FDA Module 1
Electronic Common Technical Document (eCTD) v4.0
Implementation Guide v1.7

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research
June 2024

DOCUMENT CHANGE HISTORY

Date	Version	Summary of Changes
2016-02-23	1.0	Initial Step 4 Regional Implementation Guide.
2017-03-20	1.1	Revised Step 4 Regional Implementation Guide based on review comments and consistency changes with the ICH eCTD v4.0 Implementation Guide v1.2.
2019-12-03	1.2	Revised Step 4 Regional Implementation Guide based on review comments and consistency changes with the ICH eCTD v4.0 Implementation Guide v1.3.
2021-01	1.3	Revised based on public comments from the "Electronic Common Technical Document v4.0 Technical Conformance Guide; Food and Drug Administration Electronic Common Technical Document v4.0 Module 1 Implementation Package; Request for Comments" Federal Register Notice. Changes include removal the following: 1) Two-way communications and associated data elements; 2) Regulatory Review Time; 3) Applicant DUNS Number; 4) Document media type; and 5) Category Event. In addition, changes have been made to the folder structure and additional instructions for placement of files for grouped submissions.
2021-06	1.4	Revised based on consistency review of eCTD v4.0 references (e.g., updated excluded elements for applicant) and notation of elements and attributes. No substantive changes have been made in this version.
2022-08	1.5	Revised based on changes to the ICH eCTD v4.0 Implementation package that includes eCTD v3.2.2 Forward Compatibility requirements and replaces the v4.0 Transition Mapping Message.
2024-06	1.7	Revised based on changes to the ICH eCTD v4.0 Implementation Guide and Controlled Vocabulary Package; and additional US FDA Regional clarifications for: Grouped Submissions, Forward Compatibility, Contact Type, Contact Person Address Update instructions (not needed), Allowable datatypes for Keyword code, and Application Reference instructions for references to Master Files.

TABLE OF CONTENTS Page

List of Figures

List of Tables

NOTICE TO READERS

INSTRUCTIONS TO READER

This is a technical document that provides instructions on how to implement the eCTD v4.0 specification for the FDA Module 1 submission content. The information in this document is provided in a consistent manner with the ICH eCTD v4.0 Implementation Guide. In addition, the reader may be prompted by visual cues about the context or referenced information being presented in the document.

Document Content

In the document there are several notations that are used to provide clarity to the subject matter. The first is the use of XML components (i.e., elements and attributes) versus the concept that it represents. The document text follows the notations described below:

- XML components
  - The document's narrative text is in bold, italicized text in camel case, e.g., ***contextOfUse***
  - The XML samples are as notated below in the XML Snippets section.
- Concepts without attribution to the standard and/or message
  - A defined concept, e.g., Context of Use is noted in plain text with first letter capitalized.

The following table provides visual cues that are used in the document.

Table 1: Legend of Symbols used in Document

Icon	Description
	Technical descriptions
	Items to be careful to follow
	Additional Instructions
	References to other documents

XML Snippets

The following figure indicates the color coding used in the XML snippets and any meaning that should be inferred in the samples.

Table 2: Legend for XML Snippets

Text Color	Description *Sample*
Teal	Schema components *<?xml version "1.0" encoding="UTF-8"?>*
Blue	XML notations < ....= "">
Brown	XML element *id* *code*
Red	XML attribute *root* *extension*
Black	Value of the attribute or element *2.16.840.1.113883*

The following rules were used in the development of the XML samples:

- The notation of <!--....notes….-- > was used to describe conditions that should be met for an element.
- The notation … [Description] … was used to indicate when there were additional elements not represented in the XML, but may be present in the actual XML message.

Note: *XML editors may display these XML components differently, please use the legend above for XML presented in this document.*

Location in XML

Each of the elements in this document includes a section named, “Location in XML”. The notation included uses the following convention:

Table 3: Location in XML Notation

Notation	Description	Instruction for use
>	Single arrow	The element follows the previous without indentation in the XML.
>>	Double arrow	The element follows the previous with an indentation in the XML.

For example, the following location shows both notations and is followed by the XML sample.

- ***controlActProcess>>subject>>submissionUnit>>component>>priorityNumber> contextOfUse***

Element’s location in XML

```
<controlActProcess classCode="ACTN" moodCode="EVN">
        <subject typeCode="SUBJ">
            <submissionUnit>
                <id root="e6f34476-8288-43f2-a2ea-5860d19fcf32"/>
                <code code="us_submission_unit_type_1"
                codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.13.2"/>
                <title value="Original Application- Indication: pain"/>
                <statusCode code="active"/>
                <component>
                    <priorityNumber value="1000"/>
                    <contextOfUse>
```

The priority number is represented in the path as it is a required element. In some cases optional elements will not appear in this notation. The schema is used to enforce any element sequencing requirements, but not optional elements.

Refer to the ICH eCTD v4.0 Implementation Guide for the ICH specific required elements.

Note: For FDA specific required elements, refer to Section 8.2 of this document.

XML Elements Tables

A table has been provided for each element in the XML message. When elements have multiple element parts or attributes, they are provided in one table. When there are no attributes or values for an element, the cell is grayed out to indicate that an attribute value is not required in the XML message.

Table 4: Sample XML Element Table

Table Name: <element>.<element 2>

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Conformance				
Business Rules				
Excluded Elements and/or Attributes				

Table Name: Each table is named for the elements it is representing in the XML – i.e., <element>.<element 2>. For example, the Application element has an element for the identifier, it would be represented as: ***application.id***.

Element: Identifies the XML element.

Attribute: Identifies the XML attribute.

Cardinality: Provides information on how many times the element/attribute can be repeated in the XML message. The values in this table define the cardinality to be applied in eCTD v4.0 implementation, which sometimes restrict the cardinality defined in the schema.

Value(s) Allowed/Examples: Identifies the values allowed using simple data types and any associated examples. References to controlled vocabulary are also provided.

Description/Instructions: Provides a description of the element or attribute.

Conformance: Identifies the validation requirements (e.g., XML Elements or attributes) and/or conditions that need to be met by the element.

Business Rules: Identifies any business rules that are harmonized for ICH and references to Regional/Module 1 Implementation Guides when the business rules are not harmonized.

Excluded Elements and/or Attributes: Identifies datatype elements and/or attributes that are part of the HL7 Regulated Product Submission standard and not included in the Module 1 portion of the eCTD v4.0 Implementation.

1. PURPOSE

This document serves as the implementation guide and a technical specification for the Food and Drug Administration (FDA) Electronic Common Technical Document (eCTD) v4.0 Module 1 using the Regulated Product Submission (RPS) Release 2, Normative standard. The audience for this document is mainly the individuals or organizations creating or implementing eCTD v4.0 publishing and/or review systems and its use should enable eCTD tool vendors to build a tool that publishes or displays eCTD compliant messages (i.e., utilizing the RPS standard) to the intended recipients of the information.

Note to Implementers: This implementation guide should be used in conjunction with the ICH eCTD v4.0 Implementation Guide, as the eCTD v4.0 message may be incomplete without following instructions in both implementation guides.

2. SCOPE

The RPS standard defines the message for exchanging information electronically between Regulators and Regulated Industry. The message provides the ability to describe the contents of the regulatory exchange and all information needed to process the exchange between parties. The RPS message is designed to be flexible enough to be used to support regulatory exchanges for any regulated product.

This document only includes eCTD v4.0 Module 1 instructions for the FDA regional content of the eCTD. The instructions for eCTD v4.0 Modules 2 – 5, which are shared across all ICH regions, are not included in this implementation guide. Refer to the ICH eCTD v4.0 Implementation Guide for additional instructions necessary to create a complete eCTD v4.0 message. In addition, sections in this document may also be included in the ICH eCTD v4.0 Implementation Guide and may include a reference back to that document.

3. COMPONENTS OF THE ECTD V4.0

This section provides a brief overview of the essential components of the eCTD v4.0 specification. The essential components include:

- OIDs and UUIDs (summarized in Section 3.6)
- Data Types (summarized in Section 3.7)
- ICH Implementation Guide (summarized in Section 3.8)
- Files and Folders (detailed information provided in Section 4)
- Controlled Vocabulary (detailed information provided in Section 5)
- ICH eCTD v4.0 XML Schema (detailed information provided in Section 6)
- Forward Compatibility from v3.2.2 (detailed information in Section 7)
- eCTD v4.0 XML message (detailed information provided in Section 8)

Each of these components is detailed in the subsequent sections to include specific information about the component's role in the implementation of this specification. In order to compose a complete eCTD v4.0 compliant message, the contents of this implementation guide are complemented by several other documents. The focus of this document is to outline the essential components of the eCTD v4.0 and specifically the information required to compose Module 1 of the CTD.

Note: Reference the ESTRI Website (https://www.ich.org/page/electronic-standards-estri) for complete list of documents in the ICH eCTD v4.0 Implementation and Controlled Vocabulary documents and the

FDA eCTD website for a complete list of documents for the FDA Module 1 documents for the eCTD v4.0 message.

3.1 Reference Documents

For additional regional references, the following documents should be referenced for complete regulatory and technical content:

- *FDA Guidance for Industry, Providing Regulatory Submissions in Electronic Format — Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*
- *FDA Technical Specification Document, eCTD v4.0 Technical Conformance Guide*
- *ICH eCTD v4.0 Implementation Guide*
- *ICH eCTD v4.0 and FDA Module 1 Controlled Vocabulary Spreadsheet and Genericode files*
- *ICH Specification for Submission Format for eCTD*
- *FDA Specifications for File Format Types Using eCTD Specifications*
- *FDA Study Data Technical Conformance Guide*

Note to Implementers: The FDA Module 1 Controlled Vocabulary provided in the Spreadsheet format is intended as the human readable version of the content, and the Genericode as a computable version of the content. The information provided in both files is exactly the same.

3.2 Files and Folders

For additional details regarding files and folders in Module 1, refer to Section 4 in this document.

Refer to the ICH eCTD v4.0 Implementation Guide for general information on the files and folders.

3.3 Controlled Vocabularies

The controlled vocabularies are detailed in Section 5 and examples are given for the applicable XML components in Section 8 (i.e., elements with controlled vocabulary).

Refer to the ICH eCTD v4.0 Implementation Guide for additional information about the controlled vocabulary maintained by ICH and external organizations.

3.4 ICH eCTD v4.0 XML Schema

This section outlines the required schema files for the ICH eCTD v4.0 Message.

Refer to the ICH eCTD v4.0 Implementation Guide for the schema file inventory.

3.5 The eCTD v4.0 XML Message

The eCTD v4.0 message is based on the ICH eCTD v4.0 schema and has only been constrained where noted in this Implementation Guide or the ICH eCTD v4.0 Implementation Guide. One XML message should be created for each exchange as a Submission Unit.

Refer to the ICH eCTD v4.0 Implementation Guide for additional information about the composition of the XML message.

3.6 OIDs and UUIDs

There are two types of unique identifiers, Object Identifiers (OIDs) and Universally Unique Identifiers (UUIDs). The subsections below provide additional information on how they are used by the FDA regional implementation.

3.6.1 Object Identifiers

Refer to the ICH eCTD v4.0 Implementation Guide for additional details.

The current OID for the FDA code lists is:

- FDA-ectd4-code-lists - 2.16.840.1.113883.3.989.5.1.2.2.1

The FDA OIDs are typically used as the code system value. Refer to the Module 1 Controlled Vocabulary OID list for the assigned code systems.

In addition, an OID may also be designated as the identifier ***application.id@root*** attribute (Refer to Section 8.2.10.2.1) and ***submission.id@root*** attribute (Refer to Section8.2.8.2.1), the OID is the namespace OID (provided by the FDA) and the identifier extension is a value assigned by that namespace (i.e., the application or submission number).

