The eCTD Backbone Files Specification for Module 1

The eCTD BACKBONE FILES SPECIFICATION FOR MODULE 1

Revision History

Date	Version	Summary of Changes
2003-08-13	1.0	Original version
2004-03-01	1.1	Clarifications to the original version
2006-04-13	1.2	Change to Related Sequence Example
2006-12-13	1.3	Change to XML coding for a supplement to an original application related sequence example
2012-06-01	2.0	Change to reflect major modifications to Module 1 (admin) and the use of attributes (Summary of Changes in Appendix 2)
2012-11-01	2.1	Changes include updating the DTD version references and includes a copy of the updated DTD version 3.1 in Appendix I (Summary of Changes in Appendix 2)
2013-08-23	2.2	Changes include two additional attributes for m1.15.2.1., updating the DTD version references and updating the copy of the DTD in Appendix I (Summary of Changes in Appendix 2)
2014-02-07	2.3	Modified the heading for 1.15.1.5 (Summary of Changes in Appendix 2)
2018-10-18	2.4	Changes include new eCTD submission type: REMS Supplement; updated hyperlinks which were no longer working
2020-11-09	2.5	Changes include REMS Supplement in Table 7: Group Submissions; updated eCTD header example to use https for stylesheet and DTD references in Section II
2025-03-31	2.6	Added EUA as a valid selection for Promotional Labeling Advertising in Table 2

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INTRODUCTION

This document provides specifications for creating the electronic common technical document (eCTD) backbone file for Module 1 for submission to the FDA. It should be used in conjunction with the guidance to industry: *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications.*

Font formatting conventions are used in this document to enhance its readability and emphasize items such as heading elements, attributes, titles, and file names:

- ***Bold italic*** font is used for elements and attributes.
- *Italic* font is used for links, leaf titles, publication titles, file names, and folder names.

The Module 1 eCTD Backbone File (*us-regional.xml*) includes administrative information and information for each file submitted in Module 1. The backbone file contains an XML element named ***fda-regional:fda-regional,*** which contains both the ***admin*** and ***m1-regional*** elements. The individual file information is provided within an XML element called the ***leaf*** element. The ***leaf*** elements are organized using the Module 1 section headings. The Module 1 section headings are named and organized according to the subject matter of the information contained in the files. Section headings are provided as XML elements in the ***m1-regional*** element of the backbone file. Administrative information about each submission is provided in the ***admin*** element of the backbone file.

The Module 1 eCTD Backbone File may be used in a wide range of applications and related submission types; therefore, a specific submission may not use all of the possible section heading elements. Only include the section headings that reference files in the submission. Empty section headings should not be included. The ***admin*** element should always be included, and it contains two elements named: ***applicant-info*** and ***application-set.*** These elements should be included in order as listed in *section III Admin Elements.*

The *us-regional-v3-3.dtd* file (refer to *Appendix 1*) provides the organization for each element used in the *us-regional.xml* file.

I. USE OF ATTRIBUTES

Certain ***admin*** and ***m1-regional*** heading elements require an attribute to provide information that is pertinent to the application and submission. The attribute lists are maintained as separate XML files, and each contains a standard set of codes and display names for each defined attribute type. The attribute files contain a version number, version date and coded values and display names for each value. Each coded value has a status of "active" or "inactive" to accommodate future changes; only coded values with a status of "active" should be submitted. Only the code should be provided as the attribute value in the appropriate element in the *us-regional.xml* file. The display name is shown to the reviewers in the review tool.

The following table contains the names of the attribute type lists and their respective file names.

Refer to the eCTD Submission Standards on the FDA website for the current versions of each list: https://www.fda.gov/ectd.

Table 1: Attribute List Table

Attribute Type	File Name
applicant-contact-type	*applicant-contact-type.xml*
telephone-number-type	*telephone-number-type.xml*
application-type	*application-type.xml*
submission-type	*submission-type.xml*
submission-sub-type	*submission-sub-type.xml*
supplement-effective-date-type	*supplement-effective-date-type.xml*
form-type[1]	*form-type.xml*
promotional-material-audience-type	*promotional-material-audience-type.xml*
promotional-material-doc-type	*promotional-material-doc-type.xml*
promotional-material-type	*promotional-material-type.xml*
material-id	*Provided by the applicant*
issue-date	*Provided by the applicant*

II. START OF THE MODULE 1 eCTD BACKBONE FILE

Name the Module 1 eCTD Backbone File *us-regional.xml* and place it in the *us* folder that is in the folder named *m1* as described in *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For example, the path for the *us-regional.xml* file for sequence number 0006 is 0006/m1/us/us-regional.xml. Include a reference to a ***leaf*** element in the Module 2 to 5 eCTD Backbone File (*index.xml*) for the *us-regional.xml* file. In the corresponding Module 2 to 5 eCTD Backbone File, the *operation* attribute should have a value of "new."

The header of the Module 1 eCTD Backbone File is always the same. It contains machine-readable information about the following:

- Version of XML being used
- Type of characters that are allowed in the file
- Locations of the standards that control the organization of the file

The common header is provided below:

```
<?xml version="1.0" encoding="UTF-8" standalone="no"?>
<!DOCTYPE fda-regional:fda-regional SYSTEM "https://www.accessdata.fda.gov/static/eCTD/us-regional-v3-3.dtd">
<?xml-stylesheet type="text/xsl" href="https://www.accessdata.fda.gov/static/eCTD/us-regional.xsl"?>
<fda-regional:fda-regional dtd-version="3.3" xml:lang="text" xmlns:fda-regional="http://www.ich.org/fda" xmlns:xlink="http://www.w3c.org/1999/xlink">
…
```

[1] The 356h and 1571 forms are placed in their respective application's ***admin*** section and other forms are placed in the module 1 heading element ***m1-1-forms*** using the ***form*** element.

All the heading elements and content for Module 1 should be provided after these elements and before the last element closing tag named </fda-regional:fda-regional>.

III. ADMIN ELEMENTS

Administrative information is contained in the ***admin*** element, which is contained in the ***fda-regional:fda-regional*** element. The ***admin*** element contains two child elements*:* ***applicant-info*** and ***application-set***. These elements should be placed in order as listed below.

```
…
<fda-regional:fda-regional>
    <admin>
        <applicant-info>  </applicant-info>
        <application-set>  </application-set>
   </admin>
      <m1-regional>
      </m1-regional>
 </fda-regional:fda-regional>
…
```

A. Applicant-info Element

The applicant-info element contains the following child elements: ***id***, ***company-name***, ***submission-description,*** and ***applicant-contacts***.

1. ID Element

The ***id*** element is the Data Universal Numbering System (D-U-N-S®) number that is assigned and maintained by Dun & Bradstreet. The nine (9)-digit D-U-N-S® number serves as a unique identifier (code) of a business entity and it is increasingly being used as a resource for FDA to assure accurate identification and to verify certain business information for that entity, e.g., trade names used by the entity, and addresses; the number will supplement other identifiers such as the company-name element. The D-U-N-S® number for the business entity that is the sponsor, applicant or holder of the submission should be provided and if applicable, it should match that used in the User Fee system. The same D-U-N-S® number should be used for all submissions to an application, unless there is a change in ownership of the application. Provide this element with every submission.

2. Company-name Element

The sponsor or applicant's name is located in the ***company-name*** element. An example of the ***company-name*** element for the "Very Best Drug Company" is provided below:

```
…
<company-name>Very Best Drug Company</company-name>
…
```

Provide this element with every submission.

3. Submission-description Element

The ***submission-description*** element is an optional field that allows up to 128 characters. Only the first 128 characters of the ***submission description*** element will be displayed.

- The information in the ***submission-description*** element should be a high level description of the purpose of the submission and also help differentiate between similar types of submissions.

- Some examples of helpful submission descriptions are listed below:

    - Supplement provides for new manufacturing site
    - New site for API manufacture, DSM Ltd, Groningen, NL
    - Proposed indication of an efficacy supplement
    - Pharmtox Information Amendment – Final Study Report A1001
    - Clinical Information Amendment – New Protocol A001100
    - Response to an IR letter and date
    - Type of amendment (clinical – new protocol, clinical – protocol amendment, pharmacology, toxicology, etc.)

- The field should not:
    - contain a response to FDA inquiries
    - replace the cover letter
    - pose questions to the FDA
    - contain information that is in support of an application or is needed in the approvability or acceptability of an application, or
    - contain information that is critical or needs to be reviewed.

4. Applicant-contacts Element

The ***applicant-contacts*** element contains one or more ***applicant-contact*** elements. Provide at least one complete ***applicant-contact*** element with every submission. The elements contained in the ***applicant-contact*** element are: ***applicant-contact-name***, ***telephones,*** and ***emails***. For the ***applicant-contact-name*** element, include the ***applicant-contact-type*** attribute. The ***telephones*** element contains a ***telephone*** element limited to 64 characters that requires the ***telephone-number-type*** attribute. The ***emails*** element contains an ***email*** element limited to 64 characters that does not require an attribute. When attributes are required, they should be provided as coded values from their corresponding attribute list (*applicant-contact-type.xml* and *telephone-number-type.xml*). The current valid codes for ***applicant-contact-type*** and ***telephone-number-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

An example of the ***applicant-contacts*** element containing two ***applicant-contact*** elements is shown below and includes: contact names, telephone numbers, email addresses and coded attributes. The ***applicant-contact*** element below shows Jane Smith as a regulatory contact and John Smith as the technical contact, with their respective example contact information:

```
….
<applicant-contacts>
      <applicant-contact>
            <applicant-contact-name applicant-contact-type="fdaact1">Jane Smith</applicant-contact-name>
```

```
            <telephones>
                <telephone telephone-number-type="fdatnt1">1-212-555-1234</telephone>
                <telephone telephone-number-type="fdatnt3">1-212-555-5678</telephone>
            </telephones>
            <emails>
                <email>jane.smith@gooddrugs.com</email>
            </emails>
        </applicant-contact>
        <applicant-contact>
            <applicant-contact-name applicant-contact-type="fdaact2">John Smith</applicant-contact-name>
            <telephones>
                <telephone telephone-number-type="fdatnt1">1-212-555-1213</telephone>
                <telephone telephone-number-type="fdatnt3">1-212-555-4546</telephone>
            </telephones>
            <emails>
                <email>john.smith@gooddrugs.com</email>
            </emails>
        </applicant-contact>
    </applicant-contacts>
…
```

B. Application-set Element

The ***application-set*** element may contain one or more ***application*** elements. This provides the functionality to submit a single submission to more than one application, which is also referred to as a "grouped submission" (refer to *section IV. Grouped Submissions*). If more than one ***application*** element is provided, each ***application*** element must contain the ***application-information*** and ***submission-information*** child elements.

