishment” with the same DUNS number and name as the Labeler.

Validation Procedures

- 5.1.3.1 If the document is not a NDC/NHRIC Labeler Code Request (51726-8), then there is no labeler detail information.
- 5.1.3.2 Labeler detail information has no registrant information and exactly one “Establishment”
- 5.1.3.3 Labeler detail information has exactly one “Establishment”
- 5.1.3.4 There is one id.
- 5.1.3.5 Id (DUNS Number) has the root 1.3.6.1.4.1.519.1
- 5.1.3.6 Id (DUNS Number) is the same as the id of the labeler organization.
- 5.1.3.7 Name is the same as the name of the labeler organization.
- 5.1.3.8 Labeler detail information has an address as in Section 2.1.6.

5.1.3.9 There are no further elements besides the id, name, addr, and Labeler US Agent on this level.

5.1.3.10 The DUNS number along with the labeler details' name and address information match the DUNS number record in the Dun and Bradstreet database.

5.1.4 Labeler US Agent

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
        <id extension="0001" root="2.16.840.1.113883.6.69"/>
        <name>Mann's drug Store</name>
        <contactParty>...</contactParty>

      <assignedEntity>
        <assignedOrganization>
          <assignedEntity>
            <assignedOrganization>
              <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
              <assignedEntity>
                <assignedOrganization> <!-- labeler US agent -->
                  <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
                  <name>Simmons Reps Company</name>
                  <telecom value="tel:+1-800-555-1212"/>
                  <telecom value="mailto:contact@USagent.com"/>
                </assignedOrganization>
              </performance>
            <actDefinition>
              <code code="C73330" displayName="United States agent"
                codeSystem="2.16.840.1.113883.3.26.1.1"/>
          </assignedOrganization>
        </assignedEntity>
      </assignedOrganization>
    </assignedEntity>
  </author>
</document>
```

Validation Procedures

5.1.4.1 If the country for the labeler is not “USA”, then there may be one US agent

5.1.4.2 US agent is as defined in Section 6.1.3.114

5.1.5 Labeler Operation

To describe the activity of a labeler with business operations the following structure is added.

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
        <id extension="0001" root="2.16.840.1.113883.6.69"/>
        <name>Mann's drug Store</name>
        <contactParty>...</contactParty>
      </representedOrganization>
    </assignedEntity>
  </author>
</document>
```

```

<assignedEntity>
  <assignedOrganization>
    <assignedEntity>
      <assignedOrganization>
        <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
      <assignedOrganization>
        <performance>
          <actDefinition>
            <code code="C43360" displayName="manufacture"
              codeSystem="2.16.840.1.113883.3.26.1.1"/>
            <subjectOf>
              <approval>
                <code code="C106643" displayName="Manufactures human
prescription drug products"
              codeSystem="2.16.840.1.113883.3.26.1.1"/>
              </approval>
            </subjectOf>
          </actDefinition>
        </performance>
      </assignedOrganization>
    </assignedEntity>
  </assignedOrganization>
</assignedEntity>

```

Validation Procedures

- 5.1.5.1 There are one or more labeler operation details (performance act definitions).
- 5.1.5.2 Each performance act definition (business operation) has one code.
- 5.1.5.3 Code system is 2.16.840.1.113883.3.26.1.1
- 5.1.5.4 Display name matches the code
- 5.1.5.5 The code comes from the business operations list except for *import* (C73599) and *united states agent* (C73330).
- 5.1.5.6 Each business operation code is mentioned only once.
- 5.1.5.7 There is one or more business operation qualifier except when business operation is analysis (C25391), API manufacture (C82401) , or SIP Foreign Seller (C175317).
- 5.1.5.8 Business operation qualifier has one code.
- 5.1.5.9 Code system is 2.16.840.1.113883.3.26.1.1
- 5.1.5.10 Display name matches the code
- 5.1.5.11 If the business operation is *manufacture* (C43360), then the business operation qualifier is *Manufactures human prescription drug products* (C106643), *Manufactures human over-the-counter drug products not produced under an approved drug application or under a monograph* (C131710), *Manufactures human over-the-counter drug products produced under a monograph* (C131708), *Manufactures human over-the-counter drug products produced under an approved drug application* (C131709), and/or *Contract manufacturing*

for human over-the-counter drug products produced under a monograph (C170729).

- 5.1.5.12 If the business operation is *distributes drug products under own private label (C73608)*, then the business operation qualifier is *distributes human prescription drug products (C111077)* and/or *distributes human over-the-counter drug products (C111078)*.)
- 5.1.5.13 If the qualifiers Intent to compound 506e (drug shortage) drugs (C112087), No intent to compound 506e (drug shortage) drugs (C112091), Compounding from bulk ingredients (C112092), Not compounding from bulk ingredients (C112093), Compounding sterile products (C112094), or Not compounding sterile products (C112095), then the operation is *Human drug compounding outsourcing facility (C112113)*.
- 5.1.5.14 If the business operation qualifier is *Distributes Human Prescription Drug Products (C111077)* and/or *Distributes Human Over-the-Counter Drug Products (C111078)*, then the business operation is *Distributes Drug Products under Own Private Label (C73608)*.

5.1.6 FDA-Initiated Labeler Code Inactivation

```
<document>
  <legalAuthenticator>
    <assignedEntity>
      <representedOrganization>
```

- 5.1.6.1 If the document is an FDA-initiated NDC Labeler Code Inactivation (69968-6), FDA-Initiated NDC Labeler Code Inactivation – Animal Drug (81204-0) or an FDA-Initiated NDC Labeler Code Re-Activation, then the proper legalAuthenticator element is included.
- 5.1.6.2 One id is a DUNS number with the root 1.3.6.1.4.1.519.1
- 5.1.6.3 The id with the root 1.3.6.1.4.1.519.1 (DUNS number) has a 9-digit extension
- 5.1.6.4 The proper FDA id is provided.
- 5.1.6.5 The proper FDA name is provided.
- 5.1.6.6 If the most recent document of this setId was an FDA-Initiated *NDC Labeler Code Inactivation (69968-6)* or *NDC Labeler Code Inactivation – Animal Drug (81204-0)*, then an FDA-Initiated *NDC/NHRIC Labeler Code Request (51726-8)* SPL file with <legalAuthenticator> element has been submitted before an *NDC/NHRIC Labeler Code Request (51726-8)*, *NDC Labeler Code Request - Animal Drug (72871-7)*, *NDC Labeler Code Inactivation (69968-6)*, or *NDC Labeler Code Inactivation – Animal Drug (81204-0)* can be submitted by the labeler.

5.2 *Body - Empty*

Use an empty document body:

```
<document>  
  <component>  
    <structuredBody/>
```

or

```
<document>  
  <component>  
    <nonXMLBody>  
      <text/>
```

5.2.1.1 The document body is empty

6 Establishment registration

Establishment registrations have only header information with a single registrant organization and one or more registered establishments. Aside from the proper *Establishment Registration* document type, two other document types can be used for establishment registration submissions, i.e., the *No Change Notification*, the *Establishment Deregistration* and *Out of Business Notification*.

6.1 Header

6.1.1 Document type

```
<document>
  <code code="51725-0"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="Establishment registration"/>
```

Validation Procedures

- 6.1.1.1 Document type is “Establishment registration” (51725-0), “Establishment De-Registration” (70097-1), “No change notification” (53410-7), or “Out of Business Notification” (53411-5).
- 6.1.1.2 The effective time year matches the current year.
- 6.1.1.3 There is no title
- 6.1.1.4 For a No change notification (53410-7), or Establishment De-Registration (70097-1) the set id in this document should be the same set id included in a previously submitted Establishment Registration (51725-0), No change notification (53410-7), or Establishment De-Registration (70097-1), with information about your establishment(s).
- 6.1.1.5 If a document with the same set id as the one in this file has been previously submitted, then the document type of the previously submitted file is Establishment Registration (51725-0), Establishment De-Registration (70097-1), or No change notification (53410-7).
- 6.1.1.6 “No change notification (53410-7)” documents are submitted during the time frame October 1st through December 31st of each year.
- 6.1.1.7 If the document type is *No Change Notification* (53410-7), then its most recent Establishment Registration document is not inactivated by an FDA Agency Initiated Compliance Action.

- 6.1.1.8 If the document type is *No Change Notification (53410-7)* and its most recent Establishment Registration does not have any business operation qualifiers (see Section 6.1.7), then a full Establishment Registration file must be submitted instead, except if all the business operations are only *analysis (C25391)*, *API manufacture (C82401)*, or *medicated animal feed manufacture (C84635)*.
- 6.1.1.9 If the document type is *No Change Notification (53410-7)* and its most recent Establishment Registration asserts the business operation qualifier *Manufactures human over-the-counter drug products (C106645)*, then the Establishment Registration must be updated by submitting a full Establishment Registration file.
- 6.1.1.10 If the document type is *No Change Notification (53410-7)* and its most recent Establishment Registration does not have a second id with the root 2.16.840.1.113883.4.82 (FEI number) for each establishment, then the Establishment Registration must be updated by submitting a full Establishment Registration file with FEI numbers.

6.1.2 Registrant information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
            <name>Acme drug company</name>
            <contactParty>
```

Validation Procedures

- 6.1.2.1 If the document type is “No change notification” or “Establishment De-Registration”, then there is no registrant information.
- 6.1.2.2 If the document type is “Establishment registration”, then there is registrant information.
- 6.1.2.3 There is one id, the DUNS number and name are as in Section 2.1.5.
- 6.1.2.4 The id (registrant’s DUNS Number) is not associated with any other set id of document type “Establishment registration”, except if the other set id, which was included in a previously submitted Establishment Registration SPL file, is referred in the related document (RPLC).
- 6.1.2.5 The set id is not associated with any other registrant id (DUNS Number).
- 6.1.2.6 There is one contact party as in section 2.1.8.

6.1.2.7 Establishment registration has no labeler information (no validation rules defined for it).

6.1.3 Establishment Information

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- labeler, pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
          <assignedEntity>
<assignedOrganization> <!-- establishment -->
<id extension="100000001" root="1.3.6.1.4.1.519.1"/>
<id extension="123456" root="2.16.840.1.113883.4.82"/>

<name>Middleton Manufacturing company</name>

<addr>
  <streetAddressLine>123 Burl Road</streetAddressLine>
  <city>Dublin</city>
  <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
</addr>

<contactParty>

```

Validation Procedures

- 6.1.3.1 If the document type is “establishment registration”, then there are one or more establishments.
- 6.1.3.2 If the document type is *No change notification (53410-7)* or *Establishment De-Registration (70097-1)*, then there is no establishment information.
- 6.1.3.3 Establishment has one or two id elements, one id, the DUNS number, and name are as in Section 2.1.5.
- 6.1.3.4 Establishment’s DUNS number is not associated with another establishment in the same SPL file.
- 6.1.3.5 Establishment’s DUNS number is not associated with any other set id for document type “Establishment registration”, except if the other set id, which was included in a previously submitted Establishment Registration SPL file, is referred in the relatedDocument (RPLC, see Section 2.1.11 Predecessor Document for more details).
- 6.1.3.6 The DUNS number along with the establishment name and address information match the DUNS number record in the Dun and Bradstreet database, except if all establishments have only the business operations *Medicated Animal Feed Manufacture (C84635)*.

- 6.1.3.7 If there is a second id, then its root is 2.16.840.1.113883.4.82 and the extension (FEI number) is 7 or 10 digits
- 6.1.3.8 Each establishment has an address as in Section 2.1.6.
- 6.1.3.9 There is one contact party as in Section 2.1.8.
- 6.1.3.10 There is no assigned entity other than for US Agent or Import business.
- 6.1.3.11 If the document type is *Establishment Registration* (51725-0) and there is a previously submitted document with the same set id as the one in this file where this establishment had already been mentioned, then there is a second id with the root 2.16.840.1.113883.4.82 (FEI number) for each establishment previously identified by an id (DUNS number) with the root 1.3.6.1.4.1.519.1.

6.1.4 Establishment US agent

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
<assignedOrganization> <!-- establishment -->
  <addr>
    <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
  </addr>

  <assignedEntity>
    <assignedOrganization> <!-- establishment US agent -->
      <id extension="100000001" root="1.3.6.1.4.1.519.1"/>

      <name>Simmons Reps Company</name>

      <telecom value="tel:+1-800-555-1212"/>
      <telecom value="mailto:contact@USagent.com"/>

    </assignedOrganization>

  <performance>
    <actDefinition>
      <code code="C73330" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="United States agent"/>
```

Validation Procedures

- 6.1.4.1 If the country for the establishment is not “USA”, then there is one US agent
- 6.1.4.2 US agent element has code, code system and display name are as above
- 6.1.4.3 If the country for the establishment is “USA”, then there is no US agent
- 6.1.4.4 US agent has one id, (the DUNS number), and name are as in Section 2.1.5.

- 6.1.4.5 US agent has a US telephone number and an email address.
- 6.1.4.6 The US agent's DUNS number matches the DUNS number record in the Dun and Bradstreet database and is for a USA location.
- 6.1.4.7 There is at most one US Agent.

6.1.5 Import business

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization>
            <assignedEntity> <!-- registrant -->
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedOrganization> <!-- establishment -->
  <addr>
    <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
  </addr>
  <assignedEntity>
    <assignedOrganization> <!-- establishment's importer -->
      <id extension="100000005" root="1.3.6.1.4.1.519.1"/>
      <name>Waytogo importers</name>
      <telecom value="tel:+1-800-555-1214"/>
      <telecom value="mailto:contact@waytogo.com"/>
    </assignedOrganization>
  </assignedEntity>
  <performance>
    <actDefinition>
      <code code="C73599" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="import"/>
    </actDefinition>
  </performance>

```

Validation Procedures

- 6.1.5.1 If the country code for the establishment is not “USA”, then there may be one or more import businesses.
- 6.1.5.2 Each business has code, code system and display name are as above.
- 6.1.5.3 If the country code for the establishment is USA, then there are no import businesses
- 6.1.5.4 Importer has one id, the DUNS number and name are as in Section 2.1.5.
- 6.1.5.5 Importer has a US telephone number and email address.

6.1.6 Establishment operation

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization>
      <!-- establishment -->
    </assignedOrganization>
  </assignedEntity>
  <performance>
    <actDefinition>
      <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="manufacture"/>
    </actDefinition>
  </performance>
</document>

```

Validation Procedures

- 6.1.6.1 There are one or more establishment operation details (performance act definitions).
- 6.1.6.2 Each performance act definition has one code.
- 6.1.6.3 Code system is 2.16.840.1.113883.3.26.1.1
- 6.1.6.4 Display name matches the code
- 6.1.6.5 The code comes from the business operations list except for *import* (C73599), *united states agent* (C73330), *distributes drug products under own private label* (C73608), *API/FDF analytical testing* (C101509), *clinical bioequivalence or bioavailability study* (C101511), *FDF manufacture* (C101510), *in vitro bioequivalence or bioanalytical testing* (C101512), *wholesale drug distributor* (C118411), and *third-party logistics provider* (C118412).
- 6.1.6.6 Each business operation code is mentioned only once per establishment.
- 6.1.6.7 There is no product reference.
- 6.1.6.8 If the business operation is Transfill (C125710), then the business operation qualifier is Transfills Medical Gas (C126091).

6.1.7 Business Operation Qualifier

```

<performance>
  <actDefinition>
    ...
    <subjectOf>
      <approval>
        <code code="Qualifier Code" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="Qualifier Display Name"/>
      </approval>
    </subjectOf>
  </actDefinition>
</performance>

```

Validation Procedures

- 6.1.7.1 There are one or more Business Operation Qualifiers, except if the business operation is *analysis* (C25391), *API manufacture* (C82401), *medicated animal feed manufacture* (C84635), or SIP Foreign Seller (C175317).
- 6.1.7.2 Business operation qualifier has one code.
- 6.1.7.3 Code system is 2.16.840.1.113883.3.26.1.1
- 6.1.7.4 Code is from the Business Operation Qualifier List
- 6.1.7.5 Display name matches the code

Human Drug Compounding Outsourcing Facility Operation Qualifiers

- 6.1.7.6 If the business operation is *Human drug compounding outsourcing facility* (C112113), then there are 2 or 3 operation qualifiers.
- 6.1.7.7 One of the qualifiers is *Intent to compound 506e (drug shortage) drugs* (C112087) or *No intent to compound 506e (drug shortage) drugs* (C112091).
- 6.1.7.8 Qualifiers *Intent to compound 506e (drug shortage) drugs* (C112087) and *No intent to compound 506e (drug shortage) drugs* (C112091), both should not be present at a time.
- 6.1.7.9 One of the qualifiers is *Compounding from bulk ingredients* (C112092) or *Not compounding from bulk ingredients* (C112093).
- 6.1.7.10 If one of the business operation qualifiers is compounding from *bulk ingredients* (C112092), then one of the following business operation qualifiers should be included: *Compounding sterile products* (C112094), and *Not compounding sterile products* (C112095).
- 6.1.7.11 If one of the business operation qualifiers is *Not compounding from bulk ingredients* (C112093), then the following business operation qualifiers should

not be included: *Compounding sterile products* (C112094), and *Not compounding sterile products* (C112095).

6.1.7.12 If the qualifiers Intent to compound 506e (drug shortage) drugs (C112087), No intent to compound 506e (drug shortage) drugs (C112091), Compounding from bulk ingredients (C112092), Not compounding from bulk ingredients (C112093), Compounding sterile products (C112094), or Not compounding sterile products (C112095), then the operation is Human drug compounding outsourcing facility (C112113).

Over-the-Counter Drug Operation Qualifiers

6.1.7.13 Instead of the business operation qualifier *Manufactures human over-the-counter drug products* (C106645), either *Manufactures human over-the-counter drug products produced under an approved drug application* (C131709), *Manufactures human over-the-counter drug products not produced under an approved drug application or under a monograph* (C131710), *Manufactures human over-the-counter drug products produced under a monograph* (C131708), or *Contract manufacturing for human over-the-counter drug products produced under a monograph* (C170729) must be used.

6.1.7.14 If the business operation qualifier is *Contract manufacturing for human over-the-counter drug products produced under a monograph* (C170729) or *manufactures human over-the-counter drug products produced under a monograph* (C131708), then the business operation is label (C84732), manufacture (C43360), pack (C84731), relabel (C73607), or repack (C73606).

6.2 Body - Empty

Use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>
  <component>
    <nonXMLBody>
      <text/>
```

6.2.1.1 The document body is empty

7 Out of Business Notification

The Out of Business Notification allows de-listing of all the establishments of an Establishment registration.

7.1 Header

7.1.1 Document type

```
<document>
  <code code="53411-5"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="Out of business notification"/>
```

Validation Procedures

- 7.1.1.1 Document type is “Out of business notification” (53411-5)
- 7.1.1.2 The effective time year matches the current year.
- 7.1.1.3 There is no title
- 7.1.1.4 An Establishment Registration (51725-0), Establishment De-Registration (70097-1), No change notification (53410-7), Identification of CBER-regulated generic drug facility (72090-4), Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7), or Withdrawal of Wholesale Drug Distributors and Third-Party Logistics Facility Report (77573-4) with the same set id has been previously submitted.
- 7.1.1.5 If a document with the same set id has been previously submitted, then it is an Establishment Registration (51725-0), Establishment De-Registration (70097-1), No change notification (53410-7), Identification of CBER-regulated generic drug facility (72090-4), Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7), or Withdrawal of Wholesale Drug Distributors and Third-Party Logistics Facility Report (77573-4).
- 7.1.1.6 There is no labeler, registrant, or establishment information.

7.2 Body - Empty

Use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>  
  <component>  
    <nonXMLBody>  
      <text/>
```

7.2.1.1 The document body is empty

8 Pharmacologic Class Indexing

8.1 Header

8.1.1 Document type

```
<document>
  <code code="60685-5" codeSystem="2.16.840.1.113883.6.1"
    displayName="Indexing - Pharmacologic Class"/>
```

Validation Procedures

8.1.1.1 Document code is as above

8.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

8.1.2 Author information

Pharmacologic class indexing is maintained by FDA:

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

Pharmacologic classes for Mechanism of Action (MoA), Physiologic Effect (PE), Established Pharmaceutical Class (EPC) and some extensions (EXT) and their hierarchy are maintained by the U.S. Department of Veterans Affairs's MED-RT system:

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension="926891516"/>
      <name>Department of Veterans Affairs</name>
```

Chemical structure classes and their hierarchy are maintained in the National Library of Medicine's (NLM) Medical Subject Heading (MeSH) system:

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension="015333032"/>
      <name>National Library of Medicine</name>
```

8.1.2.1 Author information for pharmacologic class indexing is as one of the above

8.2 *Body*

```
<section>
  <id root="ffabedf9-6bde-4787-beb0-abd214307427"/>
  <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="SPL Indexing Data Elements Section"/>
  <title/>
  <text/>
  <effectiveTime value="20101007"/>
  <subject>
```

Validation Procedures

8.2.1 Pharmacologic Class Indexing Section

8.2.1.1 If the document type is *Indexing – Pharmacologic Class* (60685-5), then the document contains one SPL Indexing Data Elements Section (48779-3) as above.

8.2.1.2 Value of effective time is same as value of effective time in document information.

8.2.2 Pharmacologic Class Indexing

```
<section>
  <subject>
  <identifiedSubstance>
    <id root="0987654321" extension="2.16.840.1.113883.4.9"/>
    <identifiedSubstance>
      <code code="0987654321" codeSystem="2.16.840.1.113883.4.9"/>
      <name>tazminic acid</name>
    <asSpecializedKind>
```

8.2.2.1 There is one active moiety.

8.2.2.2 There is one active moiety code.

8.2.2.3 Code system is 2.16.840.1.113883.4.9

8.2.2.4 Code and code system are the same as the parent element id's extension and root respectively.

8.2.2.5 There is one active moiety name

8.2.2.6 Active moiety name matches code

8.2.2.7 The same active moiety is not described in a pharmacologic class indexing document with a different set id.

8.2.2.8 There is no document with the same set id but a different active moiety.

8.2.2.9 There are one or more pharmacologic class components

```

<asSpecializedKind>
  <generalizedMaterialKind>
    <code code="N0000012345" codeSystem="2.16.840.1.113883.6.345"
      displayName="melhoridizing tazminate [EPC]"/>
    <name>melhoridizing tazminate (MTZ)</name>
  
```

8.2.2.10 Under each pharmacologic class component, there is a code

8.2.2.11 Code system is 2.16.840.1.113883.6.345 (MED-RT) or 2.16.840.1.113883.6.177 (MeSH)

8.2.2.12 If code system is MED-RT, then the code starts with a uppercase “N”, followed by 10 digits

8.2.2.13 If code system is MeSH, then the code starts with a uppercase “M”, followed by 7 or more digits

8.2.2.14 There is one display name

8.2.2.15 If the code system is MED-RT (2.16.840.1.113883.6.345), then display name is the formal MED-RT name with the bracket indicating the kind of concept [EPC, MoA, PE, EXT]

8.2.2.16 If the code system is MeSH (2.16.840.1.113883.6.177), then display name is the preferred MeSH name with a bracket “[CS]” indicating the kind of concept being “Chemical Structure”.

8.2.2.17 If the concept is an External Pharmacologic Class [EPC], there is a name with the preferred FDA name.

8.2.3 Pharmacologic Class Definition

```

<section>
  <subject>
    <identifiedSubstance>
      <id root="N0000012345" extension="2.16.840.1.113883.6.345"/>
      <identifiedSubstance>
        <code code="N0000012345" codeSystem="2.16.840.1.113883.6.345"
          displayName="melhoridizing tazminate [EPC]"/>
        <name use="L">melhoridizing tazminate (MTZ)</name>
        <name use="A">melhoridizing tazminate [EPC]</name>
        <name use="A">tazminic melhoridizer</name>
      
```

8.2.3.1 There are one or more pharmacologic classes.

8.2.3.2 There is one code.

8.2.3.3 The rules for the pharmacologic class code, code system and display name are as in the respective procedures 8.2.2.12 and following.

8.2.3.4 Code and code system are the same as the parent element id's extension and root respectively.

8.2.3.5 There are one or more names

8.2.3.6 One name has the use attribute "L" indicating the preferred name.

8.2.3.7 If the concept is not an Established Pharmacologic Class [EPC], then the name with the use attribute "L" is the same as the displayName.

8.2.3.8 There are zero, one or more defining super-classes

```
<asSpecializedKind>  
  <generalizedMaterialKind>  
    <code code="N0000012345" codeSystem="2.16.840.1.113883.6.345"  
      displayName="melhoridizing tazminate [EPC]"/>
```

8.2.3.9 Under each defining super-class there is a code

8.2.3.10 The rules for the defining super-class code, code system and displayName are as in the respective procedures 8.2.2.12ff

8.2.3.11 There is no other name element.

9 Dietary Supplement Labeling

Dietary supplement labeling provides a description of the product.

9.1 Header

9.1.1 Document Type

- 9.1.1.1 Document types for dietary supplement labeling is 58476-3 FDA product label Dietary supplement.
- 9.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.
- 9.1.1.3 If the document type changes from *Human Prescription Drug Label* (34391-3) or *Human OTC Drug Label* (34390-5) to *Dietary Supplement* (58476-3), then submit a new listing file with new NDC codes for the Dietary Supplement.
- 9.1.1.4 The set id is not associated with any top level product with a different Labeler Prefix

9.1.2 Labeler information

```
<document>
  <code code="58476-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="Dietary Supplement"/>
  <author>
  <assignedEntity>
    <representedOrganization>
      <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>
```

Validation Procedures

- 9.1.2.1 There is one labeler
- 9.1.2.2 There is one id, the DUNS number, and name is as in Section 2.1.5.
- 9.1.2.3 There is no other element besides id, name and registrant.

9.1.3 Registrant information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
  <assignedEntity>
    <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
```

```
<assignedOrganization>  
  <id extension="100000008" root="1.3.6.1.4.1.519.1"/>  
  <name>Acme drug company</name>
```

Validation Procedures

- 9.1.3.1 There may be registrant information
- 9.1.3.2 If there is a registrant, then there is one id, (the DUNS number) and a name as in Section 2.1.5.
- 9.1.3.3 There is no other element besides id, name and establishments.