3.6.2 Universally Unique Identifiers

Refer to the ICH eCTD v4.0 Implementation Guide for additional details.

When providing the application number assigned by the FDA for the ***application.id@root, applicationReference.id@root*** or the specific case outlined in Section 8.2.8.6 for the submission number, ***submission.id@root***, the following OID namespaces should be used instead of a universally unique identifier:

- CBER Application Id OID - 2.16.840.1.113883.3.989.5.1.2.2.1.15.1
- CDER Application Id OID - 2.16.840.1.113883.3.989.5.1.2.2.1.16.1

The following OID should only be used for ***applicationReference.id@root*** to identify related medical device applications:

- CDRH Application Id OID - 2.16.840.1.113883.3.989.5.1.2.2.1.17.1

Refer to Section 8.2.10 and 8.2.12 for additional information about the use of these OIDs.

3.7 Data Types

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

3.8 ICH eCTD v4.0 Implementation Guide for Modules 2-5

The ICH eCTD v4.0 Implementation Guide for Module 2-5 provides the instructions for organizing the documentation in the submission (i.e., the documents and placement in the CTD). The regulatory submission content for investigational or marketing information is mainly found in Module 2-5 of the CTD except for the content that is administrative and region specific.

Note to Implementers: *The information in this Implementation Guide is necessary, but not sufficient for creating the complete XML message for transmission. Please reference the ICH eCTDv4.0 Implementation Guide to send a complete XML message. The ICH eCTD v4.0 Implementation Guide is available through the ICH ESTRI website. (https://www.ich.org/page/electronic-standards-estri).*

3.9 ICH Harmonized Elements

This section outlines the XML elements that are included in the ICH eCTD v4.0 Implementation Guide and harmonized across the Regions unless otherwise noted in this document.

3.9.1 ICH Included Elements

Refer to the ICH eCTD v4.0 Implementation Guide for the ICH Included Elements.

3.9.2 ICH Excluded Elements

Refer to the ICH eCTD v4.0 Implementation Guide for the ICH Excluded Elements.

3.10 FDA-Specific Elements

The elements and business rules that are specific to the FDA are covered in this document.

3.10.1 FDA Included Elements

The following elements are included in this document with additional regional guidance:

- ***submissionUnit***
- ***keyword***
- ***submission***
- ***contactParty***
- ***application***
  - ***reference.applicationReference***
  - ***holder.applicant***
- ***contextOfUse***
  - ***subjectOf.submissionReference***

3.10.2 FDA Excluded Elements

In addition to the excluded elements in the ICH eCTD v4.0 Implementation Guide for Module 2-5, there were region-specific elements identified that may also be excluded from the FDA implementation. The

following elements are excluded from the FDA implementation of eCTD v4.0 and should not be included in the XML Message:

- ***application***
  - ***subject.ReviewProcedure***
  - ***informationRecipient.territorialAuthority***
- ***submission***
  - ***subject1.regulatoryStatus***
  - ***subject3.mode***
  - ***subject4.regulatoryReviewTime***
  - ***subject5.submissionGroup***

- ***review***
  - ***subject1.manufacturedProduct***
  - ***subject2.productCategory***
  - ***subject3.regulatoryStatus***
  - ***holder.applicant***
  - ***author.territorialAuthority***

- ***categoryEvent***

4. SUBMISSION CONTENTS, FOLDER AND FILE STRUCTURE

The folder and file structure specified for the document contents being transmitted along with the XML message should follow various specifications and rules as presented below in this section.

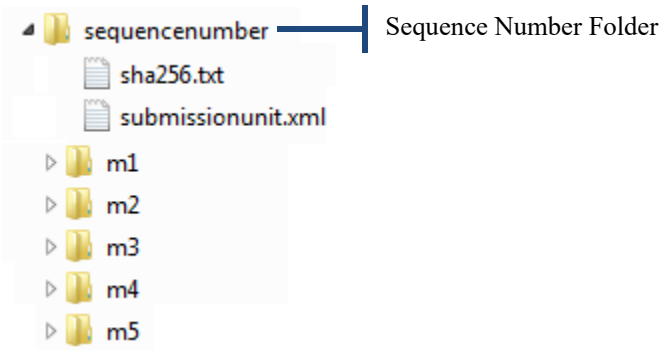
4.1 Folder Structure and Submission Unit Contents

When submitting the contents of a Submission Unit, the following structure should be used:

> The *Regionally-specified Folder* is not included in the FDA Module 1 implementation. This folder should not be included in the submission unit package.
>
> The *Sequence Number Folder* must be submitted and named with the "*sequence number"* of the Submission Unit i.e., the actual value of the sequence number (e.g., 1).

The applicant will be sending submission contents as one Submission Unit within each message transmission. All documents in the submission must be placed in a main submission folder using sequence number (which you must specify) that is unique within the application. Figure 1: Submission Unit depicts the folder structure for a Submission Unit sent by the applicant.

Figure 1: Submission Unit Folder



Refer to the ICH eCTD v4.0 Implementation Guide for additional information about the submission unit contents.

When there is more than one Submission in the Submission Unit (i.e., a grouped submission), all submitted documents must be referenced by only one application element, this is considered the primary application. The sequence number of the primary application must be designated as the sequence number folder as depicted in Figure 1. See Section 8.3 Grouped Submissions for additional information.

4.2 Naming Conventions

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

4.3 Allowable Characters

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

4.4 Length

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

4.5 Pathname Conventions and Best Practices

Refer to the ICH eCTD v4.0 Implementation Guide for details. For instruction on file reuse, see the File Reuse Appendix in Section 9.

4.6 Folder Hierarchy

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

Note: Module 1 typically has one folder. In all modules, only use subfolders if the files warrant an additional level of organization or to comply with other FDA technical specification or guidance.

4.7 File Formats

In the eCTD v4.0 message, file formats are not specified by the ICH eCTD v4.0 Implementation Guide and are not maintained in this document. Refer to Section 3.1 Referenced Documents for additional information on file formats.

4.8 Checksums

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

4.9 Compressed Archive

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

5. CONTROLLED VOCABULARIES

As described in Section 3.3, there is extensive use of controlled vocabularies in the execution of an eCTD v4.0 message. The information in the following sub-sections outline the controlled vocabulary used in developing an eCTD v4.0 message. There are several different authoritative sources for the controlled vocabulary, and as such they are categorized below by the organization that controls the content.

Note to Implementers: *The controlled vocabulary is provided both in genericode and spreadsheet file formats.*

5.1 Controlled Vocabularies Specified Regionally

The controlled vocabularies specified by the FDA for the eCTD v4.0 implementation are provided in the Module 1 Controlled Vocabulary files (e.g., genericode or spreadsheet). The ***codeSystem*** OIDs and code values for each of the code sets are defined by FDA and are available in the associated documents. The following vocabularies have additional values defined by the FDA:

- US Application Type
- US Context of Use
- US CoU Keyword Definition Type
- US Form Type
- US Promotional Document Type
- US Promotional Material Audience Type
- US Promotional Material Type
- US Submission Contact Status
- US Submission Contact Type
- US Submission Type
- US Submission Unit Status
- US Submission Unit Type
- US Telecom Capabilities
- US Telecom Use

5.2 Excluded Regional Vocabularies

The FDA controlled vocabulary is only provided for code elements that are allowed. There are elements and their code attributes which are excluded from the FDA controlled vocabulary. The excluded code lists include:

- ***applicationReference.reasonCode@code*** (Application Reference Reason)
- ***ingredientSubstance.code@code*** (Ingredient)
- ***manufacturedProduct.code@code*** (Product)
- ***mode.code@code*** (Mode)
- ***territory.code@code*** (Territorial Authority Place or Territory Named Entity)
- ***regulatoryReviewTime.code@code*** (Regulatory Review Time)
- ***reviewProcedure.code@code*** (Review Procedure)
- ***productCategory.code@code*** (Product Category)
- ***categoryEvent.code@code*** (Category Event)

Refer to Section 3.9.2 for ICH Excluded elements and 3.10.2 for FDA Excluded elements.

5.3 Controlled Vocabularies specified by ICH

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

5.4 Controlled Vocabulary specified by HL7

The controlled vocabularies are constrained in the FDA regulatory submissions as follows:

- ***submissionUnit.statusCode***
- ***submissionContact.statusCode***

5.5 Sender-defined Vocabulary

Refer to the ICH eCTD v4.0 Implementation Guide for details.

5.6 Controlled Vocabulary Versioning

The Controlled Vocabulary Versioning is used to determine the valid values accepted by the receiving system.

Refer to the ICH eCTD v4.0 Implementation Guide and Controlled Vocabulary package for details.

Refer to the FDA eCTD v4.0 Controlled Vocabulary Package for details.

6. ICH eCTD v4.0 XML Schema

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

7. FORWARD COMPATIBILITY

In addition to the instructions presented in the ICH eCTD v4.0 Implementation Guide, the FDA allows the conversion of content from eCTD v3.2.2 to v4.0 messaging features. The information provided below supplements instructions in the ICH eCTD v4.0 Implementation Guide for Forward Compatibility.

The following special instructions should be considered when moving from eCTD v3.2.2 to v4.0 submissions:

7.1 Leaf Reference

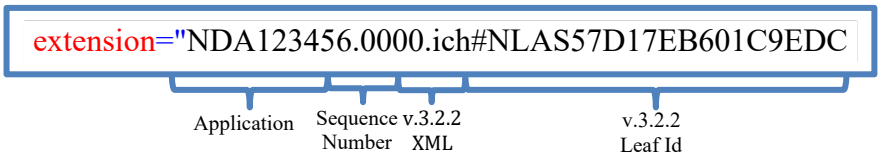
Leaf References for content life cycle will be contained in the same application and there are no additional instructions. However, when referring to eCTD v3.2.2 documents across applications, the application type and application number should be concatenated as follows:

- Application Type – use the application type prefix values in Section 10.

Note that the prefix must be in uppercase when including as a value – i.e., the application type prefix is case-sensitive.

- Application Number – as assigned to the referenced application. This should be different than the application in the submission unit. If the content is in the same application, please start your leaf reference with the appropriate sequence number in the application.

For example:



Note there is no delimiter between the application type and application number. Including a delimiter may cause an error in locating the content being referenced.

7.2 Keywords in Forward Compatibility

It is important to note that all keywords may not have existed as attributes in the ICH or FDA eCTD backbone (i.e., DTD files). Keywords therefore may need to be established from multiple locations from eCTD v3.2.2 messages. Refer to the ICH Implementation Guide (Section 8.1.2, Table 6) for ICH specific mappings. Refer to Table 5: Module 1 Attribute and Element Mappings which provides the remaining mappings for eCTD v4.0 Keywords.