Each ***application*** element has a required attribute of ***application-containing-files*** and requires a value of either "true" or "false." The purpose of the ***application-containing-files*** attribute is to indicate the application number folder where files will be stored (refer to *section IV. Grouped Submissions*). For a submission to only one application, this attribute value should be "true." For a grouped submission, a value of "true" should only be set in one application element.

The elements contained in the ***application*** element are ***application-information*** and ***submission-information***, and they should be included in order as listed here.

1. Application-information Element

The elements contained in the ***application-information*** element are ***application-number*** and ***cross-reference-application-number***.

a. Application-number element

Provide the six (6)-digit application number in the ***application-number*** element. Provide only numeric digits, including any leading zeros for the application number, without letters or dashes.

Each ***application-number*** element requires an attribute of ***application-type***, and the attribute should be provided as a coded value from its corresponding attribute list (*application-type.xml*). The current valid codes for ***application-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

The following is an example of the ***application-number*** element for NDA 456789. In this example, the application number contains the attribute value of "fdaat1" for the ***application-type***, which indicates it is a new drug application (NDA).

```
…
<application-number application-type="fdaat1 ">456789</application-number>
…
```

Provide this element and attribute with every ***application*** element in the submission.

b. Cross-reference-application-number element

This element should only be provided when an application makes reference to other applications. Cross references are unnecessary when the application(s) being referenced are in the ***application-set***.[2] A cross reference only needs to be identified once.

Provide the six (6)-digit application number in the ***cross-reference-application-number*** element. Only provide numeric digits, including any leading zeros for the application number, without letters or dashes.

Each ***cross-reference-application-number*** element requires an attribute of ***application-type*** and the attribute should be provided as a coded value from its corresponding attribute list (*application-type.xml*). The current valid codes for ***application-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

The following is an example of a ***cross-reference-application-number*** element. In this example, the application NDA 456789 cross-references DMF 012345. The ***cross-reference-application-number*** element contains the attribute value of "fdaat5" for the ***application-type***, which indicates it is a Drug Master File (DMF).

```
…
<application-number application-type="fdaat1">456789</application-number>
<cross-reference-application-number application-type="fdaat5">012345</cross-reference-application-number>
…
```

2. Submission-information element

The ***submission-information*** element contains three child elements: ***submission-id***, ***sequence-number***, and ***form***.

a. Submission-id element - <submission-id>

The ***submission-id*** element is used to identify each individual regulatory activity (original application, supplement, annual report, etc.) in an application. All submissions that belong to a specific regulatory activity (for example, a supplement and all amendments related to that supplement) should contain the same four (4)-digit number in their ***submission-id*** element. The four (4)-digit ***submission-id*** number for each regulatory activity is determined by the ***sequence-number***

[2] The cross reference electronically provides the same information found on the 356h and 1571 application forms.

of the first submission to each new regulatory activity. The ***submission-id*** should match the four (4)-digit ***sequence-number*** for that first submission to the new regulatory activity (refer to *section III.B.2.b. Sequence-number element* and *section III.B.3. Building Regulatory Activities* for additional details). Provide the four (4)-digit number in the ***submission-id*** element, including any leading zeros.

The ***submission-id*** element contains two attributes: ***submission-type*** and ***supplement-effective-date-type***. The ***supplement-effective-date-type*** attribute is only required and applicable to the submission types: efficacy supplement, labeling supplement, or chemistry manufacturing controls supplement with a ***submission-sub-type*** of "application." The attributes should be provided as coded values from their corresponding attribute lists (*submission-type.xml* and *supplement-effective-date-type.xml*). The current valid codes for ***submission-type*** and ***supplement-effective-date-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

For the correct usage of ***submission-type*** and ***supplement-effective-date-type***, refer to Tables *2* and *3* below. *Table 2* provides the descriptions of use for each ***submission-type*** and *Table 3* provides the description and usage of each ***supplement-effective-date-type***. When applying these attributes, it is important to only use them according to the "valid for" sections provided in these tables.

Below is an example of a ***submission-id*** element for a labeling supplement to an application. This ***submission-id*** element also includes the ***submission-type*** attribute and the ***supplement-effective-date-type*** attribute. In this example, the ***submission-id*** is identified as "0009" (refer to *section III.B.3. Building Regulatory Activities* for additional details on assigning the correct ***submission-id*** number to each regulatory activity), it has a ***submission-type*** attribute code of "fdast4": indicating that the submission type is a labeling supplement, and it has a ***supplement-effective-date-type*** of "fdasedt2": indicating that it is a CBE-0 supplement.

```
…
<submission-id submission-type="fdast4" supplement-effective-date-type="fdasedt2">0009</submission-id>
…
```

b. Sequence-number Element - <sequence-number>

The ***sequence-number*** element is used to uniquely identify each individual submission to an application. It must be a unique number with a maximum of four (4)-numeric digits, should start at 0001, and should not exceed 9999. The ***sequence-number*** should normally be incremented by one each time a submission is made to the application. The ***sequence-number*** element contains the attribute ***submission-sub-type***, used to further clarify the purpose of the submission. Only certain ***submission-sub-type*** attributes are applicable to certain submission types. For the correct usage of the ***submission-sub-type*** attribute, refer to *Tables 2* and *4* below. These tables provide the description for each ***submission-sub-type*** and outline the correct usage of submission sub-types for each ***submission-type***. The attribute should be provided as a coded value from its corresponding attribute list (*submission-sub-type.xml*). The current valid codes for ***submission-sub-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

In the example below, the ***sequence-number*** element contains "0004" indicating that it is the fourth submission to the application and the ***submission-sub-type*** attribute contains the code of "fdasst4"

indicating that it is an amendment.

```
…
<sequence-number submission-sub-type="fdasst4">0004</sequence-number>
…
```

c. Form Element - <form>

To accommodate grouped submissions, certain forms should only be referenced in the ***form*** element contained in the ***submission-information*** element. This will allow these forms to only display in review tools under the specified application. The ***form*** element is further described in *section VI.B. M1 Forms* and the form types with their designated reference locations are referenced in *Table 10*.[3] For all form leafs referenced in the ***form*** element or Module 1 heading element, the attribute of ***form-type*** is required and indicates the type of form being referenced and submitted.

In the example below, the ***form-type*** attribute indicates the form is Form FDA 356h. Multiple leafs can be provided for a form element in order to accommodate attachments (e.g. establishment description information).

```
…
<form form-type="fdaft2">
        <leaf ID="a11383b1215534dfdf8a81df05237f796" checksum="49e154b9bee040a2de43c459affd63e4"
checksum-type="md5" operation="new" xlink:href="356h-nda456789-0004.pdf" xlink:type="simple">
                <title>Form FDA 356h - 0004 - Amendment to Original Application</title>
        </leaf>
</form>
…
```

[3] Refer to the current version of the form-type.xml for a complete list of forms.

Table 2: Submission Types and Descriptions of Use

Submission Type	Submission Sub-Type	Supplement Effective Date Type (if applicable and *submission-sub-type* = "application")	Valid For Application Types
Original Application	Presubmission Application Amendment Resubmission		IND, NDA, ANDA, BLA, DMF, EUA
Efficacy Supplement	Presubmission		NDA, BLA
	Application	Prior Approval Supplement (PAS)	
	Amendment Resubmission		
Chemistry Manufacturing Controls Supplement	Presubmission		NDA, ANDA, BLA
	Application	Prior Approval Supplement (PAS), Changes Being Effected (CBE-0), or Changes Being Effected 30 (CBE-30)	
	Amendment Resubmission		
Labeling Supplement	Presubmission		NDA, ANDA, BLA
	Application	Prior Approval Supplement (PAS) or Changes Being Effected (CBE-0)	
	Amendment Resubmission		
REMS Supplement	Application	Prior Approval Supplement (PAS) or Changes Being Effected (CBE-30)	NDA, ANDA, BLA
	Amendment Resubmission		
Annual Report	Report Amendment		IND, NDA, ANDA, BLA, DMF
Product Correspondence	Correspondence Amendment		IND, NDA, ANDA, BLA, DMF
Postmarketing Requirements or Postmarketing Commitments	Original Amendment		NDA, BLA
Promotional Labeling Advertising	Original Resubmission Amendment		NDA, ANDA, BLA, EUA
IND Safety Reports	Report Amendment		IND
Periodic Safety Reports (Periodic Adverse Drug Experience Report	Report Amendment		NDA, ANDA, BLA

Submission Type	Submission Sub-Type	Supplement Effective Date Type (if applicable and *submission-sub-type* = "application")	Valid For Application Types
(PADER) or Periodic Safety Update Report (PSUR))			

Table 3: Supplement-Effective-Date-Types and Descriptions of Use

Supplement Effective Date Type	Description	Valid for Submission Types
Prior Approval Supplement (PAS)	The Prior Approval Supplement is a supplement submission for a major change for which distribution of the product made using the change cannot occur prior to FDA approval as provided for in 21 CFR 314.70 and 21 CFR 601.12(b).	Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement
Changes Being Effected (CBE-0)	The "Changes Being Effected" is a supplement submission for certain moderate changes for which distribution can occur when FDA receives the supplement as provided for in 21 CFR 314.70 and 21 CFR 601.12(c)(5).	Chemistry Manufacturing Controls Supplement, Labeling Supplement
Changes Being Effected 30 (CBE-30)	The "Changes Being Effected in 30 Days" is a supplement submission for certain moderate changes that must be submitted to FDA at least 30 days before the distribution of the product made using the change as provided for in 21 CFR 314.70 and 21 CFR 601.12(c).	Chemistry Manufacturing Controls Supplement, REMS Supplement