9.2 Body

9.2.1 Required Sections

Validation Procedures

- 9.2.1.1 The document body contains three or more sections
- 9.2.1.2 One section contains the product data elements
- 9.2.1.3 There is a *Package Label.Principal Display Panel* Section (51945-4) with an image of the carton/container label including the Supplement Facts.
- 9.2.1.4 There is one *Statement of Identity Section* (69718-5).
- 9.2.1.5 Aside from *SPL Listing Data Elements Section* (48780-1), *Package Label.Principal Display Panel* (51945-4) and *Statement of Identity Section* (69718-5), there are only the *Health Claim Section* (69719-3), the *Warnings Section* (34071-1) for the warning statement, the *Precautions Section* (42232-9) for the notice statement, the *Safe Handling Warning Section* (50741-8) for the safe handling statement, and the *Dosage & Administration Section* (34068-7).

10 Medical Food Labeling

Medical Food labeling provides a description of the product.

10.1 Header

10.1.1 Document Type

10.1.1.1 Document types for Medical Food labeling is 58475-5 FDA product label Medical Food.

10.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

10.1.2 Labeler information

```
<document>
  <code code="58475-5" codeSystem="2.16.840.1.113883.6.1"
    displayName="Medical Food"/>
  <author>
  <assignedEntity>
    <representedOrganization>
      <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>
```

Validation Procedures

10.1.2.1 There is one labeler

10.1.2.2 There is one id, the DUNS number, and name is as in Section 2.1.5.

10.1.2.3 The set id is not associated with any top level product with a different Labeler Prefix

10.1.2.4 There is no other element besides id, name and registrant.

10.1.3 Registrant information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
        <name>Acme drug company</name>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
    <assignedOrganization>
      <id extension="100000008" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>
```

Validation Procedures

10.1.3.1 There may be registrant information

10.1.3.2 If there is a registrant, then there is one id, (the DUNS number) and a name as in Section 2.1.5.

10.1.3.3 There is no other element besides id, name and establishments.

10.1.4 Establishment information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization <!-- Labeler -->
        <assignedEntity>
          <assignedOrganization <!-- Registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
  </assignedEntity>
  <assignedOrganization <!-- Establishment -->
    <id extension="1000000019" root="1.3.6.1.4.1.519.1"/>
    <name>Middleton Manufacturing company</name>
  </assignedOrganization>
  <performance>
    <actDefinition>
      <code code="C43360"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="manufacture"/>
    </actDefinition>
  </performance>
</document>
```

Validation Procedures

10.1.4.1 If the marketing status code for any of the products is **not completed**, then there are one or more establishments.

10.1.4.2 There is one id (the DUNS number) and name is as in Section 2.1.5.

10.1.4.3 id is not used for other establishments in the file

10.1.4.4 Establishment (“assignedOrganization”) has no other element besides id and name.

10.1.4.5 The establishment id (DUNS Number) has been submitted in a document of type “*Establishment Registration*” (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a document of type “*No Change Notification*” (53410-7) between October 1st and December 31st of the previous or the current year.

10.1.4.6 There are one or more business operations.

10.1.4.7 Act definition display name matches code

10.1.4.8 The code comes from the business operations list except for import (C73599), united states agent (C73330) and distributes drug products under own private label (C73608)

10.1.4.9 Business operation code matches a business operation code for the establishment with same id in its most recent establishment registration

10.2 Body

10.2.1 Required Sections

Validation Procedures

10.2.1.1 The document body contains two or more sections

10.2.1.2 One section contains the product data elements

10.2.1.3 There is a *Package Label.Principal Display Panel* (51945-4) Section with an image of the carton/container label.

11 Medical Device Labeling

11.1 Header

11.1.1 Document Type

11.1.1.1 Document types are *OTC Medical Device Label (69403-4)* or *Prescription Medical Device Label (69404-2)*.

11.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

11.1.2 Labeler information

```
<document>
  <code code="..." codeSystem="2.16.840.1.113883.6.1"
    displayName="..."/>
  <author>
  <assignedEntity>
    <representedOrganization>
      <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
      <name>Acme drug company</name>

      <contactParty>
        <addr>
          <streetAddressLine>1625 29th street</streetAddressLine>
          <city>Camden</city>
          <state>NJ</state> <postalCode>08101</postalCode>
          <country code="USA" codeSystem="1.0.3166.1.2.3">USA</country>
        </addr>

        <telecom value="tel:+1-800-555-1213;ext=112"/>
        <telecom value="mailto:Bob.Jones@acme.com"/>

        <contactPerson>
          <name>Bob Jones</name>
        </contactPerson>
      </contactParty>
```

Validation Procedures

11.1.2.1 There is one labeler

11.1.2.2 There is one DUNS number and name.

11.1.2.3 There are no other elements.

11.2 Body

11.2.1 Required Sections

Validation Procedures

11.2.1.1 The document body contains three or more sections

11.2.1.2 One section contains the product data elements

11.2.1.3 There is a *Package Label.Principal Display Panel* (51945-4) section with an image of the carton/container label.

12 Billing Unit Indexing

This document links the NDC for a marketed drug product with the National Council for Prescription Drug Programs (NCPDP) standard billing unit.

12.1 Header

12.1.1 Document Type

```
<document ...>
  <code code="71446-9" codeSystem="2.16.840.1.113883.6.1"
    displayName="Indexing - Billing Unit" />
```

Validation Procedures

12.1.1.1 The code for the document type is *Indexing - Billing Unit* (71446-9)

12.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type

12.1.2 Author

```
<author>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension="021660014"/>
      <name>National Council for Prescription Drug Programs</name>
```

Validation Procedures

12.1.2.1 The author is the “National Council for Prescription Drug Programs”

12.1.2.2 The DUNS Number for the author is 021660014

12.1.2.3 There are no other author elements than id and name.

12.2 Body

12.2.1 Indexing Section

```
<section>
  <id root="ffabedf9-6bde-4787-beb0-abd214307427"/>
  <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="SPL indexing data elements section" />
  <title/>
  <text/>
  <effectiveTime value="20121007"/>
  <subject>
```

Validation Procedures

12.2.1.1 If the document type is *Indexing – Billing Unit (71446-9)*, then the document contains one SPL Indexing Data Elements section as above.

12.2.1.2 Value of effective time is same as value of effective time in document information.

12.2.2 NDC

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <asContent>
          <containerPackagedProduct>
            <code code="NDC Package Code"
              codeSystem="2.16.840.1.113883.6.69"/>
          </containerPackagedProduct>
        </asContent>
      </manufacturedProduct>
    </manufacturedProduct>
  </subject>
</section>
```

Validation Procedures

12.2.2.1 There is an NDC package code inside an otherwise empty container element inside an otherwise empty manufactured product element.

12.2.2.2 NDC contains three segments divided by hyphens

12.2.2.3 Code system for NDC is 2.16.840.1.113883.6.69

12.2.2.4 The NDC matches an NDC contained in a listing / labeling document previously submitted.

12.2.2.5 The NDC is not associated with another set id with the document type Indexing - Billing Unit

12.2.3 Billing Unit

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <asContent>
          <containerPackagedProduct>
            <code code="NDC Package Code"
              codeSystem="2.16.840.1.113883.6.69"/>
          </containerPackagedProduct>
        </asContent>
      </manufacturedProduct>
    </manufacturedProduct>
  </subject>
  <subjectOf>
    <characteristic>
      <code code="NCPDPBILLINGUNIT"
        codeSystem="2.16.840.1.113883.1.11.19255"/>
      <value xsi:type="CV"
        code="Billing Unit Code"
        codeSystem="2.16.840.1.113883.2.13" xsi:type="CE"/>
    </characteristic>
  </subjectOf>
</section>
```

Validation Procedures

12.2.3.1 There is one billing unit code value

12.2.3.2 Billing unit value is “GM”, “ML” or “EA”

12.2.3.3 Code system for billing unit is 2.16.840.1.113883.2.13

12.2.3.4 There are no other package data elements

12.2.3.5 There are no other product data elements.

13 Generic User Fee Facility Self-Identification

Generic user fee facility self-identification has only header information with a single registrant organization and one or more self-identified facilities.

13.1 Header

13.1.1 Document type

```
<document>
  <code code="72090-4" codeSystem="2.16.840.1.113883.6.1"
    displayName="Identification of CBER-regulated generic drug facility"/>
```

Validation Procedures

13.1.1.1 Document type is “Identification of CBER-regulated generic drug facility” (72090-4) or “Generic Drug Facility Identification Submission” (71743-9).

13.1.1.2 The effective time year matches the current year.

13.1.1.3 There is no title

13.1.1.4 If a document with the same set id has been previously submitted, then it is of the same type.

13.1.1.5 Documents of type “Generic Drug Facility Identification Submission” (71743-9) are not submitted via the OC submission folder or the listed errors below need be corrected. (Contact CDERefacility@fda.hhs.gov for any questions.)

13.1.2 Registrant information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
      <assignedEntity>
```

```

<assignedOrganization> <!-- registrant -->
  <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
  <name>Green Clover Fine Drugs</name>
  <contactParty>
    <addr>
      <streetAddressLine>1625 29th street</streetAddressLine>
      <city>Dublin</city>
      <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
    </addr>
    <telecom value="tel:+353-12-551213"/>
    <telecom value="mailto:jmcfadden@greenclover.com"/>
    <telecom value="fax:+353-12-551214"/>
    <contactPerson>
      <name>Julie McFadden</name>
    </contactPerson>
  </contactParty>

```

Validation Procedures

13.1.2.1 There is registrant information.

13.1.2.2 There is one id, the DUNS number and name are as in Section 2.1.5.

13.1.2.3 id (document id) is not associated with any other set id of the same document type.

13.1.2.4 set id is not associated with any other registrant id of the same document type.

13.1.2.5 There is one contact party as in 2.1.8.

13.1.2.6 GDUFA facility identification submission has no labeler information.

13.1.3 Facility Information

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
              <assignedOrganization> <!-- facility -->
                <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
                <id extension="123456" root="2.16.840.1.113883.4.82"/>
                <name>Middleton Manufacturing company</name>
                <addr>
                  <streetAddressLine>123 Burl Road</streetAddressLine>
                  <city>Dublin</city>
                  <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
                </addr>
              </assignedOrganization>
            </assignedEntity>
          </assignedOrganization>
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>

```

```

<contactParty>
  <addr>
    <streetAddressLine>1625 29th street</streetAddressLine>
    <city>Dublin</city>
    <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
  </addr>
  <telecom value="tel:+353-12-551213"/>
  <telecom value="mailto:pmcdonald@middletown.com"/>
  <telecom value="fax:+353-12-551214"/>
  <contactPerson>
    <name>Patrick McDonald</name>
  </contactPerson>
</contactParty>

```

Validation Procedures

13.1.3.1 There are one or more facilities:

13.1.3.2 Facilities have two id elements, one id, the DUNS number, and name are as in Section 2.1.5.

13.1.3.3 DUNS number is not associated with another facility in the same SPL file.

13.1.3.4 DUNS number is not associated with any other set id of the same document type.

13.1.3.5 The DUNS number along with the facility name and address information match the DUNS number record in the Dun and Bradstreet database

13.1.3.6 There is a second id, the FEI with root 2.16.840.1.113883.4.82 and 7 or 10 digit extension.

13.1.3.7 Each facility has an address as in Section 2.1.6.

13.1.3.8 There is one contact party as in Section 2.1.8.

13.1.3.9 There is no further assigned entity.

13.1.4 Facility operation

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization>
      <!-- facility -->
    </assignedOrganization>
  </assignedEntity>
</document>

```

```
<performance>
  <actDefinition>
    <code code="C43360" codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="manufacture"/>
```

Validation Procedures

13.1.4.1 There are one or more facility operation details (performance act definitions).

13.1.4.2 Each performance act definition has one code.

13.1.4.3 Code system is 2.16.840.1.113883.3.26.1.1

13.1.4.4 Display name matches the code

13.1.4.5 The code comes from the business operations list.

13.1.4.6 The business operation code is one of the following: API Manufacture (C82401), FDF Manufacture (C101510), Positron Emission Tomography Drug Production (C91403), Clinical Bioequivalence or Bioavailability Study (C101511), In Vitro Bioequivalence or Bioanalytical Testing (C101512), API/FDF Analytical Testing (C101509), Pack (C84731), and Repack (C73606).

13.1.4.7 Each business operation code and qualifier is mentioned only once per facility.

13.1.5 Business Operation Qualifier

The information for all facilities submitted in a Generic Drug Facility Identification Submission and Identification of CBER-regulated Generic Drug Facility indicates that the sites are implicitly engaged in the production of generic drugs. A “non-generic qualifier” can be used to mark these facilities as *also* engaged in the production of non-generic (brand, innovator) drugs:

```
<performance>
  <actDefinition>
    ...
    <subjectOf>
      <approval>
        <code code="C101886" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="manufactures non-generics"/>
      </approval>
    </subjectOf>
```

Validation Procedures

13.1.5.1 There is zero or up to two business operation qualifiers.

13.1.5.2 The qualifier has one code.

13.1.5.3 Code system is 2.16.840.1.113883.3.26.1.1

13.1.5.4 Display name matches the code

13.1.5.5 The code is *Manufactures Non-Generics* (C101886) and/or Contract Manufacturing (C132491)

13.1.5.6 If the business operation qualifier is Contract Manufacturing (C132491), then business operation is FDF Manufacture (C101510) or Pack (C84731).

13.2 Body - Empty

Use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>
  <component>
    <nonXMLBody>
      <text/>
```

13.2.1.1 The document body is empty

14 [RESERVED]

15 Indexing - Product Concept

15.1 Header

15.1.1 Document type

```
<document>
  <code code="73815-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="Indexing - Product Concept"/>
```

Validation Procedures

15.1.1.1 Document code is as above

15.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

15.1.2 Author information

Product concept indexing is maintained by FDA:

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

15.1.2.1 Author information for Product Concept indexing is as one of the above

15.1.3 Reference Labeling

The information about a product concept is derived from Reference Labeling. The Reference Labeling is found in the SPL document submitted by the innovator, or, if the innovator has stopped marketing the product, by a designated generic manufacturer. The SPL document containing the Reference Labeling is specified using its setId as follows:

```
<document>
  ...
  <author .../>

  <relatedDocument typeCode="DRIV">
    <relatedDocument>
      <setId root="20d9b74e-e3d8-4511-9df9-cec2087372fc"/>
    </relatedDocument>
  </relatedDocument>

  <component .../>
</document>
```

Validation Procedures

15.1.3.1 There is reference labeling specified.

15.1.3.2 Type code attribute is as above.

15.1.3.3 There is no document id

15.1.3.4 There is a set id

15.1.3.5 Set id is a GUID

15.1.3.6 Reference labeling set id is the set id of a drug listing document.

15.1.3.7 If a product concept indexing file for the same reference labeling set id has been previously submitted, then it is a prior version of this indexing document with the same set id.

15.1.3.8 If a document with the same set id has been previously submitted, then it is associated with the same reference labeling set id.

15.2 Body

```
<section>
  <id root="ffabedf9-6bde-4787-beb0-abd214307427"/>
  <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="SPL Indexing Data Elements Section"/>
  <title/>
  <text/>
  <effectiveTime value="20101007"/>
  <subject>
```

15.2.1 Product Concept Indexing Section

15.2.1.1 If the document type is 73815-3, "Indexing - Product Concept", then the document contains one SPL Indexing Data Elements section as above.

15.2.1.2 There is one or more product

15.2.2 Abstract Product/Part Concept

The Abstract Product Concept is based on the level 4 Pharmaceutical Product Identifier defined as a dose form with its active ingredients and strengths.

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="ba328d9b-c64c-fca9-2ee7-9882d2ac3f32"
          codeSystem="2.16.840.1.113883.3.3389" />
```

```
<formCode code="C42916" codeSystem="2.16.840.1.113883.3.26.1.1"
  displayName="CAPSULE, EXTENDED RELEASE" />
```

Validation Procedures

- 15.2.2.1 There is a product concept code with code system 2.16.840.1.113883.3.3389.
- 15.2.2.2 Code has the format of 8-4-4-4-12 hexadecimal digits where letter digits are lower case.
- 15.2.2.3 Code value matches the specified properties according to the Abstract Product Concept Code Specification (See 15.2.4).
- 15.2.2.4 There is a form code and it comes from the Product Concept Dosage Form List

15.2.3 Ingredient

```
<ingredient classCode="ACTIM, ACTIB, or ACTIR">
  <quantity>
    <numerator value="10" unit="mg"/>
    <denominator value="1" unit="1"/>
  </quantity>
  <ingredientSubstance>
    <code code="1234567890" codeSystem="2.16.840.1.113883.4.9"/>
    <name>tazminate malate</name>
    <activeMoiety>
      <activeMoiety>
        <code code="76I7G6D29C" codeSystem="2.16.840.1.113883.4.9" />
        <name>MORPHINE</name>
      </activeMoiety>
    </activeMoiety>
  </ingredientSubstance>
</ingredient>
```

Validation Procedures

- 15.2.3.1 If the ingredient's basis of strength is the active moiety (class code is "ACTIM"), then one (and only one) active moiety, the actual basis of strength, is stated.
- 15.2.3.2 Active moiety has an active moiety UNII code.
- 15.2.3.3 If the ingredient's basis of strength is a reference substance (class code is "ACTIR"), then that reference substance is specified.
- 15.2.3.4 If the ingredient has a basis of strength other than the reference substance, then there is no reference substance.
- 15.2.3.5 Abstract product concept code should not match with any other abstract or equivalent product concept code.

15.2.3.6 Reference substance has an ingredient UNII code.

15.2.4 Abstract Product Concept Code Specification

The product concept code is created by computing the MD5 digest over a data structure describing the concept code unambiguously and uniquely, i.e., the same product concept is described by this and only this descriptor, and hence, by this and only this hash code. MD5 hash codes are 128 bit (16 byte) number which, in hexadecimal presentation, is 32 digits long. The hexadecimal digits are formatted in groups of 8-4-4-12 digits separated by hyphens.

The data structure which is the input of the MD5 digest is a pipe-delimited sequence of form code (dose form) by NCI thesaurus code only, followed by the active ingredients separated by the “pipe delimiter” (“|”) in alphabetic order of their UNII code. Each active ingredient is represented by the active ingredient code and the strength.

The dosage form code may be more generalized than the dosage form used in the SPL Listing documents. For example, “powder for solution” the code is generalized to “for solution”. Some of these more abstract dosage form codes may not be included in the dosage form table that can be chosen for drug listing submissions. For instance, POWDER, FOR SUSPENSION (C42975) is generalized to FOR SUSPENSION (C42972). The mapping between the dosage forms can be found in the Product Concept Dosage Form list on the FDA web page.

When the basis of strength is the active moiety (ingredient/@classCodde = ‘ACTIM’) and the active moiety UNII is different from the active ingredient UNII, then the active moiety UNII is appended to the active ingredient UNII with a separating tilde (“~”) character. Likewise, if the basis of strength is a reference substance, (ingredient/@classCodde = ‘ACTIR’), then the active moiety UNII is appended to the active ingredient UNII with a separating tilde (“~”) character.

The strength expression must be normalized to account for the fact that 10 mg in 5 mL are the same as 2 mg in 1 mL, and 1 g is the same as 1000 mg and appended with a pipe delimiter.

Example 1: Cefutoxime Axetil (Z49QDT0J8Z) powder for suspension (C42975) 125 mg of Cefutoxime (moiety, O1R9FJ93ED) in 5 mL is put together as “C42972|Z49QDT0J8Z~O1R9FJ93ED|2.500e1 mg/mL”, for which the MD5 digest is “7fead104-1147-b435-1545-606b40a2cd6b”.

Example 2: Trimetoprim (AN164J8Y0X) 160 mg and Sulfametoxazole (JE42381TNV) 800 mg tablet (C42998). is put together as: “C42998|AN164J8Y0X|160e-3 g|JE42381TNV|8.000e2 mg”, for which the MD5 digest is “8663a93b-5627-7466-306d-fd794b7d268a”.

The normalized strength is computed by (1) normalizing the units by scaling the numbers, (2) dividing the normalized strength numerator by the normalized denominator, and (3) writing out the normalized strength number and the combined unit.

The normalized unit for both numerator and denominator, and their factor is determined by the following 3 step algorithm: (1) if the unit is “1” the factor is 1 and the normalized unit symbol is the empty string; or (2) find the unit in the Table 17: Normalized Units; or (3) if the unit is entirely embraced in square brackets “[...]”, the factor is 1 and the normalized unit is unchanged.

Table 17: Normalized Units

| Unit | Kind of Quantity | Factor | Normalized Unit |
|-----------------|---------------------|--------------------|-----------------|
| mmol | amount of substance | 1 | mmol |
| nmol | amount of substance | 10 ⁻³ | mmol |
| meq | amount of valence | 1 | meq |
| cm ² | Area | 1 | cm ² |
| d | elapsed time | 86400 | s |
| h | elapsed time | 3600 | s |
| min | elapsed time | 60 | s |
| U | katalytic activity | 1 | U |
| g | Mass | 10 ³ | mg |
| kg | Mass | 10 ⁶ | mg |
| mg | Mass | 1 | mg |
| ng | Mass | 10 ⁻⁶ | mg |
| ug | Mass | 10 ⁻³ | mg |
| Ci | Radioactivity | 37 10 ³ | MBq |
| mCi | Radioactivity | 37 | MBq |
| L | Volume | 10 ³ | mL |
| mL | Volume | 1 | mL |
| uL | Volume | 10 ⁻³ | mL |

All units which are entirely enclosed in in brackets are represented as is with the trivial conversion factor 1.

With this the normalized strength value is computed as:

$$\begin{aligned}
 &(\text{normalized strength number}) = \\
 &\quad (\text{strength numerator number}) \times (\text{conversion factor of numerator unit}) \\
 &\quad \div [(\text{strength denominator number}) \times (\text{conversion factor of denominator unit})]
 \end{aligned}$$

In this example 125 mg in 5 mL, this is trivial because the conversion factors are 1.

$$\begin{aligned}
 &(\text{strength numerator number}) = 125 \\
 &(\text{conversion factor of numerator unit mg}) = 1 \\
 &(\text{strength denominator number}) = 5 \\
 &(\text{conversion factor of denominator unit mL}) = 1
 \end{aligned}$$

$$\begin{aligned} & \text{(normalized strength number)} = \\ & \frac{125}{5} \times \frac{1}{1} = 25. \end{aligned}$$

If the strength had been written as 125 g in 5 L, the calculation would be:

$$\begin{aligned} & \text{(strength numerator number)} = 125 \\ & \text{(conversion factor of numerator unit g)} = 1000 \\ & \text{(strength denominator number)} = 5 \\ & \text{(conversion factor of denominator unit L)} = 1000 \end{aligned}$$

$$\begin{aligned} & \text{(normalized strength number)} = \\ & \frac{125}{5} \times \frac{1000}{1000} = 25 \end{aligned}$$

Finally, the combined normalized strength number is written in the scientific notation in the format “-9.000e-9”, where “-9.000” means 4 digits, always starting with a non-zero digit before the decimal point, with an optional negative sign, and the decimal point always in the same position, “e” (lower case) is the exponent marker, verbatim as a lower case “e”, and “-9” is the exponent to base 10, with the optional negative sign followed by however many digits are required, but no zero padding. Examples 25 is formatted as “2.500e1”, 0.3766667 as “3.767e-1”, and 250×10^{10} as “2.500e12.

The normalized formatted strength number is followed by a space and then the normalized numerator unit, followed by a solidus (or “forward slash”, “/”) and the normalized denominator unit. For example, “mg” in “mL” becomes “mg/mL”). If the normalized denominator unit symbol is the empty string (i.e., the denominator unit was “1”), no solidus is appended (e.g., “mg” and the empty string becomes “mg”, not “mg/” nor “mg/1”). No attempt at canceling numerator and denominator units is made (e.g., “mg/mg” stays unchanged and is not reduced to 1.)

15.2.5 Abstract Kit Concept Code Specification

The product kit concept code is created by computing the MD5 digest over a data structure describing the concept code unambiguously and uniquely. The format of the kit concept code is the same as that of the product concept code explained in Section 15.2.4

If the form code is "kit" (C47916), the input of the MD5 digest is a pipe-delimited sequence of form code (C47916) followed by the product concept code and quantity of each part in alphabetic order of their product concept codes.

The quantity of the part must be normalized to account for the fact that 1 g is the same as 1000 mg, etc. as explained in the previous section for the normalization of strength and strength unit. The denominator value for part quantity will be always 1 and the normalization rules simplify to:

The normalized part quantity is computed by (1) normalizing the numerator unit by scaling the number and (2) writing out the normalized part quantity numerator number and unit.

The normalized part quantity numerator unit and its factor is determined by the following 3 step algorithm: (1) if the unit is “1” the factor is 1 and the normalized unit symbol is the empty string; or (2) find the unit in the Table 17: Normalized Units; or (3) if the unit is entirely embraced in square brackets “[...]”, the factor is 1 and the normalized unit is unchanged.

Example: a kit with 16.8 mL of part A (abstract concept code a46c150b-8203-ac62-31ef-adb5c0aca5a2) and 0.9 g of part B (abstract concept code bdce178d-00b2-6beb-4d96-259f444aee1d).

With this the normalized part quantity value is computed for each part as:

$$(\text{normalized part quantity numerator number}) = \frac{(\text{part quantity numerator number})}{(\text{conversion factor of numerator unit})}$$

In this example, part 1: 16.8 mL:

$$\begin{aligned} (\text{part quantity numerator number}) &= 16.8 \\ (\text{conversion factor of numerator unit mg}) &= 1 \end{aligned}$$

$$\begin{aligned} (\text{normalized part quantity number}) &= \frac{16.8}{1} = 16.8 \\ (\text{normalized part quantity unit}) &= \text{mL} \end{aligned}$$

Part 2: 0.9 g

$$\begin{aligned} (\text{part quantity numerator number}) &= 0.9 \\ (\text{conversion factor of numerator unit mg}) &= 1000 \end{aligned}$$

$$\begin{aligned} (\text{normalized part quantity number}) &= \frac{0.9}{1000} = 0.0009 \\ (\text{normalized part quantity unit}) &= \text{mg} \end{aligned}$$

Finally, the normalized part quantity number is written in the scientific notation in the format “-9.000e-9”, where “-9.000” means 4 digits, always starting with a non-zero digit before the decimal point, with an optional negative sign and the decimal point always in the same position, “e” (lower case) is the exponent marker, verbatim as a lower case “e”, and “-9” is the exponent to base 10, with the optional negative sign followed by however many digits are required, but no zero padding. Examples 16.8 is formatted as “1.680e1”, 900 as “9.000e2”, and 0.25 as “2.500e-1”.

The normalized formatted part quantity number is followed by a space and then the normalized numerator unit.

In this example; “C47916|a46c150b-8203-ac62-31ef-adb5c0aca5a2|1.680e1 mL|bdce178d-00b2-6beb-4d96-259f444aee1d|9.000e2 mg”, for which the MD5 digest is “a76b62f9-257b-7918-620e-4db706c928f8”.

15.2.6 Application Product/Kit Concept

The Application Product Concept includes the marketing application identifier in addition to the dose form with its active ingredients and strengths.

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="d5ecf7af-bb51-2003-61fe-b81973321293"
        codeSystem="2.16.840.1.113883.3.3389"/>
      <asEquivalentEntity classCode="EQUIV">
        <code code="A" codeSystem="2.16.840.1.113883.3.2964"/>
        <definingMaterialKind>
          <code code="41b5afb1-84d4-83c3-f095-5557b06994a0"
            codeSystem="2.16.840.1.113883.3.3389"/>
        </definingMaterialKind>
      </asEquivalentEntity>
    </manufacturedProduct>
  </manufacturedProduct>
</subject>
```