Table 5: Module 1 Attribute and Element Mappings

V3.2.2 Element/Attribute	Notes	V4.0 Element/Attribute	Notes
applicant-contacts	v3.2.2 Element	***contactParty***	
applicant-contact-type	v3.2.2 Attribute	***contactParty.code@code***	
applicant-contact-name	v3.2.2 Element	***contactParty.contactPerson.name.part***	Name parts are used
telephones	v3.2.2 Element	***contactParty.contactPerson.telecom.item@value***	
telephone-number-type	v3.2.2 Attribute	***contactParty.contactPerson.telecom.item@use*** ***contactParty.contactPerson.telecom.item@capabilities***	This is defined by FDA in the US Telecom Use Capabilities value set
emails	v3.2.2 Element	***contactParty.contactPerson.telecom.item@value***	
application-information	v3.2.2 Element	***application***	
application-type	v3.2.2 Attribute	***application.code@code***	
application-number	v3.2.2 Element	***application.id@extension***	
cross-reference-application-number.	v3.2.2 Element	***application.reference.applicationReference.id***	
company-name	v3.2.2 Element	***applicant.sponsorOrganization.name.part@value***	
material-id	v3.2.2 Attribute	***keyword.code@code***	This is an FDA Keyword Definition Type, and sender-defined
promotional-material-audience-type	v3.2.2 Attribute	***keyword.code@code***	These are sender- defined keywords and keyword definitions need to be

V3.2.2 Element/Attribute	Notes	V4.0 Element/Attribute	Notes
promotional-material-doc-type	v3.2.2 Attribute		established before they are referenced in the keyword element,
promotional-material-type	v3.2.2 Attribute		
promotional-material-audience-type	v3.2.2 Element		
material-id	v3.2.2 Attribute		
issue-date	v3.2.2 Attribute		
submission-description	v3.2.2 Element	***submissionUnit.title@value***	
submission-type	v3.2.2 Attribute	***submission.code@code***	
submission-sub-type	v3.2.2 Attribute	***submissionUnit.code@code***	
submission-id	v3.2.2 Element	***submission.id.item@root***	
sequence-number	v3.2.2 Element	***sequenceNumber@value***	
form-type	v3.2.2 Attribute	***keyword.code@code***	This is defined by FDA in the US Form Type value set
supplement-effective-date-type	v3.2.2 Attribute	Not included in v4.0	

7.3 Sequence Number

The sequence number follows the same instructions in the ICH eCTD v4.0 Implementation Guide unless the following scenario exists:

- Once an eCTD v4.0 message is submitted, the sequence number should continue to be assigned sequentially and issued as whole numbers instead of following the v3.2.2 instructions for 4-digit values with leading zeros.

7.4 Submission Number

The submission number follows the same instructions in the ICH eCTD v4.0 Implementation Guide unless the following scenario exists:

- If continuing a regulatory activity, the submission number should reference the initial sequence for the regulatory activity using the ***id@root*** attribute for the appropriate namespace OID (e.g., CDER or CBER OID) and ***id@extension*** attribute for the sequence number submitted for the initial submission unit for the regulatory activity. Please reference the eCTD v4.0 Technical Conformance Guide for additional information when submitting eCTD v4.0 messages to regulatory activities initiated before submitting an eCTD v4.0 submission unit.

7.5 Grouped Submission

All applications in the group should already be converted to eCTD v4.0 when a group submission is submitted in eCTD v4.0. Therefore, all keywords should be standardized across applications prior to or in the initial submission unit of the Grouped Submission.

Refer to the ICH eCTD v4.0 Implementation Guide and the eCTD v4.0 Technical Conformance Guide for additional information about the Forward Compatibility.

8. eCTD v4.0 XML Message

Refer to the ICH eCTD v4.0 Implementation Guide for details as there are no regional variations.

8.1 Message Header

The message header information provides a set of elements that are needed to specify the sender and receiver as well as the version of the ICH and Regional/Module 1 Implementation Guides used to generate the message.

8.1.1 XML Elements

The following XML shows the required elements/attributes to validate the message against the schema.

Table 6: Message Header XML Structure

XML Structure
<PORP_IN000001UV ITSVersion="XML_1.0" xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xsi:schemaLocation="urn:hl7-org:v3 PORP_IN000001UV.xsd"> <id/> <creationTime/> <interactionId/> <processingCode/> <processingModeCode/> <acceptAckCode/> <receiver> <device classCode="DEV" determinerCode="INSTANCE"> <id> <item root="" identifierName=""/>

These elements should be represented with self-closing tags as shown here.

Refer to the ICH eCTD v4.0 Implementation Guide

```
            </id>
        </device>
    </receiver>
    <sender>
        <device classCode="DEV" determinerCode="INSTANCE">
            <id/>
        </device>
    </sender>
```

Refer to the ICH eCTD v4.0 Implementation Guide

8.1.2 Required Elements

The FDA Module 1 Implementation Guide (IG) OID is required in the Message Header. If the FDA Module 1 IG OID is not present, the submission unit will be rejected. Refer to the US FDA Validation specification for specifics.

Refer to the ICH eCTD v4.0 Implementation Guide for specific information about the message header.

8.1.3 Message Header XML Sample

The following XML sample shows the content of the message header ***id*** element. The ***receiver.device.id*** element contains the IG versioning information required for the eCTD v4.0 Message XML header:

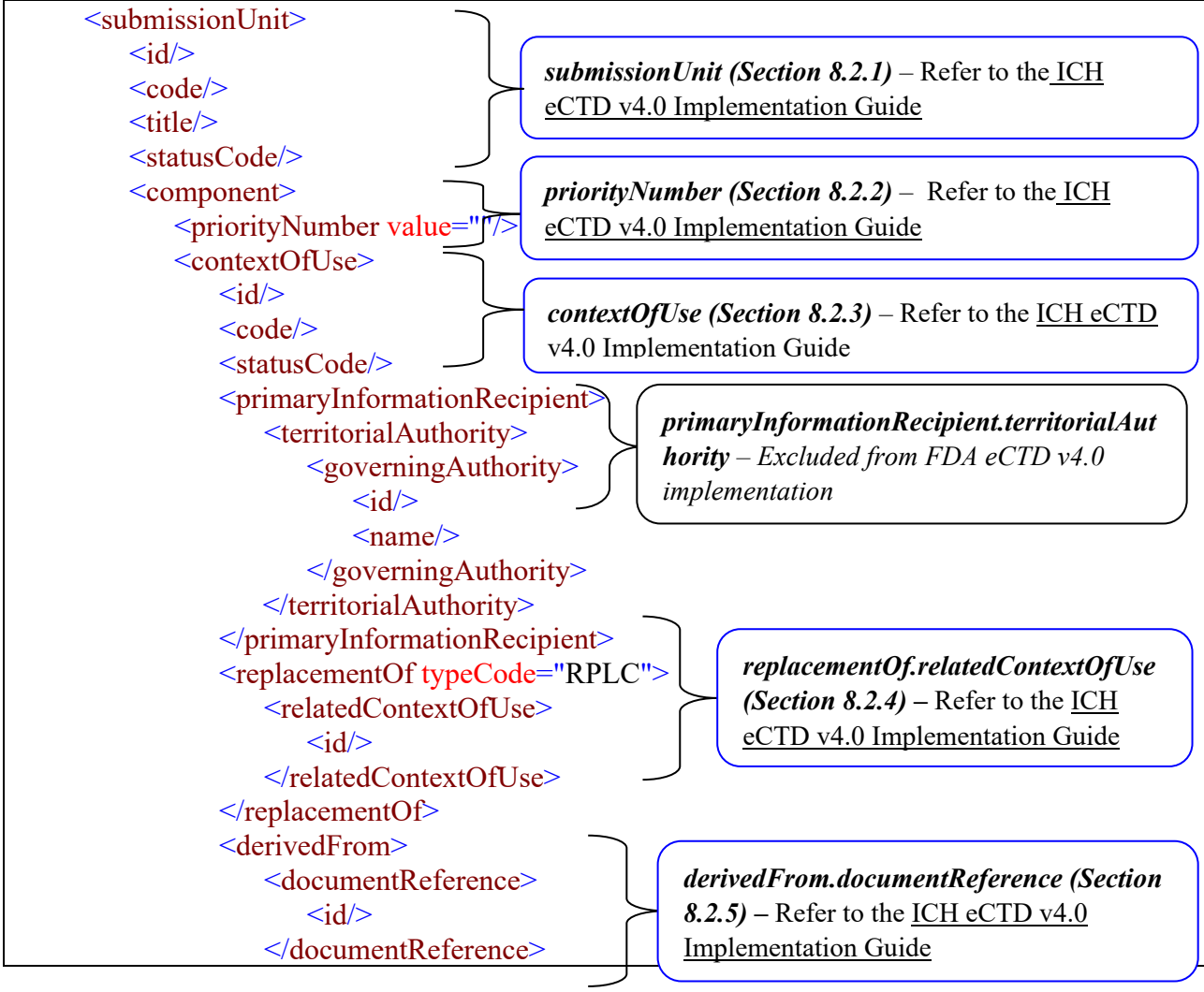
```
    <id/>
    <creationTime/>
    <interactionId/>
    <processingCode/>
    <processingModeCode/>
    <acceptAckCode/>
    <receiver typeCode="RCV">
        <device classCode="DEV" determinerCode="INSTANCE">
            <id>
              <item root="2.16.840.1.113883.3.989.2.2.1.11.4" identifierName="ICH eCTD v4.0 IG
v1.5/>
              <item root="2.16.840.1.113883.3.989.5.1.2.2.1.18.6" identifierName="FDA eCTD v4.0 IG
v1.5"/>
            </id>
        </device>
    </receiver>
    <sender typeCode="SND">
        <device classCode="DEV" determinerCode="INSTANCE">
            <id/>
        </device>
    </sender>
```

8.2 Payload Message

The following table provides a breakdown of the eCTD v4.0 XML structure noting the placement of each element in the XML Schema. The table is organized with the following three elements in the structure: ***submissionUnit***, ***submission*** and ***application***. The elements are annotated with balloon text boxes that provide references to either this document (outlined in blue and referenced by Section

number) or the ICH eCTD v4.0 Implementation Guide to identify the authoritative source of information for the element.

Table 7: eCTD v4.0 XML Message Structure

XML Structure
The eCTD v4.0 begins at the ***controlActProcess*** of the payload XML message related to Module 1 content.
<controlActProcess classCode="ACTN" moodCode="EVN"> <subject typeCode="SUBJ">
The ***submissionUnit*** element contains the following Context of Use elements and their attributes: • ***component.contextOfUse*** ○ ***primaryInformationRecipient.TerritorialAuthority*** ○ ***replacementOf.relatedContextOfUse*** ○ ***derivedFrom.documentReference*** ○ ***subjectOf.submissionReference*** ○ ***referencedBy.keyword*** Note: All of these elements are not included in this implementation guide. Refer to the ICH eCTD v4.0 Implementation Guide for additional information.


```
            </derivedFrom>
            <subjectOf negationInd="">
                <submissionReference>
                    <id><item/></id>
                </submissionReference>
            </subjectOf>

            <referencedBy typeCode="REFR">
                <keyword>
                    <code/>
                </keyword>
            </referencedBy>
        </contextOfUse>
    </component>
```