Table 4: Submission Sub-Types and Descriptions of Use

Submission Sub-Type	Description	Valid For the Listed Submission Types
Presubmission	A submission to the Agency that occurs prior to the actual submission of a full application (e.g., rolling review, reviewable unit, clinical information that the applicant requests comment on prior to submitting their application). Not all applications will have presubmissions.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement
Application	The submission that represents the application's primary supportive material. There should only be one submission with a sub-type of application within a given submission group.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement
Amendment	A submission that contains additional supportive	Original Application,

Submission Sub-Type	Description	Valid For the Listed Submission Types
	material to augment information previously submitted. Examples include responses to information requests, additional draft labeling during negotiations, etc.	Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement, Annual Report, Product Correspondence, Postmarketing Requirements or Postmarketing Commitments, Promotional Labeling Advertising, IND Safety Reports, Periodic Safety Reports (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR))
Resubmission	A submission that contains additional information for the Agency to consider following the issuance of an action communication to the applicant (e.g., complete response or inactivation). For promotional labeling and advertising, the submission of revised promotional materials that were previously submitted as an original submission sub-type. Includes requests for advisory on launch materials, requests for advisory on nonlaunch materials, pre-submission of promotional materials for accelerated approval products, and materials submitted under the Pre-Dissemination Review of Television Ads Program.	Original Application, Efficacy Supplement, Chemistry Manufacturing Controls Supplement, Labeling Supplement, REMS Supplement Promotional Labeling Advertising
Report	A submission that contains a new annual report, IND Safety Report, or Periodic Safety Report (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR)).	Annual Report, IND Safety Reports, Periodic Safety Reports (Periodic Adverse Drug Experience Report (PADER) or Periodic Safety Update Report (PSUR))
Original	Submission of original promotional materials including all promotional labeling and advertising submissions, or Postmarketing Requirements or Postmarketing Commitments	Promotional Labeling Advertising, Postmarketing Requirements or Postmarketing Commitments
Correspondence	**Routine:** administrative changes, e.g., change of address, authorized official, or meeting requests. **Donor re-entry request:** An applicant's request to re-enter a deferred donor when regulations and/or guidance do not provide a qualification method or	Product Correspondence

Submission Sub-Type	Description	Valid For the Listed Submission Types
	process for their specific situation. (21 CFR 610.41(b)) **License re-issuance:** request from applicant to change legal name. **Lot distribution report:** Postmarketing report required by 21 CFR 600.81 to be submitted every six (6) months upon approval/licensing of vaccine or biologic product. **Final labeling**	

3. Building Regulatory Activities

A regulatory activity is established, defined and identified by the submission type in an eCTD application. The purpose could be a notification of a change or a request to approve a new product or change. There can be one or more regulatory activities within an application and each regulatory activity can consist of one or more submissions.

The first submission to a regulatory activity establishes the ***submission-id*** that will be used in subsequent submissions for the same regulatory activity in an application. Using the same ***submission-id*** number for a regulatory activity allows the related submissions to be grouped together for that regulatory activity. In an eCTD submission, the ***submission-id*** element and ***submission-type*** attribute are used to group regulatory activities; the ***sequence-number*** element and ***submission sub-type*** attribute are used to indicate the order of submissions submitted for the same regulatory activity.

All submissions related to a single regulatory activity should be grouped together. This is accomplished by using the ***submission-id*** number. The number used in the ***submission-id*** element is determined by the ***sequence-number*** of the first submission to each regulatory activity. For example, if the original application is ***sequence-number*** 0001, then the ***submission-id*** for that regulatory activity is also 0001. When an amendment is submitted to this original application, the ***submission-id*** 0001 is used (to show the submissions are related), while the ***sequence-number*** is incremented by one for each subsequent submission (refer to Scenario 1 below).

The following two scenarios demonstrate the use of ***submission-id***, ***submission-type***, ***sequence-number*** and ***submission-sub-type***:

Scenario 1: In this scenario, an applicant is submitting the first submission to the original application. The ***submission-id*** should match the ***sequence-number*** since it is the first submission for this regulatory activity (original application). The ***submission-id*** and ***sequence-number*** should both contain "0001," and the appropriate ***submission-type*** code is used to indicate that it is an original application. All submissions that relate to this original application (regulatory activity) should contain the same ***submission-id*** of "0001."

Table 5: Building Regulatory Activities – Scenario 1

The Original Application regulatory activity consists of two presubmissions, the original application, and two amendments and is identified by the *submission-id* number "0001."	
Presubmission (meeting request)	

submission-id	0001
submission-type attribute	fdast1 (Original Application)
sequence-number	0001
submission-sub-type attribute	fdasst2 (presubmission)
Presubmission (meeting package)	
submission-id	0001
submission-type attribute	fdast1 (Original Application)
sequence-number	0002
submission-sub-type attribute	fdasst2 (presubmission)
Original Application	
submission-id	0001
submission-type attribute	fdast1 (Original Application)
sequence-number	0003
submission-sub-type attribute	fdasst3 (application)
Amendment #1	
submission-id	0001
submission-type attribute	fdast1 (Original Application)
sequence-number	0004
submission-sub-type attribute	fdasst4 (amendment)
Amendment #2	
submission-id	0001
submission-type attribute	fdast1 (Original Application)
sequence-number	0005
submission-sub-type attribute	fdasst4 (amendment)

Scenario 2: In this second scenario, the first submission for a new efficacy supplement (a new regulatory activity) is submitted to an application; therefore, the number used for the ***submission-id*** should match the ***sequence-number***. Since the ***sequence-number*** is incremented within the application for each submission and the last sequence number submitted to the application was "0005," both the ***submission-id*** and the ***sequence-number*** for this new efficacy supplement will be "0006." This submission and all subsequent submissions that relate to this efficacy supplement will use ***submission-id*** "0006." The ***submission-type*** code indicating it is an efficacy supplement is used for the supplement and also for all sequences related to the supplement. The ***submission-sub-type*** attribute is used (as indicated in Tables 2 and 4 above) to further clarify the purpose of each submission. The ***supplement-effective-date-type*** indicates it is a Prior Approval Supplement (PAS as indicated in Tables 2 and 3 above)

Table 6: Building Regulatory Activities – Scenario 2

The Efficacy Supplement regulatory activity below consists of three submissions and is identified by a *submission-id* number of "0006."	
Efficacy Supplement (new indication)	
submission-id	0006
submission-type attribute	fdast2 (Efficacy Supplement)
supplement-effective-date-type attribute	fdasedt1 (Prior Approval Supplement (PAS))
sequence-number	0006
submission-sub-type attribute	fdasst3 (application)

Amendment #1 to Efficacy Supplement	
submission-id	0006
submission-type attribute	fdast2 (Efficacy Supplement)
sequence-number	0008
submission-sub-type attribute	fdasst4 (amendment)
Amendment #2 to Efficacy Supplement	
submission-id	0006
submission-type attribute	fdast2 (Efficacy Supplement)
sequence-number	0010
submission-sub-type attribute	fdasst4 (amendment)

IV. Grouped Submissions

A grouped submission is a single sequence containing a *us-regional.xml*, *index.xml* and any other applicable files applied to more than one application. A grouped submission is also known as a global supplement, global submission, bundled supplement, bundled submission, multiple product submission or trans-BLA. This type of submission eliminates the need to submit multiple, identical submissions to different applications. The files referenced in the grouped submission are applied to all applications identified. The grouped submission concept does not replace or affect previously existing cross-referencing functionality (use of m1-4-4 or cross application reference links).

The files referenced in the XML backbones will physically reside in the application folder indicated with a value of "true" for the ***application-containing-files*** attribute. Only one ***application*** element in a grouped submission should contain a value of "true" for the ***application-containing-files*** attribute. The application whose ***application-containing-files*** attribute has a value of "true" is considered the primary application and should remain constant in future sequences.

When referencing or modifying files that were submitted in a grouped submission, it is possible that the files being referenced are not located in the same application type/number folder as the "new" files being submitted. In this case, the ***modified-file*** leaf attribute must also include the correct application type/number folder where the files are physically stored (refer to *section V. Leaf Element*).

The following items listed below provide general information and use limitations for submitting a grouped submission to multiple applications[4]:

General Information:

- Initial grouped submissions should only include new leaves.
- When using lifecycle operations of append, delete, or replace in a subsequent grouped submission, the lifecycle operation will apply to the modified leaf in all submissions referenced in the application set.

4 Electronic consideration(s) for grouped submissions will not supersede the policy and practice of bundled submissions as it may or may not affect user fees per the *Guidance for Industry: Guidance for Industry Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees*.

- The grouped submission's content must reside in the same exact eCTD location for all applications included in the grouped.

Use Limitations:

- Only one application type can be used in a grouped submission.
- Only one submission type can be used in a grouped submission.
- Grouped submissions are only supported using DTD version 3.3 or higher.

Table 7: Grouped Submissions Limitations and Use

Application Types Allowed	Submission Types Allowed	Center Acceptance of Grouped Submission	
		CDER	CBER
ANDA	Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	NO
BLA	Efficacy Supplement, Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	YES
DMF	Product Correspondence	YES	NO
IND	Annual Report, Product Correspondence	YES	NO
NDA	Efficacy Supplement, Labeling Supplement, Chemistry Manufacturing Controls Supplement, Product Correspondence, Promotional Labeling Advertising, REMS Supplement	YES	NO

The following two scenarios demonstrate a grouped submission for a Labeling Supplement regulatory activity to three (3) applications and an amendment to the Labeling Supplement. The scenarios also show the use of the ***supplement-effective-date-type*** attribute for the Labeling Supplement.