Validation Procedures

- 15.2.6.1 There is an product/kit concept code with code system 2.16.840.1.113883.3.3389
- 15.2.6.2 Code has the format of 8-4-4-4-12 hexadecimal digits where letter digits are lower case.
- 15.2.6.3 Code value matches the specified properties according to the Application Product Concept Code Specification (See 15.2.8).
- 15.2.6.4 There is no form code.
- 15.2.6.5 There is an equivalent product reference.
- 15.2.6.6 There is an equivalence code with code system 2.16.840.1.113883.3.2964.
- 15.2.6.7 Equivalence code is “A”, “B”, “OTC”, or “N”.
- 15.2.6.8 Equivalent product/kit concept code should not match with any other abstract or equivalent product/kit concept code.
- 15.2.6.9 There is a product/kit concept reference with code and code system same as another product/kit concept code of an Abstract or Application Product Concept in the same document.

15.2.7 Marketing Category and Application Number

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <asEquivalentEntity> ... </asEquivalentEntity>
    </manufacturedProduct>
    <subjectOf>
      <approval>
        <id extension="NDA021223" root="2.16.840.1.113883.3.150" />
        <code code="C73594" codeSystem="2.16.840.1.113883.3.26.1.1"
displayName="NDA" />
        <author>
          <territorialAuthority>
            <territory>
              <code code="USA" codeSystem="1.0.3166.1.2.3" />
            </territory>
          </territorialAuthority>
        </author>
      </approval>
    </subjectOf>
  </manufacturedProduct>
</subject>

```

Validation Procedures

15.2.7.1 There is one marketing category for every Product Equivalence

15.2.7.2 The marketing authorization should only be ANDA, BLA or NDA

15.2.8 Application Product/Kit Concept Code Specification

The Application Product Concept code is created by computing the MD5 digest over a data structure describing the Application Product concept code unambiguously and uniquely, i.e., the same equivalent product concept is described by this and only this descriptor, and hence, by this and only this hash code. MD5 hash codes are 128 bit (16 byte) number which, in hexadecimal presentation, is 32 digits long. The hexadecimal digits are formatted in in groups of 8-4-4-12 digits separated by hyphens.

The data structure which is the input of the MD5 digest is a pipe-delimited sequence of abstract product concept code and the application number separated by the “pipe delimiter” (“|”).

Example 1: Cefutoxime Axetil (Z49QDT0J8Z) powder for suspension (C42975) 125 mg of Cefutoxime (moiety, O1R9FJ93ED) in 5 mL is put together as “C42972|Z49QDT0J8Z~O1R9FJ93ED|2.500e1 mg/mL”, for which the MD5 digest is “7fead104-1147-b435-1545-606b40a2cd6b”. That is the abstract product concept.

Example 1a: a powder for suspension for 125 mg in 5 mL has the application number NDA050672, so its Application Product Concept is the MD5 hash of “7fead104-

1147-b435-1545-606b40a2cd6b|NDA050672” which is “3b35d65f-9dc2-104c-e6be-8df3d2dfb11d”.

Example 1b: Cefutoxime Axetil by Choice Pharma LLC for suspension for 125 mg in 5 mL may have the application number ANDA987654, so its Application Product Concept is the MD5 hash of “7fead104-1147-b435-1545-606b40a2cd6b|ANDA987654” which is “08007c2a-e9e4-0427-ea61-4d8197b2ef24”.

Example 2: For abstract product kit concept, MD5 digest is the sequence of form code (kit, C47916) followed by the abstract product concept code and normalized part quantity in alphabetic order of the abstract product concept code put together as "C47916|a46c150b-8203-ac62-31ef-adb5c0aca5a2|1.680e1 mL|bdce178d-00b2-6beb-4d96-259f444aee1d|9.000e2 mg", for which the MD5 digest is “a76b62f9-257b-7918-620e-4db706c928f8”. This is the abstract product kit concept code.

Example 2a: For application number BLA456789, Application Product Kit Concept is the MD5 hash of “a76b62f9-257b-7918-620e-4db706c928f8|BLA456789” which is “a071563f-e74e-a06c-33c2-2c4aee1b950”.

Note: the concept hash code for an Application Product Concept is always formed from the Abstract Product Concept and the application number despite the fact that the ANDA equivalent product references the referenced product as its equivalent. The Application Product Concept however is Independent of the choice of equivalence product only dependent on the Abstract Product Concept and the application number.

16 Lot Distribution Report

16.1 SPL Header

16.1.1 Document type

```
<document>
  <id root="50606941-3e5d-465c-b4e0-0f5a19eb41d4"/>
  <code code="66105-8" codeSystem="2.16.840.1.113883.6.1"
    displayName="Lot Distribution Data"/>
  <effectiveTime value="2010701"/>
  <setId root="a30accef-f437-4136-808c-9ed4ada5fcf8"/>
  <versionNumber value="1"/>
```

Validation Procedures

16.1.1.1 Document code is as above

16.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

16.1.2 Author information

```
<author>
  <representedOrganization>
    <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
    <id extension="Manufacturer License Number"
      root="1.3.6.1.4.1.32366.1.3.1.2"/>
    <name>Zwerg Pharma, Inc.</name>
  </representedOrganization>
  <contactParty>
    <telecom value="mailto:Bob.Jones@acme.com"/>
    <contactPerson>
      <name>Bob Jones</name>
    </contactPerson>
  </contactParty>
```

16.1.2.1 There is one author (labeler)

16.1.2.2 There are two ids

16.1.2.3 One id is the DUNS number with the root 1.3.6.1.4.1.519.1 with a 9-digit extension

16.1.2.4 One id is the manufacturer license number with the root 1.3.6.1.4.1.32366.1.3.1.2 with a 4-digit extension

16.1.2.5 There may be one contact party (see the Procedures for contact party above)

16.1.2.6 Contact party has an email address specified.

16.1.3 Bulk-Lot Manufacturers

The manufacturing establishments which will be referred to in the bulk lot suppliers are listed here.

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization> <!-- Labeler -->
        <assignedEntity>
          <assignedOrganization> <!-- Registrant -->
</assignedEntity><!-- Bulk-Lot Manufacturer 1 -->
  <confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
  <assignedOrganization> <!-- Establishment -->
    <id extension="1000000019" root="1.3.6.1.4.1.519.1"/>
    <name>Middleton Manufacturing company</name>
  </assignedOrganization>
</assignedEntity>
<assignedEntity><!-- Bulk-Lot Manufacturer 2 -->
  ...

```

Validation Procedures

- 16.1.3.1 There are one or more bulk lot manufacturers.
- 16.1.3.2 There is no registrant information.
- 16.1.3.3 Bulk-lot manufacturer has one id (the DUNS number) and a name as in Section 2.1.5.
- 16.1.3.4 Each bulk-lot manufacturer appears only once.
- 16.1.3.5 Bulk-lot manufacturer (“assignedOrganization”) has no other element besides id (the DUNS Number) and name.
- 16.1.3.6 The bulk-lot manufacturer id (DUNS Number) has been submitted in a document of type “*Establishment Registration*” (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a document of type “*No Change Notification*” (53410-7) between October 1st and December 31st of the previous or the current year.

16.2 Body

```

<component>
  <section>
    <id root="e13a985b-f706-a5c8-e8ef-73891eb1c697"/>
    <code code="48780-1"
          codeSystem="2.16.840.1.113883.6.1"
          displayName="SPL product data elements section"/>
    <effectiveTime>
      <low value="20100101"/>
      <high value="20100701" closed="false"/>
    </effectiveTime>
  </section>
</component>

```

Validation Procedures

16.2.1.1 There is a document body

16.2.2 Data Elements Section

16.2.2.1 There is an SPL Data Elements section

16.2.2.2 Effective time has low and high boundaries indicating the reporting period of the lot distribution data (reporting start date, reporting end date).

16.2.2.3 Reporting start date has at least the precision of day in the format YYYYMMDD

16.2.2.4 Reporting end date has at least the precision of day in the format YYYYMMDD

16.2.2.5 Reporting start date is before reporting end date.

16.2.2.6 Reporting end date is the same as value of effective time in document information.

16.2.2.7 Period of time represented by the reporting start and end date should not exceed 365 days.

16.2.2.8 Period of time represented by the reporting start and end date should not be less than 14 days.

16.2.3 Product Data – Single Licensed Product

```

<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="1234-5678" codeSystem="2.16.840.1.113883.6.69"/>
        <name>Multivax</name>
        <formCode code="C42973" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="POWDER, FOR SOLUTION"/>
        <ingredient classCode="ACTIB">
          <ingredientSubstance >
            <code code="KZ3L01D2PC" codeSystem="2.16.840.1.113883.4.9"/>
            <name>HUMAN VIRUS ANTIGEN</name>
          </ingredientSubstance>
        </ingredient>

        <instanceOfKind>
          <!-- DISTRIBUTION DATA, SEE BELOW -->
        </instanceOfKind>
      </manufacturedProduct>
    <subjectOf>
      <approval>
        <id extension="BLA123456" root="2.16.840.1.113883.3.150"/>
        <code code="C73585" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="BLA"/>
      </approval>
    </subjectOf>
    <consumedIn><!-- DOSING SPECIFICATION --></consumedIn>
  </manufacturedProduct>
</subject>
</section>

```

16.2.3.1 There is one or more subject manufactured products:

16.2.3.2 There is an NDC product code

16.2.3.3 The general rules about the product item code apply as per 3.1.1.1ff.

16.2.3.4 There is a trade name

16.2.3.5 Name contains no special symbols (e.g., no “®” or “™” etc) and no “USP” or dosage forms.

16.2.3.6 Name matches the NDC code submitted in drug listings.

16.2.3.7 NDC product item code has been previously submitted in an SPL listing file.

16.2.3.8 There are no other product data elements, such as generic name, product source, inactive ingredients, etc.

16.2.3.9 The same product is not described in a lot distribution report with a different set id.

16.2.3.10 There is no lot distribution report with the same set id but a different product.

16.2.4 Dosing Specification

The dosing specification is used to compute the *number of doses* in any lot, or container, such as to comply with the *number of doses in fill lot/label lot* requirement specified by the regulation.

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct><!-- NDC AND NAME --></manufacturedProduct>
    <consumedIn>
      <substanceAdministration1 classCode="SBADM" moodCode="DEF">
        <routeCode code="C38288" displayName="oral"
          codeSystem="2.16.840.1.113883.3.26.1.1"/>
        <doseQuantity value="1" unit="mL"/>
      </substanceAdministration1>
    </consumedIn>
  </subject>
</section>
```

Validation Procedures

16.2.4.1 There is a dosing specification element.

16.2.4.2 There is a route code, and the rules for route of administration code apply (3.2.20.2f).

16.2.4.3 There is a dose quantity specification with a single value and unit, except for variable dose, which do not have the dose quantity element.

16.2.4.4 Value is a number

16.2.4.5 Unit comes from the *UCUM units of measures* list

16.2.4.6 Value may be the number “0”.

16.2.4.7 Value should not include spaces.

16.2.5 Fill Lot

The fill lot is the lot of product which conforms to the specification of the product regardless of packaging, i.e., it has the form and the strength specified by the listing data for the package-Independent NDC of the product. As such the fill lot is an instance of the product regardless of packaging.

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
      <id root="{Fill Lot ID root OID}" extension="{Fill Lot ID}"/>
    </productInstance>
  </instanceOfKind>
</manufacturedProduct>
```

Validation Procedures

16.2.5.1 There is a fill lot element

16.2.5.2 The lot has an id with the following general rules for lot numbers:

16.2.5.3 There is an id extension with the reported alphanumeric lot number string

16.2.5.4 Lot number string can contain digits, upper case letters and the characters “-” and “/”.

16.2.5.5 There is a globally unique root OID

16.2.5.6 If the product item code is an NDC, then the globally unique root OID is formed by using the fixed prefix "1.3.6.1.4.1.32366.1.2.10." followed by the NDC product item code represented as a number without dashes and with initial zeroes from the labeler code segment removed (e.g., "0001-0123" becomes 10123).

16.2.5.7 If the product item code is an ISBT 128 code, then the globally unique root OID is formed by using the fixed prefix “1.3.6.1.4.1.32366.1.2.13.” followed by a decimal number value for the ISBT 128 facility identification number followed by a period “.” and a decimal number value for the ISBT 128 product code, both interpreted as a base 36 number with the digits 0-9 and A-Z, with the letter digits having the value of 9 added to the ordinal letter position (A: $1 + 9 = 10$, B = $2 + 9 = 11$, ..., Z = $26 + 9 = 35$); e.g., ISBT 128 product item code “W0123-E0404” with facility identification number “W0123” interpreted in base 36: $W = 23 + 9 = 32 \times 36 + 0) \times 36) + 1) \times 36 + 2) \times 36 + 3 = 53749083$, and ISBT 128 product code “E0404” interpreted in base 36: $E = 5 + 9 = 14 \times 36 + 0) \times 36 + 4) \times 36 + 0) \times 36 + 4 = 23519812$, resulting in “1.3.6.1.4.1.32366.1.2.13.53749083.23519812”.

16.2.6 Bulk Lot(s)

Bulk lot is the instance of raw material that goes into one or more fill lots at possibly different strengths. As such the bulk lot represents one or more ingredient instances.

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
```

```

<ingredient><!-- BULK LOT(S) -->
  <ingredientProductInstance>
    <id root="{Bulk Lot ID root OID}" extension="{Bulk Lot ID}"/>
    <asInstanceOfKind>
      <kindOfMaterialKind>
        <code code="XYZ123ABC" codeSystem="2.16.840.1.113883.4.9"/>
        <name>Mucinella Bobadis Antigen</name>
      </kindOfMaterialKind>
    </asInstanceOfKind>
  </ingredientProductInstance>

  <subjectOf>
    <productEvent>
      <code code="C43360" displayName="manufacture"
        codeSystem="2.16.840.1.113883.3.26.1.1"/>
      <performer>
        <assignedEntity>
          <representedOrganization>
            <id root="1.3.6.1.4.1.519.1" extension="DUNS number"/>
          </representedOrganization>
        </assignedEntity>
      </performer>
    </productEvent>
  </subjectOf>

```

Validation Procedures

- 16.2.6.1 There is one or more bulk lot elements
- 16.2.6.2 The lot has an id, and the general rules for lot numbers apply.
- 16.2.6.3 If the product item code is an NDC, then the globally unique root OID is formed by using the fixed prefix "1.3.6.1.4.1.32366.1.2.10." followed by the NDC Labeler Code represented as a number without initial zeroes (e.g., "0001" becomes 1).
- 16.2.6.4 If the product item code is an ISBT 128 code, then the globally unique root OID is formed by using the fixed prefix "1.3.6.1.4.1.32366.1.2.13." followed by a decimal number value for the ISBT 128 facility identification number interpreted as a base 36 number with the digits 0-9 and A-Z, with the letter digits having the value of 9 added to the ordinal letter position (A: 1 + 9 = 10, B = 2 + 9 = 11, ..., Z = 26 + 9 = 35); e.g., ISBT 128 facility identification number "W0123" interpreted in base 36: $W = 23 + 9 = 32 \times 36 + 0$, $0 = 0 \times 36 + 1$, $1 = 1 \times 36 + 2$, $3 = 3 \times 36 + 3 = 53749083$, resulting in "1.3.6.1.4.1.32366.1.2.13.53749083".
- 16.2.6.5 The bulk lot references an active ingredient
- 16.2.6.6 Code system is 2.16.840.1.113883.4.9
- 16.2.6.7 There is one ingredient name
- 16.2.6.8 Ingredient name matches the code
- 16.2.6.9 The ingredient is actually listed as an ingredient of the product
- 16.2.6.10 The bulk lot references one manufacturer (C43360).

16.2.6.11 There is one id

16.2.6.12 id is the DUNS number of the bulk lot manufacturing establishment with the root 1.3.6.1.4.1.519.1 and a 9-digit extension

16.2.6.13 Bulk-lot manufacturer (“representedOrganization”) has no other element besides id.

16.2.6.14 The bulk-lot manufacturer id is one of those listed in the bulk-lot manufacturers in the header.

16.2.6.15 The establishment id matches an establishment with same id submitted in documents of type “establishment registration” in the same or previous calendar year with business operation manufacture (C43360) or API manufacture (C82401).

16.2.6.16 The bulk lot references no other product activity

16.2.7 Label Lot(s) (Final Container Lot)

The label lot, or final container lot is the instance of the product, a portion of the fill lot that is portioned out into individual containers.

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
      <ingredient><!-- BULK LOT(S) --></ingredient>
      <member><!-- LABEL LOT -->
        <memberProductInstance>
          <id root="{Label Lot ID root OID}" extension="{Label Lot ID}"/>
          <expirationTime>
            <high value="20110417"/>
          </expirationTime>
        </memberProductInstance>
      </member>
    </productInstance>
  </instanceOfKind>
</manufacturedProduct>
```

Validation Procedures

16.2.7.1 There is one or more label lot elements

16.2.7.2 The lot has an id, and the general rules for lot numbers apply.

16.2.7.3 If the product item code is an NDC, then the globally unique root OID is formed by using the fixed prefix "1.3.6.1.4.1.32366.1.2.10." followed by the full 10-digit NDC code represented as a number without dashes and with initial zeroes from the labeler code segment removed (e.g., "0001-0123-04" becomes 1012304).

16.2.7.4 If the product item code is an ISBT 128 code, then the globally unique root OID is formed by using the fixed prefix “1.3.6.1.4.1.32366.1.2.13.” followed by a decimal number value for the ISBT 128 facility identification number followed

by a period “.” and a decimal number value for the ISBT 128 product code, both interpreted as a base 36 number with the digits 0-9 and A-Z, with the letter digits having the value of 9 added to the ordinal letter position (A: 1 + 9 = 10, B = 2 + 9 = 11, ..., Z = 26 + 9 = 35), and ending with a period “.” and the 3rd segment of the ISBT 128 package item code without leading zeroes; e.g., ISBT 128 product item code “W0123-E0404-03” with facility identification number “W0123” interpreted in base 36: W = 23 + 9 = 32 × 36 + 0) × 36) + 1) × 36 + 2) × 36 + 3 = 53749083, and ISBT 128 product code “E0404” interpreted in base 36: E = 5 + 9 = 14 × 36 + 0) × 36 + 4) × 36 + 0) × 36 + 4 = 23519812, and 3rd segment “03” without zeroes, resulting in “1.3.6.1.4.1.32366.1.2.13.53749083.23519812.3”.