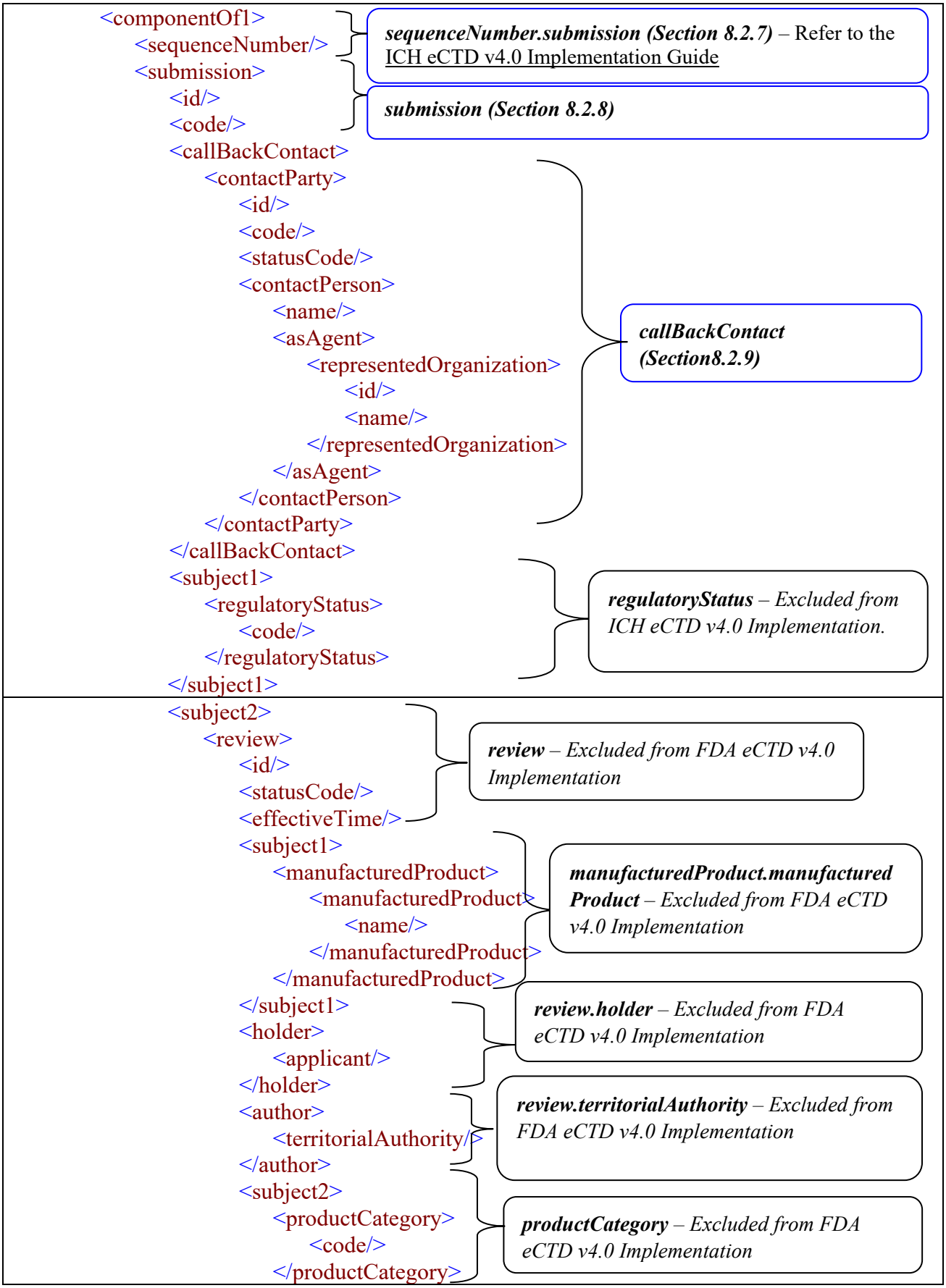
submissionReference (Section 8.3.1)

keyword (Section 8.2.6) – Refer to the ICH eCTD v4.0 Implementation Guide

This section of the XML relates to specifying the ***submission*** element. The following elements may follow the ***componentOf1.submisision*** element:

- ***sequenceNumber*** (included as an element of the relationship between ***submissionUnit*** and ***submission***)
- ***callBackContact.contactParty***
- ***subject1.regulatoryStatus***
- ***subject2.review***
    - ***subject1.manufacturedProduct***
    - ***holder.applicant***
    - ***author.territorialAuthority***
    - ***subject2.productCategory***
    - ***subject3.regulatoryStatus***
- ***subject3.mode***
- ***subject4.regulatoryReviewTime***
- ***subject5.submissionGroup***

Note: All of these elements are not included in this implementation guide. Refer to the ICH eCTD v4.0 Implementation Guide for additional information.


<componentOf1>
<sequenceNumber/>
<submission>
<id/>
<code/>
<callBackContact>
<contactParty>
<id/>
<code/>
<statusCode/>
<contactPerson>
<name/>
<asAgent>
<representedOrganization>
<id/>
<name/>
</representedOrganization>
</asAgent>
</contactPerson>
</contactParty>
</callBackContact>
<subject1>
<regulatoryStatus>
<code/>
</regulatoryStatus>
</subject1>
<subject2>
<review>
<id/>
<statusCode/>
<effectiveTime/>
<subject1>
<manufacturedProduct>
<manufacturedProduct>
<name/>
</manufacturedProduct>
</manufacturedProduct>
</subject1>
<holder>
<applicant/>
</holder>
<author>
<territorialAuthority/>
</author>
<subject2>
<productCategory>
<code/>
</productCategory>
sequenceNumber.submission (Section 8.2.7) – Refer to the ICH eCTD v4.0 Implementation Guide
submission (Section 8.2.8)
callBackContact (Section8.2.9)
regulatoryStatus – Excluded from ICH eCTD v4.0 Implementation.
review – Excluded from FDA eCTD v4.0 Implementation
manufacturedProduct.manufactured Product – Excluded from FDA eCTD v4.0 Implementation
review.holder – Excluded from FDA eCTD v4.0 Implementation
review.territorialAuthority – Excluded from FDA eCTD v4.0 Implementation
productCategory – Excluded from FDA eCTD v4.0 Implementation

```
            </subject2>
            <subject3>
                <regulatoryStatus>
                    <code/>
                </regulatoryStatus>
            </subject3>
        </review>
    </subject2>
    <subject3>
        <mode>
            <code/>
        </mode>
    </subject3>
    <subject4>
        <regulatoryReviewTime>
            <code/>
        </regulatoryReviewTime>
    </subject4>
    <subject5>
        <submissionGroup>
            <id/>
        </submissionGroup>
    </subject5>
```

regulatoryStatus – *Excluded from FDA eCTD v4.0 Implementation*

mode – *Excluded from FDA eCTD v4.0 Implementation*

regulatoryReviewTime – *Excluded from FDA eCTD v4.0 Implementation*

submissionGroup – *Excluded from FDA eCTD v4.0 Implementation*

XML Structure

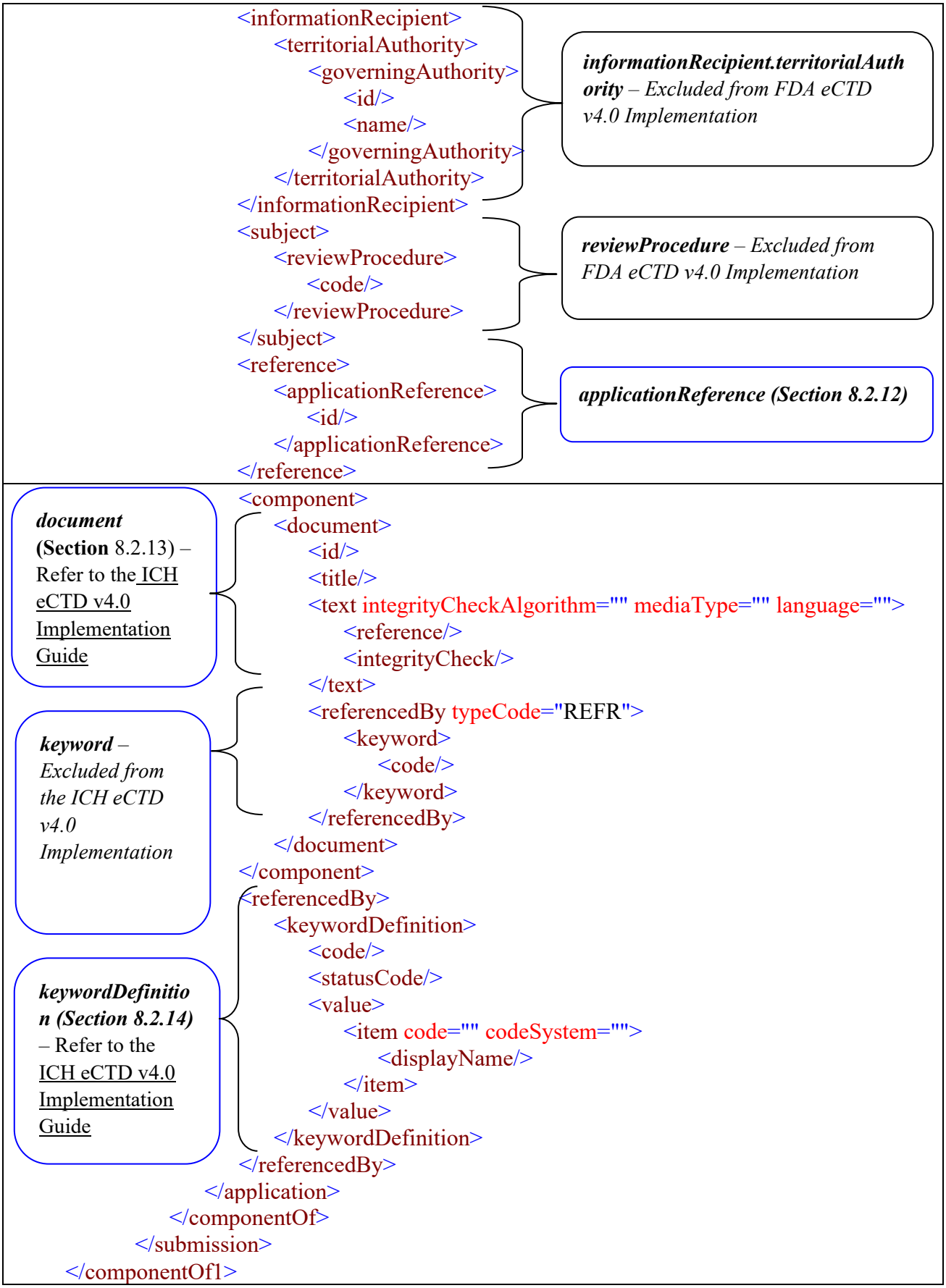
This section of the XML relates to the ***application*** element. The application section contains the following elements and their attributes:

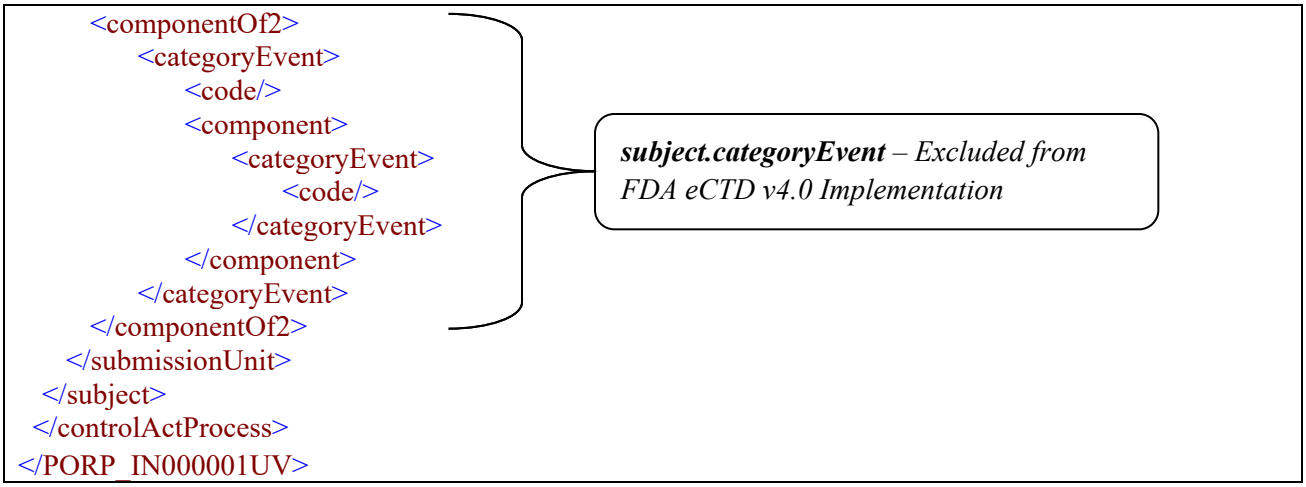
holder.applicant
informationRecipient.territorialAuthority
subject.reviewProcedure
reference.applicationReference
component.document
referencedBy.keyword
referencedBy.keywordDefinition

```
<componentOf>
    <application>
        <id>
            <item/>
        </id>
        <code/>
        <holder>
            <applicant>
                <sponsorOrganization>
                    <id></id>
                    <name></name>
                </sponsorOrganization>
            </applicant>
        </holder>
```

application (Section 8.2.10) – Refer to the ICH eCTD 4.0 Implementation Guide.