Table 8: Grouped Submission – Scenario 1

Grouped Submission Scenario 1: A grouped submission for a Labeling Supplement is being submitted to NDA 456789, 567890, and 678901. All the new files submitted are contained in the folder for NDA 456789, sequence 0011.	
NDA 456789 ***application-containing-files*** ***submission-id*** ***submission-type*** attribute ***supplement-effective-date-type*** attribute	 true 0011 fdast4 Labeling Supplement fdasedt2 (CBE-0)

sequence-number	0011
submission-sub-type attribute	fdasst3 (application)
NDA 567890	
application-containing-files	false
submission-id	0014
submission-type attribute	fdast4 Labeling Supplement
supplement-effective-date-type attribute	fdasedt2 (CBE-0)
sequence-number	0014
submission-sub-type attribute	fdasst3 (application)
NDA 678901	
application-containing-files	false
submission-id	0012
submission-type attribute	fdast4 Labeling Supplement
supplement-effective-date-type attribute	fdasedt2 (CBE-0)
sequence-number	0012
submission-sub-type attribute	fdasst3 (application)

Table 9: Grouped Submission – Scenario 2

Grouped Submission Scenario 2: An amendment is being submitted to the Labeling Supplement previously submitted as a grouped submission. Any life cycle operations on files will affect all applications indicated in the *application-set*. All the new files submitted are contained in the folder for NDA 456789, sequence 0012.	
NDA 456789	
application-containing-files	true
submission-id	0011
submission-type attribute	fdast4 Labeling Supplement
sequence-number	0012
submission-sub-type attribute	fdasst4 (amendment)
NDA 567890	
application-containing-files	false
submission-id	0014
submission-type attribute	fdast4 Labeling Supplement
sequence-number	0015
submission-sub-type attribute	fdasst4 (amendment)
NDA 678901	
application-containing-files	false
submission-id	0012
submission-type attribute	fdast4 Labeling Supplement
sequence-number	0013
submission-sub-type attribute	fdasst4 (amendment)

V. LEAF ELEMENT

Information for an individual document is contained in the ***leaf*** element, its attributes, and its ***title*** element. The ***leaf*** element is used repeatedly throughout the eCTD backbone files to provide individual information for each document being submitted. Detailed descriptions of each part of the ***leaf*** element and how to use them are found in the document, *ICH M2 technical specification,*

Electronic Common Technical Document Specification. When preparing the *us-regional.xml* file, the ***xlink:href*** and ***modified-file*** leaf attributes should reflect the path relative to the location of the *us-regional.xml* file location in the submission. The following is an example of a ***xlink:href*** attribute and its value for the 356h.pdf in Module 1 in the same submission:

```
…
xlink:href="356h.pdf"
…
```

The following is an example of a ***modified-file*** leaf attribute and its value in Module 1 in an earlier submission:

```
…
modified-file="../../../0001/m1/us/us-regional.xml#id34567"
…
```

The following is an example of a ***modified-file*** leaf attribute which is modifying a leaf that was previously submitted to a different application which contained the file. The modified-file path includes the application number for the application which contained the previously submitted file and had an ***application-containing-files*** element value of "true". In order to perform life cycle operations on leafs previously submitted in a grouped submission, the ***modified-file*** path references the application number, sequence number, and leaf id for the application where the leaf was originally submitted with the ***application-containing-files*** element value indicating "true."

```
…
modified-file="../../../../nda456789/0001/m1/us/us-regional.xml#id21342"
…
```

VI. SECTION HEADING ELEMENTS FOR MODULE 1

This section describes the heading elements relevant to Module 1. This is the equivalent to the heading elements described in the document titled, *ICH M2 technical specification, Electronic Common Technical Document Specification.*

The Module 1 section heading elements are listed in the DTD. For information on the placement of content in these headings, please refer to *The Comprehensive Table of Contents Headings and Hierarchy.* ***Leaf*** elements should only be referenced at the lowest level section/sub-section of the hierarchy for each heading element. If a section heading does not contain references to files or documents, omit the element for that heading in the eCTD backbone file.

A. M1 Regional Section Headings Requiring Attributes

Certain Module 1 heading elements require the use of an attribute to describe the information referenced in those sections. The heading elements that require an attribute are provided below:

- the ***form*** element under ***m1-1-forms*** requires an attribute indicating the ***form-type*** <attribute = ***form-type***>
- ***m1-15-promotional-material*** requires an attribute to indicate the ***promotional-material-audience-type*** <attribute = ***promotional-material-audience-type***>

- ***m1-15-2-materials*** requires an attribute to indicate the purpose of the promotional submission <attribute = ***promotional-material-doc-type***>
- ***m1-15-2-1-material*** requires attributes to indicate the type of media/delivery method of the promotional material, the applicant's identifier for the material and the date of the initial dissemination of the promotional labeling or the date of initial publication for an advertisement (only provided when the ***promotional-material-doc-type*** is a promotional 2253 submission) <attribute = ***promotional-material-type, material-id,*** and ***issue-date***>.

B. M1 Forms

The ***m1-1-forms*** heading element contains the ***form*** element. When a leaf is placed under the ***form*** element, an attribute is required and is used to indicate the type of form being submitted. Each ***form*** element requires an attribute of ***form-type*** and the attribute should be provided as a coded value from its corresponding attribute list (*form-type.xml*). Multiple leafs can be provided for a form element in order to accommodate attachments. The current valid codes for ***form-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

In the example below, the ***form-type*** attribute indicates the coded value for the Form FDA 2253.

```
…
<m1-1-forms>
      <form form-type="fdaft5">
        <leaf ID=" a11383b1215534dfdf8a81em95237f796"
        checksum="49e154b9bee094a2de43c459affd63e4" checksum-type="md5" operation="new"
        xlink:href="2253-nda456789-0016.pdf" xlink:type="simple">
                <title>Form 2253 Professional sales aid 20120415</title>
          </leaf>
      </form>
</m1-1-forms>
…
```

Table 10: Form Types and eCTD Location

Form Type	Reference Location
Form FDA 1571: Investigational New Drug Application (IND)	***form*** element within the ***submission-information*** element
Form FDA 356h: Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use"	***form*** element within the ***submission-information*** element
Patent Forms (Form FDA3542a and Form FDA 3542)	***m1-3-5-1-patent-information*** element within the ***m1-3-5-patent-and-exclusivity*** element
All other forms[5]	***form*** element within the ***m1-1-forms*** element

C. Module 1.15 — Promotional Material

When providing information in Module 1.15, the leaves should be referenced at the lowest heading

[5] Refer to the current version of the form-type.xml for a complete list of forms.

elements. The ***m1-15-promotional-material*** heading element requires an attribute of ***promotional-material-audience-type***. When a leaf is referenced in any subsection of Module 1.15, the attribute must be provided as a coded value from its corresponding attribute list (promotional-material-audience-type.xml). The current valid codes for ***promotional-material-audience-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

When providing information in a subsection of Module 1.15.2 Materials, three attributes are required: ***promotional-material-doc-type***, ***promotional-material-type***, and ***material-id***. An additional optional attribute, ***issue-date***, should only be provided when the ***promotional-material-doc-type*** is a promotional 2253 submission. The attribute ***promotional-material-doc-type*** should be provided with the ***m1-15-2-materials*** heading element and the attributes ***promotional-material-type***, ***material-id***, and ***issue-date*** (if applicable) should be provided with the ***m-1-15-2-1 material*** heading element. The attributes for ***promotional-material-doc-type*** and ***promotional-material-type*** should be provided as coded values from their corresponding attribute list (*promotional-material-doc-type.xml* and *promotional-material-type.xml*). The ***material-id*** attribute may consist of alpha and/or numeric characters and should not exceed 30 characters. The ***issue-date*** attribute, if applicable, should follow the date format as yyyymmdd (4-digit year, 2-digit month, and 2-digit day). The current valid codes for ***promotional-material-doc-type*** and ***promotional-material-type*** are available in the eCTD Submission Standards on the FDA website: https://www.fda.gov/ectd.

In the example below, the ***promotional-material-audience-type*** indicates the promotional material is intended for healthcare professionals, the ***promotional-material-doc-type*** indicates that the submission is a Form FDA 2253 submission, the ***promotional-material-type*** indicates the material being submitted is a sales aid, the ***material-id*** provided by the applicant is “65no35482”, and the ***issue-date*** provided by the applicant is “20120415” (April 15, 2012 formatted as YYYYMMDD).

```
…
<m1-15-promotional-material promotional-material-audience-type="fdapmat2">
      <m1-15-2-materials promotional-material-doc-type="fdapmdt1">
            <m1-15-2-1-material promotional-material-type="fdapmt25" material-id=”65no35482” issue-
            date=”20120415”>
                  <m1-15-2-1-1-clean-version>
                        <leaf ID="b21383b1215534dfdf8a81df05237f704"
                        checksum="49e154b9bee040a2de43c459affd6304" checksum-type="md5"
                        operation="new" xlink:href="clean-sales-aid.pdf" xlink:type="simple">
                              <title> SALES AID 65NO35482 Considerations for treatment 20120415</title>
                        </leaf>
                  </m1-15-2-1-1-clean-version>
            </m1-15-2-1-material>
      </m1-15-2-materials>
</m1-15-promotional-material>
…
```

Table 11: Promotional Material Audience Types and Descriptions

Promotional Material Audience Type	Description
Consumer	Promotional materials directed to consumers
Professional	Promotional materials directed to health care professionals

Table 12: Promotional Material Doc Types and Descriptions

Promotional Material Document Type	Description
Promotional 2253	Form and materials required from submitter at first publication of marketing and advertising materials
Request for Advisory Launch	Voluntary submission of launch promotional materials for FDA review and comment sent prior to dissemination/publication
Request for Advisory Non-Launch	Voluntary submission of promotional materials for FDA review and comment sent prior to dissemination/publication
Pre-submission Accelerated Launch	Promotional materials intended to be used in the first 120 days after approval that are submitted to FDA prior to dissemination/publication as required by 21 CFR 314.550 and 601.45
Pre-submission Accelerated Non-Launch	Promotional materials intended to be used after the 120-day post approval period that are submitted to FDA prior to dissemination/publication as required by 21 CFR 314.550 and 601.45
Pre-Dissemination Review of Television Ads	Television advertisements submitted to FDA under the Pre-Dissemination Review of Television Ads Program

Table 13: Material ID and Issue Date Descriptions

M1-15-2-1 Applicant Defined Attributes	Description
Material ID	The applicant's identification code or other designation of the specific promotional material. The material-id may consist of alpha and/or numeric characters and has a 30 character limitation.
Issue date	The date of the initial dissemination of the promotional labeling or the date of initial publication for an advertisement. The format of the date should be YYYYMMDD.