16.2.7.5 There is an expiration time with a high boundary.

16.2.7.6 Expiration time has at least the precision of month in the format YYYYMM

16.2.8 Container Data Elements

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
      <ingredient><!-- BULK LOT(S) --></ingredient>
      <member><!-- LABEL LOT -->
        <memberProductInstance>
          <asContent>
            <quantity>
              <numerator value="2" unit="mL"/>
              <denominator value="1" unit="1"/>
            </quantity>
            <container>
              <code code="1234-5678-01" codeSystem="2.16.840.1.113883.6.69"/>
              <formCode code="C43169" displayName="bottle"
                codeSystem="2.16.840.1.113883.3.26.1.1"/>
            </container>
          </asContent>
        </memberProductInstance>
      </member>
    </productInstance>
  </instanceOfKind>
</manufacturedProduct>
```

Validation Procedures

16.2.8.1 There is a container reference

16.2.8.2 There is a quantity with a numerator and denominator

16.2.8.3 Numerator has a value greater than zero and a unit

16.2.8.4 Numerator unit matches the dosing specification unit.

16.2.8.5 Denominator has value 1 and either no unit or unit “1”

16.2.8.6 The container form code and quantity is the same as the package of the product as described in the listing for the package NDC.

16.2.8.7 There is a container packaged product code

16.2.8.8 Container packaged product item code is an NDC or based on ISBT-128

16.2.8.9 There is a form code and display name

16.2.8.10 Code system for form code is 2.16.840.1.113883.3.26.1.1

16.2.8.11 Display name matches form code

16.2.8.12 The container form code matches the form code specified for the container in the listing data.

16.2.9 Containers Distributed

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
      <ingredient><!-- BULK LOT(S) --></ingredient>
      <member><!-- LABEL LOT -->
        <memberProductInstance>
          <asContent>
            <container><!-- container reference --></container>
          </asContent>
        </memberProductInstance>
      </member>
    </productInstance>
  </instanceOfKind>
  <subjectOf>
    <quantity value="1000" unit="1"/>
    <productEvent>
      <code code="C106325"
        displayName="Distributed per reporting interval"
        codeSystem="2.16.840.1.113883.3.26.1.1"/>
      <effectiveTime>
        <low value="20100101"/>
      </effectiveTime>
    </productEvent>
  </subjectOf>
```

Validation Procedures

16.2.9.1 There are one or more product events

16.2.9.2 There is one quantity (Final Containers Distributed)

16.2.9.3 Quantity value is the integer number of final containers distributed.

16.2.9.4 Quantity unit is “1” or there is no unit.

16.2.9.5 There is a product event code

16.2.9.6 Code system is 2.16.840.1.113883.3.26.1.1

16.2.9.7 The code is from the LDD *Distribution Codes* list and display name matches the code.

16.2.9.8 There is one distribution product event

16.2.9.9 Container distribution event has an effective time with low boundary specifying the Initial Distribution Date.

16.2.9.10 Initial distribution date has at least the precision of day in the format YYYYMMDD

16.2.9.11 There should be a initial distribution date.

16.2.10 Containers Returned Data

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance><!-- FILL LOT -->
      <ingredient><!-- BULK LOT(S) --></ingredient>
      <member><!-- LABEL LOT -->
        <memberProductInstance>
          <asContent>
            <container><!-- container reference --></container>
          </asContent>
        </memberProductInstance>
      </member>
    </productInstance>
  </instanceOfKind>
  <subjectOf>
    <quantity value="1000" unit="1"/>
    <productEvent>
      <code code="C106328"
        displayName="Returned"
        codeSystem="2.16.840.1.113883.3.26.1.1"/>
    </productEvent>
  </subjectOf>
```

16.2.10.1 There is one returned product event

16.2.10.2 Returned product event has no effective time

16.2.10.3 There is no other product event

16.2.11 Product Data – Kit with Multiple Licensed Products

When the licensed product is only part of a kit, but the kit itself is not tracked as a “package lot”, the lot data is specified under the appropriate part of the kit, and all the validation procedures specified for fill lot, bulk lot and label lot apply as above.

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="1234-5679" codeSystem="2.16.840.1.113883.6.69"/>
      <name p:de="Trade Name">Multivax (MixKit)</name>
    <part>
      <partProduct>
        <instanceOfKind>
          <productInstance>

```

If in addition the kit itself is tracked as a “package lot”, then the package lot data is specified for the entire kit as follows:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <code code="1234-5679" codeSystem="2.16.840.1.113883.6.69"/>
      <name p:de="Trade Name">Multivax (MixKit)</name>
      <instanceOfKind>
        <productInstance><!-- PACKAGE LOT -->
          <id root="{Package Lot root OID}" extension="{Package Lot ID}"/>
          <part><!-- LABEL LOT -->
            <partProductInstance>
              <id root="{Label Lot root OID}" extension="{Label Lot ID}"/>
            </partProductInstance>
          </part>
        </productInstance>
        <subjectOf><!-- product events --></subjectOf>
      </instanceOfKind>

```

Validation Procedures

- 16.2.11.1 The rules for product code and name are as for simple products
- 16.2.11.2 There is one or more parts, referencing label lots of these parts.
- 16.2.11.3 There is a product event code
- 16.2.11.4 There is a label lot specified elsewhere in the lot distribution report.
- 16.2.11.5 There are one or more product events
- 16.2.11.6 There is one distribution product event
- 16.2.11.7 There may be one returned product event
- 16.2.11.8 There is no other product event

17 [RESERVED]

18 Wholesale Drug Distributor/Third-Party Logistics Facility Report

Wholesale Drug Distribution submissions have only header information with data for one or more reported facilities.

18.1 Header

18.1.1 Document type

```
<document>
  <code code="75030-7"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="wholesale drug distributor/third-party logistics
facility reporter"/>
```

Validation Procedures

18.1.1.1 Document type is *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*

18.1.1.2 The effective time year matches the current year.

18.1.1.3 There is no title.

18.1.1.4 If a document with the same set id has been previously submitted, then it is a *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*.

18.1.1.5 For *Withdrawal of Wholesale Drug Distributors and Third-Party Logistics Facility Report (77573-4)* the set id in this document should be the same set id included in a previously submitted *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*, with information about your establishment(s).

18.1.2 Reporter information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- facility, may be pass-through -->
        <assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedOrganization> <!-- reporter -->
    <id extension="100000002" root="1.3.6.1.4.1.519.1"/>
    <name>ACME Drug Logistics, Inc.</name>
    <contactParty>
```

Validation Procedures

18.1.2.1 If the document type is *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*, then there is reporter information.

18.1.2.2 There is one id (the DUNS Number) and name as in Section 2.1.5.

18.1.2.3 id (reporter's DUNS Number) is not associated with any other set id of document type *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*

18.1.2.4 The set id is not associated with any other reporter id (DUNS Number).

18.1.2.5 There is one contact party as in Section 2.1.8.

18.1.2.6 The Reporter's DUNS number matches the DUNS number record in the Dun and Bradstreet database.

18.1.2.7 Facility submission has no labeler information (no validation rules defined for it.)

18.1.3 Facility Information

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
<confidentialityCode code="B" codeSystem="2.16.840.1.113883.5.25"/>
<assignedOrganization> <!-- facility -->
  <id root="1.3.6.1.4.1.519.1" extension="449819433"/>
  <name>Acme, LLC</name>
  <addr>
    <streetAddressLine>325 Good Hope Avenue</streetAddressLine>
    <city>Milwaukee</city>
    <state>WI</state>
    <postalCode>53014</postalCode>
    <country code="USA" codeSystem="1.0.3166.1.2.3">USA</country>
  </addr>
  <asNamedEntity> <!-- other "doing business as" name -->
    <code code="C117113" displayName="doing business as"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <name>A.C.M.E. Logistic</name>
  </asNamedEntity>
  <contactParty .../>

```

The confidentiality code “B” may be used at the facility level to indicate that the street address of this facility should be suppressed in public data releases.

Validation Procedures

- 18.1.3.1 If the document type is *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*, then there are one or more facilities.
- 18.1.3.2 Facility has a name and optionally one id (the DUNS Number) as in Section 2.1.5.
- 18.1.3.3 DUNS number, if present, is not associated with another facility in the same SPL file.
- 18.1.3.4 DUNS number, if present, is not associated with any other set id for document type *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)*
- 18.1.3.5 DUNS number, if present, along with the facility name and address information match the DUNS number record in the Dun and Bradstreet database
- 18.1.3.6 Each facility has an address as in Section 2.1.6.
- 18.1.3.7 There is one contact party as in Section 2.1.8.
- 18.1.3.8 There is no further assigned entity under the facility.
- 18.1.3.9 There may be zero or more “doing business as” names (DBA names).
- 18.1.3.10 DBA names has code C117113 and code system 2.16.840.1.113883.3.26.1.1.
- 18.1.3.11 DBA name has one name element.
- 18.1.3.12 There may be a suffix beginning with space, and the abbreviation WDD or 3PL in square brackets.
- 18.1.3.13 If the suffix is [WDD], then one business operation for this facility is *Wholesale Drug Distributor (C118411)*.
- 18.1.3.14 If the suffix is [3PL], then one business operation for this facility is *Third-Party Logistics Provider (C118412)*.
- 18.1.3.15 If the facility has the same “doing business as” (DBA) name regardless of business operation, then no suffix is specified.
- 18.1.3.16 The facility should not have the same “doing business as” (DBA) name with the same business operation.

18.1.4 Facility Business Operation

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- reporter -->
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization>
      <!-- facility -->
    </assignedOrganization>
  </assignedEntity>
  <performance>
    <actDefinition>
      <code code="C118411" displayName="wholesale drug distribution"
        codeSystem="2.16.840.1.113883.3.26.1.1"/>
    </actDefinition>
  </performance>

```

Validation Procedures

- 18.1.4.1 There are one or two facility business operation details (performance act definitions).
- 18.1.4.2 Act definition (business operation) code is *Wholesale Drug Distributor* (C118411) or *Third-Party Logistics Provider* (C118412) and code system is 2.16.840.1.113883.3.26.1.1.
- 18.1.4.3 Act definition (business operation) display name matches corresponding business operation code.
- 18.1.4.4 Each business operation code is mentioned only once per facility.
- 18.1.4.5 There is no product reference.

18.1.5 License

License information is specified as shown below:

```

<performance>
  <actDefinition>
    <code code="C118411" displayName="wholesale drug distribution"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
  </actDefinition>
  <subjectOf>
    <approval>
      <id extension="License Number"
        root="State license authority OID (see text)"/>
      <code code="C118777" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="licensing"/>
      <statusCode code="License Status"/>
      <effectiveTime>
        <high value="License Expiration Date"/>
      </effectiveTime>
    </approval>
  </subjectOf>

```

```

<author>
  <territorialAuthority>
    <territory>
      <code code="State code from ISO 3166-2, e.g. US-MD"
            codeSystem="1.0.3166.2"/>
    </territory>
  </territorialAuthority>
</author>

```

Example:

```

<performance>
  <actDefinition>
    <code code="C118411" displayName="wholesale drug distribution"
          codeSystem="2.16.840.1.113883.3.26.1.1"/>

    <subjectOf>
      <approval>
        <id extension="2013-WL-123456"
            root="1.3.6.1.4.1.32366.4.840.805"/>
        <code code="C118777"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="licensing"/>
        <statusCode code="completed"/>
        <effectiveTime>
          <high value="20140824"/>
        </effectiveTime>

        <author>
          <territorialAuthority>
            <territory>
              <code code="US-MD" codeSystem="1.0.3166.2"/>
            </territory>
          </territorialAuthority>
        </author>

```

If the issuer of the license is not a state, but it is valid in the entire federal territory then the ISO 3166-1 country CODE “USA” is provided and the DUNS number of the federal agency.

```

<author>
  <territorialAuthority>
    <territory>
      <code code="USA" codeSystem="1.0.3166.1.2.3"/>
    </territory>
    <governingAgency><!-- if territory code is USA -->
      <id extension="Agency DUNS Number" root="1.3.6.1.4.1.519.1"/>
      <name>Agency Name</name>
    </governingAgency>
  </territorialAuthority>
</author>

```

In case of the Drug Enforcement Agency (DEA) that DUNS number is 004234790.

```

<author>
  <territorialAuthority>
    <territory>
      <code code="USA" codeSystem="1.0.3166.1.2.3"/>
    </territory>
    <governingAgency><!-- if territory code is USA -->
      <id extension="004234790" root="1.3.6.1.4.1.519.1"/>
      <name>DEA</name>
    </governingAgency>
  </territorialAuthority>
</author>

```

Validation Procedures

- 18.1.5.1 There is one or more licenses, except if the business operation is *Third-Party Logistics Provider* (C118412).
- 18.1.5.2 License Code is from the License Type Code list.
- 18.1.5.3 Display name matches the code.
- 18.1.5.4 Code system is 2.16.840.1.113883.3.26.1.1.
- 18.1.5.5 If the license is issued by a state, then the territorial authority territory is specified with the ISO 3166-2 US state codes with code system 1.0.3166.2.
- 18.1.5.6 License has an id with the license number.
- 18.1.5.7 id has an extension, the license number.
- 18.1.5.8 If the license is issued by a state authority, then the id has a root beginning with “1.3.6.1.4.1.32366.4.840” followed by a period “.” and a decimal number equal to the value of the 2-letter ISO 3166-2 U.S. state code interpreted as a base 36 number with the digits 0-9 and A-Z, with the letter digits having the value of 9 added to the ordinal letter position (A: 1 + 9 = 10, B = 2 + 9 = 11, ..., Z = 26 + 9 = 35); e.g., Arizona, having the ISO 3166-2 “US-AZ”, i.e., the 2-letter state code “AZ” with (A =) (1 + 9) × 36 + (Z =) (26 + 9) = 10 × 36 + 35 = 395, resulting in “1.3.6.1.4.1.32366.4.840.395”.
- 18.1.5.9 License has a status code with values *active*, *suspended*, *aborted* (meaning “revoked”), or *completed* (meaning “expired”).
- 18.1.5.10 License has an effective time high value (expiration date).
- 18.1.5.11 License has no effective time low value (license issue date not reported).
- 18.1.5.12 The effective time high boundary has at least the precision of day in the format YYYYMMDD

- 18.1.5.13 If the status code is *completed*, then the current date is later than the effective time high value.
- 18.1.5.14 If the current date is later than the effective time high value, then the status code is not *active*.
- 18.1.5.15 The combination of license number, license type and business operation, and license issuing state is not associated with any other set id of document type *Wholesale Drug Distributors and Third-Party Logistics Facility Report (75030-7)* (see also 18.1.5.16 for further details).
- 18.1.5.16 The license id root *should be* followed by a suffix “.2”, “.3”, “.4”, or “.5” as follows: “.2” for *Third-Party Logistics Provider (C118412)* facility in licensing state, “.3” for *Wholesale Drug Distributor (C118411)* facility in licensing state, “.4” for *Third-Party Logistics Provider (C118412)* out of licensing state, and “.5” for *Wholesale Drug Distributor (C118411)* facility out of licensing state; in the absence of this suffix such suffix will be imputed for the purpose of the preceding procedure 18.1.5.15.
- 18.1.5.17 If the license id root has the suffix “.1”, then the license issuing state and the facility address state are not the same.
- 18.1.5.18 If the license id root has the suffix “.2”, then the business operation is *Third-Party Logistics Provider (C118412)* and the license issuing state and the facility address state are the same.
- 18.1.5.19 If the license id root has the suffix “.3”, then the business operation is *Wholesale Drug Distributor (C118411)* and the license issuing state and the facility address state are the same.
- 18.1.5.20 If the license id root has the suffix “.4”, then the business operation is *Third-Party Logistics Provider (C118412)* and the license issuing state and the facility address state are not the same.
- 18.1.5.21 If the license id root has the suffix “.5”, then the business operation is *Wholesale Drug Distributor (C118411)* and the license issuing state and the facility address state are not the same.
- 18.1.5.22 There are no other suffixes to the license id root.
- 18.1.5.23 If the territory code is “USA”, then the code system is 1.0.3166.1.2.3
- 18.1.5.24 If the territory is “USA”, then the issuing governing agency is specified with a DUNS number and name.
- 18.1.5.25 If the territory is not “USA”, then there is no governing agency specified.

18.1.5.26 If the issuing governing agency is DEA, then the DUNS number is 004234790 and the name “DEA”.

18.1.5.27 If the issuing governing agency is DEA then the license id root OID is 1.3.6.1.4.1.32366.4.840.1.

18.1.5.28 A DEA license is specified only with disciplinary actions.

18.1.5.29 There is one license per state, except a second state license can occur if there are disciplinary actions with it.

18.1.5.30 The combination of license number, license type (business operation), license issuing state and establishment address is not mentioned more than once in the same document.

18.1.6 Business Operation Qualifier

```
<performance>
  <actDefinition>
    <code code="C118412" displayName="third-party logistics provider"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
    <subjectOf>
      <approval>
        <code code="C123274" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="warehouses human prescription drug products"/>

```

18.1.6.1 There may be one business operation qualifier if the business operation is third-party logistics provider (C118412).

18.1.6.2 There is no id.

18.1.6.3 Business operation qualifier is warehouses human prescription drug products (C123274).

18.1.6.4 Display name matches the code.

18.1.6.5 Code system is 2.16.840.1.113883.3.26.1.1.

18.1.6.6 Business operation is third-party logistics provider (C118412).

18.1.7 Approval Disciplinary Action

```
<approval>
  <subjectOf>
    <action>
      <code code="disciplinary action code"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName=" disciplinary action name"/>
      <effectiveTime value="disciplinary action effective time"/>

```

```

<subjectOf>
  <document>
    <text mediaType="application/pdf">
      <reference value="suspension01.pdf"/>
    </text>
  </document>
</subjectOf>

```

When action is “other” a brief text description of the nature of the action should be included:

```

<approval>
  <subjectOf>
    <action>
      <code code="C118472"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="other"/>
      <text xsi:type="ST">brief description of nature of action</text>
      <effectiveTime value="disciplinary action effective time"/>
    </action>
    <subjectOf>
      <document>
        <text mediaType="application/pdf">
          <reference value="suspension01.pdf"/>
        </text>
      </document>
    </subjectOf>
  </subjectOf>

```

Validation Procedures

- 18.1.7.1 There is a disciplinary action code.
- 18.1.7.2 Code comes from the *Approval action* list.
- 18.1.7.3 Display name matches the code
- 18.1.7.4 Code system is 2.16.840.1.113883.3.26.1.1.
- 18.1.7.5 If action is “other” (C118472), then there is a text element containing a brief description of the nature of the action:
- 18.1.7.6 Text must be of xsi:type “ST” (plain text string).
- 18.1.7.7 Disciplinary action has an effective time.
- 18.1.7.8 The effective time value has at least the precision of day in the format YYYYMMDD.
- 18.1.7.9 Disciplinary actions are in chronological order, i.e., most recent action last.
- 18.1.7.10 If the last disciplinary action is a *suspension* (C118406), then the license status code is *suspended* or *completed*.

- 18.1.7.11 If the last disciplinary action is a revocation (C118407, *revoked*), then the license status code is *aborted*.
- 18.1.7.12 If the last disciplinary action is *(re-)activation* (C118408), then the license status code is *active*.
- 18.1.7.13 If the last disciplinary action is a resolution (C118471, *resolved*), then the license status code is *active* or *completed*.
- 18.1.7.14 If the last disciplinary action is “other” (C118472), then the license status code is active, completed, suspended or aborted.
- 18.1.7.15 There may be one or more disciplinary action document references.
- 18.1.7.16 Document reference has a text element with mediaType and reference.
- 18.1.7.17 Reference value is the file name for a valid document attachment.
- 18.1.7.18 Size of document attachment is less than 1 MB.
- 18.1.7.19 File name extension matches the media type “.pdf”.
- 18.1.7.20 All pdf files associated with the document must be actually referenced from that *Wholesale Drug Distributors and Third-Party Logistics Facility Report* (75030-7) document.

18.2 Body - Empty

Use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>
  <component>
    <nonXMLBody>
      <text/>
```

19 40 CFR 180 TOLERANCE

19.1 Header

19.1.1 Document type

```
<document>
  code code="3565717"
  codeSystem="2.16.840.1.113883.6.275.1"
  displayName="40 CFR 180 Tolerance"/>
```

Validation Procedures

19.1.1.1 Document type is “40 CFR 180 TOLERANCE” (3565717).

19.1.1.2 Code comes from the *EPA Document type* list

19.1.1.3 Code system is 2.16.840.1.113883.6.275.1

19.1.1.4 Display name matches the code

19.1.1.5 If a document with the same set id has been previously submitted, then it is of the same type.

19.1.2 Author Information

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension="057944910"/>
      <name>US Environmental Protection Agency</name>
```

Validation Procedures

19.1.2.1 There is an author.

19.1.2.2 There are no other elements than id and name.

19.1.2.3 There is one company name.

19.1.2.4 The name matches the name in the Company Number List.

19.1.3 Docket Number

The Docket Number is specified as follows:

```

<document>
  ...
  <author .../>

  <relatedDocument typeCode="XFRM">
    <relatedDocument>
      <id extension="docket number" root="docket number root OID"/>
    </relatedDocument>
  </relatedDocument>

  <component .../>
</document>

```

19.2 Body

19.2.1 Main Sections

The main sections of the SPL document represent the first level paragraphs, (a), (b), (c), etc. of the section in the regulation.

```

<section>
  <id .../>
  <code code="3145478" codeSystem="2.16.840.1.113883.6.275.1"
    displayName="(a) General"/>
  <title>(a) General.</title>
  <text/>
  <effectiveTime .../>

```

Validation Procedures

19.2.1.1 Section codes must come from list CFR_40_180_SECTION_PARAGRAPHS.

19.2.1.2 Code system is 2.16.840.1.113883.6.275.1.

19.2.1.3 Display name matches the code.

19.2.1.4 Title of the section matches the display name of the section code.

19.2.2 Sub-Section

The first level sub sections of the SPL document represent the second level sub-paragraphs, (1), (2), (3), etc. in the regulation.

```

<section>
  ...
  <component>
    <section>
      <id .../>
      <title>(1)</title>
      <text>...</text>
      <effectiveTime .../>
    </section>
  </component>

```

Validation Procedures

19.2.2.1 There is no section code.

19.2.2.2 There is a title with an Arabic ordinal number in parentheses, e.g., “(1)”, “(2)”, etc.

19.2.3 Tolerance Specification

```

<section>
  <component>
    <section>
      <subject>
        <identifiedSubstance>
          <id extension="..." root="2.16.840.1.113883.4.9"/>
          <identifiedSubstance>
            <code code="..." codeSystem="2.16.840.1.113883.4.9"/>
            <name>...</name>
          </identifiedSubstance>
        </subject>
        <subjectOf>
          <substanceSpecification>
            <code code="40-CFR-..."
              codeSystem="2.16.840.1.113883.3.149"/>
          </substanceSpecification>
          <component>
            <observation moodCode="DEF">
              <code code="" displayName="" codeSystem=""/>
            </observation>
            <analyte>
              <identifiedSubstance>
                <id extension="..." root="2.16.840.1.113883.4.9"/>
                <identifiedSubstance>
                  <code code="..."
                    codeSystem="2.16.840.1.113883.4.9"/>
                  <name>...</name>
                </identifiedSubstance>
              </identifiedSubstance>
            </analyte>
            <referenceRange>
              <observationCriterion>
                <value xsi:type="IVL_PQ">
                  <high value="" unit="[ppm]"/>
                </value>
              </observationCriterion>
              <subject>
                <presentSubstance>
                  <presentSubstance>
                    <code code="..."
                      codeSystem="2.16.840.1.113883.6.275.1"
                      displayName="..."/>
                    <name>...</name>
                  </presentSubstance>
                </presentSubstance>
              </subject>
              <subjectOf>
                <approval>
                  <code code="3565718"
                    codeSystem="2.16.840.1.113883.6.275.1"
                    displayName="General Tolerance"/>
                  <text>text note about this tolerance</text>
                  <effectiveTime xsi:type="IVL_TS">
                    <high value="expiration/revocation date"/>
                  </effectiveTime>
                </approval>
              </subjectOf>
            </referenceRange>
          </component>
        </subjectOf>
      </section>
    </component>
  </section>
</section>

```

Validation Procedures

- 19.2.3.1 There is one identified substance with UNII code or EPA SRS tracking number.
- 19.2.3.2 There is one substance code.
- 19.2.3.3 Code system is 2.16.840.1.113883.4.9 (UNII) or 2.16.840.1.113883.6.275 (EPA SRS tracking number).
- 19.2.3.4 Code and code system are the same as the parent element id's extension and root respectively.
- 19.2.3.5 There is one substance name.
- 19.2.3.6 If the code system is UNII, then code comes from the substance name list.
- 19.2.3.7 Substance name matches code.
- 19.2.3.8 The substanceSpecification code is formed by using the fixed prefix "40-CFR-" followed by the section number present in document title.
- 19.2.3.9 Code system is 2.16.840.1.113883.3.149.
- 19.2.3.10 There is a code (Enforcement Analytical Method).
- 19.2.3.11 Code comes from the Enforcement Analytical Method list.
- 19.2.3.12 Display name matches the code.
- 19.2.3.13 There is are or more analytes, the substance(s) being measured.
- 19.2.3.14 Each analyte refers to one substance measured.
- 19.2.3.15 The rules for substance code and name are as in 19.2.3.2ff

19.2.4 Tolerance Range and Commodity

```

<substanceSpecification>
  <component>
    <observation moodCode="DEF">
      <referenceRange>
        <observationCriterion>
          <value xsi:type="IVL_PQ">
            <high value="" unit="[ppm]"/>
          </value>
          <interpretationCode code="N"/>
          <subject>
            <presentSubstance classCode="LOCE">
              <presentSubstance>
                <code code="..."
                  codeSystem="2.16.840.1.113883.6.275.1"
                  displayName="..."/>
                <name>...</name>
              </presentSubstance>
            </presentSubstance>
          </subject>
          <subjectOf>
            <approval>
              <code code="3565718"
                codeSystem="2.16.840.1.113883.6.275.1"
                displayName="General Tolerance"/>
              <text>text note about this tolerance</text>
              <effectiveTime xsi:type="IVL_TS">
                <high value="expiration/revocation date"/>
              </effectiveTime>
            </approval>
          </subjectOf>
        </referenceRange>
      </observation>
    </component>
  </substanceSpecification>

```

19.2.4.1 There are one or more reference ranges (tolerances)

19.2.4.2 Reference ranges have a value

19.2.4.3 Value is of xsi type IVL_PQ

19.2.4.4 There is a high boundary with value and unit

19.2.4.5 There is no low boundary

19.2.4.6 High boundary value is a number.

19.2.4.7 High boundary unit is “[ppm]”.

19.2.4.8 There may be a commodity specified for the tolerance.

19.2.4.9 There is a tolerance commodity code.

19.2.4.10 Code system is 2.16.840.1.113883.6.275.1.

19.2.4.11 Code comes from the Tolerance Commodity list.

19.2.4.12 Display name matches code.

- 19.2.4.13 There is an application type (approval).
- 19.2.4.14 There is an application type (approval) code.
- 19.2.4.15 Code system is 2.16.840.1.113883.6.275.1.
- 19.2.4.16 Code comes from the Application Type list.
- 19.2.4.17 Display name matches code.
- 19.2.4.18 There may be an expiration or revocation date.
- 19.2.4.19 Expiration or revocation date has a high boundary
- 19.2.4.20 Expiration or revocation date value has the format YYYYMMDD
- 19.2.4.21 Expiration or revocation date has no low boundary
- 19.2.4.22 There may be a text annotation.