holder.applicant (Section 8.2.11)


<informationRecipient>
<territorialAuthority>
<governingAuthority>
<id/>
<name/>
</governingAuthority>
</territorialAuthority>
</informationRecipient>
informationRecipient.territorialAuthority – Excluded from FDA eCTD v4.0 Implementation
<subject>
<reviewProcedure>
<code/>
</reviewProcedure>
</subject>
reviewProcedure – Excluded from FDA eCTD v4.0 Implementation
<reference>
<applicationReference>
<id/>
</applicationReference>
</reference>
applicationReference (Section 8.2.12)
document (Section 8.2.13) – Refer to the ICH eCTD v4.0 Implementation Guide
<component>
<document>
<id/>
<title/>
<text integrityCheckAlgorithm="" mediaType="" language="">
<reference/>
<integrityCheck/>
</text>
<referencedBy typeCode="REFR">
<keyword>
<code/>
</keyword>
</referencedBy>
keyword – Excluded from the ICH eCTD v4.0 Implementation
</document>
</component>
<referencedBy>
<keywordDefinition>
<code/>
<statusCode/>
<value>
<item code="" codeSystem="">
<displayName/>
</item>
</value>
</keywordDefinition>
keywordDefinition (Section 8.2.14) – Refer to the ICH eCTD v4.0 Implementation Guide
</referencedBy>
</application>
</componentOf>
</submission>
</componentOf1>



All information in this section is organized in order that the eCTD v4.0 XML components appear within the schema with the exception of special types of submissions (e.g., grouped submissions).

8.2.1 Submission Unit

The ***submissionUnit*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.1.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.1.2 *XML Elements*

The following tables provide a subset of XML elements and attributes required for the ***submissionUnit*** element, and any special instructions.

*The **classCode** and **moodCode** are not required in the eCTD v4.0 XML message. The **classCode** is fixed to "ACT" and **moodCode** is fixed to "EVN". If the XML message contains any other values for these attributes it will be invalid against the schema.*

Conditions that apply to the ***submissionUnit*** element:

- Only one ***submissionUnit*** element can exist for a message.

8.2.1.2.1 *submissionUnit.title*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
title		[0..1]		This is the container element that provides a sender-defined description of the Submission Unit.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	value	[1..1]	Text	The ***value*** attribute of the ***title*** element indicates the reason for sending the Submission Unit.
Conformance	If the ***title*** element is provided, the ***value*** attribute is required.			
Business Rules	The ***submissionUnit.title*** element is an optional value that allows up to 128 characters. Only the first 128 characters of the ***submissionUnit.title@value*** attribute will be displayed. This additional information allows for a brief description of the purpose of the Submission Unit, but should not contain any reviewable information. The value 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.			

8.2.1.2.2 *submissionUnit.statusCode*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
statusCode		[0..1]		This is the container element that indicates the status of the Submission Unit.
	code	[1..1]	Alpha *active*	The ***code*** attribute of the ***statusCode*** element indicates the status of the Submission Unit.
Conformance	If the ***statusCode*** element is provided, the ***code*** attribute is required.			
Business Rules	The ***statusCode@code*** must always be active. See instruction on how to withdraw Submission Unit and its contents in Section 8.4.			

8.2.1.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[1]

[1] Final Implementation Terminology is provided on the FDA website.

8.2.1.4 *Excluded Elements*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

8.2.2 Priority Number for Context of Use

The ***priorityNumber*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.2.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.3 Context of Use

The ***contextOfUse*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.3.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.4 Related Context of Use (Context of Use Life Cycle)

The ***relatedContextOfUse*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.4.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.5 Document Reference

The ***documentReference*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.5.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations. Also see Section 7 Forward Compatibility for any clarifications on referencing a v.3.2.2 document from another application using the leaf reference.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.6 Keyword

The ***Keyword*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.6.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.6.2 *XML Elements*

The following table provides a subset of XML elements and attributes required for the ***keyword*** element, and any special instructions.

*The **classCode** and **moodCode** are not required in the eCTD v4.0 XML message. The **classCode** is fixed to "OBS" and **moodCode** is fixed to "EVN". If the XML message contains any other values for these attributes it will be invalid against the schema.*

8.2.6.2.1 *keyword.code*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This is the container element that identifies the keyword.
	code	[1..1]	Text *e.g., ich_route_1, MANU001 or MFR_001 for Manufacture Site*	The ***code*** attribute identifies the code value for the keyword.
	codeSystem	[1..1]	Text *e.g., OID value or Sender-defined text*	The ***codeSystem*** attribute is a unique identifier that indicates the controlled vocabulary system.
Conformance	The ***code*** and ***codeSystem*** attribute values are required. A keyword can only have one code.			
Business Rules	For Module 1 keywords, the code should be a valid value from the controlled list of FDA Module 1 keywords or provided as a keyword definition for the application. Grouped submissions should use the same keyword codes across applications.			

8.2.6.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[2].

8.2.6.4 *Excluded Elements*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

8.2.7 Sequence Number

The ***sequenceNumber*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

See Section 8.3 Grouped Submissions for specific instructions for that type of Submission Unit – i.e., this is the only variation for sequence numbers.

8.2.7.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.8 Submission

The ***submission*** element describes the regulatory activity within an application.

8.2.8.1 *Location in XML*

The ***submission*** element in the XML message is in the following location for the regulatory activity:

- ***submissionUnit>> componentOf1>> submission***

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.8.2 *XML Elements*

The following tables provide a complete set of XML elements and attributes required for the ***submission*** element, and any special instructions.

*The **classCode** and **moodCode** are not required in the eCTD v4.0 XML message. The **classCode** is fixed to "ACT" and **moodCode** is fixed to "EVN". If the XML message contains any other values for these attributes it will be invalid against the schema.*

*The **id@xsi:type** is not required in the eCTD v4.0 XML message. The **xsi:type** is fixed to "DSET_II". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

[2] Final Implementation Terminology is provided on the FDA website.

8.2.8.2.1 *submission.id*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is the container element of the following elements and attributes by which it uniquely identifies the Submission.
id.item	***root***	[1..1]	Valid UUID or OID	The ***root*** attribute of the ***id.item*** element provides a unique identifier (UUID) or the namespace for existing submissions (OID).
	extension	[0..1]	Text	The ***extension*** attribute of the ***id.item*** element provides the sequence number for the first sequence in the regulatory activity.
Conformance	The ***id.item@root*** attribute is required for the ***submission*** element.			
Business Rules	Only one ***item*** element should be provided for a new v4.0 submission and must be a unique identifier (UUID). For open regulatory activities initiated with eCTD v3.2.2, two item elements should be provided when sending the first v4.0 Submission Unit for the Submission. • The first item should be a unique identifier (UUID). • The second item value should indicate an OID for the namespace (associated with the FDA Center) for the ***root*** attribute and the first sequence number submitted for the regulatory activity for the ***extension*** attribute. This value will be used to ensure the submission contents is linked to the correct submission. Note: If the Submission Unit type indicates it is an amendment to an open regulatory activity and the submission UUID is not on file, it will not be accepted. Therefore, the instructions above for open regulatory activities should be applied to prevent any submission rejections. Multiple ***submission*** elements in a Submission Unit are only accepted if a grouped submission is submitted. Refer to Section 8.3 on Grouped Submissions.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***id.item @controlInformationExtension*** • ***id.item @controlInformationRoot*** • ***id.item@displayable*** • ***id.item @flavorId*** • ***id.item@identifierName*** • ***id.item @nullFlavor*** • ***id.item@reliability*** • ***id.item@scope*** • ***id.item @validTimeLow*** • ***id.item @validTimeHigh*** • ***id.item @updateMode*** • ***id.item@xsiType*** • ***id@controlInformationRoot*** • ***id@controlInformationExtension*** • ***id@flavorId*** • ***id@nullFlavor*** • ***id@updateMode*** • ***id@validTimeLow*** • ***id@validTimeHigh***			

8.2.8.2.2 *submission.code*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This is the container element that organizes the coded value for the Submission.
	code	[1..1]	Text	The ***code*** attribute indicates a coded value for the type of Submission being sent.
	codeSystem	[1..1]	Valid OID	The ***codeSystem*** attribute is a unique identifier that indicates the controlled vocabulary system. *This should be the OID registered for the code system.*
Conformance	There must be one and only one ***code@code*** and its associated ***code@codeSystem*** attribute specified for a Submission.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Business Rules	Valid ***code*** and ***codeSystem*** attributes should be provided based on the FDA's controlled vocabulary. Refer to the eCTD v4.0 Technical Conformance Guide and the Controlled Vocabulary files for specific rules for the allowable submission types for each application.			
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***code.displayName*** • ***code.originalText*** • ***code.source*** • ***code.translation*** • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@codingRationale*** • ***code@controlInformationExtension*** • ***code@controlInformationRoot*** • ***code@flavorId*** • ***code@id*** • ***code@nullFlavor*** • ***code@updateMode*** • ***code@validTimeHigh*** • ***code@validTimeLow*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@xsiType***			

8.2.8.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[3]

8.2.8.4 *Excluded Elements*

The following elements are not valid in messages sent to the FDA. If any of the elements are submitted, they will not be incorporated in the systems available to the reviewers.

- ***submissionGroup*** – this element is not required and will be ignored if submitted.
- ***mode*** - this element is not required and will be ignored if submitted.
- ***review*** - this element is not required and will be ignored if submitted.
- ***regulatoryStatus*** - this element is excluded from the eCTD implementation.

8.2.8.5 *XML Samples*

The following is an example of the XML for the ***submission*** element.

[3] Final Implementation Terminology is provided on the FDA website.

8.2.8.5.1 *New Regulatory Activities – Submitted as v4.0 Messages*

The following sample depicts the required elements for sending a new regulatory activity as a v4.0 message. This should be used for the initial and any subsequent submission units to a regulatory activity.

```
<componentOf1>
    <sequenceNumber value="1"/>
        <submission>
            <id>
                <item root="20b45e49-a226-4bd4-a716-bb54eba3b0ed"/>
            </id>
            <code code="us_submission_type_1"
            codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.12.5"/>
```

8.2.8.6 *Open Regulatory Activities Initiated with eCTD v3.2.2 - Initial v4.0 Message*

The following sample depicts the required elements for sending the initial v4.0 message to an open regulatory activity. This should be used only for the first submission unit to an open regulatory activity initiated with eCTD v3.2.2. All subsequent submission units should reference the UUID established for the regulatory activity.

```
<componentOf1>
    <sequenceNumber value="11"/>
        <submission>
            <id>
                <item root="20b45e49-a226-4bd4-a716-bb54eba3b0ed"/>
                <item root="2.16.840.1.113883.3.989.5.1.2.2.1.16.1" extension="0010"/>
            </id>
            <code code="us_submission_type_3"
            codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.12.5"/>
```

Note the Submission number (e.g., 0010) is noted in the v3.2.2 format of four digits. All submission numbers in v4.0 will be assigned a whole number (e.g., 10).