APPENDIX 1: M1 Document Type Definition (DTD) Version 3.3

```
<?xml version="1.0" encoding="UTF-8"?>
<!--version 3-1 Modified the m1-16 heading and added sub-headings-->
<!--version 3-2 Two additional attributes were added to the m1-15-2-1-material sub-heading-->
<!--version 3-3 Modified the m1-15-1-5 heading-->
<!ELEMENT fda-regional:fda-regional (admin, m1-regional?)>
<!ATTLIST fda-regional:fda-regional
    xmlns:fda-regional CDATA #FIXED "http://www.ich.org/fda"
    xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
    xml:lang CDATA #IMPLIED
    dtd-version CDATA #FIXED "3.3"
>
<!ELEMENT leaf (title, link-text?)>
<!ATTLIST leaf
    ID ID #REQUIRED
    application-version CDATA #IMPLIED
    version CDATA #IMPLIED
    font-library CDATA #IMPLIED
    operation (delete | new | append | replace) #REQUIRED
    modified-file CDATA #IMPLIED
    checksum CDATA #IMPLIED
    checksum-type CDATA #IMPLIED
    keywords CDATA #IMPLIED
    xlink:type CDATA #FIXED "simple"
    xlink:role CDATA #IMPLIED
    xlink:href CDATA #IMPLIED
    xlink:show (embed | none | other | new | replace) #IMPLIED
    xlink:actuate (onLoad | none | other | onRequest) #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT title (#PCDATA)>
<!ATTLIST title
    ID ID #IMPLIED
>
<!ELEMENT link-text (#PCDATA | xref)*>
<!ATTLIST link-text
    ID ID #IMPLIED
>
<!ELEMENT xref EMPTY>
<!ATTLIST xref
    ID ID #IMPLIED
    xlink:type CDATA #FIXED "simple"
    xlink:role CDATA #IMPLIED
    xlink:title CDATA #REQUIRED
    xlink:href CDATA #REQUIRED
```

```
    xlink:show (embed | none | other | new | replace) #IMPLIED
    xlink:actuate (onLoad | none | other | onRequest) #IMPLIED
>
<!ELEMENT node-extension (title, (leaf | node-extension)+)>
<!ATTLIST node-extension
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT admin (applicant-info, application-set)>
<!ELEMENT applicant-info (id, company-name, submission-description?, applicant-contacts)>
<!ELEMENT id (#PCDATA)>
<!ELEMENT company-name (#PCDATA)>
<!ELEMENT submission-description (#PCDATA)>
<!ELEMENT applicant-contacts (applicant-contact+)>
<!ELEMENT applicant-contact (applicant-contact-name, telephones, emails)>
<!ELEMENT applicant-contact-name (#PCDATA)>
<!ATTLIST applicant-contact-name
    applicant-contact-type CDATA #REQUIRED
>
<!ELEMENT telephones (telephone+)>
<!ELEMENT telephone (#PCDATA)>
<!ATTLIST telephone
    telephone-number-type CDATA #REQUIRED
>
<!ELEMENT emails (email+)>
<!ELEMENT email (#PCDATA)>
<!ELEMENT application-set (application+)>
<!ELEMENT application (application-information, submission-information)>
<!ATTLIST application
    application-containing-files (false | true) #REQUIRED
>
<!ELEMENT application-information (application-number, cross-reference-application-
number*)>
<!ELEMENT application-number (#PCDATA)>
<!ATTLIST application-number
    application-type CDATA #REQUIRED
>
<!ELEMENT cross-reference-application-number (#PCDATA)>
<!ATTLIST cross-reference-application-number
    application-type CDATA #REQUIRED
>
<!ELEMENT submission-information (submission-id, sequence-number, form?)>
<!ELEMENT submission-id (#PCDATA)>
<!ATTLIST submission-id
    submission-type CDATA #REQUIRED
    supplement-effective-date-type CDATA #IMPLIED
```

```
>
<!ELEMENT sequence-number (#PCDATA)>
<!ATTLIST sequence-number
    submission-sub-type CDATA #REQUIRED
>
<!ELEMENT form ((leaf | node-extension)*)>
<!ATTLIST form
    form-type CDATA #REQUIRED
>
<!ELEMENT m1-regional (m1-1-forms?, m1-2-cover-letters?, m1-3-administrative-
information?, m1-4-references?, m1-5-application-status?, m1-6-meetings?, m1-7-fast-track?,
m1-8-special-protocol-assessment-request?, m1-9-pediatric-administrative-information?, m1-10-
dispute-resolution?, m1-11-information-amendment-information-not-covered-under-modules-2-
to-5?, m1-12-other-correspondence?, m1-13-annual-report?, m1-14-labeling?, m1-15-
promotional-material?, m1-16-risk-management-plan?, m1-17-postmarketing-studies?, m1-18-
proprietary-names?, m1-19-pre-eua-and-eua?, m1-20-general-investigational-plan-for-initial-
ind?)>
<!ATTLIST m1-regional
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-1-forms (form*)>
<!ELEMENT m1-2-cover-letters ((leaf | node-extension)*)>
<!ATTLIST m1-2-cover-letters
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-administrative-information (m1-3-1-contact-sponsor-applicant-
information*, m1-3-2-field-copy-certification*, m1-3-3-debarment-certification*, m1-3-4-
financial-certification-and-disclosure*, m1-3-5-patent-and-exclusivity*, m1-3-6-tropical-disease-
priority-review-voucher*)>
<!ATTLIST m1-3-administrative-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-contact-sponsor-applicant-information (m1-3-1-1-change-of-address-or-
corporate-name*, m1-3-1-2-change-in-contact-agent*, m1-3-1-3-change-in-sponsor*, m1-3-1-4-
transfer-of-obligation*, m1-3-1-5-change-in-ownership-of-an-application-or-reissuance-of-
license*)>
<!ATTLIST m1-3-1-contact-sponsor-applicant-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-1-change-of-address-or-corporate-name ((leaf | node-extension)*)>
<!ATTLIST m1-3-1-1-change-of-address-or-corporate-name
    ID ID #IMPLIED
```

```
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-2-change-in-contact-agent ((leaf | node-extension)*)>
<!ATTLIST m1-3-1-2-change-in-contact-agent
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-3-change-in-sponsor ((leaf | node-extension)*)>
<!ATTLIST m1-3-1-3-change-in-sponsor
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-4-transfer-of-obligation ((leaf | node-extension)*)>
<!ATTLIST m1-3-1-4-transfer-of-obligation
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-1-5-change-in-ownership-of-an-application-or-reissuance-of-license ((leaf |
node-extension)*)>
<!ATTLIST m1-3-1-5-change-in-ownership-of-an-application-or-reissuance-of-license
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-2-field-copy-certification ((leaf | node-extension)*)>
<!ATTLIST m1-3-2-field-copy-certification
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-3-debarment-certification ((leaf | node-extension)*)>
<!ATTLIST m1-3-3-debarment-certification
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-4-financial-certification-and-disclosure ((leaf | node-extension)*)>
<!ATTLIST m1-3-4-financial-certification-and-disclosure
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-5-patent-and-exclusivity (m1-3-5-1-patent-information*, m1-3-5-2-patent-
certification*, m1-3-5-3-exclusivity-claim*)>
<!ATTLIST m1-3-5-patent-and-exclusivity
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-5-1-patent-information ((leaf | node-extension)*)>
<!ATTLIST m1-3-5-1-patent-information
```

```
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-5-2-patent-certification ((leaf | node-extension)*)>
<!ATTLIST m1-3-5-2-patent-certification
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-5-3-exclusivity-claim ((leaf | node-extension)*)>
<!ATTLIST m1-3-5-3-exclusivity-claim
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-3-6-tropical-disease-priority-review-voucher ((leaf | node-extension)*)>
<!ATTLIST m1-3-6-tropical-disease-priority-review-voucher
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-4-references (m1-4-1-letter-of-authorization*, m1-4-2-statement-of-right-of-
reference*, m1-4-3-list-of-authorized-persons-to-incorporate-by-reference*, m1-4-4-cross-
reference-to-previously-submitted-information*)>
<!ATTLIST m1-4-references
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-4-1-letter-of-authorization ((leaf | node-extension)*)>
<!ATTLIST m1-4-1-letter-of-authorization
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-4-2-statement-of-right-of-reference ((leaf | node-extension)*)>
<!ATTLIST m1-4-2-statement-of-right-of-reference
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-4-3-list-of-authorized-persons-to-incorporate-by-reference ((leaf | node-
extension)*)>
<!ATTLIST m1-4-3-list-of-authorized-persons-to-incorporate-by-reference
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-4-4-cross-reference-to-previously-submitted-information ((leaf | node-
extension)*)>
<!ATTLIST m1-4-4-cross-reference-to-previously-submitted-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
```

```
>
<!ELEMENT m1-5-application-status (m1-5-1-withdrawal-of-an-ind*, m1-5-2-inactivation-request*, m1-5-3-reactivation-request*, m1-5-4-reinstatement-request*, m1-5-5-withdrawal-of-an-unapproved-bla-nda-anda-or-supplement*, m1-5-6-withdrawal-of-listed-drug*, m1-5-7-withdrawal-of-approval-of-an-application-or-revocation-of-license*)>
<!ATTLIST m1-5-application-status
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-1-withdrawal-of-an-ind ((leaf | node-extension)*)>
<!ATTLIST m1-5-1-withdrawal-of-an-ind
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-2-inactivation-request ((leaf | node-extension)*)>
<!ATTLIST m1-5-2-inactivation-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-3-reactivation-request ((leaf | node-extension)*)>
<!ATTLIST m1-5-3-reactivation-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-4-reinstatement-request ((leaf | node-extension)*)>
<!ATTLIST m1-5-4-reinstatement-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-5-withdrawal-of-an-unapproved-bla-nda-anda-or-supplement ((leaf | node-extension)*)>
<!ATTLIST m1-5-5-withdrawal-of-an-unapproved-bla-nda-anda-or-supplement
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-6-withdrawal-of-listed-drug ((leaf | node-extension)*)>
<!ATTLIST m1-5-6-withdrawal-of-listed-drug
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-5-7-withdrawal-of-approval-of-an-application-or-revocation-of-license ((leaf | node-extension)*)>
<!ATTLIST m1-5-7-withdrawal-of-approval-of-an-application-or-revocation-of-license
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
```

```
<!ELEMENT m1-6-meetings (m1-6-1-meeting-request*, m1-6-2-meeting-background-materials*, m1-6-3-correspondence-regarding-meetings*)>
<!ATTLIST m1-6-meetings
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-6-1-meeting-request ((leaf | node-extension)*)>
<!ATTLIST m1-6-1-meeting-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-6-2-meeting-background-materials ((leaf | node-extension)*)>
<!ATTLIST m1-6-2-meeting-background-materials
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-6-3-correspondence-regarding-meetings ((leaf | node-extension)*)>
<!ATTLIST m1-6-3-correspondence-regarding-meetings
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-7-fast-track (m1-7-1-fast-track-designation-request*, m1-7-2-fast-track-designation-withdrawal-request*, m1-7-3-rolling-review-request*, m1-7-4-correspondence-regarding-fast-track-rolling-review*)>
<!ATTLIST m1-7-fast-track
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-7-1-fast-track-designation-request ((leaf | node-extension)*)>
<!ATTLIST m1-7-1-fast-track-designation-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-7-2-fast-track-designation-withdrawal-request ((leaf | node-extension)*)>
<!ATTLIST m1-7-2-fast-track-designation-withdrawal-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-7-3-rolling-review-request ((leaf | node-extension)*)>
<!ATTLIST m1-7-3-rolling-review-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-7-4-correspondence-regarding-fast-track-rolling-review ((leaf | node-extension)*)>
<!ATTLIST m1-7-4-correspondence-regarding-fast-track-rolling-review
```

```
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-8-special-protocol-assessment-request (m1-8-1-clinical-study*, m1-8-2-
carcinogenicity-study*, m1-8-3-stability-study*, m1-8-4-animal-efficacy-study-for-approval-
under-the-animal-rule*)>
<!ATTLIST m1-8-special-protocol-assessment-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-8-1-clinical-study ((leaf | node-extension)*)>
<!ATTLIST m1-8-1-clinical-study
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-8-2-carcinogenicity-study ((leaf | node-extension)*)>
<!ATTLIST m1-8-2-carcinogenicity-study
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-8-3-stability-study ((leaf | node-extension)*)>
<!ATTLIST m1-8-3-stability-study
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-8-4-animal-efficacy-study-for-approval-under-the-animal-rule ((leaf | node-
extension)*)>
<!ATTLIST m1-8-4-animal-efficacy-study-for-approval-under-the-animal-rule
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-pediatric-administrative-information (m1-9-1-request-for-waiver-of-
pediatric-studies*, m1-9-2-request-for-deferral-of-pediatric-studies*, m1-9-3-request-for-
pediatric-exclusivity-determination*, m1-9-4-proposed-pediatric-study-request-and-
amendments*, m1-9-6-other-correspondence-regarding-pediatric-exclusivity-or-study-plans*)>
<!ATTLIST m1-9-pediatric-administrative-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-1-request-for-waiver-of-pediatric-studies ((leaf | node-extension)*)>
<!ATTLIST m1-9-1-request-for-waiver-of-pediatric-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-2-request-for-deferral-of-pediatric-studies ((leaf | node-extension)*)>
<!ATTLIST m1-9-2-request-for-deferral-of-pediatric-studies
```

```
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-3-request-for-pediatric-exclusivity-determination ((leaf | node-extension)*)>
<!ATTLIST m1-9-3-request-for-pediatric-exclusivity-determination
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-4-proposed-pediatric-study-request-and-amendments ((leaf | node-
extension)*)>
<!ATTLIST m1-9-4-proposed-pediatric-study-request-and-amendments
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-9-6-other-correspondence-regarding-pediatric-exclusivity-or-study-plans ((leaf
| node-extension)*)>
<!ATTLIST m1-9-6-other-correspondence-regarding-pediatric-exclusivity-or-study-plans
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-10-dispute-resolution (m1-10-1-request-for-dispute-resolution*, m1-10-2-
correspondence-related-to-dispute-resolution*)>
<!ATTLIST m1-10-dispute-resolution
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-10-1-request-for-dispute-resolution ((leaf | node-extension)*)>
<!ATTLIST m1-10-1-request-for-dispute-resolution
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-10-2-correspondence-related-to-dispute-resolution ((leaf | node-extension)*)>
<!ATTLIST m1-10-2-correspondence-related-to-dispute-resolution
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-11-information-amendment-information-not-covered-under-modules-2-to-5
(m1-11-1-quality-information-amendment*, m1-11-2-nonclinical-information-amendment*, m1-
11-3-clinical-information-amendment*, m1-11-4-multiple-module-information-amendment*)>
<!ATTLIST m1-11-information-amendment-information-not-covered-under-modules-2-to-5
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-11-1-quality-information-amendment ((leaf | node-extension)*)>
<!ATTLIST m1-11-1-quality-information-amendment
    ID ID #IMPLIED
```

```
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-11-2-nonclinical-information-amendment ((leaf | node-extension)*)>
<!ATTLIST m1-11-2-nonclinical-information-amendment
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-11-3-clinical-information-amendment ((leaf | node-extension)*)>
<!ATTLIST m1-11-3-clinical-information-amendment
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-11-4-multiple-module-information-amendment ((leaf | node-extension)*)>
<!ATTLIST m1-11-4-multiple-module-information-amendment
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-other-correspondence (m1-12-1-pre-ind-correspondence*, m1-12-2-
request-to-charge-for-clinical-trial*, m1-12-3-request-to-charge-for-expanded-access*, m1-12-4-
request-for-comments-and-advice*, m1-12-5-request-for-a-waiver*, m1-12-6-exception-from-
informed-consent-for-emergency-research*, m1-12-7-public-disclosure-statement-for-exception-
from-informed-consent-for-emergency-research*, m1-12-8-correspondence-regarding-exception-
from-informed-consent-for-emergency-research*, m1-12-9-notification-of-discontinuation-of-
clinical-trial*, m1-12-10-generic-drug-enforcement-act-statement*, m1-12-11-anda-basis-for-
submission-statement*, m1-12-12-comparison-of-generic-drug-and-reference-listed-drug*, m1-
12-13-request-for-waiver-for-in-vivo-studies*, m1-12-14-environmental-analysis*, m1-12-15-
request-for-waiver-of-in-vivo-bioavailability-studies*, m1-12-16-field-alert-reports*, m1-12-17-
orphan-drug-designation*)>
<!ATTLIST m1-12-other-correspondence
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-1-pre-ind-correspondence ((leaf | node-extension)*)>
<!ATTLIST m1-12-1-pre-ind-correspondence
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-2-request-to-charge-for-clinical-trial ((leaf | node-extension)*)>
<!ATTLIST m1-12-2-request-to-charge-for-clinical-trial
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-3-request-to-charge-for-expanded-access ((leaf | node-extension)*)>
<!ATTLIST m1-12-3-request-to-charge-for-expanded-access
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
```

```
>
<!ELEMENT m1-12-4-request-for-comments-and-advice ((leaf | node-extension)*)>
<!ATTLIST m1-12-4-request-for-comments-and-advice
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-5-request-for-a-waiver ((leaf | node-extension)*)>
<!ATTLIST m1-12-5-request-for-a-waiver
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-6-exception-from-informed-consent-for-emergency-research ((leaf | node-
extension)*)>
<!ATTLIST m1-12-6-exception-from-informed-consent-for-emergency-research
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-7-public-disclosure-statement-for-exception-from-informed-consent-for-
emergency-research ((leaf | node-extension)*)>
<!ATTLIST m1-12-7-public-disclosure-statement-for-exception-from-informed-consent-for-
emergency-research
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-8-correspondence-regarding-exception-from-informed-consent-for-
emergency-research ((leaf | node-extension)*)>
<!ATTLIST m1-12-8-correspondence-regarding-exception-from-informed-consent-for-
emergency-research
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-9-notification-of-discontinuation-of-clinical-trial ((leaf | node-
extension)*)>
<!ATTLIST m1-12-9-notification-of-discontinuation-of-clinical-trial
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-10-generic-drug-enforcement-act-statement ((leaf | node-extension)*)>
<!ATTLIST m1-12-10-generic-drug-enforcement-act-statement
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-11-anda-basis-for-submission-statement ((leaf | node-extension)*)>
<!ATTLIST m1-12-11-anda-basis-for-submission-statement
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
```

```
>
<!ELEMENT m1-12-12-comparison-of-generic-drug-and-reference-listed-drug ((leaf | node-extension)*)>
<!ATTLIST m1-12-12-comparison-of-generic-drug-and-reference-listed-drug
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-13-request-for-waiver-for-in-vivo-studies ((leaf | node-extension)*)>
<!ATTLIST m1-12-13-request-for-waiver-for-in-vivo-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-14-environmental-analysis ((leaf | node-extension)*)>
<!ATTLIST m1-12-14-environmental-analysis
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-15-request-for-waiver-of-in-vivo-bioavailability-studies ((leaf | node-extension)*)>
<!ATTLIST m1-12-15-request-for-waiver-of-in-vivo-bioavailability-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-16-field-alert-reports ((leaf | node-extension)*)>
<!ATTLIST m1-12-16-field-alert-reports
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-12-17-orphan-drug-designation ((leaf | node-extension)*)>
<!ATTLIST m1-12-17-orphan-drug-designation
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-annual-report (m1-13-1-summary-for-nonclinical-studies*, m1-13-2-summary-of-clinical-pharmacology-information*, m1-13-3-summary-of-safety-information*, m1-13-4-summary-of-labeling-changes*, m1-13-5-summary-of-manufacturing-changes*, m1-13-6-summary-of-microbiological-changes*, m1-13-7-summary-of-other-significant-new-information*, m1-13-8-individual-study-information*, m1-13-9-general-investigational-plan*, m1-13-10-foreign-marketing*, m1-13-11-distribution-data*, m1-13-12-status-of-postmarketing-study-commitments-and-requirements*, m1-13-13-status-of-other-postmarketing-studies-and-requirements*, m1-13-14-log-of-outstanding-regulatory-business*, m1-13-15-development-safety-update-report-dsur*)>
<!ATTLIST m1-13-annual-report
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
```

```
<!ELEMENT m1-13-1-summary-for-nonclinical-studies ((leaf | node-extension)*)>
<!ATTLIST m1-13-1-summary-for-nonclinical-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-2-summary-of-clinical-pharmacology-information ((leaf | node-
extension)*)>
<!ATTLIST m1-13-2-summary-of-clinical-pharmacology-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-3-summary-of-safety-information ((leaf | node-extension)*)>
<!ATTLIST m1-13-3-summary-of-safety-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-4-summary-of-labeling-changes ((leaf | node-extension)*)>
<!ATTLIST m1-13-4-summary-of-labeling-changes
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-5-summary-of-manufacturing-changes ((leaf | node-extension)*)>
<!ATTLIST m1-13-5-summary-of-manufacturing-changes
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-6-summary-of-microbiological-changes ((leaf | node-extension)*)>
<!ATTLIST m1-13-6-summary-of-microbiological-changes
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-7-summary-of-other-significant-new-information ((leaf | node-
extension)*)>
<!ATTLIST m1-13-7-summary-of-other-significant-new-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-8-individual-study-information ((leaf | node-extension)*)>
<!ATTLIST m1-13-8-individual-study-information
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-9-general-investigational-plan ((leaf | node-extension)*)>
<!ATTLIST m1-13-9-general-investigational-plan
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
```