19.2.5 Specific Sections and Sub-Sections

- 19.2.5.1 There is a section (a) General.
- 19.2.5.2 There is a section (b) Section 18 Emergency exemptions.
- 19.2.5.3 There is a section (c) Tolerances with regional restrictions.
- 19.2.5.4 There is a section (d) Indirect or inadvertent residues
- 19.2.5.5 There may be a section (e) Revoked tolerances subject to the channel of trade provisions
- 19.2.5.6 There may be a section (f) Import tolerances

20 Indexing - Biologic or Drug Substance

This document communicates the FDA-preferred non-proprietary name (specified substance name) for the drug or biologic product associated with the application number included in this indexing SPL document.

20.1 Header

20.1.1 Document Type

```
<document>
  <code code="77648-4" codeSystem="2.16.840.1.113883.6.1"
    displayName="Indexing - Biologic or Drug Substance"/>
```

Validation Procedures

20.1.1.1 The code for the document type is Indexing - Biologic or Drug Substance (77648-4).

20.1.1.2 If a document with the same set id has been previously submitted then it is of the same type.

20.1.2 Author

The drug/biologic substance indexing is maintained by FDA:

```
<document ...>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id root="1.3.6.1.4.1.519.1" extension=""/>
        <name>Food and Drug Administration</name>
```

Validation Procedures

20.1.2.1 Author information for drug/biologic substance indexing is as one of the above.

20.1.2.2 The author is Food and Drug Administration (FDA).

20.1.2.3 There are no other author elements than id and name.

20.1.3 Related Document

The information in the drug/biologic substance indexing SPL file may be automatically linked to the SPL document submitted by the biologic or drug product's distributor or manufacturer using the related document element which contains the set

ID of the biologic or drug product's SPL document. The related document SPL is specified using its setId as follows:

```
<document>
...
<author .../>

<relatedDocument typeCode="XCRPT">
  <relatedDocument>
    <setId root="fe707775-a0ae-41b5-a744-28c41889fce8"/>
  </relatedDocument>
</relatedDocument>
```

Validation Procedures

20.1.3.1 There may be a specified related document.

20.1.3.2 Type code attribute is as above.

20.1.3.3 There is no document id.

20.1.3.4 There is a set id.

20.1.3.5 Set id is a GUID.

20.1.3.6 Related document's set id is the set id of a drug listing document.

20.1.3.7 If a drug/biologic substance indexing file for the same related document's set id has been previously submitted, then it is a prior version of this indexing document with the same set id.

20.1.3.8 If a document with the same set id has been previously submitted, then it is associated with the same related document's set id.

20.2 Body

```
<document>
  <component>
    <structuredBody>
      <component><!-- old data element section -->
        <section>
          <id .../>
          <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
            displayName="SPL indexing data elements section"/>
          <effectiveTime>
            <low value="old data effective start date"/>
            <high value="old data effective end date"/>
          </effectiveTime>
          <subject ... old data ... />
        </section>
      </component>
```

```
<component><!-- new data element section -->
  <section>
    <id .../>
    <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
      displayName="SPL indexing data elements section"/>
    <effectiveTime>
      <low value="new data effective star date"/>
    </effectiveTime>
    <subject ... new data ... />
  </section>
```

Validation Procedures

20.2.1.1 There is a document body.

20.2.1.2 Document body contains one or two sections of type SPL Indexing Data Elements.

20.2.2 Index Data Element Section(s) in General

```
<document>
  <component>
    <structuredBody>
      <component>
        <section>
          <id .../>
          <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
            displayName="SPL indexing data elements section"/>
          <effectiveTime>
            <low value="old data effective start date"/>
            <high value="old data effective end date"/>
          </effectiveTime>
          <subject ... old data ... />
        </section>
      </component>
    </structuredBody>
  </component>
```

Validation Procedures

20.2.2.1 Effective time has a low boundary indicating the period for the use of the specified substance name (FDA-preferred non-proprietary name) (data effective start date).

20.2.2.2 Data Elements section start date has at least the precision of day in the format YYYYMMDD.

20.2.2.3 Data Elements section end date has at least the precision of day in the format YYYYMMDD.

20.2.2.4 Data Elements section start date is before data elements section end date.

20.2.2.5 Data elements section contains information for a drug or biologic product.

20.2.3 New (or only) Index Data Element Section

```

<document>
  <component>
    <structuredBody>

    <component ... old data element section, if any ... />

    <component><!-- new or only data element section -->
      <section>
        <id .../>
        <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
          displayName="SPL indexing data elements section"/>
        <effectiveTime>
          <low value="new data effective star date"/>
        </effectiveTime>
        <subject ... new data ... />
      </section>

```

Validation Procedures

20.2.3.1 Data effective start date is same as the effective time in document information.

20.2.4 Old Index Data Element Section

```

<document>
  <component>
    <structuredBody>

    <component><!-- old data element section -->
      <section>
        <id .../>
        <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
          displayName="SPL indexing data elements section"/>
        <effectiveTime>
          <low value="old data effective start date"/>
          <high value="old data effective end date"/>
        </effectiveTime>
        <subject ... old data ... />
      </section>
    </component>

    <component ... new data element section ... />

```

Validation Procedures

20.2.4.1 Old data elements section contains effective time high boundary (old data effective end date).

20.2.4.2 Old data element section comes before the new data element section.

20.2.4.3 Old SPL indexing data elements section has been submitted in the previous version of the document.

20.2.4.4 New SPL indexing data elements section data should not match exactly to the old SPL indexing data elements section.

20.2.4.5 The end date of old data elements section is equal to the start date of new data elements section.

20.2.5 Biologic/Drug Product Information

```

<section>
  ...
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="61314-304" codeSystem="2.16.840.1.113883.6.69"/>
        <name>ZARXIO</name>
        <ingredient classCode="ACTIB">
          <ingredientSubstance>
            <code code="PVI5M0M1GW"
              codeSystem="2.16.840.1.113883.4.9"/>
            <name>filgrastim-SNDZ</name>
          </ingredientSubstance>
          <subjectOf ... substance specification .../>
        </ingredient>
      </manufacturedProduct>
    <subjectOf>
      <approval>
        <id extension="BLA125553" root="2.16.840.1.113883.3.150"/>
        <code code="C73585" codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="BLA"/>
        <author>
          <territorialAuthority>
            <territory>
              <code code="USA" codeSystem="1.0.3166.1.2.3"/>
            </territory>
          </territorialAuthority>
        </author>
      </approval>
    </subjectOf>
  </subject>
</section>

```

Validation Procedures

20.2.5.1 There is a name, i.e., proprietary name of the product as used in product labeling (see subsection 3.2.1.17 and following).

20.2.5.2 There is one active ingredient according to subsection 3.2.11.

20.2.5.3 The strength is not specified for the active ingredient.

20.2.5.4 The active moiety is not specified for the active ingredient.

20.2.5.5 Active ingredient is actually in the product, with the same basis of strength (classCode).

20.2.5.6 There is a marketing category and application number as per subsection 3.1.7.

20.2.6 Specified Substance

```

<ingredient classCode="ACTIB"/>
<ingredientSubstance .../>

<subjectOf>
  <substanceSpecification>
    <code code=" PVI5M0M1GW-SNDZ-1" codeSystem="2.16.840.1.113883.3.6277"
      displayName="filgrastim-SNDZ"/>
  </substanceSpecification>
</subjectOf>

```

Validation Procedures

20.2.6.1 There is a specified substance code with code and code system.

20.2.6.2 Code system is 2.16.840.1.113883.3.6277.

20.2.6.3 There is a specified substance code display name.

20.2.6.4 Display name matches the specified substance code.

21 Indexing - Warning Letter Alert

This document is to be used to connect the content of an FDA warning letter to the product SPL document of the product(s) described in the warning letter.

21.1 Header

21.1.1 Document Type

```
<document>
  <code code="77288-9" codeSystem="2.16.840.1.113883.6.1"
    displayName="Indexing - Warning Letter Alert" />
```

Validation Procedures

21.1.1.1 The code for the document type is Indexing - Warning Letter Alert (77288-9).

21.1.1.2 If a document with the same set id has been previously submitted then it is of the same type.

21.1.2 Author

The Indexing – Warning Letter Alert file is maintained by FDA:

```
<document ...>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id root="1.3.6.1.4.1.519.1" extension="" />
        <name>Food and Drug Administration</name>
```

Validation Procedures

21.1.2.1 Author information for Indexing - Warning Letter is as one of the above.

21.1.2.2 Author organization is FDA.

21.1.2.3 There are no other author elements than id and name.

21.1.3 Reference Labeling

The information in the warning letter alert indexing SPL file may be automatically linked to the SPL document submitted by the biologic or drug product's distributor or manufacturer using the related document element which contains the set ID of the biologic or drug product's SPL document. The SPL document containing the Reference Labeling is specified using its setId as follows:

```

<document>
  ...
  <author .../>

  <relatedDocument typeCode="XCRPT">
    <relatedDocument>
      <!-- <id root="2608fb41-083b-402b-94a0-0629fa484bb7"/> -->
      <setId root="5dd66ebe-31b8-4319-9ff2-c37baaa138e6"/>
    </relatedDocument>
  </relatedDocument>

```

Validation Procedures

21.1.3.1 There is related document specified.

21.1.3.2 Type code attribute is as above.

21.1.3.3 There is no document id.

21.1.3.4 There is a set id.

21.1.3.5 Set id is a GUID.

21.1.3.6 Related document set id is the set id of a drug listing document.

21.1.3.7 If a warning letter alert indexing file for the same related document set id has been previously submitted, then it is a prior version of this indexing document with the same set id.

21.1.3.8 If a document with the same set id has been previously submitted, then it is associated with the same related document set id.

21.2 Body

```

<document>          <!-- SPL header material here -->
  <component>
    <structuredBody><!-- SPL body material here -->
      <component>
        <section>    <!-- Product data element section -->
          <code code="48780-1" codeSystem="2.16.840.1.113883.6.1"
            displayName="SPL product data elements section"/>
          <subject>
            <manufacturedProduct>
              <!-- product data elements -->
            </manufacturedProduct>
          </subject>
        </section>
      </component>
      <!-- Other content of labeling material -->
    <component>
      <!-- ... -->
    </component>
  </structuredBody>
</component>

```

21.2.1 Indexing Section

Validation Procedures:

21.2.1.1 If the document type is Indexing – Warning Letter Alert (77288-9) then the document contains one or more SPL Indexing Data Elements section as above.

21.2.1.2 Value of effective time is same as value of effective time in document information.

21.2.2 Warning Letter Alert Data Element

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <name>proprietary name <suffix>suffix to name</suffix></name>
      <formCode code="C42998" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="tablet"/>
      <asEntityWithGeneric>
        <genericMedicine>
          <name>non-proprietary name</name>
        </genericMedicine>
      </asEntityWithGeneric>
    </manufacturedProduct>
  </manufacturedProduct>
</subject>
```

Validation Procedures:

21.2.2.1 There is a name, i.e., proprietary name of the product as used in product labeling SPL.

21.2.2.2 There is a generic medicine name as used in product labeling SPL.

21.2.2.3 There is a form code (dosage form).

21.2.2.4 Form code (dosage form) has the code system 2.16.840.1.113883.3.26.1.1.

21.2.2.5 There are one or more strength amounts with a numerator and denominator for the active ingredient.

21.2.2.6 There is one or more product item codes.

21.2.2.7 If the product item code is an NDC/NHRIC (i.e., if the root is “2.16.840.1.113883.6.69”), then the following procedures apply:

21.2.2.8 Code (NDC/NHRIC product code) has two segments separated by a hyphen.

21.2.2.9 The first segment (NDC/NHRIC labeler code) is numeric.

21.2.2.10 Segments (NDC/NHRIC product codes) follow the pattern of 4-4, 5-4 or 5-3.

21.2.3 Warning Letter Date Element

If the issue described in the warning letter has been resolved, there are date elements which can automatically inform the receiving system that the matter has been closed.

21.2.3.1 Effective time has a low boundary indicating the date the alert was issued.

21.2.3.2 Effective time may have a high boundary indicating when the issue described in the letter has been resolved.

21.2.3.3 Warning letter alert date has at least the precision of day in the format
YYYYMMDD

21.2.3.4 Warning letter alert closure date has at least the precision of day in the format
YYYYMMDD

21.2.3.5 Warning letter alert date is before reporting end date.

22 [RESERVED]

23 Risk Evaluation and Mitigation Strategy (REMS)

23.1 REMS Document

REMS are programs designed to ensure that the benefits of certain drugs outweigh their risks.

23.1.1 Document type

All REMS documents have the following document type code. See Section 1 and 2 of the SPL Implementation Guide and Validation Procedures for general rules.

```
<document>
  <id root="Document Id (UUID)"/>
  <code code="82351-8" codeSystem="2.16.840.1.113883.6.1"
    displayName="Risk Evaluation & Mitigation Strategies"/>
  <title>Risk Evaluation and Mitigation Strategy (REMS)</title>
  <effectiveTime value="YYYYMMDD"/>
  <setId root="Document Set Id (UUID)"
    <versionNumber value="1"/>
```

Validation Procedures

23.1.1.1 Document type is *Risk Evaluation & Mitigation Strategies* (82351-8)

23.1.1.2 There is an author.

23.1.1.3 If a document with the same set id has been previously submitted, then it is of the same type.

23.1.1.4 There is a title with the Risk Evaluation and Mitigation Strategy (REMS) Document [PROPRIETARY (established/proper name)] or [Established/Proper/Class Name] [Shared System] REMS.

23.1.1.5 The effectiveTime should be the date of the most recent revision or modification of the REMS.

23.1.2 REMS Author information

```
<document ...>
  <author>
    <assignedEntity>
      <representedOrganization>
        <id root="1.3.6.1.4.1.519.1" extension="Sponsor DUNS"/>
        <name>Sponsor Name</name>
```

Validation Procedures

23.1.2.1 There is one (author of document)

23.1.2.2 There is one id, the sponsor's DUNS number, and name is as in Section 2.1.5.

23.1.2.3 There is no other element besides id (the sponsor's DUNS Number) and name.

23.1.3 REMS Related Document

The REMS are provided for a drug or biologic product represented by the related document(s) SPL. As such, REMS append the related document(s) with more detail how to evaluate and manage risks regarding the product described in the related document(s). The related document(s) SPL document is referred to by its setId as follows:

```
<document>
...
<author .../>
<relatedDocument typeCode="SUBJ">
  <relatedDocument>
    <setId root="97cf7820-4bfe-4caa-86f1-a97bfcf1917a"/>
  </relatedDocument>
</relatedDocument>
<component .../>
</document>
```

Validation Procedures

23.1.3.1 There is at least one related document specified.

23.1.3.2 Type code for the related document is as above.

23.1.3.3 There is a set id with root and no extension.

23.1.3.4 Set id root is a GUID.

23.1.3.5 Related document set id is the set id of a product document of the specified type.

23.1.3.6 If a REMS document file for the same related document set id has been previously submitted, then it is a prior version of this REMS document with the same set id.

23.1.3.7 If a document with the same set id has been previously submitted, then it is associated with the same related document set id.

23.2 Body

23.2.1 REMS Sections and Subsections

See subsection 2.1.1 of the FDA's SPL Implementation Guide with Validation Procedures document for general section and subsection information.

Validation Procedures

- 23.2.1.1 REMS document may have a REMS Timetable for Submission Assessments (82352-6) section.
- 23.2.1.2 REMS documents may have a REMS Administrative Information (87523-7) section.
- 23.2.1.3 If there is a REMS Administrative Information (87523-7) section, then the REMS document must have the following sections: REMS Goals (82349-2) and REMS Requirements (87524-5.)
- 23.2.1.4 If there is a REMS Administrative Information (87523-7) section, then the REMS document must not have the section REMS Summary (82347-6).
- 23.2.1.5 If there is a REMS Requirements (87524-5), then the REMS document must have the subsection REMS Applicant Requirements (87526-0.)
- 23.2.1.6 REMS documents that have REMS Requirements (87524-5) may have the subsection REMS Participant Requirements (87525-2.)
- 23.2.1.7 If there is no REMS Administrative Information (87523-7) section, then the REMS document may have the following sections:REMS Goals (82349-2), REMS Medication Guide (82598-4), REMS Elements to Assure Safe Use (82345-0), REMS Communication Plan (82344-3), and REMS Implementation System (82350-0).
- 23.2.1.8 If there is no REMS Administrative Information (87523-7) section, then the REMS document must not have the section REMS Requirements (87524-5.)
- 23.2.1.9 REMS documents with REMS Elements to Assure Safe Use (82345-0) may also have REMS Summary (82347-6).
- 23.2.1.10 If the REMS document has any attachments, then the attachments are referenced from within the REMS Material (82346-8) section.

23.2.2 REMS Product

REMS product description contains less detail than the description of the product found in the related document SPL.

The beginning of the product data elements is as follows

```

<component>
  <section>
    <id root="Section UUID"/>
    <code code="48780-1"
      codeSystem="2.16.840.1.113883.6.1"
      displayName="SPL product data elements section"/>
    <effectiveTime value="YYYYMMDD"/>
    <subject>
      <manufacturedProduct>

```

The limited data elements for REMS products:

```

<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <name>proprietary name (except for shared system REMS)</name>

      <asEntityWithGeneric>
        <genericMedicine>
          <name>non proprietary name</name>
        </genericMedicine>
      </asEntityWithGeneric>
    </manufacturedProduct>

  <subjectOf>
    <approval>
      <!-- marketing category and application number -->

```

Validation Procedures

23.2.2.1 Code, code system and display name are as above

23.2.2.2 There is an effective time with at least the precision of day in the format YYYYMMDD.

23.2.2.3 There are one or more products

23.2.2.4 There is no product item code.

23.2.2.5 There is a generic name.

23.2.2.6 There is a proprietary name, except in a shared system REMS document.

23.2.2.7 There are no ingredients stated.

23.2.2.8 There is no package information.

23.2.2.9 There is no route of administrations in REMS documents.

23.2.2.10 There are no other product characteristics in REMS documents.

23.2.3 Marketing Category and Application Number

The approval structure specifies in the <code> the marketing category under which the product is approved for marketing. Products marketed under an approved application have an application number in the <id extension> and application tracking system under <id root>.

```

<manufacturedProduct>
  <manufacturedProduct> ... </manufacturedProduct>
  <subjectOf>
    <approval>
      <id extension="applicationnumber"
        root="FDA document tracking system OID"/>
      <code code="code for marketing category"
        codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="display name"/>

      <holder>
        <role>
          <playingOrganization>
            <id root="1.3.6.1.4.1.519.1"
              extension="Application Holder DUNS"/>
            <name>Application Holder Name</name>
          </playingOrganization>
        </role>
      </holder>

      <author>
        <territorialAuthority>
          <territory>
            <code code="USA" codeSystem="1.0.3166.1.2.3"/>
          </territory>
        </territorialAuthority>
      </author>
    </approval>
  </subjectOf>
</manufacturedProduct>

```

Validation Procedures

- 23.2.3.1 There is one marketing category for every product.
- 23.2.3.2 There is a marketing category code.
- 23.2.3.3 In a REMS SPL document, the marketing category is only ANDA (C73584), BLA (C73585), or NDA (C73594.)
- 23.2.3.4 Display name matches the code
- 23.2.3.5 Code system is 2.16.840.1.113883.3.26.1.1
- 23.2.3.6 Territorial authority is as above
- 23.2.3.7 Marketing authorization holder is specified with DUNS number and name as above.

23.2.4 REMS Summary

REMS with the section REMS Elements to Assure Safe Use (ETASU) typically include a REMS Summary. REMS with the section REMS Participant Requirements (87525-2) should not include a REMS Summary section. The REMS Summary is an overview of what stakeholders who participate in REMS with Elements to Assure Safe Use (ETASU), such as healthcare providers, patients, and distributors, are required to do under the REMS' Elements to Assure Safe Use and Implementation System. The information in the summary is presented as a series of tables that show what clinical or administrative activity each stakeholder must carry out at each point in the medication use process. It is designed to be a reader-friendly summary of the REMS program requirements as well as a tool to facilitate the coding of REMS SPL data elements.

The REMS Summary includes all requirements in the REMS document that are directed towards stakeholders other than the application holder, but the summary should not include activities that REMS participants learn about or must be aware of but do not agree to undertake. For example, when filling out a form to enroll in the REMS, a prescriber may be asked to understand the importance of monitoring patients regularly. Unless they also agree to perform this monitoring, it would not be included in the summary.

The summary is intended to be rendered as a series of tables as per the following template, including one table for each stakeholder who participates in the REMS.

[Stakeholder Name]

| | |
|------------|---------------|
| [Protocol] | [Requirement] |
| | [Requirement] |
| [Protocol] | [Requirement] |

In the table above, each item in brackets represents a “summary item”, and should be replaced with appropriate text as follows:

[Stakeholder] is replaced with a description of the participant to whom the REMS requirements apply, such as “Healthcare Providers who prescribe [drug]”. In most cases, simply identifying the role of the participant is sufficient, but in other cases the text will need to be more specific about the setting in which the drug is used, such as, “Healthcare Providers who prescribe the drug in outpatient settings” or “Closed-system outpatient pharmacies that dispense.”

[Protocol] is replaced with the step of the medication use process (prescribing, dispensing, etc.) at which the requirement must be met, such as “Before the first prescription ” or “After discontinuation”. Requirements in the summary are

organized by the timing at which they should be carried out – not when they are agreed to or acknowledged.

[Requirement] is replaced with the clinical, administrative, or operational activities that the participant must carry out as part of the REMS, such as “Enroll the patient by completing and submitting the Patient Enrollment Form”.

The language used in the requirement section is generally short and succinct, and no more than one or two sentences in length. To facilitate transmission of the text across the healthcare system, it should be in plain text and not use formatting such as bullets or indentations.

When the requirement mentions a material such as an enrollment form that is also attached or referenced in the REMS materials section, it includes a hyperlink to that material.

When a requirement applies only to a subset of patients (e.g., the requirement applies only to females of childbearing potential or a specific age group), the text is preceded by a description of the patient population followed by a colon, as in the following example: “For a female of childbearing potential: Counsel the patient on contraception” and “For patients younger than age 3: assess the patient’s response to the treatment”.

Within a single step of the medication use process there can be more than one requirement. When the REMS specifies a certain order in which requirements are to be carried out, the summary lists the requirements in that order.

In certain cases multiple stakeholders may play a similar role in the medication use process (e.g., inpatient pharmacies and outpatient pharmacies that dispense the drug) but be subject to significantly different REMS requirements. In these cases the summary should include a separate table and stakeholder item for each of those stakeholders.

Validation Procedures

23.2.4.1 REMS with the section REMS Elements to Assure Safe Use (82345-0) may include a REMS Summary (82347-6.)

23.2.4.2 REMS with REMS Participant Requirements (87525-2) should not include a REMS Summary section (82347-6).

23.2.5 REMS Data Elements

REMS Data Elements allow standardized terminology to be applied to the items in the REMS Summary (82347-6) and REMS Participant Requirements (87525-2). All

items that appear in the REMS Summary and REMS Participant Requirements have corresponding data elements coded using the appropriate standardized term. If an application holder includes an item in their REMS Summary or REMS Participant Requirements to which no standardized term applies, the application holder should contact FDA for further assistance. REMS Data Elements allow standardized terminology to be applied to the items in the REMS Summary (82347-6) and REMS Participant Requirements (87525-2). All items that appear in the REMS Summary and REMS Participant Requirements have corresponding data elements coded using the appropriate standardized term. If an application holder includes an item in their REMS Summary or REMS Participant Requirements to which no standardized term applies, the application holder should contact FDA for further assistance.

23.2.6 REMS Data Elements: Protocol

REMS requirements are presented as the substance administration of the drug being a component of a REMS protocol described in the REMS Summary or REMS Participant Requirements which then has the requirements as other components of that protocol. The basic structure is as follows:

```

<section>
  ...
  <subject2>
    <substanceAdministration>
      <componentOf>
        <sequenceNumber value="2"/>
        <protocol>
          <code code="REMS Protocol Code"
            codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="REMS Protocol Code Display Name"/>
          <component>
            <sequenceNumber value="REMS Requirement Sequence Number"/>
            <requirement>

```

Note that sequenceNumber under the <componentOf> element is fixed as value 2. This means that the substance administration of the drug under REMS is step 2 in the REMS summary protocol. Step 2 means that requirements can be meant to occur before (step 1), during (step 2), or after (step 3) the substance administration.

Substance administration is potentially a series of substance administrations depending on the type of protocol (protocol code). If the protocol guides the overall treatment, then substance administration represents the overall treatment beginning with the first prescription, and ending with the last dose. If the protocol guides a course of treatment, then the substance administration represents that course of treatment. This is coded in the protocol code.

Validation Procedures

23.2.6.1 If there is a REMS Participant Requirements (87525-2) section or a REMS Summary (82347-6) section then there is a <protocol> data element within that section.

23.2.6.2 The REMS protocol is linked with a componentOf relationship with sequence number 2.

23.2.6.3 REMS protocol has a code.

23.2.6.4 REMS protocol code comes from the REMS Protocol Type list

23.2.6.5 REMS protocol code system is 2.16.840.1.113883.3.26.1.1.

23.2.6.6 REMS protocol display name matches the code.

23.2.7 REMS Data Elements:Requirement

The requirement is specified under a protocol as follows

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/>
    <protocol>
      <component>
        <sequenceNumber value="1"/>
      </component>
    </protocol>
  </componentOf>
  <requirement><!-- or <monitoringObservation> -->
    <code code="REMS Requirement Code"
      displayName="REMS Requirement Code"
      codeSystem="2.16.840.1.113883.3.26.1.1">
      <originalText>
        <reference value="#R003"/>
      </originalText>
    </code>
    <effectiveTime>
      <period value="10" unit="min"/>
    </effectiveTime>
    <participation typeCode="PPRF">
      <stakeholder>
        <code code="C0SH01" displayName="prescriber"
          codeSystem="2.16.840.1.113883.3.26.1.1"/>
      </stakeholder>
    </participation>
  </requirement>
  <subject>
    <documentReference>
      <id .../>
    </documentReference>
  </subject>
</substanceAdministration>
```

The requirement code original text contains a reference linking to the content of the text which describes this requirement.