8.2.9 Contact Party

8.2.9.1 *Location in XML*

The ***contactParty*** element in the XML message is in the following location for contacts:

submissionUnit>>componentOf1>>submission>>callBackContact>>contactParty>contactPerson

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.9.2 *XML Elements*

The following tables provide a complete set of XML elements and attributes required for the ***contactParty*** element, and any special instructions.

*The **callBackContact@typeCode** is not required in the eCTD v4.0 XML message. The **typeCode** is fixed to "CALLBCK". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

*The **contactParty@classCode** is not required in the eCTD v4.0 XML message. The **classCode** is fixed to "CON". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

*The **contactPerson@classCode** is not required in the eCTD v4.0 XML message. The **classCode** is fixed to "PSN". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

*The **asAgent@classCode** is not required in the eCTD v4.0 XML message. The **classCode** is fixed to "AGNT". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

*The **representedOrganization@classCode** is not required in the eCTD v4.0 XML message. The **classCode** is fixed to "ORG". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

A submission should have one or more contacts provided. Contact(s) should be provided for each new regulatory activity and should include the appropriate regulatory and technical contacts. Only changes to the contact parties (additions, suspensions, or modifications) should be provided in future submission units of the regulatory activity. Only the elements listed for the Contact Party are expected for each contact. If additional information is sent, it will be ignored by the receiving system. See Section 8.2.9.6 for additional information about life cycling contact party information within a regulatory activity.

8.2.9.2.1 *Contact Party*

8.2.9.2.1.1 *callBackContact.contactParty.id*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is a container element that organizes the contact party's identifier.
	root	[1..1]	Valid UUID	The ***root*** attribute is for a global unique identifier for the contact party.
Conformance	The contact party ***id@root*** attribute is required if the element is provided.			
Business Rules	If contacts need to be updated the ***id@root*** value should remain the same to ensure only one contact record is on file for an individual per contact type.			
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***id@extension*** • ***id@identifierName*** • ***id@scope*** • ***id@reliability*** • ***id@displayable*** • ***id@validTimeLow*** • ***id@validTimeHigh***			

	• ***id@controlInformationRoot*** • ***id@controlInformationExtension*** • ***id@nullFlavor*** • ***id@flavorId*** • ***id@updateMode***

8.2.9.2.1.2 ***callBackContact.contactParty.code***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This is a container element that organizes the coded value for the Contact Party.
	code	[1..1]	Text *e.g., us_submission_contact_type_1*	The ***code*** attribute is a unique value that indicates the type of Contact Party based on Regional controlled vocabulary.
	codeSystem	[1..1]	Valid OID	The ***codeSystem*** attribute is a unique identifier that indicates the controlled vocabulary system. *This should be the OID registered for the code system.*
Conformance	The ***code@code*** and ***code@codeSystem*** values are required if the contact party element is provided.			
Business Rules	Valid ***code*** and ***codeSystem*** attributes should be provided based on the FDA's controlled vocabulary. Refer to the Controlled Vocabulary files for the contact party type. Note: Contact type should not be changed (i.e., there is no way to update the ***contactParty.code*** value). If the Contact Person has a new role, a new callBackContact element should be submitted. See 8.2.9.6.2.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@codingRationale*** • ***code@controlInformationExtension*** • ***code@controlInformationRoot*** • ***code.displayName*** • ***code@flavorId*** • ***code@id*** • ***code@nullFlavor*** • ***code.originalText*** • ***code.source*** • ***code.translation*** • ***code@updateMode*** • ***code@validTimeHigh*** • ***code@validTimeLow*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@xsiType***			

8.2.9.2.1.3 ***callBackContact.contactParty.statusCode***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
statusCode		[1..1]		This is a container element that organizes the status code value for the Contact Party.
	code	[1..1]	Alpha *e.g., active or suspended*	The ***code*** attribute is a unique value that indicates the status of the Contact Party and is based on HL7 controlled vocabulary constrained by the region.
	updateMode	[0..1]	Alpha *e.g., R for Replace*	The ***updateMode*** attribute provides the coded value to indicate if the ***statusCode*** element has been changed for the Contact Party.
Conformance	A ***statusCode@code*** value should be provided if the ***contactParty*** element is provided.			
Business Rules	The status code should either be active or suspended.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***statusCode.part*** • ***statusCode@controlInformationRoot*** • ***statusCode@controlInformationExtension*** • ***statusCode@flavorId*** • ***statusCode@nullFlavor*** • ***statusCode@updateMode*** • ***statusCode@validTimeLow*** • ***statusCode@validTimeHigh***			

8.2.9.2.2 *Contact Person*

8.2.9.2.2.1 *callBackContact.contactParty.contactPerson.name*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
name.part		[1..1]		This is a container element that organizes the value of contact person's name.
	value	[1..1]	String *e.g., Jane*	The ***value*** attribute is for the value of the name part of the Contact Party.
	type	[1..1]	Alpha e.g., GIV * *note this is a controlled list from HL7 and included in the schema*	The ***type*** attribute is for the type of the name part – e.g., family name, given name (including first name and middle name or initial).
	qualifier	[0..1]	Alpha e.g., MID, IN * *note this is a controlled list from HL7 and included in the schema*	The ***qualifier*** attribute is a subtype of the name part – e.g., middle name or initial.
Conformance	If a name is provided, both the ***part@value*** and ***part@type*** attributes should be provided for each name part.			

Business Rules	Each part of a person's name will have its own ***item*** element and should include the appropriate HL7 name parts. • ***name.part@type*** as "GIV" for a first name • ***name.part@type*** as "FAM" for a last name • ***name.part@qualifier*** as "IN" for middle initial • ***name.part@qualifier*** as "MID" for middle name
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***name.part@code*** • ***name.part@codeSystem*** • ***name.part@codeSystemVersion*** • ***name.part@language*** • ***name.part@nullFlavor*** • ***name.part@xsi:type***

8.2.9.2.2.2 *callBackContact.contactParty.contactPerson.telecom*

The ***xsi:type*** for the ***telecom*** attribute should be listed as an unordered list or "BAG_TEL".

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
item		[1..1]		This is a container element that organizes the Contact Party's contact information (e.g., telephone and email).
	value	[1..1]	String *e.g.,* tel:+1(111)999-9999	The ***value*** attribute provides the Contact Party's contact information (e.g., telephone and email).
	use	[1..1]	String *e.g., WP, MC*	The ***use*** attribute indicates the telecom connection (e.g., workplace or mobile contact).
	capabilities	[1..1]	String *e.g., voice, fax*	The ***capabilities*** attribute indicates the telecom service (e.g., voice or fax).
Conformance	An ***item*** element should have a ***value*** attribute.			

Business Rules	The phone number ***value*** should follow the following format: • domestic phone number has no more than 15 digits, tel:"+", formatted as follows: "country code", "(area code)", "3-digit prefix", '-" "4-digit number"; "postd:"up to 10-digit extension". o For example tel:+1(111)999-9999;postd:12345 • international phone number has no more than 20 digits, formatted as follows: tel:"+", "phone country", "(phone city)", "phone local"; "postd:"up to 10-digit extension". o For example "tel:+011(123)1234567890" or if no phone city, tel:+011()1234567890 The phone number – i.e., the item element requires both the ***use*** and ***capabilities*** attribute values. Refer to the Controlled Vocabulary for the telecom use valid values. The email value should follow the following format: • ***value*** should be formatted as: "mailto:johndoe@acme.com"
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***telecom.item@controlInformationRoot*** • ***telecom.item@controlInformationExtension*** • ***telecom.item@flavorId*** • ***telecom.item@nullFlavor*** • ***telecom.item@updateMode*** • ***telecom.item@validTimeLow*** • ***telecom.item@validTimeHigh*** • ***telecom.item@xsi:type***

8.2.9.2.2.3 ***callBackContact.contactParty.asAgent.representedOrganization.name***

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
name.part		[1..1]		This is a container element that organizes the value for the represented Organization's name.
	value	[1..1]	String *e.g., Acme Pharmaceuticals*	The ***value*** attribute provides the organization's name.
Conformance	If a contact party is provided, the organization represented should also be provided, and the ***part@value*** attribute is required.			
Business Rules	The name of the organization should be provided only when the contact party is initialized or changed.			

Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***name.part@code*** • ***name.part@codeSystem*** • ***name.part@codeSystemVersion*** • ***name.part@language*** • ***name.part@nullFlavor*** • ***name.part@qualifier*** • ***name.part@xsi:type***

8.2.9.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[4]

8.2.9.4 *Excluded Elements*

The following class attributes are excluded from the FDA implementation:

- ***contactPerson.id*** – note this is an additional identifier for the named individual instead of their ***contactParty.id***. Only the ***contactParty.id*** element is used.

8.2.9.5 *XML Sample*

The following XML snippet is an example of a new contact party:

```
<callBackContact>
    <contactParty>
        <id root="417e5c25-2001-40d1-af34-f1f285614187"/>
        <code code="us_submission_contact_type_1"
codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.11.3"/>
        <statusCode code="active"/>
        <contactPerson>
            <name>
                <part type="GIV" value="Jane"/>
                <part type="GIV" value="Mary" qualifier="MID"/>
                <part type="FAM" value="Smith"/>
            </name>
            <telecom xsi:type="BAG_TEL">
                <item value="tel:+1(212)555-1234" use="WP" capabilities="voice"/>
                <item value="tel:+1(212)555-5678" use="MC" capabilities="voice"/>
                <item value="tel:+1(111)999-9999" use="WP" capabilities="fax"/>
                <item value="mailto:jane.smith@gooddrugs.com"/>
            </telecom>
            <asAgent>
                <representedOrganization>
                    <name>
                        <part value="Good Drugs"/>
                    </name>
```

[4] Final Implementation Terminology is provided on the FDA website.

```
            </representedOrganization>
        </asAgent>
    </contactPerson>
</contactParty>
</callBackContact>
```

8.2.9.6 *Contact Party Life cycle*

The Contact Party for a Submission should be provided in the initial Submission Unit and any time the Contact Party is added, removed or contact information needs to be updated. To change the contact's type, suspend the previous contact and send a new contact party element with the new type. To assign more than one contact type for an individual, send multiple contact party elements. For Grouped Submissions, only one set of contacts should be provided under the primary application.

The following sections describe how to life cycle a contact's information for a Submission – i.e., suspending and updating one or more parts of the contact party's information.

8.2.9.6.1 *Suspending a Contact*

The contacts for a regulatory activity may change during the course of the submission review. If that happens and a contact is no longer active, the contact should be suspended.

When suspending a contact, the ***contactParty*** element should use the same ***id@root*** attribute value to identify the contact party and change to the status code from active to suspended using the ***updateMode*** attribute. The sample below shows the required elements and attributes:

```
<callBackContact>
    <contactParty>
        <id root="417e5c25-2001-40d1-af34-f1f285614187"/>
        <code code="us_submission_contact_type_1"
codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.11.3"/>
        <statusCode code="suspended" updateMode="R" />
    </contactParty>
<callBackContact>
```

Note: Only the required elements for the contact party are sent when suspending a contact.

8.2.9.6.2 *Updating Contact Information*

When updating contact information, use the same ***id@root*** attribute value to identify the contact party and indicate the changed element by providing the ***updateMode*** attribute for that element. The following subsections outline the instructions for updating each element of the Contact's information. There is also a complete XML sample to show the use of the ***updateMode*** attribute.