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>
<!ELEMENT m1-13-10-foreign-marketing ((leaf | node-extension)*)>
<!ATTLIST m1-13-10-foreign-marketing
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-11-distribution-data ((leaf | node-extension)*)>
<!ATTLIST m1-13-11-distribution-data
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-12-status-of-postmarketing-study-commitments-and-requirements ((leaf |
node-extension)*)>
<!ELEMENT m1-13-13-status-of-other-postmarketing-studies-and-requirements ((leaf | node-
extension)*)>
<!ATTLIST m1-13-13-status-of-other-postmarketing-studies-and-requirements
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-14-log-of-outstanding-regulatory-business ((leaf | node-extension)*)>
<!ATTLIST m1-13-14-log-of-outstanding-regulatory-business
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-13-15-development-safety-update-report-dsur ((leaf | node-extension)*)>
<!ATTLIST m1-13-15-development-safety-update-report-dsur
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-labeling (m1-14-1-draft-labeling*, m1-14-2-final-labeling*, m1-14-3-
listed-drug-labeling*, m1-14-4-investigational-drug-labeling*, m1-14-5-foreign-labeling*, m1-
14-6-product-labeling-for-2253-submissions*)>
<!ATTLIST m1-14-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-draft-labeling (m1-14-1-1-draft-carton-and-container-labels*, m1-14-1-
2-annotated-draft-labeling-text*, m1-14-1-3-draft-labeling-text*, m1-14-1-4-label-
comprehension-studies*, m1-14-1-5-labeling-history*)>
<!ATTLIST m1-14-1-draft-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-1-draft-carton-and-container-labels ((leaf | node-extension)*)>
<!ATTLIST m1-14-1-1-draft-carton-and-container-labels
    ID ID #IMPLIED
```