The timing of the requirement is specified using the sequence number. Because the substance administration step is fixed at sequence number 2, if a requirement is to occur before the start of the drug step, the requirement's sequence number is set to 1. To occur after the end of the drug step, the requirement's sequence number is set to 3. To occur after the start of and along with the drug step, the requirement's sequence number is set to 2 as well.

The pause quantity element allows placing of requirement at a certain distance from the drug step. For instance,

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/><!-- always fixed -->
    <protocol>
      <code ...step in the medication use process .../>
      <component>
        <sequenceNumber value="3"/>
        <pauseQuantity value="2" unit="wk"/>
      <requirement>
```

means that the required action is to occur 2 weeks after the end of the step in the medication use process. And the following:

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/><!-- always fixed -->
    <protocol>
      <code ...step in the medication use process .../>
      <component>
        <sequenceNumber value="2"/>
        <pauseQuantity value="1" unit="h"/>
      <requirement>
```

means that the required action is to occur 1 hour after the start of the step in the medication use process, this often means “during” the medication process, e.g., during a treatment course, measure blood pressure. However, the pause quantity can delay this step a lot more, allowing us to say “2 months after the initiation of treatment”.

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/><!-- always fixed -->
    <protocol>
      <code ...step in the medication use process .../>
      <component>
        <sequenceNumber value="2"/>
        <pauseQuantity value="2" unit="mo"/>
      <requirement>
```

The pause quantity always determines a delay between the previous step and this step. In the two examples above, the required action occurred after the start or the end of the step in the medication use process. When the required action is to occur *before* the

step in the medication use process, the pause quantity moves to the next step, the one with sequence number 2.

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/><!-- always fixed -->
    <pauseQuantity value="1" unit="h"/>
    <protocol>
      <code ...step in the medication use process .../>
    <component>
      <sequenceNumber value="1"/>
    <requirement>
```

To understand this, think about a simple 3 step action list:

1. do preparatory work
2. do the step in the medication use process
3. do follow up work

In the data model serialized into XML, we simply enter at number 2, the step in the medication use process. We then use sequence number 1 to represent preparatory work done before that step, and sequence number 3 to represent follow-up work done after that step.

2. do the step in the medication use process
 1. do preparatory work
3. do follow up work.

However, the data model associates the pause with the step that is delayed. So for example:

1. do preparatory work
2. one hour after previous step, do the step in the medication use process
3. two weeks after the previous step, do follow up work

Additionally, a requirement can be said to repeat at a certain period duration. For example, we can say measure blood pressure 20 minutes after start of treatment and then every 10 minutes:

```
<substanceAdministration>
  <componentOf>
    <sequenceNumber value="2"/><!-- always fixed -->
    <protocol>
      <code ...treatment .../>
      <component>
        <sequenceNumber value="2"/>
        <pauseQuantity value="20" unit="min"/>
        <monitoringObservation>
          <code ... blood pressure ..../>
          <effectiveTime>
            <period value="10" unit="min"/>
          </effectiveTime>
        </monitoringObservation>
      </component>
    </protocol>
  </componentOf>
</substanceAdministration>
```

Validation Procedures

- 23.2.7.1 There is a REMS Requirement.
- 23.2.7.2 REMS requirement component has a sequence number with value 1, 2, or 3.
- 23.2.7.3 If sequence number is 2 or 3, then there may be a pause quantity element.
- 23.2.7.4 If sequence number is not 2 or 3, then there is no pause quantity element.
- 23.2.7.5 If sequence number is 1, a pause quantity element may be under the componentOf parent element of the protocol ancestor element.
- 23.2.7.6 If sequence number is not 1, then there is no pause quantity element under the componentOf parent element of the protocol ancestor element.
- 23.2.7.7 REMS Requirement has a code
- 23.2.7.8 REMS Requirement code system is 2.16.840.1.113883.3.26.1.1
- 23.2.7.9 REMS Requirement code comes from the REMS Requirement list.
- 23.2.7.10 REMS Requirement display name matches the code.
- 23.2.7.11 Every text element in the REMS summary has an associated summary requirement code.
- 23.2.7.12 REMS Requirement code has an original text element with reference value.
- 23.2.7.13 Reference value links to the content ID of the section text of the section in which it is contained.
- 23.2.7.14 Reference value can not be the same as that of a different requirement data element.

- 23.2.7.15 There may be an <effectiveTime> with a <period> element to indicate repetition.
- 23.2.7.16 If there is an effectiveTime, then it has only a <period> child element.
- 23.2.7.17 REMS Requirements have a stakeholder
- 23.2.7.18 Stakeholder participation type code is PPRF.
- 23.2.7.19 Stakeholder has a code with code system 2.16.840.1.113883.3.26.1.1.
- 23.2.7.20 Stakeholder code comes from the Stakeholder list.
- 23.2.7.21 Stakeholder display name matches the code.
- 23.2.7.22 REMS Requirements may have a document reference (also considered “topic” reference).
- 23.2.7.23 Document reference has an id with root and no extension.
- 23.2.7.24 The value of the root matches an id of a document cited as a REMS Material (see Section 23.2.9)

23.2.8 REMS Approval

The Risk Evaluation and Mitigation Strategy (REMS) has a date of initial approval by the agency, which means, it is approved by the agency and this is represented by the following approval structure at the very first time a REMS substanceAdministration with protocol is mentioned in the REMS document.

```

<subject2>
  <substanceAdministration>
    <componentOf>
      <sequenceNumber value="2"/>
      <protocol>
        ...
      </protocol>
    </componentOf>
    <subjectOf>
      <approval>
        <code code="C128899"
              codeSystem="2.16.840.1.113883.3.26.1.1"
              displayName="REMS Approval"/>
        <effectiveTime>
          <low value="Date of REMS Approval [YYYYMMDD]"/>
        </effectiveTime>
      </approval>
    </subjectOf>
  </substanceAdministration>
</subject2>

```

```
<author>
  <territorialAuthority>
    <territory>
      <code code="USA" codeSystem="1.0.3166.1.2.3"/>
    </territory>
  </territorialAuthority>
</author>
</approval>
</subjectOf>
</substanceAdministration>
</subject2>
```

Validation Procedures

23.2.8.1 The first mention of a REMS protocol in the summary has a REMS approval structure (i.e. a subjectOf / approval element under the subject2 / substanceAdministration).

23.2.8.2 Only the first mention of a REMS protocol in the summary has a REMS approval structure (i.e. only the first subject2 / substanceAdministration has a subjectOf / approval element).

23.2.8.3 There is a code for *REMS Approval* (C128899).

23.2.8.4 Code system is 2.16.840.1.113883.3.26.1.1

23.2.8.5 Display name matches the code.

23.2.8.6 There is an Initial REMS Program Approval Date (effectiveTime)

23.2.8.7 REMS Program Approval Date has at least the precision of day (YYYYMMDD.)

23.2.9 REMS Material

Materials referenced from the REMS document under the section of type "REMS Materials". There is a subject manufactured product with no code and only subjectOf/document elements each of which then contain one reference.

For example, the material may be an attached PDF file to the REMS submission:

```

<section>
  ...
  <subject>
    <manufacturedProduct>
      <manufacturedProduct/>
      <subjectOf>
        <document>
          <id root="00000000-0000-0000-0000-000000000001"/>
          <title>REMS SPL Pilot Counseling Material
Placeholder<reference value="#T001"/>
          </title>
          <text mediaType="application/pdf">
            <reference value="Drug X_2015-11-01_Counseling
Material.pdf"/>
          </text>
        </document>
      </subjectOf>

```

The material may be a PDF file which is a form with instructions on where to send the form which was filled in:

```

<subjectOf>
  <document>
    <id root="00000000-0000-0000-0000-000000000003"/>
    <title>REMS SPL Pilot Dispenser Enrollment and
Agreement Form Placeholder<reference value="#T003"/>
    </title>
    <text mediaType="application/pdf">
      <reference value="drug-x-dispenser-encollment-
form.pdf"/>
    </text>
  </document>
</subjectOf>

```

Validation Procedures

- 23.2.9.1 Each reference document has an id root
- 23.2.9.2 Document reference has a title element with reference (title reference).
- 23.2.9.3 Title reference value is present in the content ID of the section text.
- 23.2.9.4 Document reference has a text element with mediaType and reference (text reference).
- 23.2.9.5 Text reference value is the file name for a valid document attachment.
- 23.2.9.6 File name extension matches the media type “.pdf”.
- 23.2.9.7 Same file name cannot occur under a different document id and the same document id cannot be used with different file name.
- 23.2.9.8 id (document id) does not match any other id across all sections, documents, or any id other than the id of the same document previously submitted.

23.2.10 REMS Electronic Resource Information

REMS may include references to electronic resources used to help carry out REMS activities. This information is captured using the document element and may be referenced within the REMS Summary using the documentReference data element </subjectOf>

REMS resources may be referenced as web content with an absolute URL reference with the “http://” or https://” protocol:

```
<subjectOf>
  <document>
    <id root="00000000-0000-0000-0000-000000000004"/>
    <title>REMS SPL Pilot Prescriber Enrollment and
      Agreement Form Placeholder
    <reference value="#T004"/>
    </title>
    <text>
      <reference value="https://company.com/drug-x-
        prescriber-encollment.html"/>
    </text>
  </document>
```

In cases where stakeholders are required to exchange data with the applicant, electronic data standards such as NCPDP telecommunications standards may be referenced. These consist of a special universal resource name (URN) which is formed with the prefix “urn:”. For example the URN “urn:NCPDP:D.0:P1:610674:000000000000-0000-0000-000000000005”, has five segments of text separated by colons following the prefix “urn:”. The segments are

- (1)the developer of the standard (e.g., “NCPDP”)
- (2)the standard version (e.g. “D.0”),
- (3)the transaction (e.g. “P1”)
- (4)the destination address such as a BIN number (e.g., “610674”)
- (5)the id of a REMS material document which provides instructions for how to carry out the transaction.

```
<subjectOf>
  <document>
    <id root="00000000-0000-0000-0000-000000000006"/>
    <title>REMS SPL Pilot - NCPDP D0 - Patient Data </title>
    <text>
      <reference value="urn:NCPDP:D.0:P1:610674:00000000-0000-0000-0000
        -000000000005"/>
    </text>
  </document>
</subjectOf>
```

Validation Procedures

23.2.10.1 Each reference document has an id root.

- 23.2.10.2 Document reference has a title element with reference (title reference) .
- 23.2.10.3 Title reference value is present in the content ID of the section text.
- 23.2.10.4 Document reference has a text element with reference (text reference) but no mediaType.
- 23.2.10.5 Text reference value is a URI starting with a URI scheme (“http://” or “urn:”).
- 23.2.10.6 If the text reference value begins with “urn:”, as for example in “urn:NCPDP:D.0:P1:610674:000000000000-0000-0000-0000-00000000”, then it is referencing an electronic data standard specification with five segments of text separated by colons; (1) the first segment after the prefix “urn:” being the organization that develops the standard (e.g., “NCPDP”), (2) the second segment being the standard version (e.g. “D.0”), (3) the third segment being the transaction (e.g. “P1”), (4) the fourth being destination address, such as a BIN number (e.g., “610674”), and (5) the fifth segment being the id of a REMS material document which provides instructions for how to carry out the transaction

24 [RESERVED]

25 [RESERVED]

26 [RESERVED]

27 [RESERVED]

28 Blanket No Changes Certification of Product Listing Data

The following data elements are being collected in the Blanket No Changes Certification of Product Listing Data:

28.1 Header

28.1.1 Document type

```
<document>
  <code code="86445-4"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="BLANKET NO CHANGES CERTIFICATION OF PRODUCT LISTING"/>
```

Validation Procedures

28.1.1.1 Document type is “Blanket No Changes Certification of Product Listing” (86445-4).

28.1.1.2 The effective time year matches the current year.

28.1.1.3 There is no title

28.1.1.4 If a document with the same set id as the one in this file has been previously submitted, then the document type is the same.

28.1.1.5 “Blanket No Changes Certification of Product Listing” documents are submitted during the time frame October 1st through December 31st of each year.

28.1.2 Establishment Information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- manufacturer, no data here -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant, no data here -->
            <assignedEntity>
              <assignedOrganization> <!-- establishment -->
                <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
                <name>Establishment Name</name>
```

Validation Procedures

28.1.2.1 There are one or more establishment(s).

28.1.2.2 The establishment id (DUNS Number) has been submitted in a document of type *Establishment Registration* (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a

document of type *No Change Notification* (53410-7) between October 1st and December 31st of the previous or the current year.

28.1.2.3 Establishment has one id element, the DUNS number, and name as in Section 2.1.5.

28.1.2.4 The most recent Establishment Registration document for this establishment is not inactivated by an FDA Agency Initiated Compliance Action.

28.1.3 NDC/ISBT Product Codes

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- manufacturer, no data here -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant, no data here -->
            <assignedEntity>
              <assignedOrganization> <!-- establishment -->
    </performance>
    <actDefinition>
      <product>
        <manufacturedProduct classCode="MANU">
          <manufacturedMaterialKind>
            <code code="NDC/ISBT Product Item Code"
              codeSystem="2.16.840.1.113883.6.69"/>

```

Validation Procedures

28.1.3.1 Each establishment is linked to at least one NDC product code or ISBT code referenced in this document

28.1.3.2 Each NDC product code or ISBT code is linked to an establishment in this document.

28.1.3.3 There are one or more establishments.

28.1.3.4 There is no act definition code.

28.1.3.5 With the exception of the NDC product codes or ISBT codes for the inner components of kits (co-packaged products), there are one or more NDC product codes or ISBT codes.

28.1.3.6 Code system is 2.16.840.1.113883.6.69 (NDC) or 2.16.840.1.113883.6.18 (ISBT).

28.1.3.7 Each product item code (NDC or ISBT) mentioned in this *Blanket No Changes Certification of Product Listing* (86445-4) file has been previously submitted in a drug/biological product listing file with a marketing status of “active”.

- 28.1.3.8 The current version of the previously submitted drug/biological product listing file for this NDC or ISBT product item code conforms to current validation procedures.
- 28.1.3.9 The NDC product code in a *Blanket No Changes Certification of Product Listing* (86445-4) may not have been previously included in an *OTC Animal Drug Label* (50577-6), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type B Medicated Feed Animal Drug Label* (50574-3), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Prescription Animal Drug Label* (50578-4), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), or *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5).
- 28.1.3.10 If the drug listing file associated with this NDC has been identified as having a listing deficiency, then it cannot be re-certified; the deficiency must be corrected first. Please contact eDRLS@fda.hhs.gov for additional details.
- 28.1.3.11 Each establishment DUNS Number associated with the product item code via its listing file has been submitted in a document of type ‘*Establishment Registration*’ (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a document of type “*No Change Notification*” (53410-7) between October 1st and December 31st of the previous or the current year.
- 28.1.3.12 The NDC product code in this *Blanket No Changes Certification of Product Listing* (86445-4) file may not have been previously included in a document of type *Bulk Ingredient* (53409-9) with the marketing category of *Bulk Ingredient for Animal Drug Compounding* (C98252).
- 28.1.3.13 The current version of the previously submitted drug/biological product listing file for this NDC or ISBT product item code may not be implicated in an FDA-Initiated Compliance Action – Drug Listing Inactivation with any open compliance actions.
- 28.1.3.14 The NDC or ISBT product item code has been listed as the top-level product in a listing file on or after January 1st of the previous year, or certified in a *Blanket No Changes Certification of Product Listing* (86445-4) file on or after October 1st but on or before December 31st of the previous year.
- 28.1.3.15 The product listing’s labeler DUNS number has been associated with the NDC labeler code segment of the product through the most recent labeler code request file.

28.1.4 Authorized Agent

```

<document>
  <author> .../
  <legalAuthenticator>
    <assignedEntity>
      <representedOrganization>
        <id extension="Authorized Agent's DUNS Number"
          root="1.3.6.1.4.1.519.1"/>
        <name>Authorized Agent Company Name</name>
      <contactParty>
        <telecom value="tel:+1-301-241-4445"/>
        <telecom value="mailto:authorized.agents@usagents.com"/>
      <contactPerson>
        <name>Name of Authorized Agent's Contact Person</name>
    </assignedEntity>
  </legalAuthenticator>
</document>

```

Validation Procedures

28.1.4.1 There is one Authorized Agent

28.1.4.2 There is one id, (the DUNS number), and name are as in Section 2.1.5.

28.1.4.3 There is a contact party's name as in Section 2.1.8.

28.1.4.4 There is a telephone number and email address.

28.2 Body - Empty

Use an empty document body:

```

<document>
  <component>
    <structuredBody/>
  </component>
</document>

```

or

```

<document>
  <component>
    <nonXMLBody>
      <text/>
    </nonXMLBody>
  </component>
</document>

```

28.2.1.1 The document body is empty

29 Human and Animal Salvaged Drug Products

29.1 Header

29.1.1 Document type

The document type can be any of the human and animal or biologic drug products listing document types. The salvaged drug product file is not distinguished by a certain document type, but by the fact that salvage establishments and salvaged lot numbers are mentioned inside the document.

```
<document>
  <code code="50578-4"
        displayName="PRESCRIPTION ANIMAL DRUG LABEL"
        codeSystem="2.16.840.1.113883.6.1"/>
```

Validation Procedures

29.1.1.1 Document type is *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *OTC Animal Drug Label* (50577-6), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type B Medicated Feed Animal Drug Label* (50574-3), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Plasma Derivative* (60683-0), *Prescription Animal Drug Label* (50578-4), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *Standardized Allergenic* (60682-2), *Vaccine Label* (53404-0), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), or *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5).

29.1.1.2 The effective time year matches the current year.

29.1.1.3 There is title

29.1.1.4 If a document with the same set id as the one in this file has been previously submitted, then the document type is the same.

29.1.2 Establishment Information

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- manufacturer, no data here -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant, no data here -->
            <assignedEntity>
<assignedOrganization> <!-- establishment -->
  <id extension="DUNS Number" root="1.3.6.1.4.1.519.1"/>
  <name>Establishment Name</name>

```

Validation Procedures

29.1.2.1 There is one establishment.

29.1.2.2 There is no other establishment.

29.1.2.3 Establishment has one id element, the DUNS number, and name as in Section 2.1.5.

29.1.2.4 The establishment id (DUNS Number) has been submitted in a document of type “*Establishment Registration*” (51725-0) on or after October 1st of the previous year, or, if earlier, that Establishment Registration has been followed by a document of type “*No Change Notification*” (53410-7) between October 1st and December 31st of the previous or the current year.

29.1.3 Business operation

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- manufacturer, no data here -->
        <assignedEntity>
          <assignedOrganization> <!-- registrant, no data here -->
            <assignedEntity>
              <assignedOrganization> <!-- establishment -->
<performance>
  <actDefinition>
    <code code="C70827"
      codeSystem="2.16.840.1.113883.3.26.1.1"
      displayName="SALVAGE"/>
  </actDefinition>

```

Validation Procedures

29.1.3.1 There are one or more establishment operation details (performance act definitions).

29.1.3.2 There is one business operation, salvage (C70827).

29.1.3.3 If have one salvage operation, then all operations are salvage.

29.1.3.4 There is act definition code.

29.1.3.5 Code system is 2.16.840.1.113883.3.26.1.1

29.1.3.6 Display name matches the code

29.2 Body

29.2.1.1 If the document type is *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *OTC Animal Drug Label* (50577-6), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type B Medicated Feed Animal Drug Label* (50574-3), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Plasma Derivative* (60683-0), *Prescription Animal Drug Label* (50578-4), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *Standardized Allergenic* (60682-2), *Vaccine Label* (53404-0), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), or *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), then the document contains data elements section as above.

29.2.1.2 Value of effective time is same as value of effective time in document information.

29.2.2 Lot number

The label lot, or final container lot is the instance of the product, a portion of the fill lot that is portioned out into individual containers.