8.2.9.6.2.1 *Contact Person's Name*

To make updates to a contact party's information, the entire ***callBackContact*** element should be sent. The values for the ***updateMode*** are indicated below depending on whether or not there is a change to the ***contactPerson.name*** element.

- For a change – indicate by using an “R” as the ***name@updateMode*** attribute value.
- For no change – indicate by using an “N” as the ***name@updateMode*** attribute value.

8.2.9.6.2.2 *Contact Person’s Telecom*

To make updates to a contact party’s information, the entire ***callBackContact*** element should be sent. The values for the ***updateMode*** attribute are indicated below depending on whether or not there is a change to the ***contactPerson.telecom*** element.

- For a change – indicate by using an “R” as the ***telecom@updateMode*** attribute value.
- For no change – indicate by using an “N” as the ***telecom@updateMode*** attribute value.

8.2.9.6.2.3 *Represented Organization’s Name*

To make updates to a contact party’s information, the entire ***callBackContact*** element should be sent. The values for the ***updateMode*** attribute are indicated below depending on whether or not there is a change to the ***representedOrganization.name*** element.

- For a change – indicate by using an “R” as the ***name@updateMode*** attribute value.
- For no change – indicate by using an “N” as the ***name@updateMode*** attribute value.

8.2.9.6.3 *XML Sample – Updating Contact Party*

The following XML snippet depicts how to send a change to the contact record. The contact’s information should be complete each time it is submitted – i.e., each element of the contact’s information is replaced by the update. Note that the ***id*** and ***code*** elements cannot be updated. If the ***id*** or ***code*** element is changed, the contact will not exist and therefore cannot be changed.

```
<callBackContact>
    <contactParty>
        <id root="417e5c25-2001-40d1-af34-f1f285614187"/>
        <code code="us_submission_contact_type_1"
codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.11.3"/>
        <statusCode code="active" updateMode="N"/>
        <contactPerson>
            <name updateMode="N">
                <part type="GIV" value="Jane"/>
                <part type="GIV" value="Mary" qualifier="MID"/>
                <part type="FAM" value="Smith"/>
            </name>
            <telecom xsi:type="BAG_TEL" updateMode="R">
                <item value="tel:+1(212)555-9997" use="WP" capabilities="voice"/>
                <item value="tel:+1(212)555-9998" use="MC" capabilities="voice"/>
                <item value="tel:+1(111)999-9999" use="WP" capabilities="fax"/>
                <item value="mailto:jane.smith@acme.com"/>
            </telecom>
            <asAgent>
                <representedOrganization>
                    <name updateMode="N">
                        <part value="Good Drugs"/>
                    </name>
```

```
            </representedOrganization>
        </asAgent>
    </contactPerson>
</contactParty>
</callBackContact>
```

8.2.10 Application

The ***application*** element is presented in this section of the Implementation Guide as it is the connection point for the ***document*** and ***keywordDefinition*** elements in the XML message. The concept of Application differs across regions.

Note: *Application is also a Module 2-5 concept that will also be provided in the ICH eCTD v4.0 Implementation Guide. Additional Regional information is provided in this document.*

8.2.10.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.10.2 *XML Elements*

The following tables provide a complete set of XML elements and attributes required for the ***application*** element, and any special instructions.

*The **classCode** and **moodCode** are not required in the eCTD v4.0 XML message. The **classCode** is fixed to "ACT" and **moodCode** is fixed to "EVN". If the XML message contains any other values for these attributes it will be invalid against the schema.*

*The **id@xsi:type** is not required in the eCTD v4.0 XML message. The **xsi:type** is fixed to "DSET_II". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

Conditions that apply to the ***application*** element:

- Only one ***application*** element can be provided for each ***submission*** element.
- An ***application*** element is required to have one and only one ***id.item@root*** attribute.

8.2.10.2.1 *application.id*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is the container element of the following elements and attributes by which it uniquely identifies the application.
id.item		[1..1]		This is the container element of the following attributes by which it uniquely identifies the application. ***Note:*** *This is an FDA constraint.*
	root	[1..1]	Valid OID *e.g., 2.16.840.1.113883.3.989.5.1.2.2.1.16.1*	The ***root*** attribute of the ***id.item*** element provides a namespace unique identifier for the FDA Center.
	extension	[1..1]	Text *e.g., 123456*	The ***extension*** attribute of the ***id.item*** element provides a location to specify the FDA application tracking number.
Conformance	The ***id.item@root*** attribute is required for the ***application*** element.			
Business Rules	Only one ***id.item*** element should be submitted for FDA applications. If more than one application number is submitted for a Submission, the message will not be accepted. Multiple ***application*** elements in a Submission Unit are only accepted if a grouped submission is submitted (i.e., multiple ***submission*** elements will also exist with one application element per submission). Refer to Section 8.3 on Grouped Submissions. The ***id.item@root*** attribute is an OID namespace for the FDA Center assigned application number provided in the ***id.item@extension*** attribute. This information will be static through the entire life cycle of the application. The ***extension*** value is the 6-digit value for the application number.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***id.item @controlInformationExtension*** • ***id.item @controlInformationRoot*** • ***id.item@displayable*** • ***id.item @flavorId*** • ***id.item@identifierName*** • ***id.item @nullFlavor*** • ***id.item@reliability*** • ***id.item@scope*** • ***id.item @validTimeLow*** • ***id.item @validTimeHigh*** • ***id.item @updateMode*** • ***id.item@xsiType*** • ***id@controlInformationRoot*** • ***id@controlInformationExtension*** • ***id@flavorId*** • ***id@nullFlavor*** • ***id@updateMode*** • ***id@validTimeLow*** • ***id@validTimeHigh***			

8.2.10.2.2 *application.code*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
code		[1..1]		This is the container element that organizes the coded value for the application.
	code	[1..1]	Text *e.g., us_application_type_1*	The ***code*** attribute is a unique value that indicates the type of application based on the FDA controlled vocabulary (e.g., NDA, ANDA, BLA, etc.).
	codeSystem	[1..1]	Valid OID *2.16.840.1.113883.3.989.5.1.2.2.1.1.2*	The ***codeSystem*** attribute is a unique identifier that indicates the controlled vocabulary system. *This should be the OID registered for the code system.*
Conformance	There must be one and only one ***code@code*** attribute specified for an application.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Business Rules	Valid ***code*** and ***codeSystem*** attributes should be provided based on the FDA's controlled vocabulary. Refer to the Controlled Vocabulary files for the application code rules and usage.			
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***code@controlInformationExtension*** • ***code@controlInformationRoot*** • ***code@codeSystemName*** • ***code@codeSystemVersion*** • ***code@codingRationale*** • ***code.displayName*** • ***code@flavorId*** • ***code@id*** • ***code@nullFlavor*** • ***code.originalText*** • ***code.translation*** • ***code.source*** • ***code@updateMode*** • ***code@validTimeHigh*** • ***code@validTimeLow*** • ***code@valueSet*** • ***code@valueSetVersion*** • ***code@xsiType***			

8.2.10.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[5]

8.2.10.4 *Excluded Elements*

The following elements are not valid in messages sent to the FDA. If any of the elements are submitted, they will not be incorporated in the systems available to the reviewers.

- ***informationRecipient.TerritorialAuthority*** – this information is not required and will be ignored if submitted.
- ***subject.ReviewProcedure*** – this element is not required and will be ignored if submitted.

8.2.10.5 *XML Samples*

The following is an example of the XML for the application information. The application enters as a ***componentOf*** element between ***submission*** and ***application*** elements.

[5] Final Implementation Terminology is provided on the FDA website.

```
…
[This XML section will repeat for each application element.  A submission element is a componentOf
an application element]
…

<componentOf>
    <application>
        <id>
            <item root="2.16.840.1.113883.3.989.5.1.2.2.1.16.1" extension="456789"/>
        </id>
      <code code="us_application_type_1" codeSystem="2.16.840.1.113883.3.989.5.1.2.2.1.1.4"/>
                …
                [Additional information may appear after the addition of the application.code, for
                example any of the following elements related to application – component,
                referencedBy, reference, or holder]
                …
    </application>
</componentOf>
```

See XML Color Legend for color usage

8.2.11 Applicant

The applicant included in the message should be the same applicant on any forms submitted for the submission unit. The applicant should be identified by the Company Name.

8.2.11.1 *Location in XML*

The ***applicant*** element in the XML message is in the following location for documents:

- ***controlActProcess>> subject>> submissionUnit>>componentOf>>submission>> componentOf>>application>>applicant***

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.11.2 *XML Elements*

The following tables provide a complete set of XML elements and attributes required for the ***applicant*** element, and any special instructions.

*The **classCode** is not required in the eCTD v4.0 XML message. The **classCode** is fixed to "SPNSR". If the XML message contains any other values for this attribute, it will be invalid against the schema.*

8.2.11.2.1 *applicant.name*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
name.part		[1..1]		This is a container element that organizes the value of applicant's name.
	value	[1..1]	String *e.g., Acme*	The ***value*** attribute provides the name part of the Applicant.
Conformance	The ***name.part@value*** attribute is required.			
Business Rules	The applicant's name should represent the applicant/sponsor of the application.			
Excluded Elements and/or Attributes	The following datatype elements and attributes may not be required by eCTD v4.0: • ***name.part@code*** • ***name.part@codeSystem*** • ***name.part@codeSystemVersion*** • ***name.part@language*** • ***name.part@nullFlavor*** • ***name.part@qualifier*** • ***name.part@xsi:type***			

8.2.11.3 *Terminology*

There is no controlled terminology for this element.

8.2.11.4 *Excluded Elements*

The following class attributes are not valid in messages sent to the FDA. If any of the values are submitted, they will be ignored.

- ***applicant.sponsoringOrganization.id***
- ***applicant.sponsoringOrganization.addr***
- ***applicant.sponsoringOrganization.telecom***

To provide contact information, see Section 8.2.9 for contact party instructions.

8.2.11.5 *XML Samples*

The following is an example of the XML for the applicant information. The ***applicant*** element follows the ***application.code*** element.

```
<holder>
    <applicant>
        <sponsorOrganization>
            <name >
                <part value="Acme Pharmaceuticals"/>
            </name>
        </sponsorOrganization>
    </applicant>
```

</holder>

8.2.12 Application Reference

An application may reference another application that was previously sent to the FDA, the ***applicationReference*** element should be used to indicate the related application. The sender may reference applications in other FDA Centers, however content[6] (i.e., documents or files) may not be reused by reference. When referencing a Drug Master File application in the message, the reference should be to an application number submitted to the same FDA Center.

8.2.12.1 *Location in XML*

The ***application*** element in the XML message is in the following location for documents:

- ***controlActProcess>> subject>> submissionUnit>>componentOf>>submission>> componentOf>>application>>reference>>applicationReference***

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.12.2 *XML Elements*

The following tables provide a complete set of XML elements and attributes required for the ***applicationReference*** element, and any special instructions.

*The **classCode** and **moodCode** are not required in the eCTD v4.0 XML message. The **classCode** is fixed to "ACT" and **moodCode** is fixed to "EVN". If the XML message contains any other values for these attributes, it will be invalid against the schema.*

The application may have zero to many application references. For each application reference, an ***applicationReference*** element should be provided.

8.2.12.2.1 *applicationReference.id*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is the container element of the following elements and attributes by which it uniquely identifies the referenced application.
	root	[1..1]	Valid OID *2.16.840.1.1138 83.3.989.5.1.2.2. 1.16.1*	The ***root*** attribute of the ***id*** element provides a namespace unique identifier for the FDA Center.