```
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-2-annotated-draft-labeling-text ((leaf | node-extension)*)>
<!ATTLIST m1-14-1-2-annotated-draft-labeling-text
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-3-draft-labeling-text ((leaf | node-extension)*)>
<!ATTLIST m1-14-1-3-draft-labeling-text
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-4-label-comprehension-studies ((leaf | node-extension)*)>
<!ATTLIST m1-14-1-4-label-comprehension-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-1-5-labeling-history ((leaf | node-extension)*)>
<!ATTLIST m1-14-1-5-labeling-history
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-2-final-labeling (m1-14-2-1-final-carton-or-container-labels*, m1-14-2-2-
final-package-insert-package-inserts-patient-information-medication-guides*, m1-14-2-3-final-
labeling-text*)>
<!ATTLIST m1-14-2-final-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-2-1-final-carton-or-container-labels ((leaf | node-extension)*)>
<!ATTLIST m1-14-2-1-final-carton-or-container-labels
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-2-2-final-package-insert-package-inserts-patient-information-medication-
guides ((leaf | node-extension)*)>
<!ATTLIST m1-14-2-2-final-package-insert-package-inserts-patient-information-medication-
guides
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-2-3-final-labeling-text ((leaf | node-extension)*)>
<!ATTLIST m1-14-2-3-final-labeling-text
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
```

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<!ELEMENT m1-14-3-listed-drug-labeling (m1-14-3-1-annotated-comparison-with-listed-drug*, m1-14-3-2-approved-labeling-text-for-listed-drug*, m1-14-3-3-labeling-text-for-reference-listed-drug*)>
<!ATTLIST m1-14-3-listed-drug-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-3-1-annotated-comparison-with-listed-drug ((leaf | node-extension)*)>
<!ATTLIST m1-14-3-1-annotated-comparison-with-listed-drug
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-3-2-approved-labeling-text-for-listed-drug ((leaf | node-extension)*)>
<!ATTLIST m1-14-3-2-approved-labeling-text-for-listed-drug
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-3-3-labeling-text-for-reference-listed-drug ((leaf | node-extension)*)>
<!ATTLIST m1-14-3-3-labeling-text-for-reference-listed-drug
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-4-investigational-drug-labeling (m1-14-4-1-investigational-brochure*, m1-14-4-2-investigational-drug-labeling*)>
<!ATTLIST m1-14-4-investigational-drug-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-4-1-investigational-brochure ((leaf | node-extension)*)>
<!ATTLIST m1-14-4-1-investigational-brochure
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-4-2-investigational-drug-labeling ((leaf | node-extension)*)>
<!ATTLIST m1-14-4-2-investigational-drug-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-5-foreign-labeling ((leaf | node-extension)*)>
<!ATTLIST m1-14-5-foreign-labeling
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-14-6-product-labeling-for-2253-submissions ((leaf | node-extension)*)>
<!ATTLIST m1-14-6-product-labeling-for-2253-submissions
    ID ID #IMPLIED
```

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    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-promotional-material (m1-15-1-correspondence-relating-to-promotional-materials?, m1-15-2-materials?)>
<!ATTLIST m1-15-promotional-material
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
    promotional-material-audience-type CDATA #REQUIRED
>
<!ELEMENT m1-15-1-correspondence-relating-to-promotional-materials (m1-15-1-1-request-for-advisory-comments-on-launch-materials?, m1-15-1-2-request-for-advisory-comments-on-non-launch-materials?, m1-15-1-3-pre-submission-of-launch-promotional-materials-for-accelerated-approval-products?, m1-15-1-4-pre-submission-of-non-launch-promotional-materials-for-accelerated-approval-products?, m1-15-1-5-pre-dissemination-review-of-television-ads?, m1-15-1-6-response-to-untitled-letter-or-warning-letter?, m1-15-1-7-response-to-information-request?, m1-15-1-8-correspondence-accompanying-materials-previously-missing-or-rejected?, m1-15-1-9-withdrawal-request?, m1-15-1-10-submission-of-annotated-references?, m1-15-1-11-general-correspondence?)>
<!ATTLIST m1-15-1-correspondence-relating-to-promotional-materials
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-1-request-for-advisory-comments-on-launch-materials ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-1-request-for-advisory-comments-on-launch-materials
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-2-request-for-advisory-comments-on-non-launch-materials ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-2-request-for-advisory-comments-on-non-launch-materials
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-3-pre-submission-of-launch-promotional-materials-for-accelerated-approval-products ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-3-pre-submission-of-launch-promotional-materials-for-accelerated-approval-products
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-4-pre-submission-of-non-launch-promotional-materials-for-accelerated-approval-products ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-4-pre-submission-of-non-launch-promotional-materials-for-accelerated-approval-products
    ID ID #IMPLIED
```

```
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-5-pre-dissemination-review-of-television-ads ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-5-pre-dissemination-review-of-television-ads
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-6-response-to-untitled-letter-or-warning-letter ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-6-response-to-untitled-letter-or-warning-letter
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-7-response-to-information-request ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-7-response-to-information-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-8-correspondence-accompanying-materials-previously-missing-or-
rejected ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-8-correspondence-accompanying-materials-previously-missing-or-rejected
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-9-withdrawal-request ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-9-withdrawal-request
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-10-submission-of-annotated-references ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-10-submission-of-annotated-references
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-1-11-general-correspondence ((leaf | node-extension)*)>
<!ATTLIST m1-15-1-11-general-correspondence
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-2-materials (m1-15-2-1-material*)>
<!ATTLIST m1-15-2-materials
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
    promotional-material-doc-type CDATA #REQUIRED
>
<!ELEMENT m1-15-2-1-material (m1-15-2-1-1-clean-version?, m1-15-2-1-2-annotated-
version?, m1-15-2-1-3-annotated-labeling-version?, m1-15-2-1-4-annotated-references?)>
```

```
<!ATTLIST m1-15-2-1-material
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
    promotional-material-type CDATA #REQUIRED
    material-id CDATA #REQUIRED
    issue-date CDATA #IMPLIED
>
<!ELEMENT m1-15-2-1-1-clean-version ((leaf | node-extension)*)>
<!ATTLIST m1-15-2-1-1-clean-version
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-2-1-2-annotated-version ((leaf | node-extension)*)>
<!ATTLIST m1-15-2-1-2-annotated-version
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-2-1-3-annotated-labeling-version ((leaf | node-extension)*)>
<!ATTLIST m1-15-2-1-3-annotated-labeling-version
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-15-2-1-4-annotated-references ((leaf | node-extension)*)>
<!ATTLIST m1-15-2-1-4-annotated-references
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-risk-management-plan (m1-16-1-risk-management-non-rems?, m1-16-2-
risk-evaluation-and-mitigation-strategies-rems?)>
<!ATTLIST m1-16-risk-management-plan
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-1-risk-management-non-rems ((leaf | node-extension)*)>
<!ATTLIST m1-16-1-risk-management-non-rems
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-risk-evaluation-and-mitigation-strategies-rems (m1-16-2-1-final-rems?,
m1-16-2-2-draft-rems?,    m1-16-2-3-rems-assessment?, m1-16-2-4-rems-assessment-
methodology?, m1-16-2-5-rems-correspondence?, m1-16-2-6-rems-modification-history?)>
<!ATTLIST m1-16-2-risk-evaluation-and-mitigation-strategies-rems
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-1-final-rems ((leaf | node-extension)*)>
```