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance>
      <member><!-- LABEL LOT -->
        <memberProductInstance>
          <id root="{Label Lot ID root OID}" extension="{Label Lot ID}"/>
          <expirationTime>
            <high value="20110417"/>
          </expirationTime>
        </memberProductInstance>
      </member>
    </productInstance>
  </instanceOfKind>
</manufacturedProduct>
```

Validation Procedures

- 29.2.2.1 If the lot number is included *Bulk Ingredient* (53409-9), *Bulk Ingredient – Animal Drug* (81203-2), *Cellular Therapy* (60684-8), *Drug for Further Processing* (78744-0), *Human OTC Drug Label* (34390-5), *Human Prescription Drug Label* (34391-3), *License Blood Intermediates/Paste Label* (53407-3), *Licensed Minimally Manipulated Cells Label* (53408-1), *Licensed Vaccine Bulk Intermediate Label* (53406-5), *Non-Standardized Allergenic Label* (53405-7), *OTC Animal Drug Label* (50577-6), *OTC Type A Medicated Article Animal Drug Label* (50576-8), *OTC Type B Medicated Feed Animal Drug Label* (50574-3), *OTC Type C Medicated Feed Animal Drug Label* (50573-5), *Plasma Derivative* (60683-0), *Prescription Animal Drug Label* (50578-4), *Recombinant Deoxyribonucleic Acid Construct Label* (78745-7), *Intentional Animal Genomic Alteration Label* (101437-2), *Standardized Allergenic* (60682-2), *Vaccine Label* (53404-0), *VFD Type A Medicated Article Animal Drug Label* (50575-0), *VFD Type B Medicated Feed Animal Drug Label* (50572-7), *VFD Type C Medicated Feed Animal Drug Label* (50571-9), or *Animal Cells, Tissues, and Cell and Tissue Based Product Label* (98075-5), then the only business operation is salvage (C70827.)
- 29.2.2.2 There is one or more label lot elements
- 29.2.2.3 The lot has an id, and the general rules for lot numbers apply.
- 29.2.2.4 There is an id extension with the reported alphanumeric lot number string
- 29.2.2.5 Lot number string can contain digits, upper case letters and the characters “-” and “/”.
- 29.2.2.6 There is a globally unique root OID
- 29.2.2.7 If the product item code is an NDC, then the globally unique root OID is formed by using the fixed prefix "1.3.6.1.4.1.32366.1.2.10." followed by the full 10-digit NDC code represented as a number without dashes and with initial zeroes from the labeler code segment removed (e.g., "0001-0123-04" becomes 1012304).
- 29.2.2.8 If the product item code is an ISBT 128 code, then the globally unique root OID is formed by using the fixed prefix “1.3.6.1.4.1.32366.1.2.13.” followed by a decimal number value for the ISBT 128 facility identification number followed by a period “.” and a decimal number value for the ISBT 128 product code, both interpreted as a base 36 number with the digits 0-9 and A-Z, with the letter digits having the value of 9 added to the ordinal letter position (A: 1 + 9 = 10, B = 2 + 9 = 11, ..., Z = 26 + 9 = 35), and ending with a period “.” and the 3rd segment of the ISBT 128 package item code without leading zeroes; e.g., ISBT 128 product item code “W0123-E0404-03” with facility identification number “W0123”

interpreted in base 36: $W = 23 + 9 = 32 \times 36 + 0) \times 36) + 1) \times 36 + 2) \times 36 + 3 = 53749083$, and ISBT 128 product code “E0404” interpreted in base 36: $E = 5 + 9 = 14 \times 36 + 0) \times 36 + 4) \times 36 + 0) \times 36 + 4 = 23519812$, and 3rd segment “03” without zeroes, resulting in “1.3.6.1.4.1.32366.1.2.13.53749083.23519812.3”.

29.2.2.9 There is an expiration time with a high boundary.

29.2.2.10 Expiration time has at least the precision of month in the format YYYYMM

29.2.3 Container Data Elements

```
<manufacturedProduct>
  <instanceOfKind>
    <productInstance>
      <member><!-- LABEL LOT -->
        <memberProductInstance>

<asContent>
  <quantity>
    <numerator value="2" unit="mL"/>
    <denominator value="1" unit="1"/>
  </quantity>
  <container>
    <code code="1234-5678-01" codeSystem="2.16.840.1.113883.6.69"/>
    <formCode code="C43169" displayName="bottle"
      codeSystem="2.16.840.1.113883.3.26.1.1"/>
  </container>
```

Validation Procedures

29.2.3.1 There is a container reference.

29.2.3.2 There is a quantity with a numerator and denominator.

29.2.3.3 Numerator has a value greater than zero and a unit.

29.2.3.4 Numerator unit matches the dosing specification unit.

29.2.3.5 Denominator has value 1 and either no unit or unit “1”

29.2.3.6 The container form code and quantity is the same as the package of the product as described in the listing for the package NDC.

29.2.3.7 There is a container packaged product code

29.2.3.8 Container packaged product item code is an NDC or based on ISBT-128.

29.2.3.9 There is a form code and display name

29.2.3.10 Code system for form code is 2.16.840.1.113883.3.26.1.1

29.2.3.11 Display name matches form code

30 FDA-Initiated Compliance Action – Drug Listing Inactivation

30.1 Header

30.1.1 Document type

```
<document>
  <code code="89600-1" codeSystem="2.16.840.1.113883.6.1"
    displayName="FDA-Initiated Compliance Action Drug Registration and
    Drug Listing Inactivation"/>
```

Validation Procedures

30.1.1.1 The document type is *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation (89600-1)* or *FDA-Initiated Compliance Action – Drug Registration and Listing Inactivation - Animal Drug (99282-6)*.

30.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

30.1.2 Author information

FDA-initiated compliance action inactivation data is maintained by FDA:

```
<author>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

Validation Procedures

30.1.2.1 Author information for drug listing inactivation is as above

30.1.2.2 The author is FDA.

30.1.2.3 There are no other author elements than id and name.

30.1.3 Reference Document

The subject of a drug listing inactivation is a referenced listing SPL document.

```

<document>
  ...
  <author .../>
  <relatedDocument typeCode="SUBJ">
    <relatedDocument>
      <setId root="Listing SPL Document Set Id (UUID)"/>
    </relatedDocument>
  </relatedDocument>
  <component .../>
</document>

```

Validation Procedures

- 30.1.3.1 There is one reference document specified.
- 30.1.3.2 Type code attribute is as above.
- 30.1.3.3 There is no document id
- 30.1.3.4 There is a set id
- 30.1.3.5 Set id is a GUID
- 30.1.3.6 Reference document set id is the set id of a drug listing document.
- 30.1.3.7 If a drug listing inactivation file for the same reference document's set id has been previously submitted, then it is a prior version of this drug listing inactivation document with the same set id.
- 30.1.3.8 If a document with the same set id has been previously submitted, then it is associated with the same reference labeling set id.
- 30.1.3.9 If the document type is *FDA-Initiated Compliance Action Drug Registration And Drug Listing Inactivation* (89600-1), then the reference document set id is the set id of a human drug listing document.
- 30.1.3.10 If the document type is *FDA-Initiated Compliance Action Drug Registration And Drug Listing Inactivation - Animal Drug* (99282-6), then the reference document set id is the set id of an animal drug listing document.

30.2 Body

```

<document>
  ...
  <author .../>
  <relatedDocument typeCode="SUBJ"/>
  <component>
    <structuredBody>
      <component>
        <section>
          <id root="c7b4aed4-55c3-4258-a655-352ccf023473"/>
          <code code="48780-1" codeSystem="2.16.840.1.113883.6.1"
            displayName="SPL PRODUCT DATA ELEMENTS SECTION"/>
          <title/>
          <text/>
          <effectiveTime value="20160405"/>
          <subject>
            <manufacturedProduct>
              <manufacturedProduct>
                <asContent/>

```

Validation Procedures

30.2.1.1 There is one SPL Product Data Elements Section (48780-1.)

30.2.1.2 There are no subsections.

30.2.1.3 Validation procedures 2.2.1.2– 2.2.1.10 are applicable to *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation* (89600-1), and *FDA-Initiated Compliance Action – Drug Registration and Listing Inactivation - Animal Drug* (99282-6).

30.2.1.4 There is no product code or any other product data elements except one flat list of packages (asContent elements)

30.2.2 Inactivated or Reactivated Listing’s NDC(s)

```

<manufacturedProduct>
  <asContent .../>
  <asContent .../>
  <asContent>
    <containerPackagedProduct>
      <code code="NDC Package Code" codeSystem="2.16.840.1.113883.6.69"/>

```

Validation Procedures

30.2.2.1 There is at least one product package with item code.

30.2.2.2 Package item code system is NDC (2.16.840.1.113883.6.69).

30.2.2.3 NDC contains three segments divided by hyphens

30.2.2.4 The NDC matches an NDC contained in the related listing document previously submitted, except if an effective time high value (reactivation date) is present for that NDC.

30.2.2.5 The same NDC is not mentioned more than once.

30.2.2.6 Product package has no other data elements than the package item code (NDC).

30.2.3 Compliance Action – Inactivation and Reactivation Status

The compliance action is the inactivation of a listing of a particular package. It has an effective time with low (inactivation start) and high (inactivation end) date. If there is no inactivation end date, the inactivation is sustained, when there is an inactivation end date, the package is reactivated by FDA.

Each package that is being inactivated is listed directly under the manufacturedProduct regardless of intermediary packages that may exist in the listing file.

```
<asContent>
  <containerPackagedProduct>
    <code code="NDC Package Code" codeSystem="2.16.840.1.113883.6.69"/>
  </containerPackagedProduct>
  <subjectOf>
    <action>
      <code code="C162847" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="Inactivated"/>
      <effectiveTime>
        <low value="20180115"/>
      </effectiveTime>
    </action>
  </subjectOf>
```

Validation Procedures

30.2.3.1 There is one compliance action for each package.

30.2.3.2 Code is from the Regulatory Action list and display name matches the code.

30.2.3.3 There is an effective time with at least a low value (inactivation date)

30.2.3.4 The effective time low (inactivation date) and high boundary (reactivation date) have at least the precision of day in the format YYYYMMDD

30.2.3.5 If there is an effective time high value (reactivation date), then it is not less than the low value (inactivation date).

30.2.3.6 If there is an effective time high value (reactivation date), then it is not later than the document effective time.

30.2.3.7 If inactivation ending date is not present in the previous version of the file then the product package can not be dropped from this file, except if the NDC has also been dropped from the most recent version of the referenced listing file.

31 FDA-Initiated Compliance Action – Establishment Registration Inactivation

31.1 Header

31.1.1 Document type

```
<document>
  <code code="89600-1" codeSystem="2.16.840.1.113883.6.1"
    displayName="FDA-Initiated Compliance Action Drug Registration and
    Drug Listing Inactivation"/>
```

Validation Procedures

31.1.1.1 The document type is *FDA-Initiated Compliance Action Drug Registration and Drug Listing Inactivation (89600-1)* or *FDA-Initiated Compliance Action – Drug Registration and Listing Inactivation - Animal Drug (99282-6)*.

31.1.1.2 If a document with the same set id has been previously submitted, then it is of the same type.

31.1.2 Author information

FDA-initiated compliance action inactivation data is maintained by FDA:

```
<author>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

Validation Procedures

31.1.2.1 Author information for establishment registration inactivation is as above.

31.1.2.2 The author is FDA.

31.1.2.3 There are no other author elements than id and name.

31.1.3 Inactivated or Reactivated Establishments

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization>
```

```
<assignedEntity> <!-- establishment -->
  <assignedOrganization>
    <id root="1.3.6.1.4.1.519.1" extension="Establishment DUNS"/>
  </assignedOrganization>
  <subjectOf>
    <characteristic>
      <code code="C162847" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="Inactivated"/>
    </characteristic>
  </subjectOf>
  <effectiveTime .../>
```

Validation Procedures

- 31.1.3.1 There is an empty registrant level leading to the establishment.
- 31.1.3.2 The registrant level has no other element aside from the assignedEntity leading to the establishment
- 31.1.3.3 There are one or more establishments.
- 31.1.3.4 The establishment level has no other element aside from the assignedOrganization leading to the establishment and subjectOf to the compliance action (characteristic).
- 31.1.3.5 Establishment is identified by one id, the DUNS Number.
- 31.1.3.6 DUNS number has root 1.3.6.1.4.1.519.1
- 31.1.3.7 DUNS number has a 9-digit extension
- 31.1.3.8 There is no other element besides the id for the DUNS Number.
- 31.1.3.9 The establishment DUNS Number occurs only once in this file
- 31.1.3.10 The establishment id (DUNS Number) has been submitted in a related document of type “*Establishment Registration*” (51725-0).
- 31.1.3.11 If the document type is *FDA-Initiated Compliance Action Drug Registration And Drug Listing Inactivation* (89600-1), then there is a business operation except *Medicated Animal Feed Manufacture* (C84635) and *Outsourcing Animal Drug Compounding* (C122061) in the previously submitted *Establishment Registration* (51725-0).
- 31.1.3.12 If the document type is *FDA-Initiated Compliance Action Drug Registration And Drug Listing Inactivation - Animal Drug* (99282-6), then there is a business operation *Analysis* (C25391), *API Manufacture* (C82401), *Label* (C84732), *Manufacture* (C43360), *Medicated Animal Feed Manufacture* (C84635), *Outsourcing Animal Drug Compounding* (C122061), *Pack* (C84731), *Particle Size Reduction* (C84386), *Positron Emission Tomography Drug Production*

(C91403), *Relabel* (C73607), *Repack* (C73606), *Salvage* (C70827), *Sterilize* (C84382), or *Transfill* (C125710) in the previously submitted Establishment Registration (51725-0).

31.1.4 Compliance Action – Inactivation and Reactivation Status

The compliance action is the inactivation of the registration of a particular establishment. It has an effective time with low (inactivation start) and high (inactivation end) date. If there is no inactivation end date, the inactivation is sustained, when there is an inactivation end date, the establishment is reactivated by FDA.

```
<assignedEntity> <!-- establishment level -->
  <assignedOrganization ... DUNS .../>
  <subjectOf>
    <characteristic>
      <code code="C162847" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="Inactivated"/>
      <effectiveTime>
        <low value="20180115"/>
      </effectiveTime>
    </characteristic>
  </subjectOf>
```

Validation Procedures

- 31.1.4.1 There is one compliance action for each establishment.
- 31.1.4.2 Code is from the Regulatory Action list and display name matches the code.
- 31.1.4.3 There is an effective time with at least a low value (inactivation date)
- 31.1.4.4 The effective time low (inactivation date) and high boundary (reactivation date) have at least the precision of day in the format YYYYMMDD
- 31.1.4.5 If there is an effective time high value (reactivation date), then it is not less than the low value (inactivation date).
- 31.1.4.6 If there is an effective time high value (reactivation date), then it is not later than the document effective time.

31.1.5 Reference Document

The subject of an establishment registration inactivation is a referenced establishment registration SPL document.

```
<document>
  ...
  <author .../>
  <relatedDocument typeCode="SUBJ">
    <relatedDocument>
      <setId root="Listing SPL Document Set Id (UUID)"/>
    </relatedDocument>
  </relatedDocument>
  <component .../>
</document>
```

Validation Procedures

31.1.5.1 There is one reference document specified.

31.1.5.2 Type code attribute is *subject* (SUBJ).

31.1.5.3 There is no document id

31.1.5.4 There is a set id

31.1.5.5 Set id is a GUID

31.1.5.6 Reference document set id is the set id of an establishment registration document.

31.1.5.7 If an establishment registration inactivation file for the same reference document's set id has been previously submitted, then it is a prior version of this establishment registration inactivation document with the same set id.

31.1.5.8 If a document with the same set id has been previously submitted, then it is associated with the same reference labeling set id.

31.2 Body - Empty

Use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>
  <component>
    <nonXMLBody>
      <text/>
```

Validation Procedures

31.2.1.1 The document body is empty

32 Drug Interactions Indexing

32.1 Header

32.1.1 Document type

```
<document>
  <code code="93723-5" codeSystem="2.16.840.1.113883.6.1"
    displayName="INDEXING - DRUG INTERACTIONS"/>
```

Procedures

32.1.1.1 Document code is as above

32.1.1.2 If a document with the same set id has been previously submitted then it is of the same type.

32.1.2 Author information

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

32.1.2.1 Drug Interaction indexing content is maintained by FDA:

32.1.2.2 Author information for drug interactions indexing is as one of the above

32.1.3 Reference Labeling

The information about a Drug Interaction is derived from Reference Labeling. The Reference Labeling is found in the SPL document submitted by the innovator, or, if the innovator has stopped marketing the product, by a designated generic manufacturer. The SPL document containing the Reference Labeling is specified using its setId as follows:

```
<document>
  ...
  <author .../>

  <relatedDocument typeCode="DRIV">
    <relatedDocument>
      <setId root="20d9b74e-e3d8-4511-9df9-cec2087372fc"/>
    </relatedDocument>
  </relatedDocument>

  <component .../>
</document>
```

Validation Procedures

32.1.3.1 There is reference labeling specified.

32.1.3.2 Type code attribute is as above.

32.1.3.3 There is no document id

32.1.3.4 There is a set id

32.1.3.5 Set id is a GUID

32.1.3.6 Reference labeling set id is the set id of a drug listing document.

32.1.3.7 If a drug interactions indexing file for the same reference labeling set id has been previously submitted, then it is a prior version of this indexing document with the same set id.

32.1.3.8 If a document with the same set id has been previously submitted, then it is associated with the same reference labeling set id.

32.2 SPL Body

```
<document> <!-- SPL header material -->
  <component>
    <structuredBody> <!-- SPL body material -->
      <component>
        <section>
```

Validation Procedures

32.2.1.1 The document body contains one or more sections

32.2.2 Sections

The interactions are grouped under the section headings where they have been mentioned.

Validation Procedures

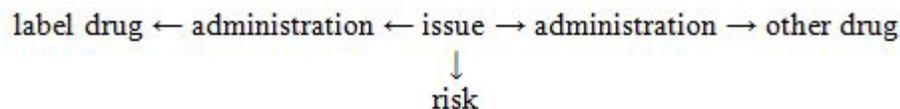
```
<section>
  <id root="dfe16f30-66af-4333-acd7-f6fa80d3d9cd"/>
  <code code="34068-7" displayName="Dosage & Administration"
    codeSystem="2.16.840.1.113883.6.1"/>
  <effectiveTime value="20200529"/>
  <subject2>
    <substanceAdministration>
      <subjectOf>
        <issue>
```

32.2.2.1 Validation procedures for sections are as in Section 2.2.1 of this document.

32.2.2.2 Each section has one or more interactions.

32.2.3 Interaction

An drug interaction is an issue related to the administration of the reference label drug document/section/subject2/substanceAdministration and then on the other hand is related to the administration of another substance (drug). So the pattern is:



The labeled drug, which is the “consumable” of the first substance administration is only implicitly given by the product(s) which are the subject of the reference label.

The administration of the “other” drug is also called the “contributing factor” to the issue with the labeled drug.

```

<substanceAdministration>
  <subjectOf>
    <issue>
      <code code="C54708" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="INTERACTION"/>
      <risk .../>
    <subject>
      <substanceAdministrationCriterion>
        <consumable .../>
  
```

Validation Procedures

32.2.3.1 There is a code for interaction (C54708).

32.2.3.2 Code system is 2.16.840.1.113883.3.26.1.1.

32.2.3.3 Display name matches the code.

32.2.4 Contributing Factor

In drug-drug interactions, the contributing factor is the administration of another drug. The other drug is “consumed” when administered, hence it is a “consumable”. The other drug can be specified as any “administrable material” usually on the level of a specific drug substance (ingredient), specified as a UNII code, or as a pharmacologic class (see Section 8).

```

<issue>
  <subject>
    <substanceAdministrationCriterion>
      <consumable>
        <administrableMaterial>
          <administrableMaterialKind>
            <code code="80061L1WGD" displayName="CIMETIDINE"
              codeSystem="2.16.840.1.113883.4.9"/>

```

Validation Procedures

- 32.2.4.1 There is a contributing factor, which is a substance administration.
- 32.2.4.2 Contributing factor substance administration has a consumable
- 32.2.4.3 Code system is UNII for specific drug substance or Med-RT or MeSH for pharmacologic class.
- 32.2.4.4 If code system is UNII, then the code comes from the UNII list.
- 32.2.4.5 The UNII display name matches the code.
- 32.2.4.6 If code system is MED-RT (2.16.840.1.113883.6.345), then the code comes from Med-RT subset for pharmacologic class indexing.
- 32.2.4.7 Med-RT display name matches the code.
- 32.2.4.8 If code system is MeSH (2.16.840.1.113883.6.177), then the code comes from the MeSH subset for pharmacologic class indexing.
- 32.2.4.9 MeSH display name matches the code.

32.2.5 Consequence (Risk)

There are 3 kinds of interactions with regard to the consequence:

1. Pharmacodynamic interactions, where the consequence is some adverse condition (medical problem).
2. Pharmacokinetic interactions, where the consequence is a change in distribution, metabolism, or elimination.
3. Unspecified interactions, where the exact consequence is not described.

All three kinds of interactions have the same interaction/code, but are distinguished by the the kind of consequence observation code, if any.

```

<issue>
  <code code="C54708" codeSystem="2.16.840.1.113883.3.26.1.1"
    displayName="INTERACTION"/>
  <risk>
    <consequenceObservation>
      <code code="C54386" codeSystem="2.16.840.1.113883.3.26.1.1"
        displayName="Pharmacokinetic effect"/>
      <value code="C54355" displayName="INCREASED DRUG LEVEL"
        codeSystem="2.16.840.1.113883.3.26.1.1" xsi:type="CE"/>
    
```

Validation Procedures

- 32.2.5.1 There may be one or more consequences or none at all (unspecified interactions).
- 32.2.5.2 There is a code for type of consequence, either *pharmacokinetic effect* (C54386, with code system 2.16.840.1.113883.3.26.1.1) or *medical problem* (44100-6, of code system 2.16.840.1.113883.6.1).
- 32.2.5.3 Display name for type of consequence matches the code
- 32.2.5.4 There is a consequence observation value.
- 32.2.5.5 Value xsi:type is as above
- 32.2.5.6 If consequence observation code is *pharmacokinetic effect* (C54386), then the consequence value comes from Pharmacokinetic Effect List.
- 32.2.5.7 Consequence value (Pharmacokinetic Effect) display name matches the code.
- 32.2.5.8 If consequence observation code is *medical problem* (44100-6), then the consequence value code system is SNOMED CT (2.16.840.1.113883.6.96).
- 32.2.5.9 If consequence value code system is SNOMED CT (2.16.840.1.113883.6.96), then the code is 6 to 18 digits.
- 32.2.5.10 If consequence value code system is SNOMED CT (2.16.840.1.113883.6.96), then the display name is the formal SNOMED CT name (fully specified name) with the parenthesis indicating the kind of concept (finding, disorder, event).

33 National Clinical Trials Number Indexing

33.1 Header

33.1.1 Document type

```
<document>
  <code code="93372-1" codeSystem="2.16.840.1.113883.6.1"
    displayName="INDEXING - NATIONAL CLINICAL TRIALS NUMBER"/>
```

Procedures

33.1.1.1 Document code is as above

33.1.1.2 If a document with the same set id has been previously submitted then it is of the same type.

33.1.2 Author information

```
<author>
  <time/>
  <assignedEntity>
    <representedOrganization>
      <id root="1.3.6.1.4.1.519.1" extension=""/>
      <name>Food and Drug Administration</name>
```

33.1.2.1 NCT Indexing content is maintained by FDA:

33.1.2.2 Author information for NCT Indexing is as one of the above

33.1.3 Reference Labeling

The NCT Indexing information is derived from Clinical Studies Section (34092-7) of Reference Labeling. The Reference Labeling is found in the SPL document submitted by the innovator, or, if the innovator has stopped marketing the product, by a designated generic manufacturer. The SPL document containing the Reference Labeling is specified using its setId as follows:

```
<document>
  ...
  <author .../>

  <relatedDocument typeCode="DRIV">
    <relatedDocument>
      <setId root="20d9b74e-e3d8-4511-9df9-cec2087372fc"/>
    </relatedDocument>
  </relatedDocument>

  <component .../>
</document>
```

Validation Procedures

33.1.3.1 There is reference labeling specified.

33.1.3.2 There is no document id

33.1.3.3 There is a set id

33.1.3.4 Set id is a GUID

33.1.3.5 Reference labeling set id is the set id of a drug listing document.

33.1.3.6 If a NCT indexing file for the same reference labeling set id has been previously submitted, then it is a prior version of this indexing document with the same set id.

33.1.3.7 If a document with the same set id has been previously submitted, then it is associated with the same reference labeling set id.

33.2 Body

```
<section>
  <id root=""/>
  <code code="48779-3" codeSystem="2.16.840.1.113883.6.1"
    displayName="SPL Indexing Data Elements Section"/>
  <effectiveTime value=""/>
```

33.2.1.1 If the document type is *INDEXING - NATIONAL CLINICAL TRIALS NUMBER* (93372-1), then the document contains one SPL Indexing Data Elements Section (48779-3) as above.

33.2.1.2 Value of effective time is same as value of effective time in document information.

33.2.2 National Clinical Trials Number

```
<subject2>
  <substanceAdministration>
    <componentOf>
      <protocol>
        <id root="2.16.840.1.113883.3.1077" extension="NCT00005094"/>
      </protocol>
    </componentOf>
  </substanceAdministration>
</subject2>
```

33.2.2.1 There is one or more NCT-References.

33.2.2.2 NCT Number has the prefix “NCT” followed by an 8-digit number.

33.2.2.3 NCT-Reference id root is 2.16.840.1.113883.3.1077.

34 [RESERVED]

35 Cosmetic Facility Registration

Cosmetic facility registrations have only header information with a single registrant organization and a facility to be registered or whose registration is to be updated.

Aside from the proper *Cosmetic Facility Registration* document type, four other document types can be used for cosmetic facility registration submissions, i.e., the *Cosmetic Facility Registration - Amendment*, *Cosmetic Facility Registration - Abbreviated Renewal*, *Cosmetic Facility Registration - Cancellation*, and *Cosmetic Facility Registration - Biennial Renewal*

Table 9: Cosmetic Facility Registration Document Types

| Code | Display Name | |
|----------|--|--|
| 103573-2 | Cosmetic Facility Registration | Contains facility details, initial submission. |
| X8888-1 | Cosmetic Facility Registration - Amendment | Contains facility details, update for any changes. |
| X8888-2 | Cosmetic Facility Registration - Abbreviated Renewal | Does not contain facility details, for biennial renewal if there is no change. |
| X8888-3 | Cosmetic Facility Registration - Cancellation | Does not contain facility details |
| X8888-4 | Cosmetic Facility Registration - Biennial Renewal | Contains facility details, for biennial renewal that is not abbreviated. |

35.1 Header

35.1.1 Document type

```
<document>
  <code code="103573-2" codeSystem="2.16.840.1.113883.6.1"
    displayName="Cosmetic Facility Registration"/>
```

Validation Procedures

35.1.1.1 Document type is *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1), *Cosmetic Facility Registration - Abbreviated Renewal* (X8888-2), *Cosmetic Facility Registration - Cancellation* (X8888-3), and *Cosmetic Facility Registration - Biennial Renewal* (X8888-4).

35.1.1.2 The effective time year matches the current year.

35.1.1.3 There is no title.

35.1.1.4 For a *Cosmetic Facility Registration – Amendment* (X8888-1), *Cosmetic Facility Registration – Abbreviated Renewal* (X8888-2), *Cosmetic Facility Registration – Cancellation* (X8888-3), and *Cosmetic Facility Registration – Biennial Renewal* (X8888-4), the set id in this document is the same set id included in a

previously submitted *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration – Amendment (X8888-1)*, or *Cosmetic Facility Registration – Biennial Renewal (X8888-4)* with information about the facility.

35.1.1.5 If a document with the same set id as the one in this file has been previously submitted, then the document type of the previously submitted file is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration – Amendment (X8888-1)*, or *Cosmetic Facility Registration – Biennial Renewal (X8888-4)*.

35.1.1.6 *Cosmetic Facility Registration – Biennial Renewal (X8888-4)* and *Cosmetic Facility Registration – Abbreviated Renewal (X8888-2)* documents are submitted every 2 years, i.e., the year of their submission is more than one year after the previous submission of any kind of *Cosmetic Facility Registration* document.

35.1.2 Authorized Agent Information (Additional Contact)

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <!-- manufacturer, may be pass-through -->
        <assignedEntity>
          <assignedOrganization> <!-- authorized agent -->
          <id root="1.3.6.1.4.1.519.1" extension=""/>
          <name>Cosmetic Company</name>
          <contactParty>
```

Validation Procedures

35.1.2.1 If the document type is *Cosmetic Facility Registration - Abbreviated Renewal (X8888-2)*, and *Cosmetic Facility Registration - Cancellation (X8888-3)*, then there is no authorized agent (additional contact).