[6] Each FDA Center has its own document repository and content cannot be referenced across Centers.

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
	extension	[1..1]	Text *e.g., MF012345*	The ***extension*** attribute of the ***id*** element provides a location to specify the FDA application tracking number being referenced.
Conformance	The ***id@root*** attribute is required for the ***applicationReference*** element.			
Business Rules	Only one ***id@root*** and ***id@extension*** attributes should be submitted for each FDA application reference. Multiple ***applicationReference*** elements may be provided for the regulatory activity/submission. The ***id@root*** attribute is an OID namespace for the FDA Center assigned application number provided in the ***id@extension*** attribute. The ***extension*** value should be composed of the case-sensitive (specifically uppercase) application type prefix (e.g., IND, MF, etc.) and the assigned value (e.g., 6 digits) for the application number. The application type prefix will be used to determine the reason for reference (e.g., MF for the Drug Master File). Refer to Section 10 for a list of valid prefixes. An Application Reference only needs to be sent once for that application.			
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***id@controlInformationRoot*** • ***id@controlInformationExtension*** • ***id@displayable*** • ***id@flavorId*** • ***id@identifierName*** • ***id@nullFlavor*** • ***id@reliability*** • ***id@scope*** • ***id@validTimeLow*** • ***id@validTimeHigh*** • ***id@updateMode*** • ***id@xsi:type***			

8.2.12.3 *Terminology*

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[7]

8.2.12.4 *Excluded Elements*

The following class attributes are excluded for the ***applicationReference*** element:

- ***applicationReference.reasonCode***

[7] Final Implementation Terminology is provided on the FDA website.

8.2.12.5 *XML Samples*

The following is an example of the XML for the application reference information. The ***applicationReference*** follows the ***holder*** element.

```
<reference>
    <applicationReference>
        id root="2.16.840.1.113883.3.989.5.1.2.2.1.16.1" extension="MF012345"/>
    </applicationReference>
</reference>
```

8.2.13 Document

The ***document*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.13.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.14 Keyword Definitions

The ***keywordDefinition*** element was outlined in the ICH eCTD v4.0 Implementation Guide and only FDA specific information is provided in this document.

8.2.14.1 *Location in XML*

Refer to the ICH eCTD v4.0 Implementation Guide for additional information as there are no regional variations.

Refer to Table 7: eCTD v4.0 XML Message Structure for the XML representation.

8.2.14.1 *Terminology*

There are additional regional keyword definition types for the Module 1 content.

All FDA controlled vocabularies are provided in the genericode and spreadsheet files.[8]

8.3 Grouped Submissions

A grouped submission is a single Submission Unit applied to more than one Submission. 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 submission units to different applications. The grouped submission concept does not replace non-eCTD cross referencing functionality (e.g., use of m1.4.4).

[8] Final Implementation Terminology is provided on the FDA website.

Grouped submissions are the only business case for sending a Submission Unit with more than one ***componentOf.submission*** element (e.g., manufacturing changes that affect more than one application). If a Submission Unit does not meet the following criteria, it should not be sent to the FDA:

- All contents in the Submission Unit relate to all Submissions in the Submission Unit.
    - The exception is the FDA Forms that should accompany each Submission.
- Each Submission in the group has a unique sequence number for that application.
- When sending any Context of Use life cycle – the operation will apply to all submissions in the group.
- The keyword definitions code and value pair should have the same codes across all applications.
    - The keyword definitions must exist for all applications in the group.
    - The keyword code and its value should be specified once per Context of Use.
- All submission contents must be placed in the primary application's sequence folder.
- All submissions in the group must have the same application code.
- All submissions in the group must have the same submission code.
- All documents must be specified under ONE application element in the submissionunit.xml file.
- If documents are included in more than one application element, the group submission will be rejected.

Grouped submissions have additional requirements in the submission unit message, which are outlined below and presented in this section:

- **Sequence Numbers** – should follow the same instructions in the ICH eCTD v4.0 Implementation Guide unless the following scenario exists:
    - There is more than one submission/regulatory activity in an application that is part of the grouped submission. In this case all regulatory activities within that application should have the same sequence number. E.g., Grouped Submission Unit includes the following:
        - Submission #10 - (Sequence Number #20) – Application #1
        - Submission #15 - (Sequence Number #20) – Application #1

  Note – the sequence number is "20" for both submissions in the application, this is because the sequence is received together and contains the same submission contents.
- **Submission Reference** (See Section 8.3.1) – this element is used to associate specific content to one or more applications in the submission on the context of use elements.

Refer to the FDA eCTD v4.0 Samples package for grouped submission examples and the Module 1 contents of its submission unit. Specific instructions are provided for the following elements when included in a grouped submission (e.g., contacts, submission references, etc.).

Refer to the FDA eCTD v4.0 Samples Package for XML Samples.

8.3.1 Submission Reference

The ***submissionReference*** element is used to indicate when a ***contextOfUse*** element is not relevant to a specific Submission within a ***submissionUnit*** element.

8.3.1.1 *Location in XML*

The ***submissionReference*** element in the XML message is in the following location:

submissionUnit>> component>>contextOfUse> replacementOf > derivedFrom > subjectOf

8.3.1.2 *XML Elements*

The following is an example of a ***submissionReference*** element:

```
<subjectOf negationInd="true">
    <submissionReference>
        <id>
            <item root="5cfec3c5-2fd2-45fb-b92f-3a70d261467b"/>
            <item root="ae57b6fe-6a18-4bac-a3aa-f7540078b25a"/>
        </id>
    </submissionReference>
</subjectOf>
```

See instructions for when to provide one or more submission reference items. These should be used only for grouped submissions.

Only one ***submissionReference*** element should be used for each ***contextOfUse*** element, but it may have multiple items.

The ***subjectOf@negationInd*** attribute value shall be "true" for any ***submissionReference*** element.

8.3.1.2.1 *submissionReference.id*

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
id		[1..1]		This is the container element of the following elements and attributes by which it uniquely identifies the referenced submission.
id.item		[1..*]		This is the container element for the attributes by which it uniquely identifies the referenced submission.
	root	[1..1]	Valid UUID	The ***root*** attribute of the ***id.item*** element provides a global unique identifier for the referenced submission in the group.
Conformance	The ***id.item@root*** attribute is required.			
Business Rules	More than one ***item*** element may be provided. This should only be used for grouped submissions to designate the FDA forms (e.g., 356h) that are not associated with a Submission. The UUID must exist as one of the submission identifiers in the grouped submission.			

Element	Attribute	Cardinality	Value(s) Allowed *Examples*	Description *Instructions*
Excluded Elements and/or Attributes	The following datatype attributes may not be required by eCTD v4.0: • ***id.item @controlInformationExtension*** • ***id.item @controlInformationRoot*** • ***id.item@displayable*** • ***id.item @flavorId*** • ***id.item@identifierName*** • ***id.item @nullFlavor*** • ***id.item@reliability*** • ***id.item@scope*** • ***id.item @validTimeLow*** • ***id.item @validTimeHigh*** • ***id.item @updateMode*** • ***id.item@xsiType*** • ***id@controlInformationRoot*** • ***id@controlInformationExtension*** • ***id@flavorId*** • ***id@nullFlavor*** • ***id@updateMode*** • ***id@validTimeLow*** • ***id@validTimeHigh***			

8.3.1.1 *Terminology*

There is no controlled terminology for this element.

8.3.1.2 *Excluded Elements*

No class elements are excluded for the ***submissionReference*** element.

8.3.2 Grouped Submission Sample

Refer to the FDA eCTD v4.0 Samples Package for XML Samples.

8.4 Withdrawing Submission Contents

If a Submission Unit is sent in error, a new Submission Unit should be submitted and all of the Context of Use elements need to either be suspended – i.e., they will be shown as inactive or a replace function needs to be provided to reinstate the previous document as the current submission contents.

Refer to the ICH eCTD v4.0 Implementation Guide for more details for suspend and replace operations.
Refer to FDA eCTD v4.0 Samples for a withdraw sample.

8.5 Promotional Materials

For Submission Units that include promotional materials, additional information (e.g., keywords) is required.

Refer to the FDA eCTD v4.0 Controlled Vocabulary Package for Module 1 Controlled Vocabulary files with the valid keyword for promotional materials.
Refer to the eCTD v4.0 Technical Conformance Guide for additional information.
Refer to the FDA eCTD v4.0 Samples Package for a promotional materials sample.

9. APPENDIX: FILE REUSE

The ***document*** element should follow the ICH eCTD v4.0 Implementation Guide, including the section "Considerations for the Document Element".

In most cases document reuse should be used when referencing previously submitted content. For any file previously submitted that requires a new title (i.e., the content does not change) a new ***document*** element may be submitted to FDA according to the following file reuse requirements.

The ***text.reference@value*** attribute must include the relative path of the file previously submitted. The file may have been referenced by a previously submitted document element in the same or different application (see examples below). To reference the file, the location of the previous file must be placed in the text reference value attribute with the following components, as applicable:

- Application Number – includes the application type prefix and the 6 digits of the application number that is represented by the application number (i.e. ***application.id.item@extension***) transmitted with the original contents. Prefix values are presented in Table 9: Application Prefix in Section 10. Note that the application number is only provided when the referenced file is in a different application.
- Sequence Number for the Submission Unit in which the file was originally submitted.
- The remainder of the path must be included as it existed when the Submission Unit was submitted to the FDA Center[9] (i.e., "m1/promotional_website.pdf")

File path example for a file in a different application:

```
<reference value="../../NDA123456/99/m1/promotional_website.pdf"/>
```

File path example for a file in the same application:

```
<reference value="../99/m1/promotional_website.pdf"/>
```

For other ***text*** elements and attributes should be the same as the previously submitted document element:

- ***text@IntegrityCheckAlgorithm***
- ***text.integrityCheck***

The following snippet provides an example of how to send a new ***document*** element for an existing file.

```
<component>
    <document>
        <id root="51a1c7d0-5275-48e3-9ebe-5a7e597612bf"/>
        <title value="New Document Title for File Reused from APP#123456"/>
```

[9] Each FDA Center has its own document repository and content cannot be referenced across Centers.

```
        <text integrityCheckAlgorithm="SHA256">
            <reference value="../../NDA123456/99/m1/promotional_website.pdf"/>
            <integrityCheck>576be0c1495daf8dfec41355654570d50f286d1266613335b7690a670746a6
        d3</integrityCheck>
        </text>
    </document>
</component>
```

Note: the document identifier and title must be unique to the new document element.

10. APPENDIX: APPLICATION PREFIX

The application prefix may be applied to the following two element values:

- ***applicationReference.id@extension*** – the value is a reference to an application previously submitted to the FDA[10] that relates to the current submission
- ***document.text.reference@value*** **–** the value indicates the relative path for the document previously submitted to the FDA Center
- ***id@extention*** **–** the value indicates the Leaf Reference's Application Identifier for Forward Compatibility (note this may be used in multiple places in the message). Refer to the ICH eCTD v4.0 Implementation Guide for additional information

The prefix must be in uppercase when including as a value – i.e., the application type prefix is case-sensitive.

Table 8: Application Prefix

Application Type	Prefix	Comments
New Drug Application	NDA	
Abbreviated New Drug Application	ANDA	
Biologic License Application	BLA	
Investigational New Drug	IND	
Drug Master File	MF	
Emergency Use Authorization	EUA	
Investigational Device Exemption	IDE	The IDE, PMA, and 510K application types should only be used in the ***applicationReference*** element along with the CDRH Application Id OID.
Premarket Approval Application	PMA	
Premarket Notification 510k	510K	

[10] The value provided may reference applications in another FDA Center