```
<!ATTLIST m1-16-2-1-final-rems
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-2-draft-rems ((leaf | node-extension)*)>
<!ATTLIST m1-16-2-2-draft-rems
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-3-rems-assessment ((leaf | node-extension)*)>
<!ATTLIST m1-16-2-3-rems-assessment
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-4-rems-assessment-methodology ((leaf | node-extension)*)>
<!ATTLIST m1-16-2-4-rems-assessment-methodology
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-5-rems-correspondence ((leaf | node-extension)*)>
<!ATTLIST m1-16-2-5-rems-correspondence
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-16-2-6-rems-modification-history ((leaf | node-extension)*)>
<!ATTLIST m1-16-2-6-rems-modification-history
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-17-postmarketing-studies (m1-17-1-correspondence-regarding-postmarketing-
commitments*, m1-17-2-correspondence-regarding-postmarketing-requirements*)>
<!ATTLIST m1-17-postmarketing-studies
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-17-1-correspondence-regarding-postmarketing-commitments ((leaf | node-
extension)*)>
<!ATTLIST m1-17-1-correspondence-regarding-postmarketing-commitments
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-17-2-correspondence-regarding-postmarketing-requirements ((leaf | node-
extension)*)>
<!ATTLIST m1-17-2-correspondence-regarding-postmarketing-requirements
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
```

```
>
<!ELEMENT m1-18-proprietary-names ((leaf | node-extension)*)>
<!ATTLIST m1-18-proprietary-names
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-19-pre-eua-and-eua ((leaf | node-extension)*)>
<!ATTLIST m1-19-pre-eua-and-eua
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
<!ELEMENT m1-20-general-investigational-plan-for-initial-ind ((leaf | node-extension)*)>
<!ATTLIST m1-20-general-investigational-plan-for-initial-ind
    ID ID #IMPLIED
    xml:lang CDATA #IMPLIED
>
```

APPENDIX 2: Summary of Changes for Versions of The eCTD Backbone Files Specification for Module 1

A. Summary of Changes for Version 2.4

1. Added eCTD Submission Type 'REMS Supplement'. The updated sections are listed below:

a. 'REMS Supplement' added to Table 2 (Submission Types and Description of Use)

b. 'REMS Supplement' added as valid submission type for PAS and CBE-30 to Table 3 (Supplement-Effective-Date-Types and Descriptions of Use)

c. 'REMS Supplement' added as valid submission type for submission sub-types of 'application', 'amendment', and 'resubmission' to Table 4 (Submission Sub-Types and Descriptions of Use).

2. Updated broken hyperlinks

B. Summary of Changes for Version 2.3

1. References to 503B were modified and/or replaced with Pre-dissemination review of television ads due to re-designation of 503B to 503C (21 USC 353c). The updated sections are listed below:

a. The description of 'Resubmission' in Table 4 (Submission Sub-Types and Descriptions of Use).

b. The promotional material doc type and its description in Table 12 (Promotional Material Doc Types and Descriptions).

2. Changed DTD version references from 3.2 to 3.3 where applicable and replaced the copy of DTD Version 3.2 in Appendix I with DTD Version 3.3.

C. Summary of Changes for Version 2.2

1. Changed DTD version references from 3.1 to 3.2 where applicable and replaced the copy of DTD Version 3.1 in Appendix I with DTD Version 3.2.

2. Revised text, revised table 1, and added table 13 to indicate the new required attribute ***material-id*** and the new optional attribute ***issue-date*** which applies to m1-15-2-1.

D. Summary of Changes for Version 2.1

1. Changed DTD version references from 3.0 to 3.1 and replaced the copy of DTD Version 3.0 in Appendix I with DTD Version 3.1.

a. Version 3.1 of the DTD includes changes to the m1-16 heading and m1-16 sub-headings were added.

E. Summary of Changes for Version 2.0

The following is a brief summary of the changes incorporated in version 2.0 of the Module 1 Backbone Files Specification. Please refer to specific sections within this document to obtain a more detailed description of the changes. The changes made are consistent with eCTD v4, to be implemented using the Regulated Product Submission (RPS) exchange standard.

1. The ***date-of-submission*** and ***product-information*** elements were removed.

2. Module 1 heading 1.9.5 "Proposal for written agreement" was removed. If leaves were previously referenced under a heading element that was removed, lifecycle operators can still be used to delete the leaves. No "new" or "replaced" leaves should be referenced under removed heading elements.

3. An ***id*** element was added under ***applicant-info*** to provide the applicant's or sponsor's corporate DUNS number issued by Dunn & Bradstreet to supplement other identifiers such as the ***company-name*** element.

4. The ***submission-description*** element was added and is optional. The element is limited to 128 characters. It allows for an additional brief description of the purpose of the submission, but should not contain any reviewable information.

5. The ***applicant-contacts*** element was added to capture contact information. One or more contact names, telephone numbers, and email addresses may be submitted for each submission, and at least one contact name is required.

6. The ***application-set*** element can contain one or many applications (i.e., grouped submission). Each application needs to have its own submission information section. When a grouped submission is submitted, the submission content will reside under a single application, but is referenced by multiple eCTD applications. The ***application-contains-files*** element was added to indicate which application contains the files in a grouped submission. This attribute will be used to identify the root application where the submission files will be stored.

7. The element ***cross-reference-application-number*** was added to provide the ability to list cross-referenced applications. An example is an ANDA referencing a DMF; the ANDA submission would reference the application type (DMF) and application number (DMF number) in the ***cross-reference-application-number*** element.

8. A new ***submission-information*** element has been introduced to group information about the submission. The ***submission-information*** element contains three elements (***submission-id, sequence-number,*** and ***form***).

9. Certain forms are provided under the ***submission-information*** element to allow each application's form to be displayed within the appropriate application.

10. Submission type was changed from an element to be an attribute of the ***submission-id*** element. In addition, an attribute of ***supplement-effective-date-type*** was added and is also an attribute of the ***submission-id*** element. The ***supplement-effective-date-type*** is only applicable if the ***submission-type*** is an efficacy, labeling or CMC supplement and the ***submission-sub-type*** is "application."

11. The ***sequence-number*** element was relocated under the ***submission-information*** element to group similar elements with information about the submission.

12. An attribute for ***submission-sub-type*** was added to more accurately reflect the nature of a submission and its relationship to the associated regulatory activity.

13. Submissions are grouped with their regulatory activity by using the ***submission-type***, ***submission-id***, and ***sequence-number***.

Example #1: The Original Application regulatory activity below has two presubmissions, the original application submission, and two amendments.		
New Module 1		**Old Module 1**
Presubmission (meeting request)		
application-containing files	true	
submission-id	0001	
submission-type attribute	fdast1 (Original Application)	Sequence: 0000
sequence-number	0001	Related Sequence: Null
submission-sub-type attribute	fdasst2 (presubmission)	
Presubmission (meeting briefing package)		
application-containing files	true	
submission-id	0001	
submission-type attribute	fdast1 (Original Application)	Sequence: 0001
sequence-number	0002	Related Sequence: Null
submission-sub-type attribute	fdasst2 (presubmission)	
Original Application		
application-containing files	true	
submission-id	0001	
submission-type attribute	fdast1 (Original Application)	Sequence: 0002
sequence-number	0003	Related Sequence: Null
submission-sub-type attribute	fdasst3 (application)	
Amendment #1		
application-containing files	true	
submission-id	0001	
submission-type attribute	fdast1 (Original Application)	Sequence: 0003
sequence-number	0004	Related Sequence: 0002
submission-sub-type attribute	fdasst4 (amendment)	
Amendment #2		
application-containing files	true	
submission-id	0001	
submission-type attribute	fdast1 (Original Application)	Sequence: 0004
sequence-number	0005	Related Sequence: 0002
submission-sub-type attribute	fdasst4 (amendment)	

Example #2: The Efficacy Supplement regulatory activity below has the supplement submission and two amendments.		
New Module 1		**Old Module 1**
Efficacy Supplement (new indication)		
application-containing files	true	
submission-id	0006	
submission-type attribute	fdast2 (Efficacy Supplement)	
supplement-effective-date-type attribute	fdasedt1 (Prior Approval	

	Supplement (PAS))	
sequence-number	0006	Sequence: 0006
submission-sub-type attribute	fdasst3 (application)	Related Sequence: Null
Amendment #1 to Efficacy Supplement		
application-containing files	true	
submission-id	0006	
submission-type attribute	fdast2 (Efficacy Supplement)	
sequence-number	0008	Sequence: 0008
submission-sub-type attribute	fdasst3 (amendment)	Related Sequence: 0006
Amendment #2 to Efficacy Supplement		
application-containing files	true	
submission-id	0006	
submission-type attribute	fdast2 (Efficacy Supplement)	
sequence-number	0010	Sequence: 0010
submission-sub-type attribute	fdasst3 (amendment)	Related Sequence: 0006

14. Certain admin and module 1 elements (***m1-1-forms*** and the sections and subsections of ***m1-15-promotional-material***) require an attribute.

15. Additional headings elements were added to *1.15 Promotional material* to further define the submission of promotional materials.

16. Additional heading elements were added or revised. Please refer to the *The Comprehensive Table of Contents Headings and Hierarchy* for the complete set of changes.

17. The *us-regional.xml* refers to and validates from supporting and required files (DTD, stylesheet, and value-type lists) located at website addresses instead of local file paths (previously required files were located in the util folder). The stylesheet (*us-regional.xsl*) was updated to refer to the new attribute value lists (XML files) and DTD for the purpose of validation and display.

18. The heading table was removed from the *Heading Elements for Module 1* section.