35.1.2.2 If the document type is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration - Amendment (X8888-1)*, or *Cosmetic Facility Registration – Biennial Renewal (X8888-4)*, then there may be authorized agent information (additional contact).

35.1.2.3 [RESERVED]

35.1.2.4 [RESERVED]

35.1.2.5 [RESERVED]

35.1.2.6 There may be one contact party (additional contact) as in Section 2.1.8.

35.1.2.7 *Cosmetic Facility Registration* has no labeler information.

35.1.3 Submitter Name and Signature (Legal Authenticator)

The authorized individual may sign for the responsible organization as follows:

```
<document>
  <author .../>
  <legalAuthenticator>
    <noteText>The data and information in this submission have been
    reviewed and, to the best of my knowledge, are certified to be true and
    accurate. I agree to report changes to this information and renew as
    required under section 607 of the Federal Food, Drug, and Cosmetic
    Act.</noteText>
    <time value= ""/>
    <signatureText mediaType="text/plain">P. Bauer</signatureText>
    <assignedEntity>
      <assignedPerson>
        <name>Peter Bauer</name>
      </assignedPerson>
    </assignedEntity>
    <representedOrganization/>
```

35.1.3.1 There may be a signature (legalAuthenticator).

35.1.3.2 If present, the signature may contains a signing statement (noteText) exactly as above.

35.1.3.3 If present, there is one signatureText element.

35.1.3.4 If present, the signatureText has mediaType “text/plain” and the electronic signature in text content.

35.1.3.5 If present, the signature contains one assigned person (the signing person).

35.1.3.6 If present, assigned person has a name

35.1.3.7 If present, assigned person has only a name, no other element.

35.1.3.8 If present, the signature contains an empty representedOrganization element (the signer signs for the responsible organization).

35.1.3.9 There is an time with at least the precision of day in the format YYYYMMDD

35.1.4 Facility Information

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization><!-- registrant -->
        </assignedEntity>
```

```

<assignedOrganization><!-- facility -->
  <id extension="100000001" root="1.3.6.1.4.1.519.1"/>
  <id extension="123456" root="2.16.840.1.113883.4.82"/>
  <name>Facility Name</name>
  <addr>
    <streetAddressLine>123 Burl Road</streetAddressLine>
    <city>Dublin</city>
    <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
  </addr>
  <contactParty .../>
  <assignedEntity ... US AGENT ... />
  <assignedEntity1 ... Parent Company .../>

```

Validation Procedures

- 35.1.4.1 If the document type is *Cosmetic Facility Registration (103573-2)*, *Cosmetic Facility Registration -- Amendment (X8888-1)*, or *Cosmetic Facility Registration – Biennial Renewal (X8888-4)*, then there is one facility.
- 35.1.4.2 If the document type is *Cosmetic Facility Registration - Abbreviated Renewal (X8888-2)* or *Cosmetic Facility Registration - Cancellation (X8888-3)*, then there is no facility information.
- 35.1.4.3 Facility has one name and one or two id elements, with the first id, the DUNS number as in Section 2.1.5 but optional.
- 35.1.4.4 There is a second id (or if there is no DUNS number, the first id), the FEI with root 2.16.840.1.113883.4.82 and 7- or 10-digit extension.
- 35.1.4.5 If present, the DUNS number along with the facility name and address information match the DUNS number record in the Dun and Bradstreet database.
- 35.1.4.6 The FEI number along with the facility name and address information match the FEI number record previously assigned by the FDA.
- 35.1.4.7 Each facility has an address as in Section 2.1.6.
- 35.1.4.8 There is one contact party as in Section 2.1.8.
- 35.1.4.9 There is no assigned entity other than for US Agent.

35.1.5 Facility US Agent

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
              <assignedOrganization><!-- facility -->
                <addr>
                  <country code="IRL"
                    codeSystem="1.0.3166.1.2.3">Ireland</country>
                </addr>
            </assignedEntity>
          <assignedOrganization><!-- facility US agent -->
            <name>Simmons Reps Company</name>

            <telecom value="tel:+1-800-555-1212"/>
            <telecom value="mailto:contact@USagent.com"/>
          </assignedOrganization>
        </performance>
        <actDefinition>
          <code code="C73330" codeSystem="2.16.840.1.113883.3.26.1.1"
            displayName="United States agent"/>
        </actDefinition>
      </representedOrganization>
    </assignedEntity>
  </author>
</document>

```

Validation Procedures

35.1.5.1 If the country for the facility is not “USA”, then there is one US agent.

35.1.5.2 US agent element has code, code system and display name are as above.

35.1.5.3 If the country for the facility is "USA", then there is no US agent.

35.1.5.4 US agent has a US telephone number (see 2.1.7.3 and following).

35.1.5.5 US agent has an e-mail address which is “N/A” if there is no email.

35.1.5.6 There is at most one US Agent.

35.1.6 Parent Company

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization><!-- registrant -->
            <assignedEntity>
              <assignedOrganization><!-- facility -->
                ...
            </assignedEntity>
          <assignedOrganization><!-- parent company -->
            <name>Parent Company Name</name>
          </assignedOrganization>
        </representedOrganization>
      </assignedEntity>
    </author>
  </document>

```

35.1.6.1 If there is a parent company, there is just one name.

35.1.7 Small Business Designation

To indicate that the facility is a small business (**except those which are not exempt per section 612b of the FD&C Act**), include the following characteristic element:

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
              <assignedOrganization .../><!-- facility -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <subjectOf>
    <characteristic classCode="OBS">
      <code code="SPLSMALLBUSINESS"
        codeSystem="2.16.840.1.113883.1.11.19255"/>
      <value xsi:type="BL" value="true"/>
    </characteristic>
  </subjectOf>
```

35.1.7.1 Code and code system is as above (for SPLSMALLBUSINESS)

35.1.7.2 There is a Boolean value as above.

35.1.7.3 Value is “true”; to indicate not a small business omit the characteristic.

35.1.8 Facility Operation

Validation Procedures

35.1.8.1 There are no facility operation details (performance act definitions).

35.2 Body

If no cosmetic product listing information is included, use an empty document body:

```
<document>
  <component>
    <structuredBody/>
```

or

```
<document>
  <component>
    <nonXMLBody>
      <text/>
```

If cosmetic product information is included there is a document body with the product data element section:

```
<document>
  <component>
    <section>
      <id root="e13a985b-f706-a5c8-e8ef-73891eb1c697"/>
      <code code="48780-1"
        codeSystem="2.16.840.1.113883.6.1"
        displayName="SPL product data elements section"/>
```

Validation Procedures

35.2.1.1 If the document is a *Cosmetic Facility Registration – Abbreviated Renewal* (X8888-2), *Cosmetic Facility Registration – Cancellation* (X8888-3), then the document body is empty

35.2.1.2 If the document is a *Cosmetic Facility Registration* (103573-2), *Cosmetic Facility Registration - Amendment* (X8888-1), or *Cosmetic Facility Registration – Biennial Renewal* (X8888-4), then there is a document body.

35.2.1.3 The document body contains one section

35.2.1.4 The one section contains the product data elements

35.2.2 Cosmetic Product

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="53-000000-000001"
          codeSystem="2.16.840.1.113883.3.9848"/>
        <name>Juvenia Soft</name>
        <asSpecializedKind>
          <generalizedMaterialKind>
            <code code="01B" codeSystem="2.16.840.1.113883.6.345"
              displayName="Baby products - Lotions, oils, powders, and creams"/>
```

The cosmetic listing number is included in any update after it has been assigned subsequent to an initial cosmetic product listing submission.

Validation Procedures

35.2.2.1 There is a name, i.e., the brand name under which the cosmetic product is sold.

35.2.2.2 Markings such as ®, or ™ should not be included.

35.2.2.3 There are one or more cosmetic product category codes (asSpecializedKind element) with a code (see Section 3.4.3).

35.2.2.4 There are no other elements besides item code, name and cosmetic product type (asSpecializedKind)

35.2.3 Responsible Person (Organization)

```
<manufacturedProduct>
  <manufacturedProduct>
    ... name, cosmetic product type ...
  </manufacturedProduct>

  <manufacturerOrganization><!-- responsible person -->
    <name>Responsible Person (Organization) Name</name>
  </manufacturerOrganization>
```

Validation Procedures

35.2.3.1 There is one responsible person (organization).

35.2.3.2 Responsible person (organization) has one name.

35.2.3.3 There are no other elements besides the name.

36 Cosmetic Product Listing

Cosmetic product listings conform to 21 U.S.C. Sec. 607 as amended by the Modernization of Cosmetics Regulation Act of 2022. Three document types can be used for Cosmetic product listing, i.e., the *Cosmetic*, *Cosmetic - Update*, *Cosmetic - Abbreviated Renewal*.

Table 10: Cosmetic Listing Document Types

| Code | Display Name | |
|----------|--------------------------------|--|
| 103572-4 | Cosmetic Product Listing | Contains cosmetic product details, initial submission. |
| X8888-5 | Cosmetic – Update | Contains cosmetic product details, update for any changes. |
| X8888-6 | Cosmetic – Abbreviated Renewal | Does not contains cosmetic product details |

36.1 Header

36.1.1 Document Type

36.1.1.1 Document types is *Cosmetic Product Listing* (103572-4), *Cosmetic – Update* (X8888-5), or *Cosmetic – Abbreviated Renewal* (X8888-6).

36.1.1.2 The effective time year matches the current year.

36.1.1.3 There is no title.

36.1.1.4 For a *Cosmetic – Update* (X8888-5), *Cosmetic – Abbreviated Renewal* (X8888-6), the set id in this document is the same set id included in a previously submitted document of type *Cosmetic Product Listing* (103572-4) or *Cosmetic – Update* (X8888-5).

36.1.1.5 If a document with the same set id as the one in this file has been previously submitted, then the document type of the previously submitted file is *Cosmetic Product Listing* (103572-4) or or *Cosmetic – Update* (X8888-5).

36.1.2 Labeler (“responsible person” as per label)

```
<document>
  <code code="..." codeSystem="2.16.840.1.113883.6.1"
    displayName="..."/>
  <author>
<assignedEntity>
  <representedOrganization>
    <id extension="100000007" root="1.3.6.1.4.1.519.1"/>
    <name>Acme cosmetics company</name>
    <telecom value="tel:+1-800-123-4567"/>
  </representedOrganization>
  <contactParty>
```

```

<addr>
  <streetAddressLine>1625 29th street</streetAddressLine>
  <city>Camden</city>
  <state>NJ</state> <postalCode>08101</postalCode>
  <country code="USA" codeSystem="1.0.3166.1.2.3">USA</country>
</addr>

<telecom value="tel:+1-800-555-1213;ext=112"/>
<telecom value="mailto:Bob.Jones@acme.com"/>

<contactPerson>
  <name>Bob Jones</name>
</contactPerson>
</contactParty>

```

Validation Procedures

36.1.2.1 There is one labeler (“responsible person”), except if the document type is *Cosmetic – Abbreviated Renewal* (X8888-6).

36.1.2.2 Responsible person has one name and may have one id element, the DUNS number as in Section 2.1.5 but optional.

36.1.2.3 Responsible person has one telephone number (see 2.1.7.3 and following).

36.1.2.4 There may be one contact party (additional contact) as in Section 2.1.8.

36.1.2.5 Responsible person may have a parent company as per Section 35.1.6

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity1>
          <representedOrganization><!-- parent company -->
            <name>Parent Company Name</name>
          </representedOrganization>

```

36.1.2.6 There is no other element besides id (the labeler’s DUNS Number), name, telephone number, parent company (assignedEntity1), contact party, and registrant (see next section).

36.1.3 Registrant

Details about the responsible person (organization) and its function as manufacturer, packer, or distributor, and other facilities where the product is manufactured or processed are reached through the otherwise empty “registrant” level:

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization>

```

Validation Procedures

36.1.3.1 There is one assignedEntity/assignedOrganization element.

36.1.3.2 There is no other element besides facilities.

36.1.4 Responsible person further details

These include the type of business (manufacturer, packer, or distributor) and whether it is a small business.

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- labeler -->
      <assignedEntity>
        <assignedOrganization><!-- registrant -->
    <assignedEntity><!-- responsible person details -->
    <assignedOrganization/>
    <subjectOf>
      <characteristic classCode="OBS">
        <code code="SPLSMALLBUSINESS"
          codeSystem="2.16.840.1.113883.1.11.19255"/>
        <value xsi:type="BL" value="true"/>
      </characteristic>
    </subjectOf>
    <performance>
      <actDefinition>
        <code code="C43360"
          codeSystem="2.16.840.1.113883.3.26.1.1"
          displayName="manufacture"/>
      </actDefinition>
    </performance>
  </assignedEntity>

```

Validation Procedures

36.1.4.1 If further details about the responsible person are provided, then they are in the first assignedEntity element under the registrant level, with an empty assignedOrganization element.

36.1.4.2 There may be a small business designation as in Section 35.1.7

36.1.4.3 There may be a performance actDefinition code as above.

36.1.4.4 Code system is 2.16.840.1.113883.3.26.1.1

36.1.4.5 Code is manufacture (C43360), pack (C84731), or distribute (C201565)

36.1.4.6 Display name matches the code.

36.1.4.7 Responsible person further details has no operation product link.

36.1.4.8 Responsible person further details has at least a small business indicator or a type of business code.

36.1.4.9 Responsible person further details has no other information besides a small business indicator or a type of business code.

36.1.5 Facility information

All other assignedEntity elements under the registrant are facilities, with only an id (the FEI) if the facility was required to be registered:

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- labeler -->
        <assignedEntity>
          <assignedOrganization><!-- registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization><!-- Facility -->
      <id extension="123456" root="2.16.840.1.113883.4.82"/>
    </assignedOrganization>
  </assignedEntity>
</document>
```

or with a name or address or FEI if, as a small business, the facility was not required for being registered and has not been registered:

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- labeler -->
        <assignedEntity>
          <assignedOrganization><!-- registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization><!-- Facility -->
      <name>Nimble Cosmetics Maker</name>
      <addr>
        <streetAddressLine>123 Burl Road</streetAddressLine>
        <city>Dublin</city>
        <country code="IRL" codeSystem="1.0.3166.1.2.3">Ireland</country>
      </addr>
    </assignedOrganization>
  </assignedEntity>
</document>
```

Facilities may also have a small business designation:

```

<document>
  <author>
    <assignedEntity>
      <representedOrganization>
        <assignedEntity>
          <assignedOrganization> <!-- registrant -->
            <assignedEntity>
              <assignedOrganization .../><!-- facility -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <subjectOf>
    <characteristic classCode="OBS">
      <code code="SPLSMALLBUSINESS"
        codeSystem="2.16.840.1.113883.1.11.19255"/>
      <value xsi:type="BL" value="true"/>
    </characteristic>
  </subjectOf>

```

Validation Procedures

- 36.1.5.1 There are one or more facilities.
- 36.1.5.2 Facility may have a small business designation (except those which are not exempt per section 612b of the FD&C Act) as in 35.1.7.
- 36.1.5.3 Facility may have an id, the FEI only.
- 36.1.5.4 The id is a FEI, with root 2.16.840.1.113883.4.82 and 7- or 10-digit extension.
- 36.1.5.5 The id (FEI) is not used for any other facilities in the file.
- 36.1.5.6 If the facility has no small business designation then there is an FEI.
- 36.1.5.7 If the facility has a small business designation then there may be an FEI.
- 36.1.5.8 If there is an id (FEI), then there may be a name or address.
- 36.1.5.9 If the facility is a small business (except those which are not exempt per section 612b of the FD&C Act) and there is no FEI, then there may be a name or address.
- 36.1.5.10 If the facility has a small business designation, then the facility may have a name .
- 36.1.5.11 If the facility has a small business designation, then the facility may have an address as in Section 2.1.6 .
- 36.1.5.12 Facility (“assignedOrganization”) has no other element besides id (the FEI Number) or name and address.

36.1.6 Facility Product Link

The following example shows how the facilities are linked to particular products. It is done by replicating the business operation (actDefinition) elements, and connecting each with one product as shown below:

```
<document>
  <author>
    <assignedEntity>
      <representedOrganization><!-- labeler -->
        <assignedEntity>
          <assignedOrganization><!-- registrant -->
        </assignedEntity>
      </representedOrganization>
    </assignedEntity>
  </author>
  <assignedEntity>
    <assignedOrganization><!-- Facility -->
      .. id or name and addr ...
    </assignedOrganization>
  </assignedEntity>
  <performance><actDefinition>
    <product>
```

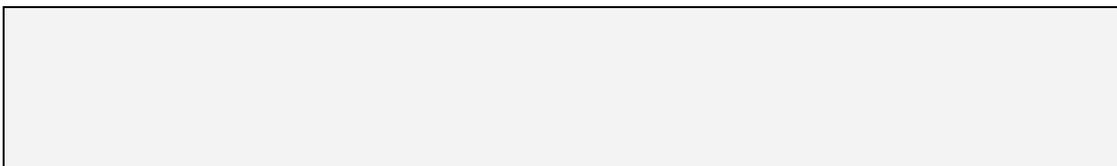
The reference to the product occurs either by listing number if that has been assigned (i.e. if the product data elements in this document already contain the listing number):

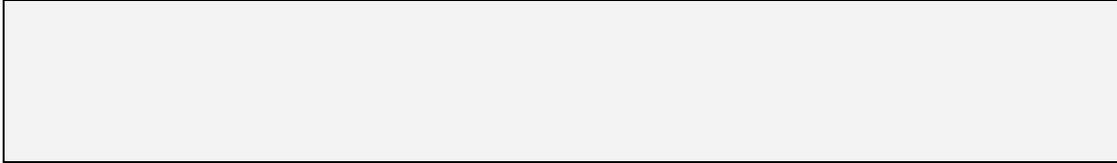
```
<product>
  <manufacturedProduct classCode="MANU">
    <manufacturedMaterialKind>
      <code code="53-XXXXXX-XXXXXX"
        codeSystem="2.16.840.1.113883.3.9848"/>
    </manufacturedMaterialKind>
  </manufacturedProduct>
</product>
```

or if the product listing number has not yet been assigned, then the reference is made by name for the cosmetic product, as such name appears on the label:

```
<actDefinition>
  <product>
    <manufacturedProduct classCode="MANU">
      <manufacturedMaterialKind>
        <code/>
        <name>Baby Shampoo</name>
      </manufacturedMaterialKind>
    </manufacturedProduct>
  </product>
```

Note that the schema still requires an empty code element.





Validation Procedures

- 36.1.6.1 There are one or more performance/actDefinition elements.
- 36.1.6.2 The performance/actDefinition element has one product reference.
- 36.1.6.3 There is either a Cosmetic Product Listing Number, or a name (but not both).
- 36.1.6.4 Product reference refers to one listed product or part product either by name or by product listing number.
- 36.1.6.5 If the facility has no small business designation, then there is an active facility registration for this facility with a cosmetic product.
- 36.1.6.6 Each listed product is linked from at least one facility.

36.1.7 Submitter Name and Signature (Legal Authenticator)

The authorized individual may sign for the responsible organization as follows:

```

<document>
  <author .../>
  <legalAuthenticator>
    <noteText>The data and information in this submission have been
    reviewed and, to the best of my knowledge, are certified to be true and
    accurate. I agree to report changes to this information as required under
    section 607 of the Federal Food, Drug, and Cosmetic Act.</noteText>
    <time value= ""/>
    <signatureText mediaType="text/plain">P. Bauer</signatureText>
  <assignedEntity>
    <assignedPerson>
      <name>Peter Bauer</name>
    </assignedPerson>
  </assignedEntity>
  <representedOrganization/>

```

- 36.1.7.1 There may be a signature (legalAuthenticator).
- 36.1.7.2 If present, the signature may contain a signing statement (noteText) exactly as above.

36.1.7.3 If present, there is one signatureText element.

36.1.7.4 If present, the signatureText has mediaType “text/plain” and the electronic signature in text content.

36.1.7.5 If present, the signature contains one assigned person (the signing person).

36.1.7.6 If present, assigned person has a name

36.1.7.7 If present, assigned person has only a name, no other element.

36.1.7.8 If present, the signature contains an empty representedOrganization element (the signer signs for the responsible organization).

36.1.7.9 There is an time with at least the precision of day in the format YYYYMMDD.

36.2 Body

36.2.1 Required Sections

Validation Procedures

36.2.1.1 If the document is a *Cosmetic – Abbreviated Renewal* (X8888-6), then the document body is empty

36.2.1.2 If the document is a *Cosmetic Product Listing* (103572-4), *Cosmetic – Update* (X8888-5), then there is a document body.

36.2.1.3 The document body contains one section, the product data element section

36.2.1.4 The section contains the product data elements

36.2.2 Cosmetic Product

```
<section>
  <subject>
    <manufacturedProduct>
      <manufacturedProduct>
        <code code="53-000000-000001"
          codeSystem="2.16.840.1.113883.3.9848"/>
        <name>Juvenia Soft</name>
        <asSpecializedKind>
          <generalizedMaterialKind>
            <code code="01B" codeSystem="2.16.840.1.113883.6.345"
              displayName="Baby products - Lotions, oils, powders, and creams"/>
          </generalizedMaterialKind>
        </asSpecializedKind>
        <ingredient>...
```

The cosmetic listing number is included in any update after it has been assigned subsequent to an initial cosmetic product listing submission.

Validation Procedures

- 36.2.2.1 If a product by the same name has been included in the previous version of the cosmetic product listing, then the assigned Cosmetic Product Listing Number is included.
- 36.2.2.2 Code system is 2.16.840.1.113883.3.9848 (Cosmetic Product Listing Number).
- 36.2.2.3 The Cosmetic Product Listing Number has the format 53-XXXXXX-XXXXXX where X stands for any digit 0 to 9.
- 36.2.2.4 The Cosmetic Product Listing Number has previously been assigned by the FDA.
- 36.2.2.5 [RESERVED]
- 36.2.2.6 The product names in the listing are unique.
- 36.2.2.7 If the products names in the listing are not unique, then there is also distinguishing information for identification purposes.
- 36.2.2.8 If the product names in the listing are not unique and the distinguishing information is confidential, then the distinguishing information is in parenthesis.
- 36.2.2.9 If the product names in the listing are unique, then there may be also distinguishing information for identification purposes.
- 36.2.2.10 If the product names in the listing are unique and distinguishing information is confidential, then the distinguishing information is in parenthesis.
- 36.2.2.11 There are one or more cosmetic product category codes (asSpecializedKind element) with a code (see Section 3.4.3).
- 36.2.2.12 Name, ingredients (including fragrance, color, and flavor) match the name for the cosmetic product, as such name appears on the label previously assigned to this listing number and the responsible person's name included in the previous version of this file.
- 36.2.2.13 Cosmetic product category matches the cosmetic product category previously assigned to this listing number.
- 36.2.2.14 There are one or more ingredients (as per Section 3.4.4)

36.2.2.15 There may be a web page link as per Section 3.4.6.2

36.2.2.16 There may be a professional use indicator as per Section 3.4.8.

36.2.2.17 There may be a label image as per Section 3.4.9.

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